TRANSLATING PATIENT INFORMATION LEAFLETS

by

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MA Thesis

Utrecht University

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April 2009

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ACKNOWLEDGEMENTS

In the first place, I would like to express gratitude towards my boyfriend Carlo, who has more or less guided me through the process of writing this thesis. His helicopter view kept me focussed at moments when I tended to lose the overview. Moreover, he tried to keep me motivated and persistent in achieving the goal of completing this thesis.

Secondly, I would like to thank my friends for taking interest in the progress of my thesis and urging me to push ahead by giving me all kinds of reasons why I should finish this thesis in time.

And last but not least, I extend my thanks to Cees Koster who patiently cleared things up at instants that I got overwhelmed by a plethora of information.

INTRODUCTION

"A complicatedly folded, thin piece of paper with an unpredictable size, printed with information on the medicine in a miniscule font size (Maes, 1993, p.13)." Despite their dubious image, these tiny pieces of paper have always interested me and I have never failed to read their contents completely in case a medicine was prescribed to me. I cannot clearly explain the origin of my interest in these leaflets – as a child I was not sickly whatsoever… – so I think it is related to a general interest in medicine combined with a small fascination for this tiny leaflet containing so much vital information.

From February to April 2008, I took the course '*Vaktaal*' (language for specific purposes) at Utrecht University, which was taught by Mariëlle Wiggerts. During this course, we were asked to analyse a patient information leaflet according to Christiane Nord's pragmatic question scheme. While performing this task, the idea of setting up a translation project around this theme was born. Therefore, to sum up, it may be stated that this thesis (or actually: translation project) is the result of an interest in medicine and patient information leaflets, translating and the '*Vaktaal*' course.

This translation project is divided into four chapters; the first three chapters are aimed at the theory of patient information leaflets and the fourth chapter is practical: an annotated translation. More specifically, chapter 1 deals with the main characteristics of patient information leaflets, chapter 2 lays out the regulation of the European Union, United Kingdom and the Netherlands regarding patient information leaflets, the differences between these regulations and the translation problems resulting from it. In chapter 3, a source text profile and a target text profile is created of the patient information leaflet that is to be translated and the project is concluded with an annotated translation from English into Dutch of an antidepressant's (Sertraline) patient information leaflet.

The outline described above results into the following, compound thesis question: What has been written about patient information leaflets regarding their text type, functions, structure, language and national and international legislation? Which translation problems arise from the differences in legislation and the source and target text profiles and how can the answers to these questions be applied to the translation process of a patient information leaflet?

1. PATIENT INFORMATION LEAFLETS

This chapter attempts to analyse the patient information leaflet by means of describing its main characteristics. In paragraph 1.1, a general definition and alternative names of a patient information leaflet are given and its realization is explained. In 1.2 is discussed that PILs have various functions, both on macro level and on micro level. Paragraph 1.3 deals with the different communicative contexts in which a PIL functions and 1.4 gives information on the contents and structure of a PIL. Paragraph 1.5 describes what kind of language should be used in PILs, keeping its different functions in mind. Finally, paragraph 1.6 discusses how lay terms should be used in PILs.

1.1 General information

A PIL is a document enclosed in the outer sales package of a medicinal product and is written in the national language(s) of the country where it is sold. Alternative names for 'patient information leaflet' are 'information leaflet', 'instruction leaflet', 'package insert', 'patient package insert', or 'consumer medicine information.' In this thesis, on consistent grounds, I will stick to using the term 'patient information leaflet' ('PIL' for short).

PILs are issued by pharmaceutical companies and have to meet the requirements of the drug regulatory agencies in the country/countries where the PIL will be issued. For European Community countries, this means that PILs will have to meet the requirements of the European Medicinal Agency (EMEA) also, on top of the requirements of the country's own drug regulatory agency.

PILs are summarized and simplified versions of core data sheets and summaries of product characteristics (SPCs). Core data sheets and SPCs are produced for the approval and development of medicines and are intended to experts. A PIL is an adapted version of these documents and it is intended to layman (Montalt Resurrecció and González Davies 68).

1.2 Functions

Not every patient uses a PIL in a similar manner. There are thousands of different types of medicines and they all need to be taken or used in a different way. Nevertheless, on macro level, a PILs function is similar to each patient, but on micro level, we may distinguish

between three ways in which a patient may read a PIL. And on a more detailed level, we can also distinguish further between primary and secondary functions of PILs.

Pander Maat and Lentz claim that the highest-level goal of a PIL is promoting the health of the population. On the next level, there are two more objectives: educating patients about health problems, and stimulating the safe and effective use of drugs. The latter two objectives are more relevant to the writers of PILs than the first-mentioned highest-level goal (Pander Maat & Lentz 138).

Maes, Ummelen, and Hoeken have similar views on the higher-level goals of a PIL. They state that PILs fulfil two important social functions: advancing the sensible use of medicines and contributing to health education (Maes, Ummelen & Hoeken 144). Contrary to Pander Maat and Lentz, they do not mention anything about promoting the health of the population in general. Maes, Ummelen, and Hoeken also describe three other functions, on a more concrete level, for which PILs could be used.

In the first place, they state that PILs could serve as an external memory, meaning that a patient consults the PIL only incidentally. The patient reads the instructions, follows them up and may then forget the information he has read. This external memory function occurs, for example, when a patient is suffering from an occasional headache and wants to take an aspirin (143).

Instead of occasional use of a medicine, a patient might have to use a medicine routinely and on a longer term. These patients use a PIL for learning and remembering (143). Patients who, for example, need to take antidepressants on a daily basis need to learn their PIL by heart. The PIL which has been translated in this translation project is an example of a PIL that is to be learned by heart since patients need to use the medicine on a daily basis and on a longer term.

A third function, and according to Maes, Ummelen, and Hoeken, the most typical, is the motivation function. In this case, the PIL is consulted by the patient in order to weigh up the medicine's pros and cons and decide if the medicine is suitable in their situation. In other words, the information in the PIL directs the patient's opinion about and conduct towards the medicine. PILs of over-the-counter medicines in particular have this motivation function (144).

As stated in the introduction to this chapter, a PIL could be classified as an instructive text. Although giving instructions might be the main function of a PIL, there are more functions. The Dutch linguistic journal *Taalbeheersing* in 1998 published an issue that was completely dedicated to instructive texts and their functions.

In the introduction article to this issue, Maes and Schellens distinguish between 'primary' and 'secondary' functions of instructive texts. The primary function of an instructive text is purely giving instructions to the reader. Instructions solely consist of procedural information. And in the same journal, Ummelen explains that procedural information consists of all of the information that instructs users what to do. These instructions do not only include the actions a user has to undertake, but also the conditions for an action and the consequences of an action (Ummelen 120). In paragraph 5 of this chapter is discussed how procedural information should be properly written.

Secondary functions in instructive texts are there to support the instructive function of the text. Examples of secondary functions are defining, describing, teaching, motivating, advising, requesting, warning, urging, signalling, and illustrating (Maes & Schellens 97). The parts of an instructive text that are defining, describing, teaching, or motivating, consist of declarative information. According to Ummelen, we may expect declarative information to contribute to factual knowledge and insight about the product the text is about (Ummelen 121).

The motivation function of an instructive text serves to motivate the reader to actually read the text, create goodwill toward the manufacturer of the product and increase identification with the manufacturer (Steehouder 102-6).

The advising, requesting, warning, and urging function of an instructive text is accomplished with the aid of politeness strategies. Steehouder says instructive texts are 'negatively face-threatening' because this text type restricts the reader's freedom of acting, by dictating what he should do and what he should refrain from. Politeness strategies are necessary for this reason to save the reader's face (106-11).

Finally, warning information in instructive texts can be conveyed by either rhetoric speech acts or semantic speech acts. Maes et al. feel that rhetoric warnings explicitly state the warning by using the word 'warning' or 'caution' for example. Semantic warnings do not use such a signal word but describe a risk which, even without a signal word, can be interpreted as a warning (Maes et al. 126-30).

An extended explanation of the linguistic means necessary to convey the secondary functions of instructive texts will be discussed in paragraph 5 of this chapter.

1.3 Type of communication

PILs are instructive texts and their main function is instructing patients on how to use their medicine safely and correctly. Pander Maat describes the context of instructive texts as "there's a will, but no way", because the reader is prepared to follow up the instructions but lacks the knowledge to do so. We could also apply this to PILs since the reader is (in most cases) willing to take the medicine he has been prescribed, but he does not know how to use it safely and correctly.

Pander Maat says instructive texts follow the phasing of the act that is to be performed, including the preparation of this act. In the case of a PIL, this means that the act is taking the medicine in a correct manner (the right dose in the right way at the right time of the day and for the right period) and the preparation is reading the PILs information on therapeutic indications, contra-indications, side effects, dosage, etc.

Instructive texts are theme-centred because the text answers a number of questions about the act that is to be performed (Pander Maat 214-15). When applying this to PILs, we could say that a PIL tries to answer two questions: is this medicine suitable for the patient, and how does he use the medicine safely and correctly? There is no main act as there is no general instruction such as 'use the medicine' that is being supported. The single steps are the instructions that matter to the reader and that need to be followed up. The reader wants to know for example how often, how much of, and in which way the medicine is to be used.

As stated in paragraph 1.1, PILs are summarized and simplified versions of core data sheets and summaries of product characteristics (SPCs). Core data sheets and SPCs are produced for the approval and development of medicines and are intended to experts. A PIL is an adapted version of these documents and it is intended to layman. Usability and readability of PILs are vital in this perspective because the patient, who is the end user and layman in many cases, must be able to have all the information at hand in order to safely and effectively use the medicine.

A medicine can either be bought over-the-counter or can be prescribed by a physician. In case it is purchased over-the-counter, there is no intervention of a physician and the patient needs to decide for himself (and/or with the help of the pharmaceutical assistant) which medicine is suitable. The pros and cons of the medicine must be considered and therefore the advice of a pharmaceutical assistant is important. Nevertheless, many patients do not consult a pharmaceutical assistant (or buy medication at the chemists' where the employees' knowledge of medication is in most cases either absent or very limited) and therefore gain no extra

information about the medicine. For this reason, the motivation function, described in the previous paragraph, is important in PILs of over-the-counter medication in order to enable the patient to weigh up the medicine's pros and cons and decide if the medicine is suitable in their situation. Homeopathic medication for example, can be purchased over-the-counter and many PILs of this type of medication have, next to a mainly instructive function, also a persuasive function. This persuasive section consists of less formal language, compared to the instructive section, and the product is praised and recommended.

In case of prescribed medication, the specific medicine has been advised by the physician and in an ideal situation the patient should be able to rely on the doctor's advice. However, physicians sometimes confine to giving the dosage and a brief explanation about the medicine's working and do not have any information (or ask about) a patient's medical history and use of other medication which could cause adverse reactions. Therefore, it is extremely important that a PIL provides information on these aspects.

1.4 Structure

The contents and structure of PILs has not remained the same in the course of time but has undergone many changes.

At the end of the eighties, the European Commission started to standardise patient information. Before that time, the individual European countries each had their own laws regarding the documentation of patient information (in the Netherlands: "*Besluit bereiding en aflevering van farmaceutische producten"*). In practice, however, these laws were often not observed very well. Therefore, in 1992, the European Commission issued the "Directive on the labelling of medicinal products for human use and on package leaflets" (a.k.a. Directive 92/27/EC, later revised in Directive 2001/83/EC and Directive 2004/27/EC). The main purpose of this directive is making sure that users are given full and comprehensible information so that medicines can be used safely and effectively (Always read the leaflet – getting the best information with every medicine 13, 14).

The Directive requires that the PIL is drawn up in accordance with the Summary of Product Characteristics and that it contains specific information in a specific order. The Directive prescribes the following seven sections within a PIL:

- **“Identification of the medicine**
  Name of the product, the active substance and details of the other ingredients, the pharmaceutical form, contents within the pack, the name and address of the marketing authorization holder and the manufacturer and the way in which the medicine works.
- **Therapeutic indications for the product**
  The conditions for which the medicine is authorised.
- **Information which patients need to be aware of prior to taking the medicine**
  Situations when the medicine should not be used, any precautions and warnings, interactions with other medicines or foods, special patient populations such as pregnant women or nursing mothers, and any effects the medicine may have on the patient’s ability to drive.
- **Dosage and usual instructions for use**
  How to take or use the medicine, how often the dose should be given, how long the course of treatment will last, what to do if a dose is missed and, if relevant, the risk of withdrawal effects.
- **Description of side effects**
  All effects which may occur under normal use of the product and what action the patient should take if any of these occur.
- **How to store the product**
- **Date on which the leaflet was prepared”** (Always read the leaflet – getting the best information with every medicine 14, 15).

The PIL must be written in the official language of the member state and must also be written in clear and understandable terms for the users.

In the case of the Netherlands and the UK, respectively the *College ter Beoordeling van Geneesmiddelen* – Medicines Evaluation Board (CBG-MEB) and the Medicines and Healthcare products Regulatory Agency (MHRA) ‘translate’ the European Commission’s laws regarding PILs into concrete guidelines which are to be applied in the country involved. Chapter 2 will give a more detailed insight into the regulation regarding PILs in the Netherlands, UK, and on European level.

1.5 Language

As we saw in paragraph 2 of this chapter, PILs and instructive texts can have different functions. A PIL could serve as an external memory, teach a procedure or motivate a reader. According to Maes, Ummelen, and Hoeken, the instructive parts of each of these types of PILs require different language.

A PIL that serves as an external memory, for example a PIL about aspirin that is taken only incidentally, should be written differently from a PIL that goes with a medicine which is used on a daily basis.

The instructions in PILs that are used as an external memory should be designed from an acting perspective, meaning that the instructions the user should follow need to be identifiable and must be described from the position of the user. To prevent the memory from being overloaded, the instructions in this type of PIL should be divided into segments. Furthermore, a graphic representation or schematic step-by-step plan could be useful with certain tasks (Maes, Ummelen & Hoeken 44, 45). Graphic representations are usually only used in PILs of medical aids, such as inhalers and band-aids. Schematic step-by-step plans are often used in PILs of medication that is to be taken. An example of a schematic plan is an algorithm. According to Jansen and Lentz, an algorithm can be described as a purely instructive design, formulated in a direct style, presented in complete fragmentation, and realized by graphic as well as linguistic means. In an algorithm, every sentence is put on a new line, preceded by a typographical sign. An algorithm should be introduced by a heading or introductive sentence to inform the reader about its goal (Jansen & Lentz 364, 65). Besides a clear segmentation, instructions in PILs that are used only incidentally should be formulated in a direct style. Maes, Ummelen, and Hoeken claim that using the imperative tense is the best way in which to formulate instructions. Moreover, the instructions should be formulated in a positive form, and negations should be refrained from (Maes, Ummelen & Hoeken 48). The last aspect attention should be paid to, is referencing. Maes, Ummelen, and Hoeken claim that instructions will only be followed up correctly if the references to objects that are involved with the act are unambiguous and clear. Most PILs in which objects are involved are medical aids, such as the previously mentioned inhalers and band-aids. The deictic and intrinsic methods are two different ways of referring to objects. In the deictic manner, objects are identified from the perspective of the user. In the intrinsic manner, objects are identified by describing them with the help of other objects. Both manners have advantages; deictic references describe a situation from the perspective of the user, and intrinsic references are

unambiguously formulated from whatever perspective. Research has made clear that testees spontaneously rather opt for the intrinsic references and that they also rank those highest. However, deictic references score higher as the text involved is being set up more explicitly from the reader's viewpoint (Maes, Ummelen & Hoeken 48, 49).

PILs that are used to learn a procedure by heart, for example PILs of medicines that must be taken daily, require different linguistic means. Learning procedures is based on declarative knowledge; this means that instructive texts should also contain conceptual information, besides procedural information. Before users of an instructive text can carry out procedures and instructions, they need to know why they are going to carry out the instructions. For instructive texts, including PILs, this means that procedural and declarative information needs to be merged into a recognisable and readable unity (Maes, Ummelen & Hoeken 52). In *Instructieve Teksten: Ontwerp, Analyse en Evaluatie,* the writers fail to give a clear description of what procedural and declarative information should actually look like. However, in the article "Procedurele en Declaratieve Informatie in Handleidingen," Ummelen defines procedural information as text that needs to support the execution of the task in a direct manner. It is all of the information that instructs users on what to do. This information does not only include the action itself, but also the condition for an action and the consequences of an action, which can concurrently be a condition for a following action. Ummelen calls this sequence an action sequence. The linguistic form in which procedural information should be shaped is:

- action verbs
- imperative
- relatively short action steering sentences
- step-by-step presentation
- if….then constructions (Ummelen 120, 21)

Declarative information should contribute to factual knowledge and insight. Ummelen proposes declarative information to denote all of the information types that do not belong to the action sequences. The linguistic form in which declarative information should be shaped is:

- modal verbs
- relatively long sentences
- many attributive adjuncts

- continual prose (Ummelen 121, 22)

The last function of an instructive text that Maes, Ummelen, and Hoeken mention is the instructive text as a motivation to (not) follow up instructions. When translating this to the situation of a PIL, we can think of a patient consulting the PIL in order to weigh up the medicine's pros and cons and decide if the medicine is suitable in their situation. PILs of over-the-counter medicines, for example, have this motivation function. In such PILs, contents and lay-out of risk information is very important. Patients have a greater tendency to follow up instructions if the consequences of not following up the instructions are considered negative. Therefore, negative consequences of misusing a medicine should be stressed. Solely stressing the negative consequences, however, is not sufficient to motivate the reader to follow up the instructions. The probability of the consequence should also be stated. Statistical information could be used for this purpose, but the downside of this is that people easily put the disadvantages of using a medicine into perspective. An alternative could be explaining the reason and background of the risk. The risk becomes more convincing this way, but still there is no guarantee that the instructions are actually being followed up. Moreover, risks should not be exaggerated, as the patient must still be willing to use the medicine (Maes, Ummelen & Hoeken 56-8). The linguistic form in which risk information should be shaped is:

- signal words or pictograms
- functional description of risks
- avoidance redundant explanations of risk information
- risk information where it is most relevant
- warnings before, not after, instructions
- integration risk information in user information
- presentation of several warnings in point-by-point list (Maes, Ummelen & Hoeken 162-4).

Maes, Ummelen, and Hoeken distinguish between four types of information in PILs: administrative information, information about effects, risk information, and information about taking. They feel that each part of a PIL should have a different design and language.

Administrative information should be put at the beginning of the PIL, in the form of a table. 'Questions' in the form of thematic catchwords should be put on the left and the ‘answers’ should be put on the right in telegram style.

Information about effects consists of conceptual information and can be designed quite similar to the traditional design of PILs: in a continuing describing style. In order to design working information in a user friendly way, the information should be split up into modules, meaning that the information should be transferred into relevant questions of the user. The information should be in question-answer form and be formulated from the perspective of the user.

Risk information consists of conceptual information (description of risks) and procedural information (what should patients do and refrain from). The linguistic means that are necessary for the conveyance of risk information has just been discussed, but I will add some more details to this. Clear signal words or pictograms should be used and they should have a warning character. Secondly, a functional description of the risks should be given, meaning that the risks, symptoms, and terms should be recognised by the user. Redundant explanations of risk information should be avoided because they will decrease the warning effect. Also, warnings should be put before, and not after, the instruction it refers to and risk information should be incorporated into user information as much as possible since this is the best guarantee that the information will be read. Finally, different warnings that are presented together should be listed in a point-by-point list (Maes, Ummelen & Hoeken 162-4).

Information about taking should start from the situation of the patient and the acts which he has to carry out. A structured text design should be used so that goal, begin situation, action, and consequence can be distinguished. If the usefulness or relevance of the act is not clear from the start, a motivation or justification should be added to the instruction so that the patient can decide if the instructions should be carried out (165-9).

1.6 Lay terms

The CBG-MEB has set up a list of acceptable lay definitions of medical terms to be used in PILs. The purpose of this is contributing to the development of more patient-friendly PILs. Another advantage is that discussions between the marketing authorization holder and the CBG-MEB concerning lay terms can be minimized. The list is published at the CBG-MEB

website and is updated regularly. Each entry consists of the medical term followed by a definition or a synonym and the medical term in parenthesis. An example of an entry:

Porfyrie	ziekte die berust op een stoornis in de aanmaak van de rode bloedkleurstof (porfyrie)
Symptomen	verschijnselen (symptomen) (Patiëntvriendelijke Termen Lijst 9, 10)

Of course, this list of patient-friendly terms is far from complete, which means that each time a medical term should be used in a PIL, there should be considered whether a definition or a synonym should be opted for.

1.7 Conclusion

'Patient information leaflets' (PILs), 'information leaflets', 'instruction leaflets', 'package inserts', 'patient package inserts', or 'consumer medicine information' are issued by pharmaceutical companies and have to meet the requirements of the drug regulatory agencies in the country/countries where the PIL will be issued**.** PILs are summarized and simplified versions of core data sheets and summaries of product characteristics (SPCs).

Higher level goals of PILs are promoting the health of the population, educating patients about health problems, and stimulating the safe and effective use of drugs. PILs can be used in three ways: as an external memory, for learning and remembering and for motivation. On a lower and more concrete level, a PIL's functions can be divided into primary and secondary functions. A PIL's primary function is instructing and the secondary functions – defining, describing, teaching, motivating, advising, requesting, warning, urging, signalling, and illustrating – serve to support the instructive function of the text.

The context of instructive texts, including PILs, is "there's a will, but no way". PILs follow the phasing of the act that is to be performed, including the preparation of this act. The act itself is taking the medicine in a correct manner and the preparation is reading the PIL's information. A PIL tries to answer two questions: is this medicine suitable for the patient, and how does he use the medicine safely and correctly? A PIL can function in two different communicative situations as the medicine can either be bought over-the-counter or can be prescribed by a physician.

Because the laws of the individual European countries concerning PILs were not sufficiently complied with, the European Commission in 1994 issued the "Directive on the labelling of medicinal products for human use and on package leaflets". The Directive prescribes seven sections within a PIL and is legally binding for all Member States. In the case of the Netherlands and the UK, respectively the *College ter Beoordeling van Geneesmiddelen* – Medicines Evaluation Board (CBG-MEB) and the Medicines and Healthcare products Regulatory Agency (MHRA) 'translate' the European Commission's laws regarding PILs into concrete guidelines which are to be applied in the country involved.

A PIL could serve as an external memory, teach a procedure or motivate a reader. The instructive parts of each of these types of PILs require different language. Furthermore, the different sections of a PIL – administrative information, information about effects, risk information and information about taking – require different linguistic means.

The CBG-MEB has set up a list of acceptable lay definitions of medical terms to be used in PILs. The purpose of this is contributing to the development of more patient-friendly PILs and minimizing discussions between the marketing authorization holder and the CBG-MEB concerning lay terms.

2. REGULATION OF THE EUROPEAN UNION, UNITED KINGDOM AND THE NETHERLANDS

The PIL that is to be translated in the practical part of this thesis has been produced in the United Kingdom and must be translated into Dutch. Therefore, I need to know in which way the guidelines regarding PILs of the British MHRA and the Dutch CBG-MEB relate to one another. These guidelines are based on the guidelines of the European Commission.

Paragraph 2.1, 2.2 and 2.3 will provide information on the history of PILs and give an overview of the guidelines of the European Union, the United Kingdom and the Netherlands. Paragraph 2.4 is a comparative analysis in which the guidelines are compared and differences are deduced which cause translation problems regarding the usability and risk and benefit information of PILs.

2.1. The European Union and patient information

Until the eighties, European countries each had their own regulation regarding patient information. These laws where not always observed and therefore in 1992 the European Commission standardised patient information for all EU-countries by means of the "Directive on the labelling of medicinal products for human use and on package leaflets" (Directive 92/27/EEC). This Directive was in 2001 revised by Directive 2001/83/EEC and in 2004 by Directive 2004/27/EEC. The Directive describes the conditions that all PILs brought onto the European market should comply with. According to article 59 of Directive 2004/27 EEC, a package leaflet should be drawn up in accordance with the Summary of Product Characteristics. It should include, in the following order:

(a) "identification of the medicinal product
    (i) name, strength and pharmaceutical form, and, if appropriate, if it is intended for babies, children or adults. The common name shall be included where the product contains only one active substance and if its name is an invented name;
    (ii) pharmaco-therapeutic group or type of activity in terms easily comprehensible for the patient;
(b) the therapeutic indications;
(c) list of information which is necessary before the medicine is taken:

(i) contra-indications;

(ii) appropriate precautions for use;

(iii) forms of interaction with other medicines and other forms of interaction (e.g. alcohol, tobacco, foodstuffs) which may affect the action of the medicine;

(iv) special warnings;

(d) the necessary and usual instructions for proper use, and in particular:

(i) the dosage;

(ii) the method, and, if necessary, the route of administration;

(iii) the frequency of administration, specifying if necessary the appropriate time at which the medicinal product may or must be administered;

and, as appropriate, depending on the nature of the product:

(iv) the duration of treatment, where it should be limited;

(v) the action to be taken in the case of an overdose (such as symptoms, emergency procedures);

(vi) what to do when one or more doses have not been taken;

(vii) indication, if necessary, of the risk of withdrawal effects;

(viii) a specific recommendation to consult the doctor or the pharmacist, as appropriate, for any clarification on the use of the product;

(e) a description of the adverse reactions which may occur under normal use of the medicine, and. if necessary, the action to be taken in such a case; the patients should be expressly asked to communicate any adverse reaction which is not mentioned in the package leaflet to his doctor of pharmacist;

(f) a reference to the expiry date on the label, with:

(i) a warning against using the product after that date;

(ii) where appropriate, special storage precautions;

(iii) if necessary, a warning concerning certain visible signs of decoration;

(iv) the full qualitative composition (in active substances and excipients) and the quantitative composition in active substances, using common names, for each presentation of the medicine;

(v) for each presentation of the product, the pharmaceutical form and content in weight, volume or units of dosage;

(vi) the name and address of the marketing authorisation holder, and, where applicable, the name of his appointed representatives in the Member States;

(vii) the name and address of the manufacturer;

(g) where the medicine is authorised in accordance with Articles 28 to 39 under different names in the Member States concerned, a list of the names authorised in each Member State;

(h) the date on which the package leaflet was last revised" (Directive 2004/27/EC of the European Parliament and of the Council 136/48-136/49).

The Directive is a legal instrument and is binding upon each Member State it is addressed to. However, the national authorities in each Member State (such as the CBG-MEB in the Netherlands and the MHRA in the United Kingdom) are allowed to adapt the Directive into a form they consider most suitable for achieving the objectives in their country (according to the EU Pharmaceutical Legislation). More details about this will follow in paragraph 2.2 and 2.3.

In 1998, the European Commission published a guideline which was especially aimed at the readability of PILs and was to supplement the existing Directive 92/27/EEC: the "Guideline on the readability of the label and package leaflet of medicinal products for human use" (more commonly known as "Guideline on readability"). In this document, requirements with regard to contents, structure, design and style of PILs had been drawn up. The guideline provides advice to marketing authorization holders and does not have legal force; the definitive legal requirements are those outlined in the Directive and national rules of the Member States. However, this guideline should be considered as a "harmonised Community position" which will simplify the assessment, approval and control of PILs. Marketing authorization holders and manufacturers of medicines are allowed to take alternative approaches regarding the readability of PILs, but they need to justify this. The Guideline on readability consists of the following directions (summarized):

- The print size and type should be 8 points Didot. The spaces between lines should measure at least 3 mm.
- Words in full capitals/upper case should be avoided.
- Colours may be used but must distinguish from the background.

- Simple punctuation should be used.
- Sentences over 20 words or 70 characters should be avoided.
- The rules concerning bullet point lists should be obeyed. A group of bullet points should be introduced with a colon and a single full stop should be placed at the end of the group. A list of bullet points should begin with the uncommon and specific case and end with the common or general case, unless this is inappropriate for the product. A minimum number of words should be used in the bullet points and never more than one sentence. There should be no more than nine items where the bullet points are simple and no more than five when they are complex.
- Abbreviations should be avoided.
- When possible ‘it' should be used for reference to the medicine, avoiding repetition.
- The paper size should be A4/A5 for long leaflets. The paper weight should be no less than 40g/m2.
- (Sub)headings should be made conspicuous (e.g. by colours) and also, headings should be numbered. No more than two levels of headings should be used.
- Sentences should be formulated in an active and direct style.
- Pictograms should only be used when they make the message clearer.
- Red colour print should only be used for very important warnings.
- Capitals should not be used indiscriminately (Guideline on the readability of the label and package leaflet of medicinal products for human use 3, 4, 11, 12).

The report on readability supplements the Directive on some aspects very well, but fails to give good advice on other key aspects of PILs. For example, “the text must be readily understandable for the patient” is very vague and can be interpreted in many different ways. The guideline fails to give concrete advice on this aspect. For this reason, several EU-countries have published additional reports on PILs’ readability. Paragraph 2.2 and 2.3 will discuss the reports that have been set up in the Netherlands and the UK in order to supplement the guideline of the European Commission.

Included in the Guideline on readability, the European Commission in 1998 designed a model leaflet in which an example PIL had been drawn up (Guideline on the readability of the label and package leaflet of medicinal products for human use 13-7). Until November 2005, PILs could be set up in two ways: either according to the Directive, or according to the example of the model leaflet. The Directive is not very specific about how a PIL should be set

up because, as we saw earlier on in this paragraph, the only concrete information the Directive gives, is about a PIL's content and structure. Until November 2005, PILs that were not designed according to the model leaflet (so according to the Directive) had to be tested.

In 2004, the revision of the European medicinal law (called Review 2001) was rounded off. The date of implementation of this review was 1 November 2005. From this date onwards, manufacturers and registration holders of medicines that were to be registered for the first time or that had changed drastically were obliged to have their PIL's readability tested. The Guideline on readability includes information on testing PILs' readability but again, the report is not very specific about what the test should entail and, moreover, the '16 out of 20' norm (16 out of 20 consumers must be able to answer each test question correctly) caused much discussion as this norm was considered too light (Guideline on the readability of the label and package leaflet of medicinal products for human use 24-6). Therefore, the individual Member States, again, set up additional reports in which the tests are elaborated on. The following paragraphs offer more information about the ways in which national authorities have elaborated on the European Commission's Directive and Guideline on readability.

2.2 Patient information in The Netherlands

In the Netherlands, medicines' registration files containing information on for example composition, risks and side effects have been documented since 1963. These files also contained medical information intended for doctors and pharmacists; the Summary of Product Characteristics (SPC, or, in Dutch: *'IB-deel'*). From 1963 onwards, patient information had to be provided with each medicine. In the beginning, the SPC functioned as patient information and doctors and pharmacists had to take the sheet away before handing the medicine to the patient. This resulted into patients not receiving any written information, but only oral instructions when the doctor or pharmacist thought it necessary.

Twelve years later, in 1975, medicine suppliers were obliged by law to distribute a special information leaflet with their medicines. This precursor of the modern PIL consisted of two versions; information for the patient and the SPC. Of course, patients would read both versions and this had a negative effect on the medicine use of patients. The government and medical branch now started realising that the patient should come first, and in 1978 this resulted into the "*Besluit bereiding en aflevering van farmaceutische producten*". In this document was written that each medicine package had to contain a patient information leaflet.

The "*Besluit"* was not sufficiently complied with because many medicines were still supplied without PIL and for this reason the "*Richtsnoer patiëntenbijsluiter"* was introduced in 1988. This law contained rules that manufacturers had to comply with when composing PILs.

After the European Commission in 1992 introduced Directive 92/27/EEC, it was in 1994 incorporated into the Dutch "*Besluit etikettering en bijsluiter farmaceutische produkten"* (a.k.a. "*Het Besluit"*). Article 7 of *Het Besluit* is in fact identical to article 59 of Directive 92/27/EEC with the exception of the information on the manufacturer of the medicine. According to the Directive, this information should be put at the end of the PIL, whereas *Het Besluit* requires information about the manufacturer to be put in the first section of the PIL.

In the Netherlands, the national authority CBG-MEB assesses and confirms PILs. It publishes additional information on the Directives of the European Commission and has been made responsible by the government for monitoring the observance of the guidelines. As stated earlier, Directive 92/27/EEC has been incorporated into *Het Besluit.* The CBG-MEB has drawn up an extensive document that gives further information about the Directive, *Het Besluit* and the Guideline on readability: "*Bijsluiter van farmaceutische producten"*. This document was first published in 2004 (MEB-5-3.0) and contains information on contents and readability of PILs. MEB-5-3.0 has recently been revised into MEB-5-4.0 but the latter document does not provide any new information which is applicable to this thesis and therefore I have used the more detailed MEB-5-3.0 to gain my information from. As became clear from the list in the previous paragraph, the Guideline on readability mainly focuses on extratextual aspects and some general grammatical aspects of a PIL and states that "the text must be readily understandable for the patient". The CBG-MEB has set up the *Bijsluiter van farmaceutische producten* in order to clarify and elaborate on the Directive and the Guideline on readability. The *Bijsluiter van farmaceutische producten* (MEB-5-3.0) consists of:

- Guidance on package leaflet sections: this part elaborates on the contents of the package leaflet sections which are stated in the Directive.
- House style: elaboration on the information about model leaflets and readability tests in the Guideline on readability.
- Model package leaflet: this is a direct translation into Dutch of annex 1a of the Guideline on readability. Seven additional aspects have been incorporated into the Dutch model leaflet which were not included in the model leaflet of the European Commission.

- Guidance on the model package leaflet: this is an adaptation of annex 1b of the Guideline on readability. The guidance is presented in the form of a table and this makes it more surveyable than annex 1b. Moreover, the guidance avoids referring to texts of law (annex 1b does not) and explains the law in its own words. The guidance also elaborates on the extratextual aspects and linguistic aspects of a PIL which annex 1b does not elaborate on.
- Declaration concerning the technical aspects of readability: this form for completion is a declaration in which can be confirmed that the aspects of section 1b in the Guideline on readability have been taken into account.
- Criteria for the assessment of a readability test: adaptation of annex 2 of the Guideline on readability. This document is presented in the form of a table which makes it more surveyable than annex 2. The document gives a clear outline of what a readability test should entail whereas annex 2 is less elaborate.
- Lay terms: the CBG-MEB has produced a list of acceptable lay versions of medical terms in the package leaflet. The Guideline on readability does not contain such a list (*Bijsluiter van farmaceutische producten* 1-45).

2.3 Patient information in the United Kingdom

Patient information with medicines has been regulated in the United Kingdom since 1977. Although few medicines at that time were supplied with leaflets, those leaflets which were produced had to comply with certain legal requirements. Those leaflets were usually inhaled medicines and others that required detailed instructions for use by patients self-medicating outside the healthcare environment.

In 1992, the European Commission issued Directive 92/27/EEC and this Directive was in 1994 implemented into UK legislation. In 1993, the then Medicines Control Agency produced a guidance document that elaborated on the Directive: “Guidance for the pharmaceutical industry on the labelling and leaflets regulation.” This guidance caused the European Commission to publish the Guideline on readability.

In the United Kingdom, the Medicines and Healthcare products Regulatory Agency (MHRA) is the government agency which is responsible for ensuring that medicines and medicinal devices work, and are acceptably safe. The Patient Information Quality Unit is part of the Vigilance and Risk Management of Medicines Division. The Unit is responsible for

policy and regulation of all types of product information and assesses labels and PILs provided by the pharmaceutical industry for compliance with the Directive.

Recently, the MHRA has published guidance on the Guideline on readability: "Always Read the Leaflet – getting the best information with every medicine". In this document is stated that the Guideline on readability has had a great impact on the quality of the information in PILs because many PILs now contain a better balance of the risks and benefits of a medicine. However, there is much more which could be achieved within the current regulatory framework and therefore the Working Group redrafted the Guideline on readability. This is comparable to the way in which the Dutch CBG-MEB redrafted the Guideline on readability by means of the *Bijsluiter van farmaceutische producten*. Always read the leaflet – getting the best information with every medicine contains the following adaptations and additions to the Directive and the Guideline on readability:

- Improvement of risk communication: annex 10 of Always read the leaflet gives extensive information on how risk information should be communicated. Attention is being paid to: key points as a summary at the start of the section, giving information on the benefits of taking the medicine and guidance on presenting statistical information (149-65).
- Improvement of usability of PILs: annex 6 of Always read the leaflet gives extensive information on how the accessibility and readability of a PIL can be improved. Attention is being paid to: writing style, typeface, design and layout, headings, use of colour and use of symbols and pictograms (97-101). Information on these aspects is much more extended than in the Guideline on readability.
- Attention is being paid to patients with special needs: annex 6 provides information on people who need PILs in a different format (102-111).
- Improvement of how to undertake user testing: annex 5 and its appendix gives extensive information on how user testing should be accomplished. Attention is being paid to: the legal basis, reasons for user testing, when to undertake tests, implementation and an illustration of one way of undertaking a test (89-96).
- Lay terms: in annex 8 of Always read the leaflet, the MHRA has produced a list of acceptable lay versions of medical terms in the package leaflet. Moreover, a list of principles for developing definitions has been given (123-8).

2.4 Comparative analysis

In the previous paragraphs has been outlined how the European Commission and the health authorities in the Netherlands and the United Kingdom have arranged their regulation regarding patient information. The Directive and Guideline on readability serve as a guiding principle for the legislation of the Member States. The PIL that is to be translated into Dutch has been set up in the United Kingdom and therefore it is important to distinguish which aspects should be taken into account when translating this PIL. I will now research in which ways the Dutch legislation deviates from the British legislation by taking Always read the leaflet – getting the best information with every medicine and *Bijsluiter van farmaceutische producten* as my frames of reference. From these differences, translation problems of the Sertraline PIL are deduced and solutions are proposed.

2.4.1 Differences between British and Dutch guidelines concerning usability

Annex 6 of the MHRA's document Always Read the Leaflet – getting the best information with every medicine gives information on the usability of PILs. This information is an elaboration upon and expansion of the guidelines of the European Commission's Guideline on readability and I will therefore use annex 6 in my comparison with the Dutch legislation. The CBG-MEB says the following about PILs' usability: "In order to promote readability, section A of the Guideline on readability provides guidance and states the requirements relating to the technical aspects of readability, such as print type and size, the use of colour, paper size and weight (see also the section on house style and the declaration concerning the technical aspects of readability" (*Bijsluiter van farmaceutische producten* 6). After comparing the European Commission's Guideline on readability with the CBG-MEB's section on house style and the declaration concerning the technical aspects of readability, it appears that the CBG-MEB does not give any new rules on usability, but sticks to those of the Guideline on readability. When comparing the MHRA's annex 6 with sections A and C of the Guideline on readability, it shows that the MHRA has elaborated on the Guideline on readability concerning the following aspects:

- "Simple words with few syllables should be used and Latinate words should be avoided.

- Five or six bullet points in a list should be the maximum. (This is an adaptation on the Guideline on readability which states that no more than nine items should be used in a list where bullet points are simple and no more than five where they are complex.)
- Font size 14 points should be used for headings and 12 points for main body text. For visually impaired the font size should be between 16 and 20 points. (This is contrary to the Guideline on readability which states that the font size should be 8 points.)
- Italic fonts and underlining should not be used.
- All text should be set horizontally.
- Spaces should be used between paragraphs to rest the eye.
- The text should be aligned to the left margin.
- Justified or centred text should not be used.
- Columns should be used to aid text navigation or vertical line when space is limited. Keep important information together so text flows easily from one column to another.
- The use of a larger font or bold text needs to be considered in the case of using reverse type for highlighting particular warnings. Reverse type is difficult for older readers" (Always read the leaflet – getting the best information with every medicine 100-1).

As we can see, the differences between the British and Dutch conventions concerning usability are not very striking. The MHRA has only elaborated on the Guideline on readability on a few linguistic and extratextual aspects and contradicts it on the aspect of font size and use of bullet points.

2.4.2 Translation problems concerning usability

The PIL that will be translated is a British leaflet which will be translated into Dutch. After having compared the British and Dutch regulation concerning PILs, two translation problems occur.

The British regulation says that five or six bullet points in a list should be the maximum,

whereas the Dutch regulation (which sticks to the Guideline on readability) states that no more than nine items should be used in a list where bullet points are simple and no more than five where they are complex. The Sertraline PIL has not complied with the British regulation since nearly all lists consist of more than six bullet points. Most lists consist of complex bullet points, which means that in the Dutch translation (in case the bullet points remain complex), no more than five bullet points can be used. A solution would be to transform the complex bullet points into simple bullet points and combining bullet points.

The second translation problem concerning usability is font size. I do not know if the Sertraline PIL has complied with the regulation in Always read the leaflet since this PIL is only available in PDF-format which makes it impossible to distinguish the font sizes. However, the proportion between headings, main text and information for the visually impaired (of which the MHRA respectively prescribes 14, 12 and 16-20 points) seems to be in accordance with the MHRA's guideline. The Guideline on readability (and the CBG-MEB accordingly) prescribes a font size and type of 8 points Didot and that (sub)headings should be made conspicuous (e.g. by colours) and headings should be numbered. In the translation, this will not be a real translation 'problem', as the font size and type, and the use of reverse type in source text can easily be converted to the Dutch prescribed situation.

For the remaining aspects regarding a PIL's usability, the target text can stick to the Guideline on readability and the prescriptions of the CGB and its model leaflet.

2.4.3 Differences between British and Dutch guidelines concerning risk and benefit information

For this comparative analysis, annex 10 of Always read the leaflet – getting the best information with every medicine needs to be compared with the chapter 'Guidance on package leaflet sections' of the CBG-MEB's *Bijsluiter van farmaceutische producten*. Annex 10 gives guidance on optimising the presentation of risk and benefit in PILs and elaborates upon the European Commission's Guideline on readability. 'Guidance on package leaflet sections' elaborates on the contents of the package leaflet sections which are stated in the Directive.

I will now compare the MHRA's and CBG-MEB's documents, and in the following paragraphs I will show the differences with regard to the presentation of key information, benefits of the medicine and side effects.

Key information or general information

The MHRA proposes an extra section with key information at the beginning of the leaflet, especially designed for people that would consider a leaflet too long or complex to read. The CBG-MEB follows the Directive (in which a similar section 'general information' is given at the end of the PIL) but states that it "is hesitant to include such as section at the end of a PIL". However, the CBG-MEB does not give any alternatives concerning the section's location. The MHRA wants the key information to be presented as a short series of bullet points and wants to include the following information:

- benefits of the product
- maximum dose or duration of treatment
- potential side effects or withdrawal reactions
- contraindications
- important drug interactions
- circumstances in which the drug should be stopped
- what to do if the medicine does not work
- where to find further information
- stimulation for reading rest of PIL
- last update PIL (Always read the leaflet – getting the best information with every medicine 151).

The CBG-MEB, in contrary, only permits the following information in its 'general information' section:

- a short description of the disease or the condition
- reference to an independent patient organisation
- general recommendations [..] such as "Return unused medicines to the pharmacy". (*Bijsluiter van farmaceutische producten* 13).

Moreover, the CBG-MEB states that "the text may not contain any information that would be better to state elsewhere in the package leaflet or that has been stated elsewhere in the package leaflet" which means that, contrary to the British situation, the CBG-MEB does not want information about maximum dose or duration of treatment, potential side effects or withdrawal reactions, contraindications, important drug interactions, circumstances in which

the drug should be stopped and what to do if the medicine does not work in its 'general information' section.

Information on the benefits of medicines

The MHRA states that the risks of a treatment should be placed in the context of the potential benefits and this could be achieved by including some general information on how the medicine works. According to the Directive, a PIL already needs to have the section 'What is your medicine and how does it work' and according to the MHRA, this section could be complemented with the following information:

- "why it is important to treat the disease and what the likely clinical outcome would be if the disease remained untreated;
- whether the treatment is for short term or chronic use;
- whether the medicine is being used to treat the underlying disease (ie curative) or for control of symptoms;
- if the latter, which symptoms will be controlled and how long the effects will last;
- whether the effects will last after the medication is stopped;
- where the medicine is used to treat two or more discrete indications, all should be succinctly described as above;
- where to obtain more information on the condition" (Always read the leaflet – getting the best information with every medicine 158).

Items which are most relevant to the patient, for example the impact of the medicine, should be given prominence by means of using specific font sizes or types.

The CBG-MEB, on the other hand, sticks to the Directive and only uses the prescribed section 'What is your medicine and how does it work', in which the pharmacotherapeutic group to which the medicine belongs and the mechanism of action or characteristics of the product is described in terms that are understandable to the patient (*Bijsluiter van farmaceutische producten* 8).

Information about side effects

There are some striking differences between the ways the MHRA and the CBG-MEB deal with side effects in PILs but on some issues they have the same opinion. Summarized, the MHRA has set up the following guidelines regarding side effects:

- The scientific term of a condition should be placed in brackets after the lay term.
- In case of serious side effects the action that is to be taken by the patient must be described.
- The duration of risk must be stated.
- A doctor should be consulted if side effects that are not mentioned in the section occur.
- Serious side effects should be mentioned first, then other possible side effects grouped by frequency (most frequent first). Body System Order Class (SOC) grouping should only be used when frequencies are not known.
- Verbal descriptors should only be used if accompanied by the equivalent statistical information of which only the upper bound should be referred to. E.g. use ’fewer than 1 in every 1,000’ rather than ‘between 1 in 10,000 and 1 in 1,000.’
- If severity of side effects is known, this should be included in the PIL.
- If a side effect is dose-related, this should be included in the PIL.
- Providing links/details of further information sources on side effects should be considered.
- Conveying imprecision of point estimates using terms such as “approximately”/”about”/”around” when referring to estimates for major safety issues (Always read the leaflet – getting the best information with every medicine 160-64).

And, summarized, the CBG-MEB has set up the following guidelines with regard to side effects:

- The scientific term of a condition should be placed in brackets after the lay term.
- In case of serious side effects the action that is to be taken by the patient must be described.
- The duration of risk must be stated.
- A doctor should be consulted if side effects that are not mentioned in the section occur.
- Side effects are to be presented in the following order: 1. SOC grouping 2. In decreasing frequency within each organ system. 3. Within each frequency group, the side effects should be listed in order of decreasing severity.
- The CBG-MEB uses the same terminology “very common, common, uncommon, rare, very rare” in combination with a different form of statistical information (very

common >1/10; common >1/100-<1/10; uncommon >1/1000-<1/100; rare >1/10.000-<1/1000; very rare <1/10.000). These patient numbers can be stated at the beginning of the section.

- Blood disorders should be included; these are not directly evident as such to the patient, but can be identified when described in the following way: blood disorders that can give rise to symptoms such as tiredness, frequent infections, bruises, etc.
- Side effects such as sudden cardiac death and risk of suicide must be included and indicating its frequency is extremely important. Although mentioning such side effects can have a negative effect on treatment compliance, it is important to include them in connection with liability considerations and the need for patients to be fully informed. These side effects should be described as follows:
    - Sudden cardiac death: “Extremely rare incidences of sudden cardiac death have been reported.”
    - Risk of suicide: “Extremely rare reports have been made of patients who have developed suicidal tendencies (for antidepressants: at the start of the treatment). If you think that you are also affected in this way, you are advised to contact your doctor immediately”.
- Related side effects can be covered by a single term. E.g. different arrhythmias could be summarised as” heart rhythm disorders” (*Bijsluiter van farmaceutische producten* 11, 12).

As we can see, the British and Dutch organisations are of the same opinion regarding the use of medical jargon, patient’s action in the case of serious side effects, duration of risk and non-mentioned side effects. They are also of the same opinion that verbal descriptors should be used in combination with statistical information but the MHRA only wants to refer to the upper bound and uses a full sentence, while the CBG-MEB gives a range of statistical information and wants these numbers to be placed at the beginning of the section.

Furthermore, the MHRA as well as the CBG-MEB advises a specific order in which the side effects should be listed but they use different criteria. The MHRA wants to list serious side effects first, followed by the rest of the side effects in decreasing frequency. The CBG-MEB, on the other hand, groups side effects by the system of Body System Order Class (SOC) in decreasing frequency within each organ system.

And additionally, the MHRA has guidelines regarding severity of side effects, dose-related side effects, further information on side effects and point estimates; subjects on which

the CBG-MEB does not have any guidelines. In retrospect, the CBG-MEB discusses issues which the MHRA does not pay attention to: inclusion of blood disorders, side effects such as sudden cardiac death and risk of suicide and using single terms for related side effects.

2.4.4 Translation problems regarding risk and benefit information

As for risk and benefit information, the first translation problem that is caused by the differences between the British and the Dutch regulation exists in the field of key/general information. The MHRA proposes an extra section with key information on risk and benefit of the medicine at the beginning of the PIL whereas the CBG-MEB sticks to the short 'general information' section prescribed by the Directive. The Sertraline PIL contains a section with 'general information' ("Eight important things you need to know about Sertraline") at the start of the PIL but this section is not completely in accordance with the content of the prescribed 'general information' section of the MHRA. In the target text, the 'general information' section should be placed at the end of the PIL, before the information on the last update, and will contain a short description of the disease or the condition, reference to an independent patient organisation and general recommendations such as "Return unused medicines to the pharmacy". No information that is stated elsewhere in the PIL is allowed in this section. This means that the information in the first section of the source text will not be translated at all since its content has already been stated elsewhere in the PIL.

Another difference between the MHRA's and CBG-MEB's guidelines exists in the field of benefit information. As I stated in the previous paragraph, the MHRA proposes to elaborate on the section "What is your medicine and how does it work", in which amongst others the benefits of the medicine should be described, thus elaborating on the Directive. The Sertraline PIL has (again) not complied with the MHRA's regulation and sticks to the Directive which means that only the pharmacotherapeutic group and the characteristics of the medicine are given in the section "What is your medicine and how does it work". As the CBG-MEB has not set up additional regulation concerning benefit information, the section "What is your medicine and how does it work" will be fully maintained in the target text.

Most differences between the MHRA's and CBG-MEB's guidelines have been encountered in the field of risk information. Both authorities are of the opinion that verbal descriptors should be used in combination with statistical information, but the MHRA only wants to refer to the upper bound and wants to use a full sentence, whereas the CBG-MEB

gives a range of statistical information and wants these numbers to be placed at the beginning of the section. The Sertraline PIL has only partly complied with the MHRA's guideline since a verbal descriptor has been used in combination with statistical information and a full sentence has been used, but the statistical information does not refer to the upper bound ("more than 1 in 10,000 patients, but less than 1 in 1,000 patients"). The CBG-MEB also wants to combine verbal descriptors with statistical information, so in the target text only the rendering of statistical information needs to be adapted and will have to look like e.g. "rare: >1/10.000-<1/1000".

Another translation problem concerning the rendering of side effects results from the differences between the order in which the side effects should be listed. The MHRA wants to list serious side effects first, followed by the rest of the side effects in decreasing frequency. The Sertraline PIL has complied with this regulation. The CBG-MEB, on the other hand, groups side effects by the system of Body System Order Class (SOC) in decreasing frequency within each organ system. This means that the side effects must be grouped according to the SOC. So the order of the lists of side effects of the Sertraline PIL must be changed drastically in the target text.

Lastly, there are aspects the CBG-MEB wants to have included in Dutch PILs, whereas the MHRA does not mention them in their guideline. These aspects are information on blood disorders, side effects such as sudden cardiac death and risk of suicide and using single terms for related side effects. The Sertraline PIL has already included information on blood disorders in the section on side effects ("low blood levels of sodium which can cause tiredness and confusion") so this aspect can be maintained in the target text. The side effect sudden cardiac death is not relevant for the Sertraline PIL as it is not stated in the PIL and is therefore not considered a side effect. Risk of suicide is mentioned in the Sertraline PIL and the information on this issue can therefore be maintained in the target text. Regarding using single terms for related side effects could be stated that none of the side effects are related, so it is not necessary to group related side effects in the target text.

2.5 Conclusion

In setting up their guidelines concerning PILs, both the British MHRA and the Dutch CBG-MEB take the European Commission's key documents, the Directive and the Guideline on readability, as their basis. As became clear from paragraph 2.1, the Directive focuses at the contents and format of PILs and the Guideline on readability is an addition to the Directive, focussing on PILs' design and style and including a model leaflet. As the Directive and the

Guideline on readability are not very elaborate and leave many questions unanswered, the MHRA set up "Always read the leaflet – getting the best information with every medicine" and the CBG-MEB drew up *"Bijsluiter van farmaceutische producten"*; both documents are an elaboration on the European Commission's guidelines.

Since this translation project results into translating the British Sertraline PIL into Dutch, I have, in this chapter, compared the British situation regarding PILs with the Dutch situation and I found differences in the fields of usability and risk and benefit information. From these differences, translation problems were deduced and solutions were proposed. In the field of usability, the differences that were detected between the MHRA's and the CBG-MEB's guidelines are not very striking. The CBG-MEB has completely retained the rules of the Guideline on readability and the MHRA has complemented the Guideline on readability (and the CBG-MEB accordingly) on a few aspects regarding word choice, font type and some aspects concerning the design of the PIL's text. Regarding font size and bullet points, the MHRA's opinion slightly differs from the Guideline on readability (and the CBG-MEB accordingly), but since the Sertraline PIL has not complied with the MHRA's regulation at all, the target text needs thorough redrafting with regard to bullet point lists and font size.

Regarding risk and benefit information, one of the differences encountered between the British and the Dutch situation is the rendering of key/general information. The MHRA proposes an extra section with key information on risk and benefit of the medicine at the beginning of the PIL whereas the CBG-MEB sticks to the short 'general information' section prescribed by the Directive. Again, the Sertraline PIL has not fully complied with the MHRA's regulation which means that in the target text, superfluous information needs be left out and the location of the 'general information' section needs to be adjusted.

The MHRA also proposes to elaborate on the section 'What is your medicine and how does it work', in which amongst others the benefits of the medicine are described. The MHRA wants to add more information on the benefits of the medicine than the Directive prescribes. The CBG-MEB has not published additional guidelines on this aspects and therefore sticks to the Directive in which only the pharmacotherapeutic group and the characteristics of the medicine are given in the section "What is your medicine and how does it work". The Sertraline PIL has (again!) not complied with the MHRA's guideline and sticks to the Directive. This means that this section can be fully maintained in the translation of the Sertraline PIL.

Most differences between the opinions of the two health authorities exist in the field of side effects, but there are also aspects on which the MHRA and CBG-MEB are of the same

opinion, such as the use of medical jargon, patient's action in the case of serious side effects, duration of risk and non-mentioned side effects. They also agree on the aspects of combining verbal descriptors with statistical information and they use a specific order for listing side effects. However, the two countries use different criteria concerning these subjects. The target text will have to comply with the Dutch regulation. Furthermore, the MHRA has guidelines regarding severity of side effects, dose-related side effects, further information on side effects and point estimates; subjects on which the CBG-MEB does not have any guidelines. In retrospect, the CBG-MEB discusses issues which the MHRA does not pay attention to: inclusion of blood disorders, side effects such as sudden cardiac death and risk of suicide and using single terms for related side effects. Information on these issues is either irrelevant for the medicine Sertraline or is already present in the source text and can be maintained in the target text (information on blood disorders and risk of suicide).

Now that the translation problems concerning usability and risk and benefit information have been discussed, the next chapter will focus on Nord's translation-oriented text analysis. As will become clear, a few sub questions of Nord's scheme for analysis have already been answered (or partly answered) and therefore chapter 3 is centred on the analysis of the vocabulary and grammar of the Sertraline PIL and its potential Dutch translation.

3. TRANSLATION-ORIENTED TEXT ANALYSIS

In this chapter, Nord's translation-oriented text analysis will be applied to the Sertraline PIL and its potential translation into Dutch. Paragraph 3.1 gives background information on Nord's theory and explains which translation problems have already been identified so far in this thesis. Paragraph 3.2 answers the sub questions of the pragmatic question scheme for either the source text as well as the target text, thus creating source and target text profiles. Lastly, paragraph 3.3 'translates' the answers to the sub questions of paragraph 3.2. into translation problems and possible solutions.

3.1 Nord's translation-oriented text analysis

Christiane Nord's conveniently arranged pragmatic question scheme is a great aid in making a translation-oriented text analysis. It is a top-down method which starts by analysing extratextual dimensions and works toward the intratextual features. The method consists of seventeen sub questions: "Who transmits to whom, what for, by which medium, where, when, why, a text with what function? On what subject matter does s/he say what, what not, in what order, using which non-verbal elements, in which words, in what kind of sentences, in which tone, to what effect?" (Nord, 235-36).

According to Nord's theory, a profile of the target text in its communicative situation in the target culture needs to be made first. After this target text profile ('desired state') the source text ('actual state') needs to be analysed with the help of the same question scheme. Personally, I prefer to answer each sub question for either the source text as well as the target text, starting with the source text and then the target text. Subsequently, these two profiles can be compared and translation problems can be identified. Nord distinguishes four types of translation problems: pragmatic, culture-specific, language pair-specific and text-specific translation problems. The differences between them will be described in paragraph 3.3.

In chapter 2, the translation problems concerning usability and risk and benefit information in the Sertaline PIL have already been identified. The translation problems in the field of usability concerned bullet point lists and font size. In advance of paragraph 3.2, the use of bullet points could be classified under sub question 15 (grammar) and font size may be classified under sub question 13 (non-verbal elements).

The translation problems in the field of risk and benefit information concerned the rendering of key/general information, benefit information, statistical information, the order of the lists of side effects and information on blood disorders, side effects such as sudden cardiac death and risk of suicide and using single terms for related side effects. As has become clear in chapter 2, the rendering of benefit information, information on blood disorders, side effects such as sudden cardiac death and risk of suicide and using single terms for related side effects will not cause any translation problems when translating the Sertraline PIL. The translation problems that follow from the differences in the rendering of key/general information, statistical information and the order of listing side effects could be classified into each of the sub questions. The issue of key/general information could be classified into sub questions 9 (subject) and 12 (segmentation). Statistical information could be classified into sub question 14 (vocabulary) and the issue of the order of lists of side effects could be classified into sub question 12.

As will become clear from the rest of this chapter, the greater part of the sub questions has already been dealt with and answered in chapter 1 and 2. The following paragraphs are therefore mainly aimed at answering sub questions 8, 9, 12, 14 and 15.

3.2 Source and target text profiles

In the following overview, the source and target text profiles have been set up with the help of Nord's pragmatic question scheme. Please note that the source text has been analysed from the actual state in which it exists. This means that the Sertraline PIL's contents and the extratextual aspects that are known have been analysed. In chapter 2, the guidelines of the MHRA have been outlined, but as will become clear, the Sertraline PIL has not complied with them all the time or only to a limited degree. Therefore I will stick to describing the actual state in which the Sertraline PIL exists and I will only elaborate on the 'desirable' state in which the MHRA wishes PILs to be in case this is relevant for answering the sub question.

In this overview, it has been indicated when no translation problems result from the analysis. In case a translation problem does appear, it is discussed in paragraph 3.3.

1. Who transmits? (sender)

- ST: Marketing authorisation holder Tillomed Laboratories Ltd is the sender and most likely the text producer. Tillomed is most likely an expert on the subject and not on text

production. Only visually impaired can ask Tillomed for more information (see Sertraline PIL: “Hard to read? Phone 0800 970 6115 for help”).

- TT: Dutch PILs are issued by Dutch marketing authorisation holders, but often a (specialized) translation agency is commissioned to translate the PIL. The sender cannot be asked for more information. However, the CBG-MEB prescribes that in the ‘general information’ section should be referred to an independent patient organisation.

→ No translation problem

2. To whom? (recipient)

- ST: Patients suffering from depression who have been prescribed Sertraline by their doctor.

- TT: Idem

→ No translation problem

3. What for? (intention)

- ST: PILs are by convention written to promote the safe and effective use of medicines. This has already been discussed in paragraph 1.2 and 1.3 of this thesis.

- TT: Idem

→ No translation problem

4. By which medium? (medium)

- ST: PILs are simplified versions of Summaries of Product Characteristics and core data sheets; documents that are intended to experts. This has already been discussed in paragraph 1.1.

- TT: Idem

→ No translation problem

5. **Where? (space)**

- ST: The text has supposedly been produced at the address of the marketing authorisation holder.

- TT: I will translate the Sertraline myself but in a professional situation the translation of a British PIL will most likely be done by a translation agency specialized in medical/pharmaceutical translations.

→ No translation problem

6. **When? (time)**

- ST: In the Sertraline PIL is stated: “This leaflet was last approved in July 2008.” The actual time of writing is unknown.

- TT: The Sertraline PIL is to be translated in March 2009.

→ No translation problem because in the past half a year, the regulation regarding patient information has not been changed so there will be no time lag between source and target text situation.

7. **Why? (motive)**

- ST: The main motive of setting up a PIL is the production of a new medicine which by law requires a PIL.

- TT: Idem

→ No translation problem

8. **With what function? (function)**

- ST: In chapter 1.2. the different functions of instructive texts have already been discussed. In order to bring this into practice, the procedural and declarative parts and corresponding text functions of the Sertraline PIL have been highlighted. As became clear from chapter 1.2, instructive texts consist of a combination of procedural (instructive, advising, requesting, warning, urging function) and declarative information (defining, describing,

teaching, motivating function). In annex 1 the procedural and declarative parts of the Sertraline PIL have been highlighted. Furthermore, the different types of sentences that have been used with either text function have been indicated. Details about this grammatical analysis can be found under sub question 15.

When looking at the highlights in the Sertraline PIL, it appears that the instructions always consist of procedural information (see yellow, green and grey highlights). On top of this, declarative sentences may have been used to support the instruction (blue highlights). Furthermore, there are sections in the PIL which are purely informative and not instructive. These parts consist of declarative information and are not part of instructions (see pink highlights).

The Guideline on readability prescribes: "Where explanations are given for instructions, the instructions should come first. For example: 'Take care with X if you have asthma –it may bring on an attack'" (11). As the MHRA has not set up any regulation with respect to this issue, the Guideline on readability must be observed. When looking at the highlighted text functions in the Sertraline PIL, we can see that it is often not the case that the instruction (yellow, green and/or grey highlight) comes first and the explanation comes second (blue highlight). So we may conclude that the Sertraline PIL has not observed the Guideline on readability regarding this issue.

- TT: The information described above with regard to text functions can also be applied to the Dutch communicative situation in which the Sertraline PIL will function.

→ Translation problem: see paragraph 3.3.

9. On what subject matter? (subject)

- ST: The MHRA has set up guidelines regarding the contents of the different sections in a PIL. As becomes clear from the Sertraline PIL, the guidelines of the MHRA are not complied with fully. The MHRA for example requires an extra section with key information at the beginning of the leaflet. The Sertraline PIL contains such a section but its content does not meet the MHRA's requirements. The Sertraline PIL consists of the following sections:
    - Identification of the medicine: name of the medicine, active substance, pharmaceutical form (partly stated)

- General/key information: “Eight important things you need to know about Sertraline”
- Stimulation to read the PIL fully and further important information
- Index
- Therapeutic indications: “What Sertraline is and what it is used for”
- Risk information: “Before you take Sertraline”
- Dosage and instructions for use: “How to take Sertraline”
- Information about side effects: “Possible side effects”
- Information about storing the medicine: “How to store Sertraline”
- Further identification of the medicine: active substance, other ingredients, pharmaceutical form (fully described), contents of the pack, information about marketing authorization holder, information about manufacturer, product licence numbers, date of last approval, information for visually impaired.

- TT: The CBG-MEB requires PILs to consist of the following sections:
  - “General characteristics-Identification of the product (name, composition, pharmaceutical form and content, pharmacotherapeutic group, name of the marketing authorization holder, recorded in the register under RVG
  - Use of the medicine (all of the indications in the SmPC)
  - Before using the medicine (Situations in which the medicine should not be used, necessary precautions during use, interactions with other medicines and other interactions that may affect the medicine’s action, special warnings)
  - Instructions for use
  - Side effects
  - Instructions for storage and expiry date
  - General information
  - Date on which the package leaflet was last revised/approved” (*Bijsluiter van farmaceutische producten* 8-13)

→ Translation problem: see paragraph 3.3.

10. What? (information)

- ST: This question has already been answered under the previous sub question (9).

- TT: This question has already been answered under the previous sub question (9).

11. What not? (presuppositions)

- ST: This question has already been answered under sub question 9.

- TT: This question has already been answered under sub question 9.

12. In what order? (segmentation)

- ST: The macrostructure of the Sertraline PIL is marked by section headings in reverse type and the use of one box. Between paragraphs, space has been used. This is partly a conventional composition for PILs since the MHRA requires following:
    - "Spaces should be used between paragraphs to rest the eye.
    - Columns should be used to aid text navigation or vertical line when space is limited. Keep important information together so text flows easily from one column to another.
    - The use of a larger font or bold text needs to be considered in the case of using reverse type for highlighting particular warnings. Reverse type is difficult for older readers" (Always read the leaflet – getting the best information with every medicine 100-1).

  The Sertraline PIL uses only one column (which includes stimulation to read the PIL fully, further important information and the index) and no vertical lines, so on this aspect it only partly complies with the MHRA's guideline. The Sertraline PIL fully complies with the MHRA's guideline regarding spaces between paragraphs and the use of bold text or larger font when reverse type is used.

- TT: The Dutch Sertraline PIL will be produced according to the model leaflet of the CBG-MEB (which the CBG-MEB has almost literally taken over from the Guideline on readability) and must have a segmentation according to the model leaflet which is stated in *Bijsluiter van farmaceutische producten* (19-22).

  The Guideline on readability (and the CBG-MEB has adopted the rules accordingly) has a few additional specific rules regarding the macro structure of a PIL. They are:

- "(Sub)headings should be made conspicuous (e.g. by colours) and also, headings should be numbered. No more than two levels of headings should be used.
- Only use pictograms when they make the message clearer.
- Columns should be used to aid text navigation or vertical line when space is limited. Keep important information together so text flows easily from one column to another.
- Only use red colour print for very important warnings" (Guideline on the readability of the label and package leaflet of medicinal products for human use 3, 4, 11, 12).

→ Translation problems: see paragraph 3.3.

13. Using which non-verbal elements? (illustrations etc)

- ST: No non-verbal elements are used, except the logo of the marketing authorisation holder Tillomed. In most PILs the logo of the marketing authorisation holder is printed at the beginning or the end of the PIL. The national health authority has not set up any regulation concerning the use of logos.
- TT: The CBG-MEB requires: "Only a logo of the marketing authorisation holder may be included and no logos of manufacturers, importers or licence authorisation holders" (*Bijsluiter van farmaceutische producten* 8).

→ No translation problem since Tillomed logo can omitted in the target text. No other logo will be used since I simply do not know who will be the Dutch marketing authorisation holder.

14. In which words? (vocabulary)

- ST: In annex 2 has been indicated in which different ways medical terms are rendered in the Sertraline PIL.

The following requirements of the MHRA's regulation concerning the correct use of lay terms (Always read the leaflet – getting the best information with every medicine 123-8) are relevant in this respect:

- “When to use lay definitions: definitions should be used when the medical term is not well known in the general population” (Sertraline PIL has complied with this rule).
- “General format: the standard format is to describe what the condition is and then what a sufferer may feel. The latter serves to help patients in identifying whether they may be suffering from the effect described. This may not be necessary if the condition is well known or the symptoms obvious from the description of the condition.” (The Sertraline PIL has also complied with this rule since it in most cases the symptoms of a condition are described (see blue highlights annex 2) and in case the symptoms are not described, the condition is well known (brown-green hightlights))
- “Inclusion of medical terms: pharmaceutical companies should also consider including the medical term where this is an important feature and may help the reader interpret other sources of information about the medicine” (The Sertraline PIL has complied with this rule since medicines are always indicated by their active substance).
- “Serious: use this term to indicate that the condition is usually medically significant (e.g. is likely to require medical attention, such as hospitalisation). For example, Stevens-Johnson syndrome causes serious blistering and anaphylaxis is a serious allergic reaction. This is not necessary when the seriousness of the condition is obvious or well known” (The Sertraline PIL has complied with this rule since the seriousness of the Stevens-Johnson syndrome and anaphylaxis is already indicated in the section heading “Serious side effects” and, moreover, “serious” is repeated in the symptom description of anaphylaxis.
- “Severe: where necessary to distinguish from symptoms or medical effects that might otherwise be considered as mild (e.g. severe headache, or severe pain accompanying myocardial infarction)” (The Sertraline PIL has complied with this rule since “severe skin reaction” is used correctly for Stevens-Johnson syndrome).
- “Brackets: use these for the medical term where it is helpful to quote this” (The Sertraline PIL has not complied with this rule in all cases. In annex 2, the red highlights do comply with the rule, except when “e.g.” is used instead of brackets for quoting the medical term. The yellow and grey highlights state the medical

term first and put the definition between brackets so these do not comply with the regulation. Only the blue markings fully observe the rule).

- TT: Concerning medical terminology, the CBG-MEB sticks to the Guideline on readability which prescribes: "Where a scientific or specialised term is used, an explanation should be given" (11).

  The CBG-MEB has also set up a list of acceptable lay definitions of medical terms to be used in PILs. The CBG-MEB "strongly recommends placing the medical term in brackets after the lay term" (*Bijsluiter van farmaceutische producten* 45).

  → Translation problem: see paragraph 3.3.

15. In what kind of sentences (grammar)

- ST: In annex 1 the procedural and declarative parts of the Sertraline PIL have been indicated. It appears that procedural information has been formulated in the following types of sentences:
  - imperative sentences, either positively or negatively formulated (yellow highlights in annex 1)
  - conditional clauses (green highlights)
  - longer 'normal' sentences with modals (should, may, might, will), either positively or negatively formulated (grey highlights, modals boxed and in red font)
  - longer 'normal' sentences without modals, either positively or negatively formulated (grey highlights)

The MHRA has not set up any specific regulation to complement on the Guideline on readability regarding the grammatical aspects of PILs. The Guideline on readability prescribes the following (Guideline on the readability of the label and package leaflet of medicinal products for human use 3, 4, 11, 12, 21):

- "An active and direct style should be used, by placing the verb at the beginning of the sentence, for example:
  - 'take 1 tablet' instead of '1 tablet should be taken'
  - 'you should' is better than 'it is recommended'

  This principle should be adapted in the case of, for example, 'If…then' instructions, such as: 'If you feel ill, tell your doctor.'" (The Sertraline PIL has not

complied with this rule; see annex 1 in which all passive sentences are highlighted by means of an orange font colour.)

- "Use simple punctuation." (The Sertraline PIL has complied with this rule.)
- "Do not use sentences over 20 words or 70 characters." (The Sertraline PIL has not complied with this rule since it contains many sentences that are longer than 20 words)
- "Be positive rather than negative, whenever possible. Negative instructions should only be used when the consumer should avoid specific actions." (The Sertaline PIL has complied with this rule as negative formulations indicate that the patient should avoid certain actions.)

- TT: The target text will be set up according to the model leaflet which means that the required, standard sentences of the model leaflet need to adopted into the target text (see instructions model leaflet in *Bijsluiter van farmaceutische producten* p.24-39).

  Furthermore, the target text needs to observe the above-mentioned regulation of the Guideline on readability concerning grammar.

  → Translation problem: see paragraph 3.3.

16. In which tone (tone)

- ST: This has already been discussed in paragraph 1.5.

- TT: Idem.

  → No translation problem

17. To what effect (effect on reader)

- ST: In case of prescribed medication, the specific medicine has been advised by the physician and in an ideal situation the patient should be able to rely on the doctor's advice. However, physicians sometimes confine to giving the dosage and a brief explanation about the medicine's working and do not have any information (or ask about) a patient's medical history and use of other medication which could cause adverse reactions. Therefore, it is extremely important that a PIL provides information on these aspects so the patient can use the medicine safely and effectively.

- TT: Idem.

→ No translation problem

3.3 Translation problems

Nord distinguishes four types of translation problems. In the first place there are pragmatic translation problems which come forth from the differences in the communicative situations in which the source text and target text function (e.g. problems because of differences in time and space and because of culturally determined different prescience of the conventions in the source and target culture). Secondly, Nord distinguishes culture-specific translation problems which come forth from the differences in norms and conventions of the source and target culture (e.g. legal guidelines for PILs). Thirdly there are translation problems that are language pair-specific which come forth from the differences in structures of the source and target language (e.g. the translation of the English modals into Dutch). Lastly there are text-specific translation problems which occur while translating individual texts of which the solution cannot be applied to other translations (e.g. the translation of puns) (Nord 237).

Virtually all of the translation problems of the Sertraline PIL could be classified as culture-specific translation problems because they come forth from the differences in regulation regarding PILs of the British MHRA and the Dutch CBG-MEB. There is only one translation problem that may be classified as language-pair specific. I have not encountered any pragmatic or text-specific translation problems. The following translation problems (solutions to the translation problems are also proposed) are culture-specific and it has been indicated which sub question the translation problem relates to.

Sub question 8: Function

- Procedural information: The Guideline on readability's rule regarding the sequence instruction-explanation has frequently been ignored in the ST but will have to be observed in the TT. This means that many instructions in the PIL require thorough redrafting so that they are all formulated in the sequence instruction-explanation.

Sub question 9: Subject

- Key/general information: The MHRA prescribes an extra section with key information on risk and benefit of the medicine at the beginning of the PIL whereas the CBG-MEB sticks

to the shorter ‘general information’ section prescribed by the Directive. In the TT, the section “Eight things you need to know about Sertraline” is superfluous and needs to omitted from the TT. Instead, a ‘general information’ section needs to added.

- Presuppositions: The Sertraline PIL contains information about the manufacturer and information for the visually impaired but the CBG-MEB does not prescribe information about these subjects. Therefore, this information needs to be omitted from the TT.

Sub question 12: Segmentation

- Macro structure: The CBG-MEB requires PILs’ headings to be numbered and the use of columns or vertical lines between sections. The Sertraline PIL lacks this but in the TT headings need to be numbered and columns or vertical lines need to be used.
- Side effects: The CBG-MEB wants side effects to be grouped by the system of Body System Order Class (SOC) in decreasing frequency within each organ system. This means that the side effects of the Sertraline PIL – which have been grouped on the basis of the frequency in which they occur – must be regrouped according to the SOC.

Sub question 13: Non-verbal elements

- Font size: The MHRA prescribes font sizes of 14 for headings, 12 for main text and 16-20 for visually impaired) whereas the Guideline on readability (and the CBG-MEB accordingly) prescribes a font size and type of 8 points Didot for all text. In the translation, this will not be a serious translation ‘problem’ as the font size and type, and the use of reverse type of the Sertraline PIL can easily be converted to the Dutch prescribed situation of 8 points Didot.

Sub question 14: Vocabulary

- Terminology: the CBG-MEB requires the medical term to be placed in brackets after the lay term or the explanation of the term. In my opinion, however, this is only possible when the explanation or lay term is an equivalent of the medical term. Therefore, putting the medical term in brackets after the lay term or explanation is only possible in case the name of the pharmacotherapeutic group is given (e.g. “watering tablets (diuretics)”) and in case of diseases/disorders (e.g. “feeling elated or over-excited, which causes unusual behaviour (mania)”). It is not possible with names of medicines – which is often the active substance of the medicine - (e.g. “pimozide (for psychiatric disorders)”). In the latter case, the medical term can simply not be preceded by an explanation (e.g. “*medicine for*

psychiatric disorders (pimozide)") as pimozide is just one of the many medicines that can be used for psychiatric disorders. Since medical terminology has been rendered in various ways in the Sertraline PIL, this aspect needs thorough redrafting in the TT. The medical term needs to be placed in brackets after the lay term or the explanation of the term.

Sub question 15: Grammar

- Bullet points: The MHRA requires five or six bullet points in a list to be the maximum, whereas the CBG-MEB states that no more than nine items should be used in a list where bullet points are simple and no more than five where they are complex. In the Sertraline PIL nearly all lists consist of more than six bullet points. Most lists consist of complex bullet points which means that in the TT (in case the bullet points remain complex) no more than five bullet points can be used. A solution would be to transform the complex bullet points into simple bullet points and to combine bullet points.
- Active sentences: Neither the MHRA, nor the CBG has set up additional regulation concerning the grammar used in PILs. This means that the Guideline on readability has to be complied with. For the TT this means that the passive sentences of the Sertraline PIL (indicated in appendix 1 by means of orange font colour) must be rewritten into active sentences.
- Sentence length: The Guideline on readability prescribes that sentences should contain 20 words or less. As many sentences in the Sertraline PIL contain more than 20 words they all need to be rewritten into sentences containing 20 words or less.
- Statistical risk information: The MHRA only wants to refer to the upper bound of the statistical information and wants to use a full sentence for this information, whereas the CBG-MEB's regulation refers to the upper and lower bound of the statistical information and does not use full sentences. The Sertraline PIL has only partly complied with the MHRA's guideline since the statistical information does not refer to the upper bound ("more than 1 in 10,000 patients, but less than 1 in 1,000 patients"). In the TT the rendering of statistical information needs to be adapted and will have to look like e.g. "rare: >1/10.000-<1/1000."

Lastly, I have identified one translation problem that can be classified as language pair-specific. This is the use of modals and this is an aspect of which there is no regulation about, but which might cause translation problems. The modal verbs 'may', 'might', 'should' and

‘will’ have been used several times in the Sertraline PIL. Per sentence should be considered how to translate the modals.

3.4 Conclusion

In this chapter, Nord’s translation-oriented text analysis has been applied to the Sertraline PIL in order to set up a source and target text profile. In a top-down method, seventeen sub questions have been answered with regard to the existing source text and the potential target text. From the answers to the sub questions, translation problems have been deduced and possible solutions have been proposed. It appeared that most translation problems are culture-specific because they result from the differences in regulation of PILs in the source and target text culture.

With regard to text function, a translation problem concerning the rendering of procedural information resulted from the differences between the Sertraline PIL and the Dutch regulation. As for a PIL’s subject matter, differences in the key/general information sections will cause translation problems. With regard to a PIL’s segmentation, translation problems regarding the macro structure (numbering of headings and separation of sections) and the order of lists of side effects came forth from the differences between the Sertraline PIL and the CBG-MEB’s regulation. The sub question ‘non-verbal elements’ resulted into a translation problem regarding font size. And, as for vocabulary, the rendering of the medical terminology needs to be thoroughly adapted in the target text. Most translation problems came forth from differences between the British and Dutch regulation concerning a PIL’s grammar; the target text needs to be rewritten with regard to bullet point lists, passive sentences, sentence length and statistical risk information.

In the next – and final – chapter of this translation project, the actual translation of the Sertraline PIL into Dutch has been made. For this purpose, the translation problems laid out in this chapter have been taken into account.

4. ANNOTATED TRANSLATION PATIENT INFORMATION LEAFLET SERTRALINE

In the final chapter of this thesis, the translation of the Sertraline PIL into Dutch has been made.

For this purpose, I made use of the model leaflet set up by the European Commission which has been adopted, complemented and adapted by the CBG-MEB and has been incorporated into "*Bijsluiter van farmaceutische producten*", the CBG-MEB's key document on regulation. Together with the model leaflet, the remaining regulation of the CBG-MEB (which is stated in *Bijsluiter van farmaceutische producten*) and the regulation laid out in the Guideline on readability must be complied with. Furthermore, the translation problems which have arisen from the differences between the MHRA's and CBG-MEB's regulation, described in chapter 3, must be taken into account as well. These translation problems concerned procedural information, key/general information, presuppositions, macro structure, side effects, font size, terminology, bullet points, active sentences, sentence length, statistical information and the use of modals (for details, see paragraph 3.3).

Paragraph 4.1 contains the actual translation of the Sertraline PIL from English into Dutch. The numbers between brackets refer to the notes that have been listed in paragraph 4.2. Paragraph 4.3 summarizes the most important findings of the translation activities.

4.1. Translation

(1)

(2)

Lees deze bijsluiter zorgvuldig door voordat u start met het gebruik van dit geneesmiddel (3).

- Bewaar deze bijsluiter, het kan nodig zijn deze nogmaals door te lezen.
- Heeft u nog vragen, raadpleeg dan uw arts of apotheker.
- Geef dit geneesmiddel niet door aan anderen, dit geneesmiddel is aan u persoonlijk voorgeschreven (4). Dit geneesmiddel kan schadelijk zijn voor anderen, zelfs als de verschijnselen dezelfde zijn als waarvoor u het geneesmiddel heeft gekregen.

Inhoud van deze bijsluiter (5)

1. Wat is Sertraline en waarvoor wordt het gebruikt?
2. Wat u moet weten voordat u Sertraline inneemt
3. Hoe wordt Sertraline ingenomen?
4. Mogelijke bijwerkingen
5. Hoe bewaart u Sertraline?
6. Algemene informatie (6)

Sertraline 50 mg filmomhulde tabletten
Sertraline 100 mg filmomhulde tabletten (7)

Het werkzame bestanddeel is sertraline hydrochloride waarvan bij Sertraline 50 mg in één tablet 50 mg aanwezig is. Bij Sertraline 100 mg is hiervan 100 mg in één tablet aanwezig (8).
Andere bestanddelen (hulpstoffen) zijn microkristallijne cellulose, calcium waterstoffosfaat, hyprolose, natriumzetmeel glycolaat, magnesium stearaat, hypromellose, talk, titaandioxide (E171) (9).

Registratiehouder: “naam, adres, plaats” (10)
(11)

In het register ingeschreven onder RVG …. (12)

(13)

1. Wat is Sertraline en waarvoor wordt het gebruikt? (14)

Farmaceutische vorm en inhoud
De tabletten zijn verkrijgbaar in blisterverpakkingen van 10, 14, 15, 20, 28, 30, 50, 50x1, 60, 98 en 100 filmomhulde tabletten. Tevens zijn er flacons verkrijgbaar met 30, 50, 100, 250, 300 en 500 filmomhulde tabletten (15).

Het is mogelijk dat niet alle verpakkingsgroottes in de handel worden gebracht (16).

Geneesmiddelengroep

Sertraline behoort tot een geneesmiddelengroep genaamd selectieve serotonine heropname remmers (SSRI's).

Toepassing van het geneesmiddel

Sertaline is een middel tegen neerslachtigheid (antidepressivum) (17) dat invloed uitoefent op het zenuwstelsel. Het wordt gebruikt voor de behandeling van ernstige neerslachtigheid (depressie).

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2. Wat u moet weten voordat u Sertraline inneemt

Gebruik Sertraline niet

- wanneer u overgevoelig bent voor sertraline of één van de andere bestanddelen van Sertraline;
- wanneer u MAO-remmers inneemt (bij depressie of ziekte van Parkinson) (18) of deze de afgelopen twee weken ingenomen heeft;
- wanneer u pimozide inneemt (bij psychiatrische aandoeningen).

Wees extra voorzichtig met Sertraline (19)

- wanneer u epilepsie heeft. In geval van epileptische aanvallen dient de behandeling met Sertraline (20) gestaakt te worden (21). Neem contact op met uw arts.
- (22)
- wanneer u schizofrenie heeft.
- wanneer u een ernstige lever- of nierfunctiestoornis heeft.
- waneer u in het verleden periodes heeft gehad van overdreven opgewektheid gepaard gaande met het hebben van veel energie (manie) (23). Wanneer u vermoedt dat u symptomen van manie heeft, dient de behandeling gestaakt te worden (24). Neem contact op met uw arts.
- wanneer u in het verleden bloedingstoornissen heeft gehad, bv. bloedingen in de maag of het darmkanaal.
- (25)

- wanneer u onlangs een hartaanval heeft gehad of wanneer u een hartaandoening heeft die niet stabiel is.
- wanneer u elektroshocktherapie (26) ondergaat.
- wanneer u een oudere persoon bent, omdat de kans op bijwerkingen dan groter is.
- (27)
- wanneer u ook nog andere medicijnen gebruikt. Zie “Gebruik van andere medicijnen” (28).

Gedachten over zelfmoord en verergering van uw depressie (29)
Raadpleeg uw arts of ga onmiddellijk naar het ziekenhuis wanneer u gedachten heeft over zelfmoord of zelfbeschadiging (30).

Wanneer u depressief bent is het mogelijk dat u gedachten heeft over zelfbeschadiging of zelfmoord. Deze gedachten kunnen versterkt worden wanneer u net begonnen bent met het innemen van antidepressiva. Deze medicijnen hebben namelijk tijd nodig om te gaan werken, gewoonlijk ongeveer twee weken maar soms langer (31). Er bestaat een grotere kans op dergelijke gedachten:

- wanneer u onlangs gedachten heeft gehad over zelfbeschadiging of zelfmoord.
- wanneer u een jongvolwassene bent. Voor volwassenen jonger dan 25 jaar met psychiatrische aandoeningen die een antidepressivum gebruiken, bestaat er een vergroot risico op zelfmoordgedrag. Klinische onderzoeken hebben dit uitgewezen (32).

(33) **Het zou kunnen helpen om familie of een goede vriend over uw depressie te vertellen** en deze bijsluiter te laten lezen. U zou kunnen vragen of ze kunnen aangeven wanneer ze denken dat uw depressie verergert. Ook zouden ze kunnen aangeven wanneer ze bezorgd zijn over veranderingen in uw gedrag (34).

Rusteloosheid/niet stil kunnen zitten of staan
Neem zo snel mogelijk contact op met uw arts (35) wanneer u vermoedt dat u de volgende symptomen heeft: rusteloosheid, behoefte aan veel bewegen en niet stil kunt zitten of staan. De grootste kans hierop is in de eerste weken van de behandeling met Sertraline (36).

Serotoninesyndroom (37)

Neem contact op met uw arts wanneer u de volgende symptomen heeft: hoge koorts, spierkrampen, verwardheid en angst. Dit zouden tekenen kunnen zijn van een aandoening die bekend staat als ‘serotoninesyndroom’. Hierop bestaat een grotere kans wanneer u tevens andere serotonine heropname remmers (SSRI’s) of MAO-remmers (bij depressie en ziekte van Parkinson) inneemt. Ook is deze kans groter wanneer u de afgelopen twee weken MAO-remmers heeft ingenomen (zie (38) “Gebruik van andere medicijnen”) (39). De behandeling met Sertraline dient mogelijk gestaakt te worden.

(40)

Gebruik bij kinderen en adolescenten jonger dan 18 jaar

In de regel dient Sertraline niet gebruikt te worden voor kinderen en adolescenten jonger dan 18 jaar. Volgens klinisch onderzoek hebben patiënten jonger dan 18 jaar die behandeld worden met Sertraline een groter risico op bepaalde bijwerkingen. Deze bijwerkingen betreffen zelfmoordpogingen, zelfmoordgedachten en vijandigheid (voornamelijk agressie, opstandig gedrag en woede) (41) (42). Ook ontbreekt er informatie over de langetermijneffecten van Sertraline op de groei, rijping en cognitieve en gedragsontwikkeling van deze leeftijdsgroep (43). Het is echter mogelijk dat uw arts Sertraline voorschrijft aan patiënten jonger dan 18 jaar wanneer dit in hun belang is. Raadpleeg uw arts wanneer u dit wilt bespreken. Raadpleeg uw arts ook wanneer bovengenoemde bijwerkingen zich ontwikkelen of verergeren (44).

Gebruik van Sertraline in combinatie met andere medicijnen

Een aantal (45) medicijnen kunnen Sertraline beïnvloeden of worden beïnvloed door Sertraline (46). Uw arts moet u mogelijk zorgvuldiger controleren en de dosis van onderstaande (47) medicijnen naar gelang aanpassen (48):

- MAO-remmers, bv. moclobemide (49) (bij depressie) en selegiline (50) (bij ziekte van Parkinson). Zie sectie “Gebruik Sertraline niet” (51);
- serotonergische medicijnen (52) zoals tryptofaan (bij slapeloosheid) (53), fenfluramine (een eetlustremmer), dextromethorfan (bij hoest), pethidine en tramadol (bij hevige pijn) (54);
- lithium (bij psychische aandoeningen);

- sumatriptan (55) en andere triptanen (bij migraine);
- fenytoïne (56) (bij epilepsie);
- diazepam (bij angst en onrust (agitatie)) (57);
- pimozide (bij psychoses);
- insuline en/of tabletten, bv. tolbutamide (58) (bij diabetes) (59). Sertraline kan invloed hebben op uw bloedsuikerspiegel die door middel van insuline en/of tabletten wordt gereguleerd (60);
- cimetidine (61) (bij maagzweren en spijsverteringsmoeilijkheden);
- diuretische medicijnen (bij hoge bloeddruk) (62);
- fenazon (63) (bij pijn);
- medicijnen voor onregelmatig hartritme bv. propafenon en flecainide (64) (65);
- kruidengeneesmiddelen (bij depressie) die sint-janskruid bevatten (*Hypericum perforatum*) (66) (67).

De volgende medicijnen verhogen het risico op bloedingen:
- bloedverdunnende medicijnen (anticoagulantia) (68), bv. warfarin (69);
- pijnstillende medicijnen van het type NSAID (niet-steroïde anti-inflammatoire preparaten) (70) bv. aspririne en ibuprofen (71);
- fenothiazines bv. perfenazine en thioridazine (72) en andere medicijnen voor psychoses;
- tricyclische antidepressiva (bij depressie) bv. clomipramine en imipramine (73).

Informeer uw arts of apotheker wanneer u andere geneesmiddelen gebruikt of kort geleden heeft gebruikt. Dit geldt ook voor geneesmiddelen die u zonder recept kunt verkrijgen. (74).

Gebruik van Sertraline in combinatie met voedsel en drank
Drink geen alcohol wanneer u wordt behandeld met Sertraline (75).

Zwangerschap (76)
Vraag uw arts of apotheker om advies voordat u een geneesmiddel inneemt (77).

Gebruik Sertraline niet wanneer u zwanger bent of zwanger wilt worden, tenzij uw arts dit geneesmiddel heeft voorgeschreven. Er zijn geen gegevens bekend over het effect van Sertraline op het ongeboren kind. (78).

Raadpleeg zo snel mogelijk uw arts of verloskundige wanneer uw baby één van de volgende symptomen heeft: slaap- en voedingsmoeilijkheden, opgewondenheid en onrust (agitatie) (79). Deze ontwenningsverschijnselen zijn gemeld bij pasgeboren baby's wanneer zwangere vrouwen aan het eind van de zwangerschap Sertraline hadden ingenomen (80).

Borstvoeding
Vraag uw arts of apotheker om advies voordat u een geneesmiddel inneemt (81).

Gebruik Sertraline niet wanneer u borstvoeding geeft, tenzij uw arts dit geneesmiddel heeft voorgeschreven. Sertraline komt in kleine hoeveelheden in de moedermelk terecht en kan mogelijk invloed hebben op zuigelingen die borstvoeding krijgen (82).

Rijvaardigheid en het gebruik van machines
Bestuur geen voertuigen en bedien geen machines wanneer u last heeft van slaperigheid, duizeligheid, wazig zicht of flauwvallen. Wees voorzichtig, totdat u weet hoe u op de behandeling met Sertraline reageert (83).

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3. Hoe wordt Sertraline ingenomen?

Volg altijd het voorschrift van uw arts op. De dosis kan voor iedere patiënt verschillen (84).

Dosering (85)
Volwassenen: De gebruikelijke dosering is 50 mg, eenmaal daags ingenomen als één 50 mg tablet of een halve 100 mg tablet. Afhankelijk van uw reactie kan de dosering in stappen van 50 mg worden verhoogd (86) tot maximaal 200 mg (vier 50 mg tabletten of twee 100 mg tabletten) (87). Tussen iedere verhoging met 50 mg dient ten minste één week te zitten (88).

Ouderen: Gelijk aan volwassenen, maar de dosering dient zo laag mogelijk te zijn.

Kinderen en adolescenten: In de regel dient Sertraline niet voor kinderen en adolescenten jonger dan 18 jaar te worden gebruikt. Zie sectie 2 "Gebruik bij kinderen en adolescenten jonger dan 18 jaar" (89).

Nierfunctiestoornissen: Gelijk aan volwassenen.

Leverfunctiestoornissen: De dosering dient te worden aangepast. Mogelijk moet de dosering worden verlaagd of de periode tussen doseringen worden verhoogd. Volg de instructies van uw arts (90).

Wijze van innemen

Neem de tabletten eenmaal daags in, 's ochtends of 's avonds. U kunt de tabletten met of zonder voedsel innemen en met een glas water (91).

Behandelingsduur

Uw behandeling met Sertraline dient voort te duren totdat u minstens 6 maanden geen symptomen van depressie meer heeft gehad. De symptomen kunnen echter binnen 7 dagen verbeteren en het maximale effect wordt doorgaans na 2-4 weken bereikt (92).

Wat u moet doen wanneer u te veel van Sertraline heeft ingenomen

Raadpleeg uw arts, EHBO of apotheek wanneer u meer Sertraline heeft ingenomen dan in deze bijsluiter staat vermeld. Doe dit ook wanneer u meer Sertraline heeft ingenomen dan uw arts heeft voorgeschreven (93).

Symptomen van overdosis zijn slaperigheid, misselijkheid, braken, snelle polsslag, trillen, onrust, duizeligheid en diepe bewusteloosheid.

Wat u moet doen wanneer u bent vergeten Sertraline in te nemen

Wanneer u bent vergeten Sertraline in te nemen, dient u gewoon door te gaan met uw gebruikelijke dosering. Neem nooit een dubbele dosis van Sertraline om zo de vergeten dosis in te halen (94).

Effecten die u kunt verwachten wanneer de behandeling met Sertraline wordt gestopt (95)

Stop alleen met de behandeling met Sertraline wanneer uw arts dit aangeeft. Gewoonlijk adviseert uw arts de dosering geleidelijk te verlagen gedurende een periode van ten minste één tot twee weken. Stop **niet** ineens met het innemen van tabletten want dan bestaat er een kans op ontwenningsverschijnselen.

De meestvoorkomende effecten zijn: duizeligheid, prikkelend/tintelend gevoel in de huid, slaapstoornissen (waaronder slapeloosheid en heftige dromen), rusteloosheid en angst, misselijkheid, braken, trillen en hoofdpijn (96). De kans op deze effecten (97) is groter wanneer u Sertraline gedurende lange tijd of in hoge doseringen heeft gebruikt. Ook is deze kans groter wanneer de dosering te snel is afgebouwd (98).

Over het algemeen zijn deze symptomen licht tot matig van aard en verdwijnen binnen twee weken. Bij sommige patiënten kunnen ze echter hevig zijn en/of langere tijd aanhouden (2-3 maanden of langer).

(99)

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4. Mogelijke bijwerkingen (100)

Zoals alle geneesmiddelen kan Sertraline bijwerkingen veroorzaken (101). Neem onmiddellijk contact op met uw arts of de EHBO wanneer één van de volgende ernstige bijwerkingen optreden:

Ernstige bijwerkingen
Zelden: >1/10.000-<1/1000 (102)

Bloed- en lymfestelselaandoeningen (103)

- abnormale bloedingen of bloeden gedurende lange tijd.

Zenuwstelselaandoeningen

- rusteloosheid, verwardheid, zweten, diarree, koorts, hoge bloeddruk, snelle hartslag, stijve spieren (symptomen van serotoninesyndroom);
- persoonlijkheidsveranderingen, mogelijk in combinatie met het zien of horen van dingen die niet echt zijn (hallucinaties) (104);
- coma;
- epileptische aanvallen.

Maag-darmstelselaandoeningen

- ontsteking van de alvleesklier die hevige pijn in de onderbuik en rug veroorzaakt (pancreatitis))105).

Lever- en galaandoeningen

- leverontsteking (hepatitis), gele verkleuring van de huid of ogen (geelzucht), leverfalen (106).

Huid- en onderhuidaandoeningen

- zwelling van het gezicht of de keel (Quincke-oedeem) (107);
- ernstige overgevoeligheidsreactie met (hoge) koorts, rode vlekken op de huid, gewrichtspijnen en/of oogontsteking (Stevens-Johnson syndroom) (108);
- ernstige, plotselinge (overgevoeligheids)reactie gepaard gaande met koorts en blaren op de huid/vervelling van de huid (toxisch epidermale necrolyse) (109).

Algemene aandoeningen

- ernstige allergische reactie die ademhalingsproblemen of duizeligheid veroorzaakt (anaphylaxis);
- allergische reactie zoals huiduitslag, jeuk of kortademigheid (110).

Overige bijwerkingen (111)

Zeer vaak	>1/10
Vaak	>1/100-<1/10
Soms	>1/1000-<1/100
Zelden	>1/10.000-<1/1000

Bloed- en lymfestelselaandoeningen

- huiduitslag door puntvormige bloedingen in de huid (purpura) (soms) (112).

Afwijkingen in de hormoonhuishouding (113)

- groeien van borsten bij mannen (gynecomastie) (zelden);

- abnormaal hoog prolactinegehalte in het bloed wat onregelmatige menstruatie en melkproductie uit de borsten kan veroorzaken (hyperprolactinemie) (zelden);
- melkvloed uit de tepels (galactorroe) (zelden);
- te traag werkende schildklier wat moeheid of gewichtstoename kan veroorzaken (hypothyreöidie) (zelden).

Voedings- en stofwisselingsstoornissen

- laag natriumgehalte in het bloed wat moeheid, verwardheid, spierkrampen, epileptische aanvallen en coma kan veroorzaken (hyponatriëmie). Dit komt vooral voor bij oudere patiënten en patiënten die plaspillen (diuretica) en andere medicijnen gebruiken (zelden).

Psychische stoornissen

- slapeloosheid (zeer vaak);
- slaperigheid (zeer vaak);
- verminderde eetlust (zeer vaak);
- gapen (vaak);
- rusteloosheid (vaak);
- angst (vaak);
- periodes van overdreven opgewektheid gepaard gaande met het hebben van veel energie (manie) (soms) (114);
- depressie verergert (soms);
- zien of horen van dingen die niet echt zijn (hallucinaties) (soms);
- verminderd seksueel verlangen (zelden);
- nachtmerries (zelden);
- agressie (zelden).

Zenuwstelselaandoeningen

- trillen (zeer vaak);
- duizeligheid (zeer vaak);
- droge mond (zeer vaak);
- hoofdpijn (vaak);
- bewegingsstoornissen zoals tandenknarsen en ongebruikelijke en onbeheersbare problemen met lopen (vaak);

- tintelen of gevoelloosheid in de handen of voeten (vaak);
- verhoogde transpiratie (vaak);
- migraine (soms);
- rusteloosheid/niet stil kunnen zitten of staan (hyperkinesie) (zie sectie 2 “Wees extra voorzichtig met Sertraline”) (zelden);
- onwillekeurige spiersamentrekkingen (zelden).

Oogaandoeningen
- verminderd gezichtsvermogen (vaak)
- verwijdde pupillen (soms)

Evenwichtsorgaan- en ooraandoeningen
- oorsuizen (zelden)

Hartaandoeningen
- pijn in de borstkas (vaak)
- hartkloppingen (vaak)
- hoge bloeddruk (soms)
- flauwvallen (soms)
- versnelde hartslag (soms)

Bloedvataandoeningen
- zwelling van de enkels, voeten, vingers of rond de ogen (oedeem) (soms)

Ademhalingsstelsel- en borstkasaandoeningen
- moeilijkheden met de ademhaling (soms)

Maag-darmstelselaandoeningen
- misselijkheid (zeer vaak)
- diarree/dunne ontlasting (zeer vaak)
- pijn in de maag/onderbuik (vaak)
- verstopping (vaak)
- overgeven (vaak)

- grotere eetlust (soms)

Huid- en onderhuidaandoeningen

- uitslag (vaak)
- jeuk (soms)
- haaruitval (soms)
- schilferen van de huid (soms)
- overgevoeligheid voor zonlicht (zelden) (115)
- jeukende uitslag (zelden)

Skeletspierstelsel- en bindweefselaandoeningen

- gewrichtspijn (soms)

Nier- en urinewegaandoeningen

- niet kunnen ophouden van urine (urine-incontinentie) (soms) (116);
- moeilijkheden met plassen (urineretentie) (zelden) (117).

Voortplantingsstelsel- en borstaandoeningen

- impotentie of problemen met de zaadlozing (zeer vaak)
- onregelmatige menstruatie (vaak)
- permanente erectie (zelden)

Algemene aandoeningen

- zich zwak voelen (vaak)
- vermoeidheid (vaak)
- opvliegers (vaak)
- afname van lichaamsgewicht (vaak)
- koorts (soms)
- zich niet lekker voelen (soms)
- toename van lichaamsgewicht (soms)

Raadpleeg uw arts of ga onmiddellijk naar het ziekenhuis wanneer u gedachten heeft over zelfmoord of zelfbeschadiging. Deze gedachten kunnen zich tijdens of vlak na het stoppen van de behandeling met Sertraline voordoen (118).

(119)

Raadpleeg uw arts of apotheker in geval er bij u een bijwerking optreedt die niet in deze bijsluiter is vermeld. Doe dit ook wanneer er een bijwerking optreedt die u als ernstig ervaart (120).

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5. Hoe bewaart u Sertraline?

Sertraline buiten bereik en zicht van kinderen houden (121).

Er zijn geen speciale bewaarinstructies (122).

Gebruik Sertraline niet meer na de datum op de verpakking achter “niet te gebruiken na” of “exp” (123).

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6. Algemene informatie (124)

Patiëntenorganisatie voor informatie over depressie:
Stichting Pandora
Helpdesk: 0900-7263672 (€0,10 pm)
Depressielijn: 0900-6120909 (€0,15 pm)
www.stichtingpandora.nl

Vraag uw apotheker op welke manier ongebruikte medicijnen weggeworpen dienen te worden. Werp geen medicijnen weg via de gootsteen of het huisvuil.

Deze bijsluiter is voor het laatst herzien/goedgekeurd in juli 2008 (125) (126).

4.2 Notes

1. In the ST, the name, strength and pharmaceutical form are given at the beginning of the PIL. The model leaflet, however, requires this information to be stated after the PIL's index (and, optionally, also at the beginning).
2. The entire section 'Eight things you need to know about Sertraline' is superfluous and has been omitted from the TT.
3. Entire section according to model leaflet. Last sentence of this section in Sertraline PIL ("If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor of pharmacist.") is not required according to the model leaflet and is therefore omitted from the TT.
4. Sentence rewritten according to instruction-explanation sequence.
5. Entire section according to model leaflet.
6. Section added to index model leaflet since CBG-MEB's "*Bijsluiter van farmaceutische producten"* prescribes this section whereas it is not in the model leaflet.
7. According to the model leaflet, the name, strength and pharmaceutical form should be stated here. Optionally, this information can also be stated at the beginning of the PIL but I have refrained from this. See also note 1.
8. Since the Sertraline PIL includes two pharmaceutical forms (50 mg and 100 mg), I have adapted this required, standard sentence of the model leaflet.
9. Translations derived from SPC Sertraline.
10. Dutch registration holder unkown.
11. According to the model leaflet, information about the manufacturer is not required in Dutch PILs and is therefore omitted from the TT.
12. Although not included in the model leaflet of the Guideline on readability, the CBG-MEB's model leaflet considers it advisable to include the RVG-number.
13. Vertical lines between sections according to regulation CBG-MEB.
14. All headings and subheadings in the TT have been formulated according to the model leaflet.
15. In the ST, this information has been given in section 6 ("Further information"). However, the model leaflet requires this type of information to be stated in section 1. The ST sentence is >20 words and has therefore been reformulated in the TT.

16. This information is not required by the model leaflet, but since it completes the information about the contents of Sertraline, it has been maintained.
17. In the ST, no definition or lay term for "antidepressant" has been given, whereas I think the term should be explained for a lay audience. Therefore, the medical term is preceded by an explanation according to the CBG-MEB's "*Patiëntvriendelijke termen lijst*."
18. Whereas the Guideline on readability prescribes that the medical term should be placed in brackets after the definition or lay term, this does not apply to names of medicines (see also paragraph 3.3 sub question 14).
19. According to the Guideline on readability, no more than five bullet points may be used where they are complex and no more than nine where they are simple. In this list, the bullet points concerning medication have been omitted since they are a repetition of the bullet points under "Taking other medicines". In the last bullet point, I have added a reference to this subsection. After having omitted the bullet points about medication, nine bullet points are left but they are complex. I do not know how to solve this since no more bullet points may be omitted and I cannot combine any bullet points as they are all about different types of diseases/disorders. Moreover, information about stopping treatment cannot be omitted and splitting this subsection into two sections (e.g. "disorders" and "other") is not possible since the Guideline does not allow using more than two levels.
20. I have made "behandeling" more explicit by adding "met Sertraline" because it is not clear which treatment is referred to.
21. According to the Guideline on readability sentences should be active instead of passive. However, the patient is not the agent in this sentence (the doctor is) and therefore it must remain passive.
22. Bullet point about diabetes omitted and transferred to section "Taking other medicines."
23. According to the Guideline on readability, the definition or lay term should come before the medical term in brackets. ST sentence
24. Idem note 21.
25. Bullet point about medicines that cause an increased risk of bleeding omitted and transferred to "Taking other medicines".

26. Translation “electric shock treatment” via http://www.mijnwoordenboek.nl/thema/ME/EN/NL/T/1.html.
27. ST bullet point about medication omitted and transferred to section “Taking other medicines”.
28. This sentence has been added as a reference to the bullet points about medication that have been deleted from this list and have been transferred to “Taking other medicines”.
29. This section should actually be part of the section “Take special care with Sertraline” since the model leaflet prescribes to include special warnings in this section. However, in the TT, the information about suicide is stated in a separate section, probably because the section is too long to incorporate into a bullet point list and contains very important information. I have therefore maintained the complete section.
30. Section rewritten according to instruction-explanation sequence.
31. The ST sentence is >20 words and has therefore been reformulated in the TT.
32. The ST sentence is >20 words and has therefore been reformulated in the TT.
33. This subsection and the next three subsections are not required by the model leaflet. However, they have been adopted from the ST because they contain vital information about Sertraline which is also stated in the SPC.
34. The ST sentence is >20 words and has therefore been reformulated in the TT.
35. Section rewritten according to instruction-explanation sequence.
36. I have made “behandeling” more explicit by adding “met Sertraline” because it is not clear which treatment is referred to.
37. Translation “serotonergic syndrome” via Wikipedia.
38. In English texts, it is more common to use “please”. I have not translated it in the TT.
39. The ST sentence is >20 words and has therefore been reformulated in the TT.
40. According to the model leaflet, the subsection “Withdrawal symptoms when stopping treatment” needs to be placed under section 3. It has therefore been omitted in this section.
41. According to the regulation, the medical term (“hostility”) should be placed in brackets after the definition. In practice however, this does not create a clear sentence since the definition is too long. The sequence of the ST in this respect has therefore been maintained.

42. The ST sentence is >20 words and has therefore been reformulated in the TT.
43. The ST sentence is >20 words and has therefore been reformulated in the TT.
44. The sequence instruction-explanation cannot be achieved in this paragraph because, if doing so, the section will lose its coherence. The sequence of the ST in this respect has therefore been maintained.
45. I have not translated "other" since it is obvious from the section heading that "other" medicines are referred to.
46. I have repeated "Sertraline" in order to improve the sentence's readability.
47. In the ST is stated "Some of these medicines are listed below". However, according to the SPC, this list is complete. I have therefore omitted "some" in the TT.
48. Section rewritten according to instruction-explanation sequence.
49. Translation "moclobemide" via Wikipedia.
50. Translation "selegiline" via Wikipedia.
51. The reference to the subsection "Take special care with Sertraline" has been omitted since the information on medication has been omitted from "Take special care with Sertraline" as it is already stated in this subsection.
52. Translation "serotonergic" via Wikipedia.
53. Earlier in this PIL, tryptophan has been referred to as "for insomnia" and therefore I will maintain this.
54. The reference to the subsection "Take special care with Sertraline" has been omitted since the information on medication has been omitted from it.
55. Translation "sumatriptan" via Wikipedia.
56. Translation "phenytoin" via www.ziekenhuis.nl/medicijngids.
57. Synonym of "agitation" given according to the "*Patiëntvriendelijke termen lijst*".
58. Translation "tolbutamide" via Wikipedia.
59. The model leaflet requires the pharmacotherapeutic group to be noted in brackets after the active substance. In the ST, the pharmacotherapeutic group has been mentioned first ("medicines for diabetes") and I have therefore changed this into mentioning the active substance first ("insuline and/or tablets, e.g. tolbutamide), followed by the pharmacotherapeutic group.
60. As this sentence concerns medication, it has been transferred from "Take special care with Sertraline" to this subsection.
61. Translation "cimetidine" via Wikipedia.

62. This bullet point has not been formulated according to the rule I have stated in note 19 because it cannot be adapted as no active substance is mentioned (all types of diuretic medication is referred to). I have therefore maintained the sentence.
63. Translation “phenazone” via www.ziekenhuis.nl/medicijngids.
64. Translation “propafenone” and “flecainide” via www.ziekenhuis.nl/medicijngids;
65. This bullet point has not been formulated according to the rule I have stated in note 19 because it cannot be adapted as the two active substances mentioned are only a few examples of medicines for irregular heart rhythm.
66. This bullet point has not been formulated according to the rule I have stated in note 19 because it cannot be adapted as this would mean that both “for depression” as well as “Hypericum perforatum” must be placed in brackets after the active substance (St. John’s wort).
67. Again, the Guideline on readability’s rule concerning lists of bullet points has proved to be impossible to comply with in all cases. This list contains 13 bullet points of which none can be combined (the bullet points are not related) or transferred into simple sentences (as this would result into sentences over 20 words).
68. This bullet point has not been formulated according to the rule I have stated in note 19 because it cannot be adapted as the active substance mentioned is only one example of blood-thinning medication. I have added “anticoagulantia” since the medical name must also be stated.
69. Translation “warfarin” via Wikipedia.
70. Translation NSAID via http://www.kennisring.nl/smartsite.dws?id=76225.
71. This bullet point has not been formulated according to the rule I have stated in note 19 because it cannot be adapted as the two active substances mentioned are only a few examples of NSAIDs.
72. Translations “perphenazine” and “thioridazine” via www.ziekenhuis.nl/medicijngids.
73. Translation “clomipramine” and “imipramine” via www.ziekenhuis.nl/medicijngids.
74. I have rewritten this paragraph according to the sequence instruction-explanation. This instruction, however, is unrelated to the long instruction above and I have therefore maintained it on the same place as in the ST. In the ST, this instruction

consists of >20 words and I have therefore translated it according to the example in the model leaflet which consists of two sentences.

75. Conform the Guideline on readability, I have changed this sentence from a passive into an active voice.
76. In the ST, “Pregnancy” and “Breast-feeding” consists of three separate sections. However, according to the model leaflet, “Pregnancy” and “Breast-feeding” should be two separate sections.
77. Required standard sentence according to the model leaflet.
78. Paragraph rewritten according to instruction-explanation sequence.
79. Synonym of “agitation” given according to the “Patient-vriendelijke termenlijst”.
80. Paragraph rewritten according to instruction-explanation sequence.
81. Required standard sentence according to the model leaflet.
82. Required standard sentence according to the model leaflet.
83. Paragraph rewritten according to instruction-explanation sequence.
84. In the ST, this section starts with “Always follow the doctor’s instructions. There are differences in what individuals need.” According to the model leaflet, this is not a required standard sentence. However, I think it is important to include it into the TT so that the patient knows that in the next section (dosage) the doctor is the agent in the sentences that are stated in the passive voice.
85. In the ST, the segmentation of this section is unclear. It seems as if all of the subsections are related to dosage. I have therefore classified “adults”, “elderly”, “children and adolescents”, “impaired kidney function” and “impaired liver function” under the heading “dosage”.
86. This paragraph is stated in the passive voice but it cannot be changed into an active voice since the doctor is the agent and not the patient himself.
87. The sections “50 mg” and “100 mg” have been combined in order to make the section more surveyable and to avoid using another level of heading.
88. From the ST, it is not apparent how big the increases may be. I have looked this up in the SPC and it appeared that the increases should be 50 mg a week. I have therefore adapted these sentences in the TT.
89. The ST contradicts itself here as in section 2 has been stated that Sertraline is sometimes used with children when the doctor has prescribed it. I have therefore adapted the ST sentence and added a reference to section 2.

90. In the ST, the sentence “Follow the doctor’s instructions” is stated right between two instructions that are related to one another. This does not seem logical and I have therefore transferred this sentence to the end of the paragraph.
91. In this paragraph, the patient is the agent. I have therefore transferred the sentences from a passive voice into an active voice.
92. Paragraph rewritten according instruction-explanation sequence.
93. The ST sentence is >20 words and has therefore been reformulated in the TT.
94. Required sentence according to model leaflet.
95. According to the model leaflet, the section on withdrawal effects should be placed here. In the ST, however, there are three sections on withdrawal effects (in section 2, 3 and 4). As I will follow the model leaflet, I have combined the ST information of section 2, 3 and 4 and placed the section on withdrawal effects here.
96. In de TT, this sentence is > 20 words. I have therefore split it.
97. In the TT, the reference “the risk” is used. I think it should be specified which risks are actually meant and I have therefore added “op deze effecten”.
98. In de TT, this sentence is > 20 words long. I have therefore split it.
99. In the ST, this section is concluded with “If you have any further questions on the use of this product, ask your doctor or pharmacist.” According to the model leaflet, this sentence is not required in Dutch PILs and I have therefore omitted it.
100. The model leaflet states “Side effects should be grouped as much as possible, but within the possibilities the IB-part (SPC) offers”. In paragraph 3.3 of this thesis, however, has been laid out that the CBG-MEB requires the side effects to be grouped according to the organ system (SOC). So the model leaflet and the CBG-MEB contradict one another on this issue. I have therefore decided to look at the most recent SPC of Sertraline and to maintain the order in which the side effects are listed. This SPC lists the side effects according to the organ system and I have therefore decided to maintain this order. The SOC-order is more suitable anyway, because, in comparison with the listing according to frequency of side effects, it will result into shorter bullet point lists.
101. Required standard sentence according to model leaflet.
102. Statistical risk information according to guideline CBG-MEB.
103. Designations and order of organ groups according to the SPC of Sertraline.
104. The CBG-MEB prescribes that in case a lay definition has been given, the medical term should be added after the lay term in brackets. This should not be

done in case short definitions have been given. In the TT, I have applied this rule which means that in some cases the medical term of a lay definition has been added in brackets. I have retrieved these medical terms from the SPC of the Sertraline PIL.

105. According to the regulation of the CBG-MEB, the medical term has been added to the lay definition.

106. According to "*Bijsluiter van farmaceutische producten*", related side effects can be covered by a single term. However, in this category of side effects (serious), it is important to mention the symptoms of the disease and I have therefore not covered the liver diseases by one term. Definition of diseases according to "*Patientvriendelijke termen lijst*".

107. In the ST, the medical term of all serious side effects where symptoms are related to a specific disease or disorder have been given, except for these symptoms. According to the SPC, swelling of the face or throat are symptoms of Quicnke's syndrome. I have therefore added this medical term after the definition (the symptoms).

108. In the ST, Stevens-Johnson syndrome and toxic epidermal necrolysis have been combined under one bullet point as they both are a type of skin disease. In the TT, however, I have split them into two bullet points because they are classified under skin disorders. Moreover, the definition of both diseases has become more extended because I have used the "*Patientvriendelijke termen lijst*" and it is therefore more surveyable to split them into two separate bullet points.

109. Definition of disease according to "*Patiëntvriendelijke termen lijst*".

110. In the ST, two types of allergic reactions are stated under one bullet point. In the TT, however, I have split them into two bullet points because they are already classified under skin disorders.

111. Frequency ("*zeer vaak*", etc) and patient numbers of other side effects stated at the beginning of the section, according to "*Bijsluiter van farmaceutische producten*" p.12.

112. As the side effects are in the first place listed according to the SOC and not according to their frequency, the frequency must be added after the side effect in decreasing frequency. Within each frequency group, the side effects should be listed according to decreasing severity ("*Bijsluiter van farmaceutische producten*" p.12).

113. The designations of the organ systems have been taken from the SPC, except "*endocriene aandoeningen*". This term is likely to be unknown to a lay audience and I have therefore used "*afwijkingen in de hormoonhuishouding*".

114. The symptoms of this side effect refer, according to the MHRA's "Glossary of medical lay terms" to mania. In the TT, I have defined mania according to the "*Patiëntvriendelijke termen lijst*" and I have added the medical term.

115. According to the SPC, "abnormal reaction of the skin to sunlight" refers to "photosensitivity". I have used the lay definition of the "*Patiëntvriendelijke termen lijst*" to translate this side effect.

116. According to the SPC, "leaking or passing urine when you do not mean to" refers to "urine incontinence". I have used the lay definition of the "*Patiëntvriendelijke termen lijst*" to translate this side effect.

117. According to the SPC, "water retention" refers to "urine retention". I have used the lay definition of the "*Patiëntvriendelijke termen lijst*" to translate this side effect.

118. The CBG-MEB requires information on side effects concerning suicidal tendencies to be included in the "Possible side effects" section and to indicate its frequency. In the Sertraline PIL this information has been stated as a separate paragraph after the lists of side effects and no information about frequency has been given. The SPC does not give any additional information about the frequency in which suicidal tendencies occur (it only gives information on when it is most likely to appear and this has already been stated in the TT in section 2) and I have therefore maintained the paragraph of the ST without adding information on frequency. However, I have split the paragraph into two sentences because the ST sentence is > 20 words. Furthermore, I have changed the paragraph into the required instruction-explanation sequence.

119. ST section on withdrawal effects omitted in TT because model leaflet requires this type of information to be placed in section 3.

120. Required, standard sentence according to model leaflet. This standard sentence, however, does not comply with the rule of <20 words per sentence and the instruction-explanation sequence and I have therefore adapted it.

121. Required standard sentence according to model leaflet.

122. The Sertraline PIL does not give any information on storing and the SPC states that there are no special instructions for storage. I think it is important to make

explicit that there are no special instructions for storage and I have therefore stated this in the TT.

123. Required standard sentence according to model leaflet.

124. The model leaflet does not prescribe it, but the CBG-MEB requires a “General information” section. I have therefore included such a section in the TT with information on an independent patient organisation and on the disposal of medicines. The CBG-MEB also allows a description of the disease or condition in this section, but this has already been given in section 1. And as the CBG-MEB does not allow any information to be repeated in this section, I have not included a description of depression.

125. Required standard sentence according to model leaflet.

126. The CBG-MEB requires a font size and type of 8 points Didot for PILs. In this thesis, however, I have not adapted the PIL’s font size since MS Word 2003 does not have the Didot font type. Regarding font size, I consider it more convenient in this thesis to maintain the font size of 12 points.

4.3 Conclusion

After having translated the Sertraline PIL, it may be concluded that the model leaflet, in many respects, is an apt frame of reference according to which a PIL can be set up. However, in some respects the model leaflet contradicts the CGB's regulation stated in "*Bijsluiter van farmaceutische producten*" and the Guideline on readability. Two of the most striking examples of these paradoxes concern sentence length and the instruction-explanation sequence. The Guideline on readability demands sentences to be shorter than 20 words and instructions to go before their explanations. It appeared that in the model leaflet, there are instances of standard sentences exceeding the maximum length and instructions not preceding their explanation. So obviously, the model leaflet has not been completely geared to the Guideline on readability.

I also noticed that some of the regulation cannot be complied with properly. An instance hereof is the Guideline on readability's regulation about bullet point lists. In some cases, I have managed to reduce the lists conform the required length, but in other cases doing so would result into incomplete information or the violation of other regulation. In the latter cases the regulation about bullet points has not been complied with as I did not find any acceptable solution to this problem.

Another interesting aspect of the translation process was that I have adopted sections or phrases of the ST – which were not required by the model leaflet – into the TT. An instance hereof is information about using Sertraline for children and adolescents. This type of information is not required by the model leaflet but cannot be omitted from the TT as it is vital information for patients.

As a last comment regarding the translation process, I would like to state that I have not made use of any Dutch translations of the Sertaline PIL (I had not intended to make use of them anyway, however, I did glance at them and found out that most Dutch Sertraline PILs do not sufficiently comply with the CBG's regulation and, in most cases, are too literally translated…). On the other hand, I did consider it necessary to use the Dutch SPC because I needed to verify ambiguous information of the ST (see note 47 for an example of this). And also, since the CBG-MEB demands inclusion of medical terms, I needed to check which disease/disorder was referred to by certain symptoms listed in the ST (see note 107 for an example of this).

CONCLUSION

All four chapters of this translation project have contributed to answering the thesis question (or actually: questions): What has been written about patient information leaflets regarding their text type, functions, structure, language and national and international legislation? Which translation problems arise from the differences in legislation and the source and target text profiles and how can the answers to these questions be applied to the translation process of the Sertraline patient information leaflet?

Chapter 1 laid the groundwork for the rest of the translation project by describing what has been written about PILs. After completing this chapter I had a thorough grasp of the different functions, the language and structure of PILs and the communicative situation in which they function. The second chapter went into the legislation of the European Commission, the United Kingdom and the Netherlands. I found a plethora of information on the legislation of PILs and found many differences between the regulation of the British authority MHRA and the Dutch authority CBG-MEB. From this, I deduced translation problems and solutions which would have to be taken into account while translating the Sertraline PIL. In chapter 3, more translation problems were detected (and solutions were proposed) by comparing the source text profile of the Sertraline PIL with the target text profile. The translation problems deduced in chapter 2 and 3 were taken into account while translating the Sertraline PIL from English into Dutch. The translation process itself went quite smoothly as I could anticipate on translation problems, and solutions to them had already been suggested in the previous chapters. However, when being put into practice, the regulation of the different authorities appeared to contradict one another at some points and some of the rules of the CBG-MEB or the European Commission's Guideline on readability proved to be impossible to obey.

As a final conclusion, I would like to comment that translating a PIL properly requires thorough research and is a very time-consuming activity because the regulation on PILs is overwhelming, sometimes inconsistent and subject to constant revision. Writing this translation project has provided me with a profound knowledge of PILs and their translation process and this knowledge could be of great assistance in my future work as a translator.

ANNEX 1

Procedural information (part of instruction):

- Imperative (43) “please” (normal font) (9) positive (italic) (30), negative (underlined) (6)
- Conditional clause (38)
- Procedural sentence positive (italic) (34), negative (underlined) (6), modals (red font, boxed) (32), other verbs (purple font) (4)
- Passive sentences (orange font colour)

Declarative information (supports instruction):

- Declarative sentence various verb forms

Declarative information (**no** part of instruction):

- Declarative sentence informative fragments and sentences

PATIENT INFORMATION LEAFLET

Sertraline 50 mg film-coated tablet
Sertraline 100 mg film-coated tablet
(Sertraline hydrochloride)

Eight important things you need to know about Sertraline

Sertraline treats depression. Like all medicines it can have unwanted effects. *It is therefore important that you and your doctor weigh up the benefits of treatment against the possible unwanted effects, before starting treatment.*

Sertraline should not be used to treat depression in children and adolescents under 18. *See section 2, Use in children and adolescents.*

Sertraline won’t work straight away. Some people taking antidepressants feel worse before feeling better. *Your doctor should see you regularly during your course of treatment. Tell your doctor if you haven’t started feeling better.*

Some people who are depressed or anxious think of harming of killing themselves. If you start to feel worse, or think of harming or killing yourself, ***see your doctor or go to a hospital straight away.***

Don’t stop taking Sertraline without talking to your doctor. If you stop taking Sertraline suddenly or miss a dose, you may get withdrawal effects. *See section 3, How to take Sertraline.*

If you feel restless and feel like you can’t sit still, *tell your doctor*. *Increasing the dose of Sertraline may make these feelings worse.*

Taking some other medicines with Sertraline can cause problems. *You may need to talk to your doctor. See section 2, Using other medicines.*

If you are pregnant or planning to get pregnant, *talk to your doctor.* *See section 2, Pregnancy and breastfeeding.*

Please read this entire leaflet carefully before you start taking this medicine.

- *Keep this leaflet. You may need to read it again.*
- If you have further questions, please ask your doctor or your pharmacist.
- This medicine has been prescribed for you personally and you should not pass it to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. **What Sertraline is and what it is used for?**
2. **Before you take Sertraline**
3. **How to take Sertraline**
4. **Possible side effects**
5. **How to store Sertraline**
6. **Further information**

1. What Sertraline is and what it is used for

Sertraline belongs to a group of medicines called selective serotonin re-uptake inhibitors (SSRIs).

Sertaline is an antidepressant medicine that acts on the nervous system. It is used for treatment of:

- Depression (Major depressive episodes)

2. Before you take Sertraline

Do not take Sertraline

- if you are hypersensitive to sertraline or any of the other ingredients of Sertraline
- if you are taking an MAO inhibitor (for depression or Parkinson's disease) or have taken them at any time within the last 14 days
- if you are taking pimozide (for psychiatric disorders)

Take special care with Sertraline

- if you have epilepsy. In the event of seizures the treatment should be stopped. *Contact your doctor*
- if you have diabetes, as Sertraline can effect the control of your blood sugar levels with insulin and/or tablets. *The dose of these medications may have to be adjusted.*
- if you have schizophrenia
- if you have severely impaired liver or kidney function

- if you have a history of mania (feeling elated or over-excited, which causes unusual behaviour). If you feel you are developing the symptoms of mania, treatment should be stopped. *Contact your doctor*
- if you have a history of bleeding disturbances, e.g. bleeding in the stomach or intestine
- if you are taking medicines that cause an increased risk of bleeding, e.g. medicines to thin the blood (anticolagulants), some medicines used to treat mental disorders (atypical antipsychotics and phenothiazines, most tricyclic antidepressants), medicines for pain and inflammation (NSAIDs) or aspirin
- if you have recently had a heart attack or have an unstable heart disorder
- if you are having electric shock treatment
- if you are elderly, as you may be more likely to have side effects
- if you are taking other medicines for depression, tryptophan (for insomnia), fenfluramine (an appetite suppressant), dextromethorphan (for cough), pethidine or tramadol (for severe pain)

Thoughts of suicide and worsening of your depression

If you are depressed you can sometimes have thoughts of harming or killing yourself. *These may be increased when first taking antidepressants,* since these medicines all take time to work, usually about two weeks but sometimes longer. **You** may be more likely to think like this:

If you have previously had thoughts about harming or killing yourself

If you are a **young adult**. Information from clinical trials has shown an increased risk of suicidal behaviour in adults aged less than 25 years with psychiatric conditions who were treated with an antidepressant.

If you have thoughts of harming or killing yourself at any time, ***contact your doctor or go to a hospital straight away.***

You may find it helpful to tell a relative or close friend *that you are depressed, and ask them to read this leaflet. You might ask them to tell you if they think your depression is getting worse, or if they are worried about changes in your behaviour.*

Restlessness/inability to sit or stand still

Sertraline can cause restlessness, the need to move often and the inability to sit or stand still. This is most likely to occur in the first few weeks of treatment. If you think you have these symptoms, *you should talk to your doctor as soon as possible.*

Serotonergic syndrome

Contact your doctor if you develop symptoms such as high fever, muscle twitching, confusion and anxiety. These may be signs of a condition known as 'serotonergic syndrome'. This is more likely to occur if you are also taking other serotonin re-uptake inhibitors (SSRIs), an MAO inhibitor (for depression or Parkinson's disease) or have been treated with an MAO inhibitor in the last 14 days (please see section "Taking other medicines"). *Treatment with Sertraline might need to be stopped.*

Withdrawal symptoms when stopping treatment with Sertraline

When you stop taking Sertraline, it is common to experience withdrawal symptoms, especially if treatment is stopped suddenly. *When stopping treatment, the dose should be reduced gradually (see section 3 'If you stop taking Sertraline' and section 4 'Possible withdrawal effects when stopping with Sertraline').*

Use in children and adolescents under 18 years of age

Sertraline should not normally be used for children and adolescents under 18 years. Clinical trials have shown that patients under 18, treated with Sertraline, have an increased risk of side effects such as suicide attempts, suicidal thoughts and hostility (predominantly aggression, oppositional behaviour and anger). Also, the long-term safety effects concerning growth, maturation and cognitive and behavioural development of Sertraline in this age group are not yet known. However, your doctor may prescribe Sertraline for patients under 18 if it is thought to be in their best interests. If you want to discuss this, please go back to your doctor. *You should also inform your doctor if any of the side effects listed above develop or become worse.*

Taking other medicines

Some other medicines can affect or be affected by Sertraline.
Some of these medicines are listed below:

- MAO inhibitors, e.g. moclobemide (for depression) and selegiline (for Parkinson's disease). Please see sections "Do not take Sertraline" and "Take special care with Sertraline"
- Serotonergic medicines such as tryptophan (to aid sleep), fenfluramin (an appetite suppressant), dextromethorphan (for cough), pethidine and tramadol (for severe pain). Please see section "Take special care with Sertraline"
- Litium (for mental disorders)
- Sumatriptan and other triptans (for migraine)
- Phenytoin (for epilepsy)
- Diazepam (for anxiety and agitation)
- Pimozide (for psychoses)
- Medicines for diabetes (insulin and/or tablets, e.g. tolbutamide)
- Cimetidine (for stomach ulcers and indigestion)
- Diutetic medicines (for high blood pressure)
- Phenazone (for pain)
- Medicines for irregular heart rhythm e.g. propafenone and flecainide
- Herbal medicines (for depression) containing St. John's wort (*Hypericum perforatum*)

The following medicines increase the risk of haemorrhages:

- Blood-thinning medicines e.g. warfarin
- Aspirin and other pain-relieving medicines of the NSAID type (non-steroidal anti-inflammatory drugs) e.g. ibuprofen
- Phenothiazines e.g. perphenazine and thioridazine and other medicines for psychoses
- Tricyclic antidepressants (for depression) e.g. clomipramine and imipramine

Your doctor may need to monitor you more carefully and adjust the dose of the above mentioned medicines as appropriate.
Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Taking Sertraline with food and drink

Drinking alcohol should be avoided if you are being treated with Sertraline.

Pregnancy and breast-feeding
Ask your doctor of pharmacist for advice before taking any medicine.

Pregnancy: It is not known if Sertraline affects the unborn child. Do not take Sertraline if you are pregnant or planning to become pregnant unless your doctor has told you to.

Withdrawal symptoms have been reported in newborn babies when expectant mothers have taken Sertraline at the end of pregnancy.
Symptoms include sleeping and feeding difficulties, excitement and agitation. If your baby has any of the above symptoms *you should contact your doctor or midwife as soon as possible.*

Breast-feeding: Sertraline passes into breast milk in small amounts and may affect breast-feeding infants. Do not take Sertraline with breast-feeding unless your doctor has told you to.

Driving and using machines
In some people Sertaline can cause side effects such as drowziness, dizziness, blurred vision or fainting. If you have these side effects do not drive or use machinery. *You should be careful, until you know how you react to Sertaline treatment.*

Continued…

3. How to take Sertraline

Always follow the doctor's instructions. There are differences in what individuals need.

Dosage

Adults
***(50 mg)**: The usual dose is 50 mg once a day, taken as one 50mg tablet. Depending on response, the dose may be increased gradually to a maximum of 200mg, taken as four 50mg tablets. Increases in the dose should be made at intervals of at least 1 week.*

***(100mg)**: The usual dose is 50 mg once a day, taken as half a 100mg tablet. Depending on response, the dose may be increased gradually to a maximum of 200mg, taken as two 100mg tablets. Increases in the dose should be made at intervals of at least 1 week.*

Elderly
As for adults, but the dose should be as low as possible.

Children and Adolescents
Sertraline should not be used for children and adolescents below18 years of age.

Impaired kidney function
As for adults

Impaired liver function

It is necessary to adjust the dose. Follow the doctor's instructions. The dose may be reduced or the interval between doses increased.

Method of administration

The tablets should be taken once daily, either in the morning or in the evening. The tablets may be taken with or without food and with a glass of water.

Duration of treatment

Although your symptoms of depression may improve within 7 days, the maximum effect is generally reached after 2-4 weeks. *Your treatment with Sertraline should continue until you have been symptom-free for at least 6 months.*

If you take more Sertraline than you should

***Contact the doctor**, accident and emergency department or pharmacy* if you have taken more Sertraline than is stated in this leaflet, or more than the doctor has prescribed.
Symptoms of overdose are drowsiness, nausea, vomiting, rapid pulse, tremor, agitation, dizziness and deep unconsciousness.

If you forget to take Sertraline

If you forget to take Sertraline, *you should simply continue with your usual dose - do not take a double dose.*

If you stop taking Sertaline

You should only stop treatment with Sertraline when your doctor tells you. Your doctor will usually advise you to reduce the dose gradually over a period of at least one to two weeks. Do **not** stop taking tablets suddenly as there is a risk you may have withdrawal effects *(see section 4, 'Possible withdrawal effects when stopping treatment with Sertraline').*

If you have any further questions on the use of this product, *ask your doctor or pharmacist.*

4. Possible side effects

Like all medicines, Sertraline can cause side effects, although not everybody gets them.
Contact the doctor or accident and emergency department immediately if you develop the following serious side effects:

Serious side effects:
Rare: (more than 1 in 10,000 patients, but less than 1 in 1,000 patients)

- Feeling agitated, confused, sweating, diarrhoea, fever, high blood pressure, rapid heart beat, muscle stiffness (symptoms of serotonin syndrome)
- Abnormal bleeding or bleeding for a long time
- Allergic reaction such as skin rash, itching, shortness of breath or serious allergic reaction which causes difficulty in breathing or dizziness (anaphylaxis)
- Personality changes which may include seeing or hearing things that are not real
- Unconsciousness
- Fits
- Inflammation of the pancreas, which causes severe pain in the abdomen and back

- Inflammation of the liver (hepatitis), yellowing of the skin or whites of the eyes (jaundice), liver failure
- Swelling of the face or throat
- Severe skin reaction, e.g. blistering of the skin, mouth, eyes or genitals (Stevens Johnson syndrome) or peeling of the upper layer of skin (toxic epidermal necrolysis).

Other side effects:
Very common (in more than 1 in 10 patients)

- Loss of appetite
- Impotence of problems with ejaculation
- Difficulty in sleeping
- Sleepiness
- Shaking
- Dizziness
- Feeling sick
- Dry mouth
- Diarrhoea/loose bowel movements

Common (more than 1 in 100, but less than 1 in 10 patients)

- Weight loss
- Agitation
- Anxiety
- Movement disorders e.g. grinding of teeth and unusual and uncontrollable problems with walking
- Tingling or numbness in the hands or feet
- Reduced sense of touch
- Headache
- Blurred vision
- Chest pain
- Feeling your heart beat
- Flushing
- Yawning
- Indigestion
- Pain in the stomach/abdomen
- Being sick
- Constipation
- Rash
- Irregular periods
- Increased tendency to sweat
- Feeling of weakness
- Tiredness

Uncommon (more than 1 in 1,000, but less than 1 in 100 patients)

- Increased appetite
- Weight gain
- Feeling elated or over-excited, which causes unusual behaviour

- Depression becomes worse
- Seeing or hearing things that are not real
- Migraine
- Enlarged pupils
- Faster heart beat
- High blood pressure
- Fainting
- Skin rash resulting from bleeding into the skin from small blood vessels
- Hair loss
- Itching
- Blistering of the skin
- Joint pain
- Leaking or passing urine when you do not mean to
- Fever
- Feeling unwell
- Swelling of the ankles, feet, fingers or around the eyes
- Abnormal laboratory test results.

Rare (more than 1 in 10,000, but less than 1 in 1,000 patients)

- Restlessness/inability to sit or stand still *(see section 2 "Take special care")*
- Discharge of milk from the nipples
- Abnormally high level of the hormone prolactin in the blood which can cause irregular periods and production of milk from breasts
- Underactive thyroid gland which can cause tiredness or weight gain
- Water retention and production of highly concentrated urine,
- Low blood vessels of sodium which can cause tiredness and confusion, muscle twitching, fits and coma (mainly occurs in elderly patients and in patients using diuretics (water tablets) and other medicines
- Enlargement of breasts in men
- Aggressiveness
- Confusion
- Reduced sexual desire
- Nightmare
- Involuntary muscle contractions
- Ringing or buzzing in the ears (tinnitus)
- Difficulty breathing
- Itchy rash
- Abnormal reaction of the skin to sunlight
- Muscle cramps
- Difficulty in urinating
- Persistent erection
- Increased cholesterol in the blood

If you have thoughts of harming or killing yourself during Sertraline therapy or soon after stopping therapy ***contact your doctor or go to a hospital straight away***.

Possible withdrawal effects when stopping treatment with Sertraline: Dizziness, prickling or tingling sensation in the skin, sleep disturbances (including not being able to sleep and intense dreams), agitation or anxiety, feeling sick and/or being sick, shaking and headache are the most commonly reported reactions. The risk is higher when Sertraline has been used for a long time, in high doses or when the dose is reduced too quickly.

Generally these symptoms are mild to moderate and stop within two weeks. However, in some patients they may be severe and/or continue for longer (2-3 months or more).
If Sertraline treatment is no longer required, *your doctor will usually advise you to reduce the dose gradually over several weeks (see section 3 "If you stop taking Sertraline").*

If you have side effects that persist and are troublesome, *tell your doctor of pharmacist.* Some side effects may require treatment.

If any of the side effects gets serious, or if you notice any side effects not listed in this leafet, please tell your doctor or pharmacist.

5. How to store Sertraline

Keep out of the reach and sight of children.

Do not use Sertraline after the expiry date which is stated on the pack.

Medicines should not be disposed of via waste water or household waste. *Ask your pharmacist how to dispose of medicines no longer required.* These measures will help to protect the environment.

6. Further information

What Sertraline contains

Sertraline 50 mg
The active substance is 50mg sertraline as sertraline hydrochloride.

Sertraline 100 mg
The active substance is 100mg sertraline as sertraline hydrochloride.

The other ingredients are microcrystalline cellulose, calcium hydrogen phosphate dihydrate, hyprolose, sodium starch glycolate (type A), magnesium stearate, hypromellose, talc, titanium dioxide (E 171).

What Sertraline looks like and contents of the pack
Sertraline 50 mg is a white, capsule shaped, scored film-coated tablet, coded SE/50 on one side.
Sertraline 100 mg is a white, capsule shaped, scored film-coated tablet, coded SE/100 on one side.

Sertraline is available in blister packs containing 10, 14, 15, 20, 28, 30, 50, 50x1, 60, 98 and 100 film-coated tablets or tablet container containing 30, 50, 100, 250, 300 and 500 film-coated tablets.

Not all pack sizes may be marketed.

Marketing Authorisation Holder:
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Manufacturer:
Sandoz llac San. Ve Ticaret A.S.
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Product License Numbers:
Sertraline 50mg tablets: PL 11311/0305
Sertraline 100mg tablets: PL 11311/0306

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ANNEX 2

- Medicine (name of active substance/pharmacotherapeutic group) + disease/condition/symptoms of disease/effects of medicine in brackets (yellow)
- Disease/condition/symptoms of disease/effects of medicine + medicine (name of active substance/pharmacotherapeutic group) in brackets or `e.g.` (red)
- Abbreviations written in full/definition of medicine or condition + abbreviation in brackets (green)
- Definition of disease/condition/symptoms + medical term in brackets (blue)
- Medical term + definition of disease/condition/symptoms in brackets (grey)
- Latinate terms (dark green)
- Medical terms without definition (brown-green)
- Lay terms or definitions without medical term (pink)

PATIENT INFORMATION LEAFLET

Sertraline 50 mg film-coated tablet
Sertraline 100 mg film-coated tablet
(Sertraline hydrochloride)

Eight important things you need to know about Sertraline

- **Sertraline treats depression**. Like all medicines it can have unwanted effects. It is therefore important that you and your doctor weigh up the benefits of treatment against the possible unwanted effects, before starting treatment.
- **Sertraline should not be used to treat depression in children and adolescents under 18**. See section 2, Use in children and adolescents.
- **Sertraline won't work straight away**. Some people taking antidepressants feel worse before feeling better. Your doctor should see you regularly during your course of treatment. Tell your doctor if you haven't started feeling better.
- **Some people who are depressed or anxious think of harming of killing themselves**. If you start to feel worse, or think of harming or killing yourself, **see your doctor or go to a hospital straight away.**
- **Don't stop taking Sertraline without talking to your doctor.** If you stop taking Sertraline suddenly or miss a dose, you may get withdrawal effects. See section 3, How to take Sertraline.
- **If you feel restless and feel like you can't sit still, tell your doctor.** Increasing the dose of Sertraline may make these feelings worse.
- **Taking some other medicines with Sertraline can cause problems.** You may need to talk to your doctor. See section 2, Using other medicines.
- **If you are pregnant or planning to get pregnant, talk to your doctor.** See section 2, Pregnancy and breastfeeding.

Please read this entire leaflet carefully before you start taking this medicine.

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- This medicine has been prescribed for you personally and you should not pass it to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

7. **What Sertraline is and what it is used for?**
8. **Before you take Sertraline**
9. **How to take Sertraline**
10. **Possible side effects**
11. **How to store Sertraline**
12. **Further information**

1. What Sertraline is and what it is used for

Sertraline belongs to a group of medicines called selective serotonin re-uptake inhibitors (SSRIs).

Sertaline is an antidepressant medicine that acts on the nervous system. It is used for treatment of:

- Depression (Major depressive episodes)

2. Before you take Sertraline

Do not take Sertraline

- if you are hypersensitive to sertraline or any of the other ingredients of Sertraline
- if you are taking an MAO inhibitor (for depression or Parkinson's disease) or have taken them at any time within the last 14 days
- if you are taking pimozide (for psychiatric disorders)

Take special care with Sertraline

- if you have epilepsy. In the event of seizures the treatment should be stopped. Contact your doctor
- if you have diabetes, as Sertraline can effect the control of your blood sugar levels with insulin and/or tablets. The dose of these medications may have to be adjusted.
- if you have schizophrenia
- if you have severely impaired liver or kidney function
- if you have a history of mania (feeling elated or over-excited, which causes unusual behaviour). If you feel you are developing the symptoms of mania, treatment should be stopped. Contact your doctor
- if you have a history of bleeding disturbances, e.g. bleeding in the stomach or intestine

- if you are taking medicines that cause an increased risk of bleeding, e.g. medicines to thin the blood (anticolagulants), some medicines used to treat mental disorders (atypical antipsychotics and phenothiazines, most tricyclic antidepressants), medicines for pain and inflammation (NSAIDs) or aspirin
- if you have recently had a heart attack or have an unstable heart disorder
- if you are having electric shock treatment
- if you are elderly, as you may be more likely to have side effects
- if you are taking other medicines for depression, tryptophan (for insomnia), fenfluramine (an appetite suppressant), dextromethorphan (for cough), pethidine or tramadol (for severe pain)

Thoughts of suicide and worsening of your depression
If you are depressed you can sometimes have thoughts of harming or killing yourself. These may be increased when first taking antidepressants, since these medicines all take time to work, usually about two weeks but sometimes longer. **You** may be more likely to think like this:

- If you have previously had thoughts about harming or killing yourself
- If you are a **young adult**. Information from clinical trials has shown an increased risk of suicidal behaviour in adults aged less than 25 years with psychiatric conditions who were treated with an antidepressant.

If you have thoughts of harming or killing yourself at any time, **contact your doctor or go to a hospital straight away.**

You may find it helpful to tell a relative or close friend that you are depressed, and ask them to read this leaflet. You might ask them to tell you if they think your depression is getting worse, or if they are worried about changes in your behaviour.

Restlessness/inability to sit or stand still *(agitation)*
Sertraline can cause restlessness, the need to move often and the inability to sit or stand still. This is most likely to occur in the first few weeks of treatment. If you think you have these symptoms, you should talk to your doctor as soon as possible.

Serotonergic syndrome
Contact your doctor if you develop symptoms such as high fever, muscle twitching, confusion and anxiety. These may be signs of a condition known as ‘serotonergic syndrome’. This is more likely to occur if you are also taking other serotonin re-uptake inhibitors (SSRIs), an MAO inhibitor (for depression or Parkinson’s disease) or have been treated with an MAO inhibitor in the last 14 days (please see section “Taking other medicines”). Treatment with Sertraline might need to be stopped.

Withdrawal symptoms when stopping treatment with Sertraline
When you stop taking Sertraline, it is common to experience withdrawal symptoms, especially if treatment is stopped suddenly. When stopping treatment, the dose should be reduced gradually (see section 3 ‘If you stop taking Sertraline’ and section 4 ‘Possible withdrawal effects when stopping with Sertraline’).

Use in children and adolescents under 18 years of age
Sertraline should not normally be used for children and adolescents under 18 years. Clinical trials have shown that patients under 18, treated with Sertraline, have an increased risk of side

effects such as suicide attempts, suicidal thoughts and hostility (predominantly aggression, oppositional behaviour and anger). Also, the long-term safety effects concerning growth, maturation and cognitive and behavioural development of Sertraline in this age group are not yet known. However, your doctor may prescribe Sertraline for patients under 18 if it is thought to be in their best interests. If you want to discuss this, please go back to your doctor. You should also inform your doctor if any of the side effects listed above develop or become worse.

Taking other medicines
Some other medicines can affect or be affected by Sertraline.
Some of these medicines are listed below:

- MAO inhibitors, e.g. moclobemide (for depression) and selegiline (for Parkinson's disease). Please see sections "Do not take Sertraline" and "Take special care with Sertraline"
- Serotonergic medicines such as tryptophan (to aid sleep), fenfluramin (an appetite suppressant), dextromethorphan (for cough), pethidine and tramadol (for severe pain). Please see section "Take special care with Sertraline"
- Litium (for mental disorders)
- Sumatriptan and other triptans (for migraine)
- Phenytoin (for epilepsy)
- Diazepam (for anxiety and agitation)
- Pimozide (for psychoses)
- Medicines for diabetes (insulin and/or tablets, e.g. tolbutamide)
- Cimetidine (for stomach ulcers and indigestion)
- Diutetic medicines (for high blood pressure)
- Phenazone (for pain)
- Medicines for irregular heart rhythm e.g. propafenone and flecainide
- Herbal medicines (for depression) containing St. John's wort (*Hypericum perforatum*)

The following medicines increase the risk of haemorrhages:

- Blood-thinning medicines e.g. warfarin
- Aspirin and other pain-relieving medicines of the NSAID type (non-steroidal anti-inflammatory drugs) e.g. ibuprofen
- Phenothiazines e.g. perphenazine and thioridazine and other medicines for psychoses
- Tricyclic antidepressants (for depression) e.g. clomipramine and imipramine

You doctor may need to monitor you more carefully and adjust the dose of the above mentioned medicines as appropriate.
Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Taking Sertraline with food and drink
Drinking alcohol should be avoided if you are being treated with Sertraline.

Pregnancy and breast-feeding
Ask your doctor of pharmacist for advice before taking any medicine.

Pregnancy: It is not known if Sertraline affects the unborn child. Do not take Sertraline if you are pregnant or planning to become pregnant unless your doctor has told you to.

Withdrawal symptoms have been reported in newborn babies when expectant mothers have taken Sertraline at the end of pregnancy.
Symptoms include sleeping and feeding difficulties, excitement and agitation. If your baby has any of the above symptoms you should contact your doctor or midwife as soon as possible.

Breast-feeding: Sertraline passes into breast milk in small amounts and may affect breast-feeding infants. Do not take Sertraline with breast-feeding unless your doctor has told you to.

Driving and using machines
In some people Sertaline can cause side effects such as drowsiness, dizziness, blurred vision or fainting. If you have these side effects do not drive or use machinery. You should be careful, until you know how you react to Sertaline treatment.

Continued…

3. How to take Sertraline

Always follow the doctor's instructions. There are differences in what individuals need.

Dosage

Adults
(50 mg): The usual dose if 50 mg once a day, taken as one 50mg tablet. Depending on response, the dose may be increased gradually to a maximum of 200mg, taken as four 50mg tablets. Increases in the dose should be made at intervals of at least 1 week.

(100mg): The usual dose if 50 mg once a day, taken as half a 100mg tablet. Depending on response, the dose may be increased gradually to a maximum of 200mg, taken as two 100mg tablets. Increases in the dose should be made at intervals of at least 1 week.

Elderly
As for adults, but the dose should be as low as possible.

Children and Adolescents
Sertraline should not be used for children and adolescents below18 years of age.

Impaired kidney function
As for adults

Impaired liver function
It is necessary to adjust the dose. Follow the doctor's instructions. The dose may be reduced or the interval between doses increased.

Method of administration
The tablets should be taken once daily, either in the morning or in the evening. The tablets may be taken with or without food and with a glass of water.

Duration of treatment
Although your symptoms of depression may improve within 7 days, the maximum effect is generally reached after 2-4 weeks. Your treatment with Sertraline should continue until you have been symptom-free for at least 6 months.

If you take more Sertraline than you should
Contact the doctor, accident and emergency department or pharmacy if you have taken more Sertraline than is stated in this leaflet, or more than the doctor has prescribed.
Symptoms of overdose are drowsiness, nausea, vomiting, rapid pulse, tremor, agitation, dizziness and deep unconsciousness *(coma).*

If you forget to take Sertraline
If you forget to take Sertraline, you should simply continue with your usual dose - do not take a double dose.

If you stop taking Sertaline
You should only stop treatment with Sertraline when your doctor tells you. Your doctor will usually advise you to reduce the dose gradually over a period of at least one to two weeks. Do **not** stop taking tablets suddenly as there is a risk you may have withdrawal effects (see section 4, 'Possible withdrawal effects when stopping treatment with Sertraline').

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, Sertraline can cause side effects, although not everybody gets them. Contact the doctor or accident and emergency department immediately if you develop the following serious side effects:

Serious side effects:
Rare: (more than 1 in 10,000 patients, but less than 1 in 1,000 patients)

- Feeling agitated, confused, sweating, diarrhoea, fever, high blood pressure, rapid heart beat, muscle stiffness (symptoms of serotonin syndrome)
- Abnormal bleeding or bleeding for a long time
- Allergic reaction such as skin rash, itching, shortness of breath or serious allergic reaction which causes difficulty in breathing or dizziness (anaphylaxis)
- Personality changes which may include seeing or hearing things that are not real
- Unconsciousness
- Fits
- Inflammation of the pancreas, which causes severe pain in the abdomen and back
- Inflammation of the liver (hepatitis), yellowing of the skin or whites of the eyes (jaundice), liver failure
- Swelling of the face or throat
- Severe skin reaction, e.g. blistering of the skin, mouth, eyes or genitals (Stevens Johnson syndrome) or peeling of the upper layer of skin (toxic epidermal necrolysis).

Other side effects:
Very common (in more than 1 in 10 patients)

- Loss of appetite
- Impotence or problems with ejaculation
- Difficulty in sleeping
- Sleepiness
- Shaking
- Dizziness
- Feeling sick *(nausea)*
- Dry mouth
- Diarrhoea/loose bowel movements

Common (more than 1 in 100, but less than 1 in 10 patients)

- Weight loss
- Agitation
- Anxiety
- Movement disorders e.g. grinding of teeth and unusual and uncontrollable problems with walking
- Tingling or numbness in the hands or feet
- Reduced sense of touch
- Headache
- Blurred vision
- Chest pain
- Feeling your heart beat
- Flushing
- Yawning
- Indigestion
- Pain in the stomach/abdomen
- Being sick
- Constipation
- Rash
- Irregular periods
- Increased tendency to sweat
- Feeling of weakness
- Tiredness

Uncommon (more than 1 in 1,000, but less than 1 in 100 patients)

- Increased appetite
- Weight gain
- Feeling elated or over-excited, which causes unusual behaviour *(agitation)*
- Depression becomes worse
- Seeing or hearing things that are not real
- Migraine
- Enlarged pupils
- Faster heart beat
- High blood pressure
- Fainting
- Skin rash resulting from bleeding into the skin from small blood vessels
- Hair loss

- Itching
- Blistering of the skin
- Joint pain
- Leaking or passing urine when you do not mean to
- Fever
- Feeling unwell(*nausea)*
- Swelling of the ankles, feet, fingers or around the eyes
- Abnormal laboratory test results.

Rare (more than 1 in 10,000, but less than 1 in 1,000 patients)

- Restlessness/inability to sit or stand still (see section 2 “Take special care”)
- Discharge of milk from the nipples
- Abnormally high level of the hormone prolactin in the blood which can cause irregular periods and production of milk from breasts
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- Difficult breathing
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- Abnormal reaction of the skin to sunlight
- Muscle cramps
- Difficulty in urinating
- Persistent erection
- Increased cholesterol in the blood

If you have thoughts of harming or killing yourself during Sertraline therapy or soon after stopping therapy **contact your doctor or go to a hospital straight away**.

Possible withdrawal effects when stopping treatment with Sertraline: Dizziness, prickling or tingling sensation in the skin, sleep disturbances (including not being able to sleep and intense dreams), agitation or anxiety, feeling sick and/or being sick, shaking and headache are the most commonly reported reactions. The risk is higher when Sertraline has been used for a long time, in high doses or when the dose is reduced too quickly.

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5. How to store Sertraline

Keep out of the reach and sight of children.

Do not use Sertraline after the expiry date which is stated on the pack.

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6. Further information

What Sertraline contains

Sertraline 50 mg
The active substance is 50mg sertraline as sertraline hydrochloride.

Sertraline 100 mg
The active substance is 100mg sertraline as sertraline hydrochloride.

The other ingredients are microcrystalline cellulose, calcium hydrogen phosphate dihydrate, hyprolose, sodium starch glycolate (type A), magnesium stearate, hypromellose, talc, titanium dioxide (E 171).

What Sertraline looks like and contents of the pack
Sertraline 50 mg is a white, capsule shaped, scored film-coated tablet, coded SE/50 on one side.
Sertraline 100 mg is a white, capsule shaped, scored film-coated tablet, coded SE/100 on one side.

Sertraline is available in blister packs containing 10, 14, 15, 20, 28, 30, 50, 50x1, 60, 98 and 100 film-coated tablets or tablet container containing 30, 50, 100, 250, 300 and 500 film-coated tablets.

Not all pack sizes may be marketed.

Marketing Authorisation Holder:
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Product License Numbers:
Sertraline 50mg tablets: PL 11311/0305
Sertraline 100mg tablets: PL 11311/0306

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