Additional information that the community pharmacists need when assessing antithrombotic prescriptions

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Inhoudsopgave

Samenvatting

Inleiding: antitrombotica zijn bedoeld om het risico op trombose te verminderen, maar verhogen in het algemeen het risico op bloedingen vanwege een verlengde stollingstijd. Apothekers komen vaak verschillende problemen tegen bij het beoordelen van antitrombotica recepten in de openbare apotheek. In dit onderzoek willen we weten welke aanvullende informatie een openbare apotheker in Nederland nodig heeft om antitrombotica recepten te beoordelen, waarom deze informatie wordt opgevraagd en of de aanvullende informatie leidt tot een interventie van de behandeling.
Methode: dit onderzoek is een semi-kwalitatief, observationeel onderzoek die is uitgevoerd in 5 openbare apotheken in Nederland. Antitrombotica voorschriften waarvoor de apotheker bij de uitgifte of controle extra informatie nodig had zijn geïncludeerd in de studie. Apothekers werd gevraagd om op een opgesteld verzamelformulier op te schrijven welke extra informatie nodig was, bij wie deze informatie opgevraagd werd, welke afwegingen de apotheker maakte bij het beoordelen van de recepten en hoe het recept afgehandeld is.
Resultaten: De aanvullende informatie die werd opgevraagd werd als volgt geclassificeerd: nierfunctie, contra-indicatie, indicatie, duur van de behandeling, dosis en anders. Aanvullende informatie over de nierfunctie werd opgevraagd voor de klasse direct orale anticoagulantia (DOAC). Apothekers vroegen aanvullende informatie op over de contra-indicatie ‘verhoogde kans op gastro-intestinale bloeding’ op voor patiënten die voornamelijk salicylaten voorgeschreven kregen. Voor de DOAC's, duale therapie en heparines is aanvullende informatie gevraagd over de indicatie. Voor patiënten die duale therapie kregen voorgeschreven, werd meer informatie gevraagd over de duur van de therapie. Er was meer informatie nodig over een interactie voor de vitamine K antagonist (VKA) acenocoumarol.
Conclusie: Aanvullende informatie over de nierfunctie wordt het meest gevraagd voor DOAC's. De leeftijd van de patiënt en het feit dat de medicatiedosering afhankelijk is van de nierfunctie van de patiënt zijn factoren waarmee apothekers rekening houden. Voor het voorschrijven van acetylsalicylzuur, inclusief carbasalaatcalcium, wordt vaak om informatie gevraagd om te beoordelen of een patiënt een verhoogd risico heeft op het ontwikkelen van een gastro-intestinale bloeding of een contra-indicatie heeft voor de plaatjesaggregatieremmer. Extra informatie over de indicatie van een DOAC werd noodzakelijk geacht in het geval een patiënt geen comedicatie gebruikte, bijvoorbeeld cardiovasculaire medicijnen. Informatie ter beoordeling van de voorgeschreven behandelingsduur werd vooral gevraagd bij het voorschrijven van combinatietherapie. Vaak werd om aanvullende informatie over dosering gevraagd, bij een geneesmiddel waarvan de doseringen per indicatie verschillen en afhankelijk zijn van de nierfunctiecomedicatie gebruikte, bijvoorbeeld cardiovasculaire medicijnen. Informatie ter beoordeling van de voorgeschreven behandelingsduur werd vooral opgevraagd bij het voorschrijven van combinatietherapie.

Introduction

Antithrombotics consist of a wide range of drugs including antiplatelets and anticoagulants and are prescribed for different indications. Antiplatelet agents are mainly used as primary and secondary prevention of (cardio)vascular events. Anticoagulants are prescribed to treat thrombosis or prevent thrombus formation in patients with atrial fibrillation. Antithrombotics are intended to reduce the risk of thrombosis, but they generally increase the risk of haemorrhage. Patients on antithrombotic drugs are at increased risk of bleeding due to a prolonged clotting time [1].
More than 1 million people in the Netherlands use antithrombotic drugs [2]. The chronic nature of the treatment, the number of interactions with other drugs, and the inherent bleeding risk contribute to the complexity of the treatment [3]. For several indications, therapy with a combination of antithrombotic medication is required. Combining multiple antithrombotics is risky from a safety perspective because it increases the risk of bleeding twofold to fourfold compared with monotherapy [1, 4]. Therefore, the balance between the occurrence of a (cardio)vascular event (efficacy) and the development of bleeding (safety) is sometimes fragile in antithrombotic treatment. [5].

Pharmacists frequently encounter a variety of issues when evaluating direct oral anticoagulation (DOAC) prescriptions. It is possible that information for determining the appropriate dosage is unknown in the pharmacy. This could include information on patient's characteristics or the indication. It is also possible that the prescribed dosage is incorrect. DOACs are vulnerable to incorrect dosing because dose adjustments for this class of antithrombotics are necessary depending on the indication and patient characteristics such as renal function, age, and weight [6]. The study of Sugrue *et al* [7], which evaluated the prevalence of incorrect DOAC dosing in patients with atrial fibrillation, found that DOAC dosing did not conform to the recommended dose in 14.8% of patients. A similar finding was made in the study by Zhang *et al.* [8], which was carried out at the St. Antonius Hospital in The Netherlands. This study showed that 17.4% of the patients received an inappropriate DOAC dose. Dosage assessment of DOACs was difficult in 7.4% of the patients due to the lack of adequate documentation of factors such as renal function, indication, and weight [8]. Joosten *et al.* [9] conducted an exploratory study in three pharmacies and a general practitioner practice in the Netherlands to determine if there is enough information readily available for community pharmacists to assess the correctness of DOACs dosage in patients, and whether additional information provided by the general practitioner is required. There was no information on indication or body weight for any of the patients, making it difficult to determine the appropriate DOAC dosage. Additional information from the general practitioner was required for the dosage assessment of 89% of the patients. This study showed that community pharmacists are unable to assess the validity of DOAC doses due to a lack of information on patient parameters [9]. The study of Joosten *et al.* has not been published. In another study by Ishikawa *et al.* [10], which was conducted at the Tohoku University Hospital in Japan, it was found that the indication is often not specified on the prescription of direct oral anticoagulants (DOAC), making it difficult to determine whether the patient was given the correct dose [10]. A cross-sectional investigation in primary care by van den Broek *et al.* [6] found that the community pharmacist may not always have access to the necessary information to do proper dose monitoring. In addition, wrong doses are regularly used because there are indications where the dose changes over time. For example, the dosage of dabigatran in patients with atrial fibrillation is reduced from 150 mg twice daily to 110 mg two times a day in patients 80 years and older [6].

Additionally, pharmacists may encounter difficulties when assessing prescriptions with antithrombotic combination therapy. It can happen that the treatment is not in accordance with the guidelines, or that no proton pump inhibitor is prescribed, despite the patient's increased risk of gastrointestinal bleeding. According to different studies, the guidelines are perceived as complicated, particularly in patients with multiple indications who need a combination of antithrombotic drugs [1,5,11]. In a study conducted by Herwaarden *et al.* [12] in a Dutch community pharmacy, it was discovered that 14 to 23 % of all dual antiplatelet therapies (DAPT) were not prescribed in accordance with the guidelines. The cause of nearly 50% of these therapies was DAPT continuation past the advised treatment period. Besides, patients on dual or triple antiplatelet medication are more likely to experience gastrointestinal bleeding. According to the research of Herwaarden et al [12], 56% of the patients with double or triple antiplatelet therapy who had an increased risk of gastric bleeding did not receive adequate gastric protection putting them at risk for gastrointestinal bleeding [12]. Due to the problems mentioned, the pharmacist may need to intervene in some cases.

The pharmacist assesses prescriptions to ensure that the medications are safe and effective. As a result, an intervention should be carried out if the pharmacist determines that the prescribed medication is unsafe or ineffective. An intervention is defined as a recommendation initiated by a pharmacist in response to a drug-related problem in an individual patient, occurring in any phase of the medication process. These interventions could be related to dosing, duration of therapy, monitoring of side effects, as well as the risk of toxicity [13,14,15]. In a prospective cohort study at a teaching hospital by Zhang *et al.* [16] an antithrombotic stewardship program was implemented to assess combined oral antithrombotic therapy. At least one intervention by the antithrombotic stewardship team was needed for 54.6% of the patients. The most frequent interventions were defining and documenting the duration of treatment for combined antithrombotic therapy (65.5%), discontinuing antithrombotic therapy because the indication was lacking (19.4%), and changing the dosage (8.1%) [16].

Because of different factors the assessment of antithrombotic prescriptions remains difficult. As previously stated, the prescribed dosage is not always correct, and the information required to assess the prescriptions is not always complete. Furthermore, guidelines are not followed when prescribing medication, and there is a lack of gastric protection in patients at high risk of gastric bleeding. In some cases, the pharmacist's intervention is required for the medication to be used safely and effectively. We are interested in the issues that come up when assessing antithrombotic prescriptions in the Dutch community pharmacy.

Aim of the study

In this study we aim to gain knowledge of what additional information a community pharmacist in the Netherlands needs to assess antithrombotic prescription, why the information is being requested, and whether the additional information leads to adjustments in the treatment.

Methods

Study design and setting

This semi-qualitative, observational study was conducted at a purposive sample of 5 community pharmacies in the Netherlands. The following antithrombotic prescriptions were included: salicylates, P2Y12-inhibitors, dipyridamole, DOACs, vitamin K antagonists (VKA), and heparins (table 1 in appendix A). The collecting period varied per pharmacy, and there were no set criteria for it. Antithrombotic prescriptions for multidose drug dispensing, as well as repeat service, were excluded. According to the law, these prescriptions must be reviewed once a year. Pharmacists repeat these prescriptions without conducting an overall assessment unless there is a change to the prescription. Therefore, for these prescriptions, an overall assessment of the prescriptions does not happen every time, which is the reason for exclusion.

This semi-qualitative study was conducted between March 2022 and June 2022. Pharmacists at the pharmacies were asked to collect antithrombotic prescriptions for which additional information was needed for the assessment. More information about how pharmacists collected the prescriptions can be found under the heading 'data collection and dataset.'

Data collection and dataset

Prescriptions for which the pharmacist needed extra information during dispensing or checking were included. This includes prescriptions that have been handled by pharmacy technicians without the involvement of a pharmacist, but for which additional information has been obtained. Additional information is all the information needed to assess the effectiveness and safety of the prescription, meaning any prescription that cannot be assessed without extra intervention. The additional information (e.g., weight, indication, medical history, duration of therapy, laboratory test results, interactions, contraindication, etc.) may be derived from consulting the prescriber, the patient, reference works, or the patient medication file. For antithrombotic prescriptions that required additional information for assessment, a 'collection form' (table 2 in appendix A) was completed. Pharmacists were instructed to write down what extra information was needed, from whom it was requested, what considerations were made when assessing the prescription, as well as how the prescription was handled. The student went to the pharmacy to analyze the prescriptions that had been collected. The supervisor approached pharmacies to participate in the study and, along with the student, conducted the post-participation evaluation with the pharmacists.

The reason for requesting additional information was examined for each case in order to assess the data saturation. Every ten cases were examined to see if there was a new reason for requesting additional information. Prior to the study, it was determined that a minimum of 50 cases would be included. We assumed that the data was saturated when there was no new reason for requesting additional information in 10 consecutive cases.

During the study the design was changed from a cross-sectional, observational study to a semi-qualitative study. The inclusion criteria were adjusted as a result. There was no uniform method of collection that had been agreed upon since each pharmacy operates differently. The manner of collecting the prescriptions, the regional and local agreements and arrangements within pharmacies were discussed in an evaluation that was done afterwards with the pharmacists. In two pharmacies the collection forms were completed during the assessment of the prescriptions and in two other pharmacies, these forms were completed afterwards. In one of the pharmacies in which the collection forms were filled out later, the pharmacist and pharmacy technicians wrote on the prescription what information was requested. Later, a search was performed and all antithrombotic prescriptions from the collection period were

retrieved. The student analyzed these prescriptions and completed the collection forms together with the pharmacist. In the other pharmacy where the collection forms were completed afterwards, the pharmacist and pharmacy technicians made notes on the prescriptions that required additional information. In this pharmacy the pharmacist performed a search as well and all antithrombotic prescriptions from the collection period were retrieved. For the prescriptions that required additional information, a collection form was completed. At one of the pharmacies, the pharmacist collected the prescriptions and emailed the information to the student. Additional questions about the prescriptions could be asked by email. Later, the student filled out the collecting forms for these prescriptions.
A dataset was created by combining the data from the collecting forms, the patient's medical record, and information obtained from conversations with pharmacists regarding the antithrombotic prescriptions. The dataset included anonymous patient data such as age and gender, as well as prescription parameters such as the antithrombotic medication prescribed, dose, frequency, duration of treatment, prescriber, etc. The dataset also contained the source of the additional information along with the reason for requesting the additional information (table 3 in appendix A).

Data analysis
Data collected through the pharmacy information system, collection forms, and conversations with pharmacists concerning the prescriptions were imported into Microsoft Excel. Descriptive statistics were used to illustrate and categorize the problems that pharmacists may encounter when assessing antithrombotic prescriptions and to analyze the considerations taken into account by pharmacists while assessing the prescription. Descriptive statistics were analyzed using IBM SPSS Statistics version 28.

Patient privacy
The privacy of the patient is guaranteed by attaching a code to each prescription that contains the pharmacy code and the prescription number. The pharmacy code can be used to identify the pharmacy from which the prescription was obtained, and the prescription number can be used to look up the prescription to request any missing information. The database contains no personal information about the patient other than age and gender. Additionally, the data is saved in a special secured database that is only accessible to the researchers.

Results

Characteristics of patients and antithrombotic prescriptions A total of 47 prescriptions from 5 different community pharmacies were included in the study (table 1). The patients' average age is 73 years old, with a range of 63 (31 – 94) and males and females are distributed in roughly equal numbers. The DOACs class encompassed most of the prescriptions (48.9%) with rivaroxaban receiving the most requests for extra information. For a VKA, additional information was only requested once. Most of the prescriptions were prescribed by a general practitioner (70.2%). Furthermore, repeat dispense accounted for 87.2% of all prescriptions.

Table 1: Population characteristics and antithrombotic prescription data

	Antithrombotic prescriptions (n=47)	
	Mean	Range
Age	73	63 (31 – 94)
	Frequency (n)	Percent (%)
Gender		
Men	23	48.9
Women	24	51.1
Polypharmacy		
Yes	27	57.4
No	20	42.6
Comorbidities		
Yes	32	68.1
No	15	31.9
Classes of antithrombotics		
Salicylates	14	29.8
P2Y12-inhibitor	2	4.3
Direct oral anticoagulant	23	48.9
Heparin	2	4.3
Salicylates + P2Y12-inhibitor	5	10.6
Vitamin K antagonist	1	2.1
Prescriber		
General practitioner	33	70.2
Specialist	14	29.8
Type of dispense		
First dispense	6	12.8
Repeat dispense	41	87.2

Requested information and considerations

We divided the information that community pharmacists requested for the assessment of antithrombotic prescriptions into the following categories: renal function, contraindication, indication, duration of treatment, dose, and other (table 4 in appendix B). When assessing antithrombotic prescriptions, pharmacists consider several factors in order to process the prescription, for example the age of the patient or a high risk of gastric bleeding. This is done to ensure that antithrombotic medication is used safely and effectively. These factors determine the type of additional information that is requested by pharmacists. In this chapter, the

requested additional information is discussed in more detail. In addition, the considerations that pharmacists make for each category of additional information are discussed.

Renal function

Every time the pharmacist required more information about the renal function, a DOAC prescription was prescribed (Table 4 in appendix B and figure 1B). Sometimes additional information was requested for the DOACs about kidney function, together with, for example, the dosage or weight. For some prescriptions, the indication was unknown. This factor wasn't always requested, therefore it wasn't considered in determining the effectiveness and safety for all prescriptions. Most prescriptions were repeat dispense prescriptions from the general practitioner.

When requesting additional information on renal function, pharmacists considered the dosage of the prescribed medication to rely on the patient's renal function. Additionally, pharmacists mention that they ask about older patients' renal function because this parameter is expected to be impaired in elderly patients. Age is a factor that is considered when requesting more information on renal function. A new renal function value was also asked for when the prior measurement was too old. According to protocol, the renal function value should not be older than 13 months, as was mentioned by one of the pharmacists.

Contraindication

Pharmacists requested more information regarding a contraindication mainly for patients who were prescribed a salicylate (table 4 in appendix B and figure 1F). It concerns the contraindication 'increased risk of gastrointestinal bleeding'. This primarily affects people who are above 80 years old. The factors age, history of ulcers and comedication are used to evaluate the bleeding risk. If there is a high risk of bleeding, the use of a proton pump inhibitor (PPI) is checked.

Indication

Additional information on the indication was requested for DOACs and dual therapy (table 4 in appendix B and figures 1B, 1E). Additional information about the indication was also requested for the heparins, in combination with the duration of treatment (table 3 in appendix and 1C). This information was considered necessary when the patient was not taking any co-medication, e.g., cardiovascular drugs. Additionally, if the patient receives dual therapy, the duration of the combination therapy relies on the indication, so information on the indication was required.

Duration of treatment

More information about the duration of therapy was requested for patients who were prescribed dual therapy (table 4 in appendix B and figure 1C). For heparins, the duration of treatment was also requested, along with the indication (figure 1E). Most of the prescriptions were repeat dispense. In dual therapy, it was also monitored to see which drug will be discontinued over time, because combination therapy is always used temporarily.

Dose

Additional information about the dosage was often requested in combination with another factor, such as indication or renal function (table 4 in appendix B and figure 1A). This information is requested regarding DOACs, dual therapy, and salicylates (figures 1B, 1E and 1F). In one of the cases the dose was lowered to a level that was inappropriate for the patient's indication. According to the pharmacist, the dosage was not in accordance with guidelines. In another case where dabigatran 150 mg twice daily was prescribed, the prescriber was asked to consider a dose reduction as the patient was approaching the age of 80. Age was taken into

consideration while deciding whether to reduce the dose in this case. Also, if the patient wanted to have a repeat prescription earlier than expected and overuse was thought to be occurring, more information on the frequency of dosing was required.

Interaction

More information regarding an interaction was needed for the VKA acenocoumarol because the patient was also using metformin, which can lower the international normalized ratio (INR) (table 4 in appendix B and figure 1G). Furthermore, no information regarding a possible interaction with other antithrombotics was requested.

Other

Additional information that could be classified as 'other' was also requested (Table 4 in appendix B). In one of the cases, the patient had a hypersensitive reaction to clopidogrel in the past and was now prescribed clopidogrel again. In another case, acetylsalicylic acid caused the patient to have itching symptoms and requested an alternative medication. The third case was a repeat dispense prescription from the hospital. A check was needed to see if the first dispense of the prescription took place in the current pharmacy and therefore regular checks of indication and renal function to ensure the correct dose is already done.

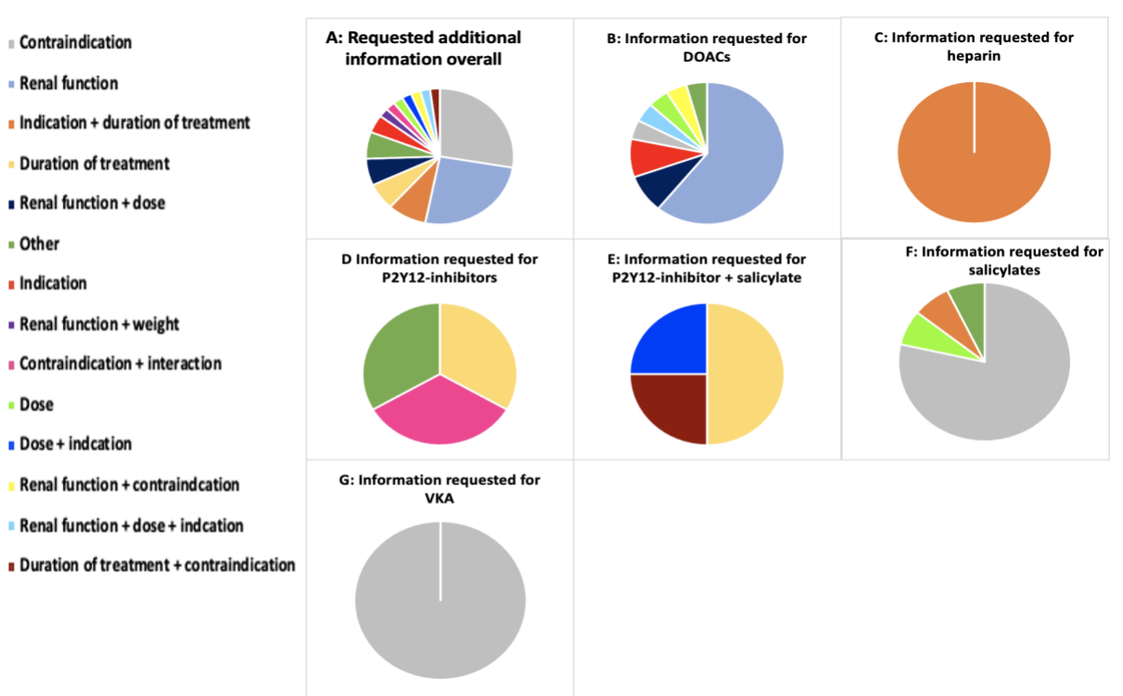

Figure 1. A: Pie chart overall requested additional information to assess antithrombotic prescriptions. Additional information required to assess B: DOACs, C: heparins, D: P2Y12-inhibitors, E: dual therapy, F: salicylates, and G: VKAs.
DOAC: Direct oral anticoagulant
VKA: Vitamin K antagonist

Cases

As described in the previous sections, pharmacists request different types of information. We will describe a few of the cases that were included in this study to get a better insight. Case 1 illustrates a request for more information about renal function and a contraindication, while case 2 illustrates a request for more information about the indication and duration of treatment. In the third case, a description of a situation is given where additional information on the dosage was needed.

Case 1: renal function and gastric protection

A 73-year-old man is prescribed apixaban 5mg 2 times a day for chronic use by his general practitioner. The indication is unknown, and it is a repeat dispense of the prescription. The patient is a polypharmacy patient with peptic ulcer, gout, and hypertension as co-morbidities. The patient is also taking the following medication:

- *Colchicine 0,5 mg 3 times a day if necessary*
- *Perindopril/indapamide 4/1,25 mg once a day*
- *Sotalol 40 mg 3 times a day*
- *Hydroxocobalamin injection 1mg=2mL*

To assess if the apixaban dosage is appropriate for the patient, the pharmacist needs to know the renal function. Because of the peptic ulcer comorbidity, the pharmacist needs to know if the patient is using a gastric protector. The renal function was looked up in the Pharmacy Information System (PIS), as well as whether the patient was using a proton pump inhibitor. The patient's renal function is 60 milliliters per minute (measured on 17-05-21), and he is taking pantoprazole 40 mg once daily. The apixaban has been delivered to the patient as prescribed.

Case 2: indication and duration of treatment

A 54-year-old woman is prescribed carbasalate calcium 100mg once a day by the specialist. This is the first dispense of the medication. The patient is already taking clopidogrel 75 mg once a day. The patient is a polypharmacy patient with hypertension and COPD as co-morbidities. The patient is also taking the following medication:

- *Amlodipine 10mg once a day*
- *Enalapril 10 mg once a day*
- *Ipratropium 40 microgram 3-4 times a day*
- *Simvastatin 40 mg once a day*
- *Formoterol/beclomethasone 100/6 2 inhalations per day*
- *Ethinylestradiol/desogestrel 0,03/0,15 1 pill every day for 21 consecutive days*

The pharmacist wants to know what the indication for the prescription is, how long the combination of the platelet aggregation inhibitors will be given, and which of the two medicines will be discontinued over time. This information is requested from the prescriber. The indication is a cerebrovascular accident. The patient had previously suffered a stroke and had been taking clopidogrel 75mg once daily since 12-01-21. The specialist prescribes carbasalate calcium 100 mg 1 time daily because the patient has had a second stroke. The carbasalate calcium and clopidogrel combination should be taken for three months. Carbasalate calcium should be discontinued after three months, and the patient should continue to take clopidogrel for the rest of her life. The carbasalate calcium has been delivered to the patient as prescribed.

Case 3: dose

A 31-year-old woman is prescribed acetylsalicylic acid 80mg once a day by the specialist. The patient has previously been given this medication in the dosage of two tablets once daily. The dosage has now been reduced to one tablet once a day. It is a repeat dispense of the prescription and the indication is pre-eclampsia prophylaxis. The patient is not a polypharmacy patient and has the comorbidities of iron deficiency and nausea. The pharmacist wants to check with the patient whether the dosage has been reduced to 80 mg one time daily. The pharmacist wants to know this because the recommended dosage for the indication is 160 to 200 mg once daily. The patient says that, as far as she is aware, the dosage has not changed. The pharmacist gives the patient acetylsalicylic acid and advises her to take two pills once a day. Also, a question regarding this handling was forwarded to the prescriber.

Source of additional information

In our results we see that the PIS is the most frequent source of requesting additional information for prescription assessment (figure 2). For example, the renal function was often checked in the PIS, or whether the patient was using a PPI. The PIS was also frequently checked to see if the patient's file contains a stop date when combination therapy is prescribed. Another frequently consulted source of additional information was the prescriber. Data requested from the prescriber includes information about the prescribed dose and indication. To further explain this, an illustration is given in case 4, where the prescriber is asked for more information concerning the dosage and indication. In some cases, the patient was asked for additional information. For heparins, for example, an indication or duration of treatment was requested (figure 1). In addition, the patient was sometimes asked if the medication is being taken as directed. Finally, the literature was also consulted for additional information. For example, online sources were used to determine whether a dosage is appropriate, or for more information about a contraindication.

Case 4: dose and indication

An 80-year-old woman is given a loading dose of carbasalate calcium 300 mg and clopidogrel 300 mg on day one, by her general practitioner. Acetylsalicylic acid 80mg once daily for three weeks and clopidogrel 75mg once daily for three months are prescribed starting on day two. The patient has no comorbidities and is not a polypharmacy patient. The pharmacist wants to know why a double loading dose is prescribed and what the indication is. This information has been requested from the prescriber. A transient ischemia attack is most likely the cause. With the doctor's approval, the carbasalate calcium loading dose was removed and only clopidogrel was given as a loading dose.

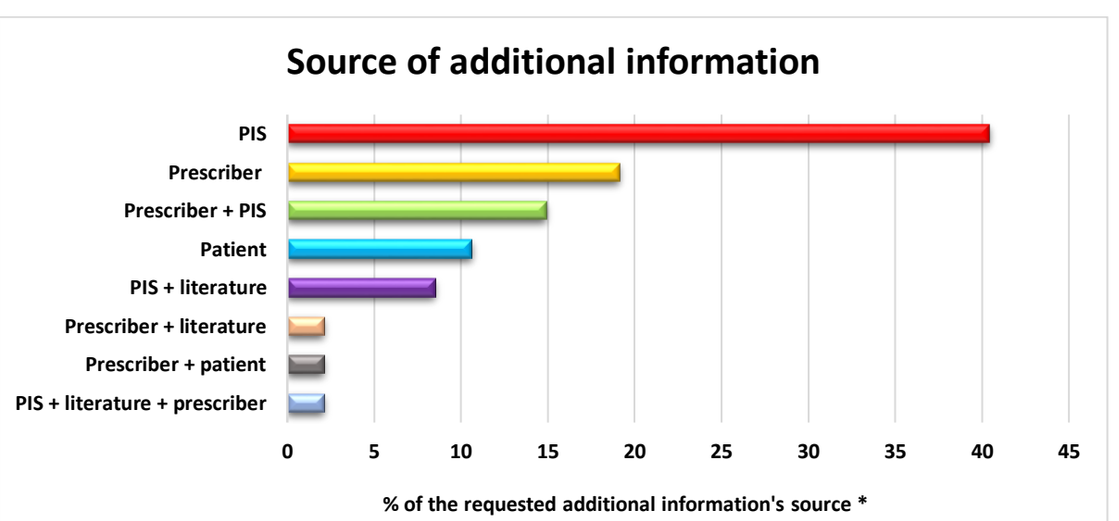

Figure 2: The source from which additional information is requested to review antithrombotic prescriptions.
** The cases mentioned in this study constitute the basis for these percentages. It can provide guidance, but we are unsure if it is an accurate reflection of practice. No values can be attached to these percentages.*
PIS: Pharmacy information system

Pharmacist interventions

The pharmacist intervened in 4 of the 47 prescriptions. In two prescriptions a PPI was added to the medication because the patient had a high risk of gastric bleeding and did not use a PPI. The dosage was changed in another case because the prescriber had prescribed a double loading dose. In the last case, the pharmacist substituted acetylsalicylic acid for carbasalate calcium due to the patient's adverse reactions to the prescribed medication. This was done with the prescriber's approval.

Regional and local agreements and arrangements within pharmacies

After the collection period, an evaluation was conducted with the pharmacists. During this conversation, information on regional and local agreements as well as arrangements made inside the pharmacy regarding antithrombotic prescriptions were obtained. These agreements vary by pharmacy. One of the pharmacies has reached a regional agreement with prescribers from hospitals to note the indication, renal function, and duration of treatment on prescriptions. In another pharmacy, the pharmacy and prescribers have reached an agreement that the following information is gathered from each DOAC user via a fixed procedure: age, weight, lab value measurement date, renal function, and indication. These factors are used to determine whether the dosage is appropriate for the patient. At the third pharmacy for all patients over the age of 70, a renal function value is requested from the prescriber and documented in the patient file. Doctors have agreed to forward the renal function value at the fourth pharmacy when the prescribed medication is dosed based on renal function. There is also a regional agreement that the end date of dual therapy should be stated on the prescription.

There was one thing that the pharmacies had in common regarding arrangements within the pharmacy. There is no physical prescription of the multidose drug dispensing prescriptions and automatically repeated prescriptions. In 4 of the 5 pharmacies, these prescriptions are reviewed at the start of treatment and repeated without an overall assessment. It is only reassessed if there is a change in the prescription. In one of the pharmacies, prescriptions for these patients are evaluated once every three months. Lawfully, a new prescription for these patients should be provided annually, and the pharmacist should assess this. A new prescription is accredited by the general practitioner in one of the pharmacies once every six months or once a year. We don't have information about how other pharmacies handle this because we didn't ask pharmacists if they utilize this practice.

Data saturation

The reason for requesting additional information was examined for each case to determine whether the data was saturated in this study. A bar was added to the figure for each case in which a new reason for requesting additional information was observed. It was decided in advance that 50 cases would be included, after which data saturation would be evaluated. Figure 2 shows after 31 cases, no new reason for requesting additional information was included. This means that the data has been saturated, even though the total of 50 prescriptions has not been reached (figure 3).

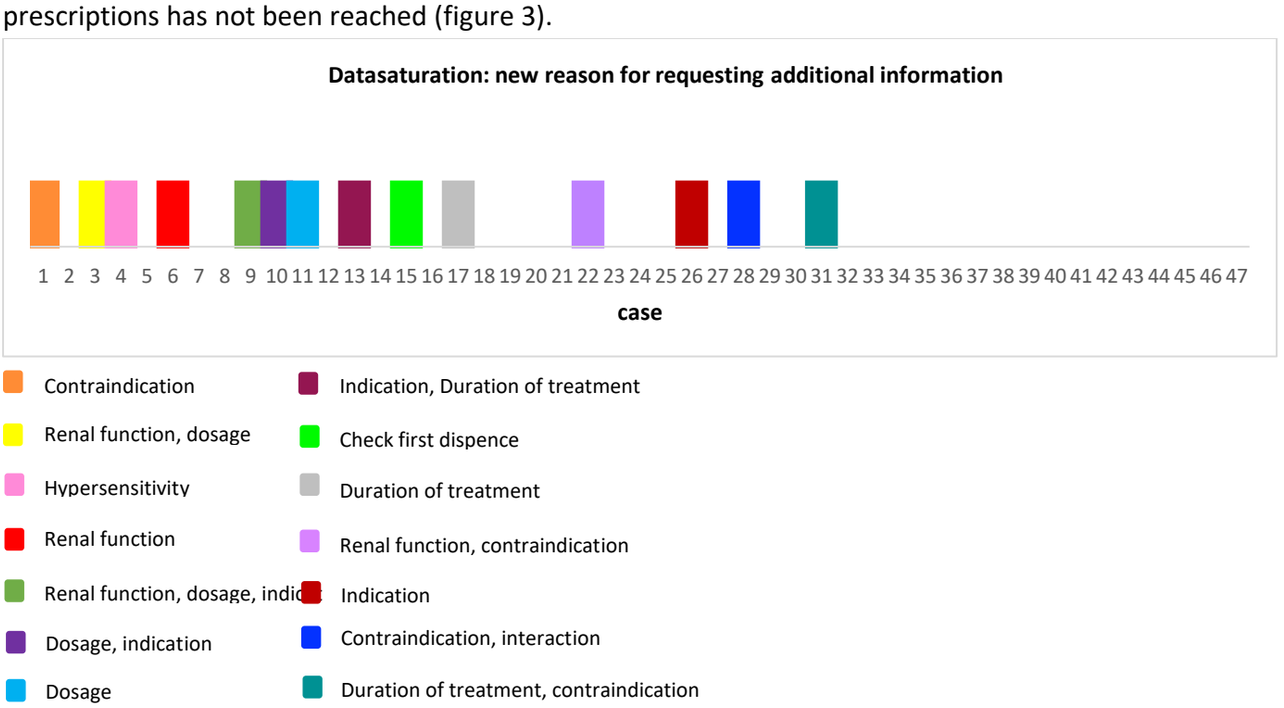

Figure 3: An overview of the data saturation of the cases included in this study

Discussion

The aim of this semi-qualitative study was to see which additional information pharmacists in community pharmacies need to assess antithrombotic prescriptions and what their considerations are when assessing these prescriptions. Additional information on renal function is most frequently requested for DOACs. The patient's age and the fact that medication dosage is dependent on the renal function of the patient are factors that pharmacists consider. For prescriptions of acetyl salicylic acid, including carbasalate calcium, information to assess whether a patient has an increased risk of developing a gastrointestinal bleeding or has a contraindication for the antiplatelet drug, is frequently requested. Extra information about the indication of a DOAC was considered necessary in case of a patient not taking any co-medication e.g., cardiovascular drugs. Information to assess the prescribed duration of treatment was primarily requested for combination therapy prescriptions. Additional information on dosage was often requested, in case of a drug with dosages that differ between indications and are dependent on renal function.
The requested and obtained information could cause an intervention by the pharmacist, such as adding a proton pump inhibitor to the medication or adjusting the dosage.

According to the findings of this study, pharmacists most frequently require additional information on renal function for the assessment of DOAC prescriptions. In general, factors to consider when treating patients with DOACs are age and the fact that medication dosage is dependent on the renal function. The study by Joosten *et al.* [9], a cross-sectional pilot study which looked at whether enough information is available for the community pharmacist to assess the dosage of DOAC prescriptions, found that information about the patient's renal function was present in 30% of patients at the start of DOAC treatment. For 24% of patients this information could be obtained from the PIS. The study did not specify where this information was available in the pharmacy for the remaining 6% of patients. This means that additional information about renal function had to be obtained from a source other than the PIS for 76% of the patients [9]. However, there are several differences between the study of Joosten *et al.* and our study, making it difficult to compare the results. To begin with, our study included patients who had a prescription for any antithrombotic, whereas the study of Joosten *et al.* focused on only DOACs. Our study looked at prescriptions for all types of antithrombotics and what information the pharmacist requests for their assessment, whereas Joosten *et al*. looked at whether information about the indication, renal function measured in the previous 6 months, and body weight was available in the pharmacy for DOAC-users. As a result, other issues that pharmacists may encounter when evaluating DOAC prescriptions may go unmentioned. Pharmacists in our study stated that they consider the patient's age when requesting information about renal function because renal function is more likely to be impaired in elderly people. This stated consideration is supported by the study of Mallappallil *et al.* [17]. According to this research, the renal function declines by 10 ml/min every decade after the age of 40, so that by the age of 70, this parameter has declined by about 30 ml/min. Information regarding contraindication is frequently requested for acetylsalicylic acid and carbasalate calcium, prescriptions. Pharmacists say they consider the patient's age and other factors which increase the risk of bleeding such as specific concomitant medication when requesting more information about the contraindication such as a history of a gastric ulcer. In the ASPirin in Reducing Events in the Elderly (ASPREE) trial, which involved healthy people aged 70 years or older from Australia and the United States, there was a higher risk of upper gastrointestinal bleeding with 100 mg of enteric-coated aspirin taken daily, compared to placebo [18]. The study by Garca Rodriguez *et al.* [19], a population-based observational study examining the impact of PPIs on the risks of upper and lower gastrointestinal bleeding among

users of low-dose aspirin, found that maintenance PPI treatment provides gastroprotection to prevent upper gastrointestinal bleeding in individuals treated with low-dose aspirin. The findings of the last two studies support the considerations mentioned by pharmacists when requesting more information about the contraindication.

Extra information about the indication of a DOAC was considered necessary in case of a patient who was not taking any co-medication e.g., cardiovascular drugs. DOACs are frequently prescribed for atrial fibrillation, which often occurs in elderly patients with cardiovascular disease which almost always involves polypharmacy [20]. It is understandable that a pharmacist would require the indication when receiving and assessing a prescription for a patient on DOAC monotherapy because these patients frequently take multiple medications to treat their disease. An indication for which DOACs can be used as monotherapy is deep venous thrombosis. Patients are given an anticoagulant to prevent a pulmonary embolism or thrombosis expansion. So, when a pharmacist receives a prescription with DOAC monotherapy, it is possible that he or she will inquire whether the medication is being used to treat deep vein thrombosis. If so, the pharmacist could also check whether the prescribed dosage is appropriate and whether the duration of treatment is known. The duration of therapy is determined by several factors, such as the type of thrombus and the patient's risk factors [21]. Information on the duration of treatment was primarily requested for combination therapy prescriptions. This includes dual antiplatelet therapy (DAPT) (P2Y12-inhibitor and acetylsalicylic acid). According to the guidelines, antithrombotic combination therapy should be used for a limited time. The duration of the combination therapy varies depending on the indication [22]. In a study conducted by Herwaarden *et al.* [12] in a Dutch community pharmacy, it was discovered that 14 to 23% of all DAPT were not prescribed in accordance with the guidelines. The cause of nearly 50% of these therapies was DAPT continuation past the advised treatment period. In this study, the initiator of antithrombotic combination therapy is advised to inform the general practitioner and/or community pharmacy of the intended duration of therapy to avoid the patient taking DAPT for an unnecessarily long period of time [12]. For many years, only patients with an acute coronary syndrome received DAPT for one year with acetylsalicylic acid monotherapy to be continued as monotherapy after one year. Nowadays guidelines recommend personalized durations of DAPT. In recent years, DAPT is also being utilized to treat neurological conditions such as transient ischemic attack. Both the CHANCE (Clopidogrel in high-risk patients with acute nondisabling cerebrovascular events) study [23] and POINT (Platelet-Oriented Inhibition in New Transient Ischaemic Attack and Minor Ischemic Stroke) study [24] studied the use of acetylsalicylic acid in combination with clopidogrel in the treatment of a TIAs. The guidelines state that it is possible to treat a TIA with a combination of acetylsalicylic acid and clopidogrel for the first three weeks and then continue with chronic clopidogrel use [25]. Because the duration of treatment is related to the indication, pharmacists should inquire about both the duration of treatment and the indication.

Additional information on dosage was often requested, in case of a drug with dosage regimens that depend on the indications and/or renal function. According to the research of Dominguez-Erquicia *et al.* [26] the use of an inappropriate dose of DOAC in elderly patients is approximately 40%. An inappropriate dosing prescription was associated with high blood pressure, weight, and renal function. It is therefore necessary to carefully assess the patient's characteristics in order to prescribe the appropriate DOAC dose. Furthermore, some indications require an adjusted dose of a DOAC (rivaroxaban) when combined with a platelet aggregation inhibitor [27]. It is therefore reasonable to check the indication to ensure the correct dosage. The requested and obtained information could lead to an intervention by the pharmacist. In the study by Zhang *et al.* [16] in which an antithrombotic stewardship program was implemented to assess combined oral antithrombotic therapy, at least one intervention by the antithrombotic

stewardship team was needed for 54.6% of the patients. The three interventions that were made the most frequently were: (1) defining and documenting the maximum duration of the combination antithrombotic therapy required (65.5%); (2) discontinuing antithrombotic therapy because the proper indication was missing (19.4%); and (3) adjusting the dosage (8.1%) [16]. The dose-adjustment interventions were carried out in prescriptions containing a DOAC. A number of interventions were also carried out in our study with antithrombotic prescriptions. However, comparing the interventions in our study to the interventions done in the study of Zhang et al. [16] is difficult because the interventions in the study of Zhang et al. [16] were related to combination therapy. Interventions with other antithrombotics are not considered in the study by Zhang *et al.* [16].

Strengths and limitations of the study

One of our study's strengths is the use of the PIS systems to retrieve prescription and patient data. This data reflects real-world information and was collected in a relatively easy and trustable manner. Another strength of our study is that it included all antithrombotics. This way it is made sure that problems that may occur when assessing all types of antithrombotics are covered rather than being limited to a single class. However, there are also some limitations to the current study. One of the limitations is that the prescriptions were gathered by pharmacists. It is possible that for some prescriptions for which additional information was requested, no collection form was completed, and thus it was missed in the data. However, this is only a limitation if it overlooks a case in which a new type of additional information has been requested. This is not expected based on data saturation, as the data is saturated after 31 cases (figure 2). Another limitation is that only a small number of pharmacies participated in the study. Other types of additional information may have been requested when assessing antithrombotic prescriptions, but due to the small sample size and limited number of participating pharmacies, these cases might have been missed.

Future recommendations

Additional information on patient characteristics is frequently requested when assessing antithrombotic prescriptions. Therefore, introducing a system that allows the transfer of patient data, such as clinical laboratory data and data on the indication, to community pharmacies are important to improve clinical risk management of antithrombotic therapy by pharmacists. Furthermore, it may be beneficial to make regional (or national) agreements between health care providers including pharmacists about the exchange of treatment characteristics such as the duration of dual therapy. This might make the assessment process go more quickly.

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Appendix A: Data collection of antithrombotic prescriptions

Table 1: antithrombotic drugs that are included in the study

Classes of antithrombotics	**Drugs of the class included in the study**
Salicylates	Acetylsalicylic acid, carbasalate calcium
P2Y12 inhibitors	Clopidogrel, prasugrel, ticagrelor
Direct oral anticoagulants	Apixaban, edoxaban, rivaroxaban, dabigatran
Vitamin K antagonist	Acenocoumarol, fenprocoumon
Heparines	Dalteparin, enoxaparin, fondaparinux, nadroparin, tinzaparin
Dipyridamole	Dipyridamole

Table 2: Collection form

Prescription number	☑	Reason for collecting	Considerations
Sex: Male/Female/x Age: …… year		Additional information from reference work:	
		indication	
		dosage	
		interactions	
		contraindication	
		other:	
		Additional oral information from the patient:	
		Lab values	
		Weight	
		indication	
		Medical history	
		Duration of treatment	
		Wants and needs	
		other:	
		Additional information from PIS:	
		Lab value	
		Medical history	
		Electronic patient file	
		indication	
		Other:	
		Additional information from the prescriber:	
		Lab value	
		Weight	
		indication	
		Medical history	
		Duration of treatment	
		Consideration when choosing medication	
		Consultation about medication monitoring signal	
		Other	

Table 3: Collected information about the prescriptions

Age	Gender	Medication	Class	Dose	Frequency	Indication	Duration of treatment	Type of dispense	polypharmacy	Comorbidities	Source of additional information	Reason

Appendix B: Results

Table 4: A description of the cases examined in this study
PIS: Pharmacy information system
TIA: transient ischemic attack
PPI: Proton pump inhibitor
INR: International normalized ratio

Renal function									
Age of the patient	*Medication and dose*	*Indication*	*Prescriber*	*Type of dispense*	*Polypharmacy*	*Comorbidities*	*Source of additional information*	*Considerations of the pharmacist*	*Summary*
71	Rivaroxaban 10mg 1 time a day	deep vein thrombosis	General practitioner	Repeat dispense	No	COPD, IBD, Asthma	PIS, Prescriber	Renal function according to PIS: 86 mL/min measured on 20-01-21. According to protocol, renal function should not be older than 13 months.	New renal function requested from prescriber: 86 mL/min. Prescription approved.
68	Edoxaban 60 mg 1 time a day	peripheral arterial disease	General practitioner	Repeat dispense	Yes	COPD, hypertension, gout	Prescriber	Renal function needed for dose assessment. Weight was not	Renal function according to PIS: 90 mL/min measured on

								requested because the patient has been seen often in the pharmacy and the pharmacist knows that the patient is overweight.	25-01-22. Prescription approved.
79	Apixaban 5 mg 2 times a day	Unknown	General practitioner	Repeat dispense	No	Hypertension, ischemic heart disease	PIS	Weight has not been requested because it is known that the patient is a little bit overweight.	Renal function according to PIS: 84 mL/min measured on 16-03-22. Prescription approved.
88	Dabigatran 110 mg 2 times a day	Essential hypertension without organ damage	General practitioner	Repeat dispense	No	None	PIS, prescriber	Dosage check based on renal function.	Renal function not documented in PIS. Requested from prescriber: 34 mL/min measured on 03-12-21. Prescription approved.
82	Edoxaban 30 mg 1 time a day	transient ischemic attack	General practitioner	Repeat dispense	Yes	Hypertension	PIS, prescriber	Dosage depends on renal function. Renal function according to PIS: 38 mL/min measured on 06-11-20. New renal function needed.	A new renal function test was requested from the prescriber. Prescription approved.
84	Apixaban 5 mg 2 times a day	unknown	General practitioner	Repeat dispense	Yes	Heart failure, Angina Pectoris	PIS	Dosage control based on renal function. Renal function is expected to be impaired in elderly patients	Renal function according to PIS: 37 mL/min measured on 03-12-21. Prescription approved.
91	Rivaroxaban 15 mg 1 time a day	venous thromboembolism	General practitioner	Repeat dispense	Yes	Hypertension	PIS	Dosage depends on renal function of the patient.	Renal function according to PIS: 40 mL/min measured on 07-04-22. Prescription approved.

80	Rivaroxaban 20 mg 1 time a day	peripheral arterial disease	General practitioner	Repeat dispense	Yes	Hypertension, COPD	PIS	Patient is old and the dosage depends on the renal function.	Renal function according to PIS: 63 mL/min measured on 30-11-21. Prescription approved.
67	Apixaban 5 mg 2 times a day	Unknown	specialist	Repeat dispense	Yes	Asthma, COPD, diabetes mellitus	PIS	Renal function needed for dosage assessment apixaban.	Renal function checked in PIS. Prescription approved.
60	Rivaroxaban 20 mg 1 time a day	venous thromboembolism	General practitioner	Repeat dispense	Yes	Schizophrenia, depression, glaucoma	PIS, prescriber	Renal function according to PIS: 63 mL/min, measured on 05-09-20. The renal function documented in the PIS is too old.	A new renal function was requested from the prescriber. Prescription approved.
82	Apixaban 5 mg 2 times a day	Unknown	General practitioner	Repeat dispense	No	Hypertension, hyperthyroidism	PIS, prescriber	Renal function documented in PIS: 57 mL/min measured on 03-10-17. This is too old.	Prescriber: new renal function was requested. Prescription approved.
68	Rivaroxaban 20mg 1 time a day	Atrial fibrillation	Specialist	Repeat dispense	Yes	No	PIS	Dosage depends on the renal function.	PIS: Renal function 89 mL/min measured May 2022. Prescription approved.
Renal function + Dose									
79	Dabigatran 150 mg 2 times a day	Unknown	General practitioner	Repeat dispense	No	None	PIS, literature, prescriber	New measurement of renal function needed, and prescriber is asked to consider dose reduction because patient approaches 80 years of age.	Renal function according to PIS: 84 mL/min. Literature: check if dosage is appropriate for renal function.
73	Rivaroxaban 15mg 1 time a day	atrial fibrillation	General practitioner	Repeat dispense	Yes	Diabetes mellitus, Heart failure	Patient, PIS	The pharmacist suspects that the medication is being overused because the patient wants to have a	Daily dosage is correct based on renal function: 44 mL/min. Patient: daily dosage is 15 mg 1 time a day. Patient lost a package

								repeat prescription earlier than expected.	of the medication and wants a new one. Prescription approved.
84	Dabigatran 110 mg 2 times a day	Unknown	Specialist	Repeat dispense	No	None	PIS, literature	Dose control based on renal function.	Renal function according to PIS: 45 mL/min measured on 10-05-21. Literature: check if dosage is appropriate for renal function. Prescription approved.
83	Apixaban 2,5 mg 2 times a day	unknown	General practitioner	Repeat dispense	Yes	None	PIS, literature	Renal function needed for dose assessment.	Renal function: 48 ml/min (9-2-22). Literature: check if dosage is appropriate for renal function. Prescription approved.
Renal function + contraindication									
73	Apixaban 5 mg 2 times a day	unknown	General practitioner	Repeat dispense	Yes	Peptic ulcer, gout, hypertension	PIS	- Patient has had a peptic ulcer in the past. Renal function looked up in PIS.	Renal function according to PIS: 60 mL/min measured on 17-05-21. Contraindication: patient already takes Pantoprazole 40 mg. Prescription approved.
Renal function + weight									
80	Apixaban 5 mg 2 times a day	unknown	General practitioner	Repeat dispense	No	None	PIS	Apixaban is dosed based on weight, renal function, and age.	Renal function: 54 mL/min (measured March 2022) Weight: 83 kg (measured March 2022). Prescription approved.

Renal function + dose + indication									
55	Apixaban 5 mg 2 times a day	unknown	Specialist	First dispense	No	None	PIS and literature	Not mentioned	Renal function: 100 mL/min (4-05-22) Indication: Start 4 weeks before the ablation treatment Dosage: check in literature
Indication									
75	Edoxaban 60 mg 1 time a day	atrial fibrillation	General practitioner	Repeat dispense	No	None	Prescriber	The indication is required because the patient is not using any comedication.	Indication: according to the general practitioner the patient had cardioversion. It is unknown if edoxaban should be continued. The decision of whether to keep using edoxaban is submitted to the cardiologist.
51	Rivaroxaban 10 mg 1 time a day	recurrence deep vein thrombosis	General practitioner	Repeat dispense	No	None	Patient	The pharmacist wants to know what the indication is because the patient does not use any comedication. Renal function is unknown, but it's not expected to be poor based on age and absence of co-morbidities.	Indication: recurrence deep vein thrombosis. Prescription approved.
Dose									
31	Acetylsalicylic acid 80 mg 1 time a day	Pre-eclampsia prophylaxis	Specialist	Repeat dispense	No	iron deficiency, nausea	Patient	The dosage for pre-eclampsia prophylaxis according to guidelines is 160 - 200 mg once a day	According to the patient the dosage has not been adjusted. As a result, the prescription is written

									for 80 mg twice a day. The specialist has yet to respond to an email asking if he or she agrees with this handling.
Dose + indication									
80	Day 1: - carbasalate calcium 300 mg - Clopidogrel 300 mg From day 2: - Clopidogrel 75 mg 1 time a day Acetylsalicylic acid 80 mg 1 time a day	suspected transient ischemic attack (TIA)	General practitioner	First dispense	No	None	Prescriber	Prescribing a double loading dose is not common.	Double loading dose prescribed. Indication and clarification for double loading dose requested. Indication: probably a TIA. Carbasalate calcium loading dose removed and only clopidogrel given as a loading dose.
Duration of treatment									
81	Clopidogrel 75 mg 1 time a day	acute coronary syndrome	General practitioner	Repeat dispense	Yes	Asthma, COPD, ischemic heart disease	Prescriber	The duration of therapy mentioned on the prescription by the prescriber does not match the length of treatment recorded in the PIS.	After a check with the prescriber, the duration of treatment recorded in the PIS is correct. Prescription approved.
70	Carbasalate calcium 100 mg 1 time a day and Prasugrel 10 mg 1 time a day	Unknown	Specialist	Repeat dispense	Yes	Diabetes mellitus, hypertension, breast carcinoma	PIS	Combination of 2 platelet aggregation inhibitors. Verify whether a note has been made about the duration of treatment in the PIS.	Duration of combination therapy already documented in PIS: end 02-23. After that, only carbasalate calcium should be continued for chronic use. Prescription approved.

54	Prasugrel 10 mg 1 time a day and acetylsalicylic acid 80 mg 1 time a day	unknown	specialist	Repeat dispense	Yes	peptic ulcer, morbid obesity, ischemic heart disease	PIS	Combination therapy should be used temporarily.	Duration of combination therapy: end 26-06-23. After that only acetyl salicylic should be continued for chronic use. Prescription approved.
Indication + duration of treatment									
54	Carbasalate calcium 100 mg 1 time a day Already in use but not on prescription: clopidogrel 75mg 1 time a day	cardiovascular event	specialist	First dispense	Yes	COPD, hypertension	Prescriber	Combination therapy. Duration of combination therapy depends on indication. Also, which of the 2 will be discontinued over time?	Indication: cardiovascular event Duration of treatment: 3 months. Clopidogrel is then used permanently, and carbasalate calcium is discontinued. Prescription approved.
82	Fraxiparine 2850 IE/0,3 mL	Postoperative prevention of thrombosis	specialist	Repeat dispense	Yes	Heart failure, hypertension	Patient	First dispense was in the hospital. Current pharmacy needs information for assessment of prescription.	Duration of treatment: 5 weeks Indication: postoperative shoulder and hip surgery. Prescription approved.
53	Fraxiparine 2850 IE/0,3 mL	prevention of thrombosis due to bone fracture	Specialist	Repeat dispense	No	None	Patient	Check whether the patient truly needed to continue injecting fraxiparine, as in some cases the patient must/may stop sooner (eg because INR is normal again or because patient is mobile again). - To avoid waste	Duration of treatment: 4 weeks Indication: prevention of thrombosis due to bone fracture. Prescription approved.

Contraindication									
80	acetylsalicylic acid 80 mg 1 time a day	Unknown	Specialist	First dispense	No	Angina Pectoris, Asthma, COPD	PIS	First dispense of acetylsalicylic acid, patient has no gastric protection in use.	Omeprazole 20 mg added to the medication.
82	Carbasalate calcium 100 mg 1 time a day	Unknown	General practitioner	Repeat dispense	Yes	COPD	PIS	Gastric protection needed because of an increased risk of ulcer.	Patient is already taking omeprazole 20 mg. Prescription approved.
83	acetylsalicylic acid 80 mg 1 time a day	peripheral arterial disease	General practitioner	Repeat dispense	Yes	Hypertension, hyperthyroidism	PIS	Increased risk of ulcer based on age and comedication paroxetine.	Patient is already taking Pantoprazole 40 mg. Prescription approved.
94	Clopidogrel 75 mg 1 time a day	Transient ischemic attack	General practitioner	Repeat dispense	No	Hypertension, gout, peptic ulcer	PIS	Increased risk of ulcer based on age.	Patient is already taking pantoprazole 20 mg. Prescription approved.
81	Carbasalate calcium 100 mg 1 time a day	Unknown	General practitioner	Repeat dispense	No	None	PIS, prescriber	Gastric protection needed based on age.	Patient has no PPI in use. pantoprazole 20 mg added to the medication and a prescription for the PPI requested from the prescriber.
76	acetylsalicylic acid 80 mg 1 time a day	Unknown	General practitioner	Repeat dispense	Yes	Hypertension, ulcus pepticum	PIS	Increased risk of ulcer based on age and peptic ulcer in the past.	Patient is already taking esomeprazole 40 mg. Prescription approved.
81	acetylsalicylic acid 80 mg 1 time a day	Unknown	General practitioner	Repeat dispense	Yes	Asthma, COPD, hypertension	PIS	Increased risk of ulcer based on age.	Patient is already taking pantoprazole 40. Prescription approved.
68	Rivaroxaban 2,5 mg 2 times a day	Unknown	specialist	First dispense	Yes	Diabetes mellitus, peptic ulcer	PIS, literature	Patient has had a peptic ulcer in the past.	Literature: information regarding the interaction. PIS: Patient already

									takes omeprazole 40 mg. Prescription approved.
61	Acetylsalicylic acid 80 mg 1 time a day	Unknown	General practitioner	Repeat dispense	Yes	Diabetes mellitus, depression	PIS	Increased risk of ulcer based on comedication (Sertraline and acetylsalicylic acid)	PIS: The patient hasn't had an ulcer before, so no PPI required. Prescription approved.
81	Acetylsalicylic acid 80 mg 1 time a day	Unknown	General practitioner	Repeat dispense	Yes	Hypertension, diabetes mellitus, renal impairement	PIS	Increased risk of ulcer based on age.	Patient is already taking omeprazole 20 mg. Prescription approved.
87	Acetylsalicylic acid 80 mg 1 time a day	Unknown	General practitioner	Repeat dispense	Yes	Hypertension, diabetes mellitus, asthma	PIS, patient	Increased risk of ulcer based on age.	Patient is already taking omeprazole 20 mg, but it should have been finished by now. The patient was asked if she still uses it. Patient indicates that she still uses it but that she had collected more a while ago, so that she has sufficient stock. Prescription approved.
86	Acetylsalicylic acid 80 mg 1 time a day	Transient ischemic attack	General practitioner	Repeat dispense	No	Diabetes mellitus, hypertension	PIS	Increased risk of ulcer based on age.	Patient is already taking omeprazole 20. Prescription approved.
54	Acetylsalicylic acid 80 mg 1 time a day	Unknown	General practitioner	Repeat dispense	Yes	None	PIS	Increased risk of ulcer based on comedication (prednisolone)	Since the patient is under 60 years old, no PPI is necessary. Prescription approved.
Duration of treatment + contraindication									
55	Ticagrelor 90 mg 2 times a day and acetylsalicylic acid 80 mg 1 time a day	Unknown	General practitioner	Repeat dispense	Yes	ischemic heart disease	PIS	Combination therapy: - Increased risk of bleeding	Duration of combination therapy: until 10-08-22. Only acetylsalicylic acid

								- Combination therpay should be used temporarily	should be continued after that time. Prescription approved.
Contraindication + interaction									
56	Acenocoumarol 1 mg according to thrombosis service	venous thromboembolism	General practitioner	Repeat dispense	Yes	Diabetes mellitus, peptic ulcer	PIS	- Metformin lowers INR. Risk factors for bleeding	Patient is already taking omeprazole 20. The use of metformin has already been reported to the thrombosis service. Prescription approved.
Other									
69	Clopidogrel 75 mg 1 time a day	Percutaneous coronary intervention	specialist	First dispense	No	None	Prescriber, patient	PIS gave a notification of a previously recorded intolerance to clopidogrel. Patient was asked about the intolerance but nothing was discussed her.	Switched to ticagrelor but patient got many side effects. Patient is going to try clopidogrel again. Prescriber was asked what to do with the hypersensitivity. Prescriber indicates that the patient should try clopidogrel.
69	Rivaroxaban 20 mg 1 time a day	deep vein thrombosis	specialist	Repeat dispense	No	None	PIS, prescriber	Repeat prescription from hospital. Check is needed to see if this prescription is already dispensed in the current pharmacy and therefor regular checks of indication and renal function (to ensure correct dose) are already done.	First dispense took place on 10-02-22. Indication and renal function documented in PIS.

68	Acetylsalicylic acid 80mg 1 time a day	peripheral arterial disease	General practitioner	Repeat dispense	Yes	Diabetes mellitus	Prescriber	The patient thinks that the itching symptoms she experiences are due to acetylsalicylic acid.	Patient switched to carbasalate calcium 100 mg