NON-INTERVENTIONAL (NI) STUDY PROTOCOL

Study information

Title	Evaluating the Effectiveness of Eliquis® Additional Risk Minimization Measures in Kingdom of Saudi Arabia
Protocol number	B0661194
Protocol version identifier	1.0
Date	16 May 2025
EU Post Authorization Study (PAS) register number	EUPAS1000000270
Active substance	Apixaban; direct factor Xa inhibitor ATC code: B01AF02
Medicinal product	Eliquis® (Apixaban)
Research question and objectives	The overall objective of this study is to evaluate the effectiveness of the additional RM tools for Eliquis®, in terms of their key safety messages, by conducting a survey in the KSA where the RM tools have been implemented. **Primary objective will be to**: 1. Assess HCPs' knowledge of RM tools (ie, Prescriber Guide and Patient Alert Card) with regards to the bleeding risk associated with Eliquis® treatment. **Secondary objectives will be to:** 1. Assess utilization of Eliquis® RM tools (ie, Prescriber Guide and Patient Alert Card) by HCPs. 2. Assess HCPs' self-declared behavior with regards to the specific guidance related to the prevention and management of bleeding associated with Eliquis® treatment.
Country of study	Kingdom of Saudi Arabia
Author	Redacted

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2. LIST OF ABBREVIATIONS

Abbreviation	Definition
ADR	Adverse Drug Reaction
AE	Adverse Event
AEM	Adverse Event Monitoring
AF	Atrial Fibrillation
aRMM	Additional Risk Minimization Measure
ASA	Acetylsalicylic Acid
ATC	Anatomical Therapeutic Chemical
CI	Confidence Interval
CrCl	Creatinine Clearance
DCE	Data Check Edit
DCTs	Data Collection Tools
DSU	Drug Safety Unit
DVT	Deep Vein Thrombosis
EC	Ethics Committee
EDP	Exposure During Pregnancy
FDA	Food and Drug Authority
GI	Gastrointestinal
GORD	Gastro-Oesophageal Reflux Disease
GPP	Good Pharmacoepidemiology Practices
GVP	Good Pharmacovigilance Practices
HCP	Health Care Professional
HMA-EMA	Heads of Medicines Agencies-European Medicines Agency

INR	International Normalized Ratio
ISTH	International Society on Thrombosis and Hemostasis
IRB	Institutional Review Board
ISPE	International Society for Pharmacoepidemiology
KSA	Kingdom of Saudi Arabia
MAH	Marketing Authorization Holder
NI	Non-interventional
NIS	Non-Interventional Study
NVAF	Non-Valvular Atrial Fibrillation
NYHA	New York Heart Association
PAS	Post-Authorization Study
PASS	Post-Authorization Safety Study
PE	Pulmonary Embolism
P-gp	P-glycoprotein
RDG	Random Data Generation
RM	Risk Minimization
RMP	Risk Management Plan
RWD	Real-world Data
SAP	Statistical Analysis Plan
SAS	Statistical Analysis System
SFDA	Saudi Food and Drug Authority
SmPC	Summary of Product Characteristics
SOP	Standard Operating Procedure
TIA	Transient Ischemic Attack
USA	United States of America

VKA	Vitamin K Antagonist
VTE	Venous Thromboembolic Event
VTEp	VTE Prevention
VTEt	VTE Treatment
YRR	Your Reporting Responsibilities

3. RESPONSIBLE PARTIES

Principal Investigator(s) of the Protocol

Name, Degree(s)	Job Title	Affiliation	Address
Redacted			

4. ABSTRACT

Title

Evaluating the Effectiveness of Eliquis® Additional Risk Minimization Measures in Kingdom of Saudi Arabia

Protocol version and date

Version 1.0, 16 May 2025

Name and affiliation of main author

Redacted

Rationale and Background

The Eliquis® (apixaban) risk management plan (RMP) contains additional risk minimization (RM) tools, comprising a *Prescriber Guide* and a *Patient Alert Card*. These originally applied only for the indication of Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation (NVAF), with one or more risk factors, such as prior stroke or transient ischemic attack (TIA); age ≥ 75 years; hypertension; diabetes mellitus; symptomatic heart failure (New York Heart Association [NYHA] Class ≥ II).

An updated Prescriber Guide and Patient Alert Card were subsequently also required for the two other Eliquis® indications, Prevention of venous thromboembolic (VTE) events in adult patients who have undergone elective hip or knee replacement surgery ('VTEp'), and Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE) and prevention of recurrent DVT and PE in adults ('VTEt'). The objective of the RM tools is to minimize the important identified risk of bleeding when Eliquis® is used for all its indications. The purpose of this study is to assess whether implementation of the RM tools has led to effective understanding and reinforcement of key safety messages outlined in the Summary of Product Characteristics (SmPC) and Package Leaflet.

The study comprises online surveys of representative samples of healthcare professionals (HCPs) in the Kingdom of Saudi Arabia (KSA). These surveys will provide information on distribution, usage, knowledge, and behavior associated with the success of RM tool implementation. The study results will be analyzed to determine if the current RM tools lead to effective understanding and reinforcement of key safety messages and whether any modification is required either to the tools or the way they are implemented.

Research Question and Objectives

The overall objective of this study is to evaluate the effectiveness of the additional RM tools for Eliquis®, in terms of their key safety messages, by conducting a survey in the KSA where RM tools have been implemented.

Primary Objective

The primary objective of this study will be to:

1. Assess HCPs' knowledge of RM tools (ie, Prescriber Guide and Patient Alert Card) with regards to the bleeding risk associated with Eliquis® treatment.

Secondary Objectives

The secondary objectives will be to:

1. Assess utilization of Eliquis® RM tools (ie, Prescriber Guide and Patient Alert Card) by HCPs.

2. Assess HCPs' self- declared behavior with regards to the specific guidance related to the prevention and management of bleeding associated with Eliquis® treatment.

Study Design

This will be a non-interventional PASS, cross-sectional study to evaluate the effectiveness of RM tools for Eliquis® in the KSA. The study objectives will be accomplished by means of a cross-sectional survey among HCPs who prescribe and/or dispense Eliquis® in the KSA. Data will be collected during the data collection period of approximately 4-6 months. The study aims to obtain completed surveys from 20 HCPs. The data from the HCPs will be collected using a structured self-administered questionnaire to gather evaluation metrics related to the utilization and understanding of RM tool content and messages. In addition, the survey will assess behaviors, including a set of hypothetical scenarios for HCPs. The surveys are not intended to be a mechanism for collecting adverse events (AEs), nor are they intended to result in minimizing the numbers of AEs reported.

Primary Endpoint

1. The proportion of targeted HCPs' who responds to the knowledge-related questions in agreement with the RM tools for Eliquis®.

Secondary Endpoints

1. The proportion of targeted HCPs using Eliquis® for any approved indication who have utilized the RM tools
2. The proportion of targeted HCPs whose responses to the practice-related questions, self-declared behavior, are in agreement with the RM tools

Population

Potential prescribers or dispenser of Eliquis® (HCPs) in the KSA will be invited to participate in this survey.

Inclusion Criteria

The HCPs must meet all of the following criteria to be eligible for inclusion in the survey:

1. Involved in the treatment of at least one patient with Eliquis® within the last 12 months
2. Willing to participate in the self-administered HCP survey by providing voluntary consent to participate in this survey conducted in the KSA

Exclusion Criteria

The HCPs meeting any of the following criteria will not be included in the study:

1. Employed in full time research or hospital administration (ie, non-practicing physicians)
2. Employment by Pfizer, Inc or any research organization/vendor contracted by Pfizer to administer the survey.

Variables

The variables related to HCP demographics and medical background are:

1. Demographic information (age range, gender, and location [city])
2. HCP type (physician, pharmacist or other)
3. Medical specialty (cardiology, general [internal] medicine/internist, other medical specialty)
4. Practice setting (Primary Care vs Secondary/Tertiary Care office or clinic vs hospital)

5. Role in Eliquis® treatment (initiating prescribing, continuing prescribing, or dispensing Eliquis®)
6. Length of professional practice as a HCP (the number of years practicing as a HCP)
7. Regular vs. occasional ('Regular' is defined as ≥1 patient/month and 'occasional' is defined as <1 patient/month during last the 6 months) treatment with Eliquis®
8. Eliquis® indication treated

The primary endpoint is:

1. The proportion of targeted HCPs who responds to the knowledge-related questions in agreement with the RM tools for Eliquis®

Secondary endpoints are:

1. The proportion of targeted HCPs using Eliquis® for any approved indication who have utilized the RM tools
2. The proportion of targeted HCPs whose responses to the practice-related questions, self-declared behavior, are in agreement with the RM tools

Data Source (Survey)

A structured web-based, cross-sectional self-administered questionnaire comprised of closed ended questions or statements with multiple response choices (ie, questions or statements asking the HCPs to choose from a defined list of responses) will be used to collect the survey data. The questionnaire will collect data on HCP characteristics in addition to their responses pertaining to the effectiveness of the RM tools. It is estimated to take 20 to 25 minutes to complete the HCP questionnaire.

Study Size

At the time of protocol writing, approximately 85 HCPs were prescribing/dispensing Eliquis® in KSA, and around 73 of these have received the RM tools in-person and 12 by email, per Pfizer Inc.'s Distribution List. Given this relatively small pool of HCPs, an empirical sample size of 20 HCPs is proposed. It is important to note that the final survey sample size will depend on HCPs' willingness to participate in the survey. All completed surveys received during the data collection period of approximately 4-6 months will be included in the final study report.

A threshold of 80% correct responses per risk questions will be used to define the success of the program. However, this criterion will not be used for formal statistical testing. The selection of this threshold for success was regarded as being subjective and not based on prior knowledge, experience, or established scientific criteria.

Data Analysis

The statistical analysis will be conducted using the SAS® software V9.4 (SAS Institute North Carolina, USA), or R version 3.6 or higher on Windows™. All the analyses will be descriptive. Continuous variables will be described by their number (of valid cases, of missing values), mean, standard deviation, and median, Q1, Q3, minimum and maximum. Categorical variables will be described as the total number and relative percentage per category.

In case of multiple-choice questions, the frequency of each option provided by the HCPs will be reported as the total number and relative percentage per category. Different combinations of the answers provided (if any) will not be considered.

Wilson CIs of 95% will be evaluated on the overall result.

The participation rate will be analyzsed overall for HCPs.

The proportion of correct and desirable answers to the selected questions asked in the questionnaire will be expressed for HCPs who provide answers to those questions (the missing data will not be counted as a denominator in proportions). Success indicators by objectives will be presented for HCPs.

Milestones

Milestone	Planned Date
Start of data collection	01 June 2025
End of data collection	15 October 2025
Registration in the HMA-EMA Catalogues of RWD Studies	25 May 2025
Final study report	30 December 2025

5. AMENDMENTS AND UPDATES

None

6. MILESTONES

Milestone	Planned Date
Start of data collection	01 June 2025
End of data collection	15 October 2025
Registration in the HMA-EMA Catalogues of RWD Studies	25 May 2025
Final study report	30 December 2025

7. RATIONALE AND BACKGROUND

Eliquis® (apixaban) is a reversible and highly potent inhibitor of factor Xa with rapid absorption, a 12-hour half-life, and 25% renal excretion. It has been co-developed by Bristol-Myers Squibb and Pfizer as an anticoagulant and antithrombotic agent in non-valvular atrial fibrillation (NVAF) and venous thromboembolic events (VTE). Apixaban was approved in 2014 by the Saudi Food and Drug Authority (SFDA) and the three approved indications include[1]:

- Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation (NVAF) with one or more risk factors, such as prior stroke or transient ischemic attack (TIA); age ≥ 75 years; hypertension; diabetes mellitus; symptomatic heart failure (New York Heart Association [NYHA] Class ≥ II)
- Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults
- Prevention of venous thromboembolic events (VTE) in adult patients who have undergone elective hip or knee replacement surgery

NVAF is a cardiac arrhythmia, which is a significant etiological risk factor for cardiogenic thromboembolism resulting in embolic ischemic stroke or other systemic embolism. These sequelae are associated with high patient morbidity and mortality, and substantial healthcare burden; therefore, the prevention of thromboembolism in NVAF cases is of significant importance.

In patients with atrial fibrillation (AF) who were not candidates for vitamin K antagonists (eg, warfarin), Eliquis® has been shown to reduce the rate of stroke or systemic embolism by 55% compared with aspirin, without increasing the risk of major bleeding.[2] While the global prevalence of AF is estimated to be 0.1-4% in community-based studies,[3, 4] the prevalence of AF among the Saudi Arabia population is still unclear. However, the burden of illness associated with AF in Saudi Arabia is considered high.[5] Additionally, the findings of a registry study among Saudi patients with AF revealed a higher use of oral anticoagulants compared with global data [6] yet significant safety associated knowledge gaps exist in Saudi patients with AF taking oral anticoagulants.[7] Furthermore, a recent observational study in Saudi Arabia reported medication errors related with the use of direct oral anticoagulant in clinical practice, and highlighted the need for risk prevention and reduction strategies to enhance safety associated with anticoagulant use.[1]

Venous Thromboembolism (VTE) is a condition with different manifestations: Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE). Any episode of DVT significantly increases the risk of further VTE and may lead to a PE or post-thrombotic syndrome that includes venous ulceration, debilitating pain, and intractable oedema. It is estimated that approximately 25,000 people are affected in the

Kingdom of Saudi Arabia (KSA) annually.[8] PE is the most serious complication of DVT, as the embolized blood clot lodges in the lung vasculature and obstructs blood flow through the lungs, leading to cardiopulmonary compromise, which has a high risk of death.

The safety of apixaban has been investigated in 4 Phase III clinical studies including more than 15,000 patients: more than 11,000 patients in NVAF studies and more than 4,000 patients in the VTE treatment (VTEt) studies, for an average total exposure of 1.7 years and 221 days respectively. Common adverse reactions were hemorrhage, contusion, epistaxis, and hematoma.

- In the NVAF studies, the overall incidence of adverse reactions related to bleeding with apixaban was 24.3% in the apixaban vs warfarin study and 9.6% in the apixaban vs acetylsalicylic acid study.
- In the apixaban vs warfarin study the incidence of ISTH (International Society on Thrombosis and Hemostasis) major gastrointestinal bleeds (including upper GI, lower GI, and rectal bleeding) with apixaban was 0.76%/year. The incidence of ISTH major intraocular bleeding with apixaban was 0.18%/year.
- In the VTEt studies, the overall incidence of adverse reactions related to bleeding with apixaban was 15.6% in the apixaban vs enoxaparin/warfarin study and 13.3% in the apixaban vs placebo study.

As directed by the SFDA, the Marketing Authorization Holder (MAH) agreed to provide educational materials as part of additional risk minimization measures (aRMMs), targeting all healthcare professionals (HCPs) who are expected to prescribe/use Eliquis® for any of the approved indications. The educational materials include risk minimization (RM) tools which comprise a Prescriber Guide and a Patient Alert Card. These originally applied only for the indication of Prevention of stroke and systemic embolism in adult patients with NVAF, with one or more risk factors.

An updated Prescriber Guide and Patient Alert Card were subsequently also required for the two other Eliquis® indications, Prevention of VTE events in adult patients who have undergone elective hip or knee replacement surgery, and Treatment of DVT and PE and prevention of recurrent DVT and PE in adults. The RM tools are designed for use in all three indications for Eliquis® with an aim to increase awareness of the important identified risk of bleeding during treatment with Eliquis® and provide guidance on how to manage that risk. A description of the key safety messages of each RM tool is as follows:

The Prescriber Guide (*see* Annex 3.1)

- Details of populations potentially at higher risk of bleeding
- Recommended dosages and guidance on the posology for different indications
- Recommendations for dose adjustment in at risk populations, including renal or hepatic impairment patients
- Guidance regarding switching from, or to, Eliquis® treatment
- Guidance regarding surgery or invasive procedures, and temporary discontinuation
- Management of overdose situations and hemorrhage
- The use of coagulation tests and their interpretation
- That all patients should be provided with a Patient Alert Card, and be counseled about its key safety messages

The Patient Alert Card (*see* Annex 3.2)

- Signs and symptoms of bleeding and when to seek attention from an HCP
- Importance of treatment compliance
- Necessity to carry the Patient Alert Card with them at all times
- The need to inform HCPs that they are taking Eliquis® if they need to have any surgery or invasive procedure

This study, therefore, is intended to assess whether implementation of the RM tools has led to effective understanding and reinforcement of key safety messages outlined in the Summary of Product Characteristics (SmPC) and Package Leaflet. Pfizer has committed to do this using a survey-based approach. The survey will be comprised of questions aimed at assessing the success of RM tool implementation:

- Utilization of the RM tools
- Knowledge and comprehension of the RM tool key safety messages
- Self-declared behaviors (including hypothetical risk-based scenarios).

This non-interventional study is designated as a post-authorization safety study (PASS) and is a commitment to SFDA.

8. RESEARCH QUESTION AND OBJECTIVES

The overall objective of this study is to evaluate the effectiveness of the additional RM tools for Eliquis®, in terms of their key safety messages, by conducting a survey in the KSA where the RM tools have been implemented.

8.1. Objectives

8.1.1. Primary Objective

The primary objective of this study will be to:

1. Assess HCPs' knowledge of RM tools (ie, Prescriber Guide and Patient Alert Card) with regards to the bleeding risk associated with Eliquis® treatment.

8.1.2. Secondary Objectives

The secondary objectives of this study are to:

1. Assess utilization of Eliquis® RM tools (ie, Prescriber Guide and Patient Alert Card) by HCPs.
2. Assess HCPs' self- declared behavior with regards to the specific guidance related to the prevention and management of bleeding associated with Eliquis® treatment.

9. RESEARCH METHODS

This section presents methods that will be employed to evaluate the effectiveness of the RM tools in KSA.

9.1. Study Design

This will be a cross-sectional non-interventional PASS to evaluate the effectiveness of RM tools for Eliquis® in the KSA. The study objectives will be accomplished by means of a cross-sectional survey among HCPs who prescribe and/or dispense Eliquis® in the KSA. Data will be collected during the data collection period of approximately 4-6 months. The study aims to obtain completed surveys from 20

HCPs. The data from the HCPs will be collected using a structured self-administered questionnaire to gather evaluation metrics related to the utilization and understanding of RM tool content and messages. In addition, the survey will assess behaviors, including a set of hypothetical scenarios for HCPs. The surveys are not intended to be a mechanism for collecting adverse events (AEs), nor are they intended to result in minimizing the numbers of AEs reported.

Potential prescribers or dispenser of Eliquis® (HCPs) in the KSA will be invited to participate in this survey

9.1.1. Primary Endpoint

1. The proportion of targeted HCPs who respond to the knowledge-related questions in agreement with the RM tools for Eliquis®.

9.1.2. Secondary Endpoints

1. The proportion of targeted HCPs using Eliquis® for any approved indication who have utilized the RM tools.
2. The proportion of targeted HCPs whose responses to the practice-related questions, self-declared behavior, are in agreement with the RM tools.

9.2. Setting

9.2.1. Study Population

HCPs will be considered for participation in the study if they prescribe/dispense Eliquis® for any of the three currently approved indications, including the following subgroups:

- Cardiologists (including allied specialties, eg, angiologists, electrophysiologists)
- General practitioners/internal medicine physicians
- Other HCPs (eg, clinical pharmacists).

9.2.2. Inclusion Criteria

The HCPs must meet all of the following criteria to be eligible for inclusion in the survey:

1. Involved in the treatment of at least one patient with Eliquis® within the last 12 months
2. Willing to participate in the self-administered HCP survey by providing voluntary consent to participate in this survey conducted in the KSA

9.2.3. Exclusion Criteria

The HCPs meeting any of the following criteria will not be included in the study:

1. Employed in full time research or hospital administration (ie, non-practicing physicians)
2. Employment by Pfizer, Inc or any research organization/vendor contracted by Pfizer to administer the survey

9.2.4. Method of HCP Recruitment for Participation

At the time of protocol writing, approximately 85 HCPs were prescribing/dispensing Eliquis® in KSA and around 73 of these received the RM tools in-person and 12 by email, per Pfizer Inc.'s Distribution List. Given this relatively small pool of HCPs, an empirical sample size of 20 HCPs is proposed.

HCPs recruitment and survey will be conducted by the following process:

- HCPs who meet the eligibility criteria will be invited to participate in the survey* by email and/or phone. An email invitation will include a web link directing to a webtool named 'Decipher', where the survey questionnaire will be available. In the invitation, the survey background and objectives, and the contact information for questions will be explained to the HCPs. Instructions detailing the survey requirements will be displayed at the start of the survey.

  (**Pre-testing of the HCP structured questionnaire will be performed prior to implementation of the survey*)

- After sending the initial inviation with the web link, following steps would be followed:
  - If the HCPs agree to participate in the survey, they can access the survey and the instructions for the web questionnaire by clicking on the web link included in the email.
  - If the web questionnaire is not completed in the first attempt, HCPs will receive a reminder email and/or phone call (first reminder) 1 week after the initial invitation.
  - If the web questionnare remains incomplete, a second reminder will be sent about 2 weeks after the initial invitation.
  - If the web questionnaire still remains incomplete, a third (and final) reminder will be sent 3 weeks after the initial invitation.

An HCP will be considered unreachable if he/she has been contacted up to 3 times without an answer. For each recruited HCP, the number of times the HCP is contacted, as well as the date when he/she is contacted and the date and time when he/she completes the web questionnaire, will be recorded. HCP recruitment will be competitive, meaning the first 20 HCPs completing the web survey will be included in the final analysis.

9.3. Variables

The following screening questions will be presented to the HCPs:

- Consent to participate.
- Whether the HCP managed patient(s) treated with Eliquis® during the last 12 months period preceding the survey.
- Employment by Pfizer or any research organization/vendor contracted by Pfizer to administer the survey.

The following variables will be collected through the HCP survey.

9.3.1. HCP Demographics and Medical Background

The variables related to HCP demographics and medical background are presented in Table 1.

Table 1 : HCP Demographics and Medical Background

Variable	Operational Definition
Demographic information (age range, gender, and Location [city])	Defined as the age range and gender of the HCP and the city where the HCP practices

HCP type	Defined as physician, pharmacist or other
Medical specialty	Defined as: cardiology (including allied specialties, eg, angiology, electrophysiology), general [internal] medicine/ internist, other medical specialty
Length of professional practice as a HCP	Defined as the number of years practicing as a HCP
Practice setting	Defined as the Primary Care vs Secondary/Tertiary Care office or clinic vs hospital setting where the HCP is involved in Eliquis® treatment
Role in Eliquis® treatment	Defined as whether the HCP is involved in initiating prescribing, continuing prescribing or dispensing Eliquis®
Eliquis® indication treated	Defined as the approved Eliquis® indication where the HCP has been involved in treatment
Regular vs. occasional treatment with Eliquis®	The average number of Eliquis® patients per month treated by the HCP for any approved indication during the last 6 months. 'Regular' is defined as ≥1 patient/month and 'occasional' is defined as <1 patient/month

9.3.2. Outcomes/Endpoint Variables

The primary endpoint is:

1. The proportion of targeted HCPs who responds to the knowledge-related questions in agreement with the RM tools for Eliquis®.

The secondary endpoints are:

1. The proportion of targeted HCPs using Eliquis® for any approved indication who have utilized the RM tools.
2. The proportion of targeted HCPs whose responses to the practice-related questions, self-declared behavior, are in agreement with the RM tools.

Table 2: Operational definitions of primary and secondary endpoints

Variable	Operational definition
Knowledge and comprehension	In the context of this protocol "Knowledge" is defined as being able to recall key information related to the risk minimization of Eliquis® (identified risk of bleeding) and "Comprehension" is defined as the ability to understand the content of the RM tools. Specific questions will be used to assess these variables.
Utilization of the RM tools	"Tool Usage" is defined as the extent of use of the appropriate educational materials (Prescriber Guide and Patient Alert Card). Specific questions will be used to assess the proportions of HCPs using Eliquis® for any approved indication who have utilized the RM tools.

Self-declared behavior	"Self-declared behavior " is defined as the attitudes and actions toward the prevention and management of bleeding. Specific questions will be used to assess this variable.

The key survey effectiveness evaluation metrics per tool are shown in Table 3:

Table 3 Key effectiveness evaluation metrics

Metrics	RM Tool	
	Prescriber Guide	**Patient Alert Card**
Utilization	X	X
Knowledge and comprehension		
Early recognition of symptoms that require immediate contact with HCP	X	X
Dosage/administration in the appropriate indications	X	X
Patients at risk and contraindications	X	
Monitoring treatment	X	
Self-declared behavior		
Counsel patient on key safety messages	X	
Actions if hemorrhagic ADRs are identified	X	
Immediate notification of hemorrhagic ADRs, when appropriate, to a HCP	X	X
Distribute Patient Alert Card to patients	X	
Ability to respond correctly to hypothetical risk scenarios	X	

Table 4 shows the specific survey items that are intended to be used to evaluate the primary and secondary objectives, by measuring the aggregated responses from multiple survey participants.

Table 4 Survey Questionnaire Design

Survey Questions	Location
Questions examining HCPs demographics and medical background	Annex 1.2 - Section 2 (Q1 to Q14)
Questions designed to understand knowledge	Annex 1.2 - Section 3 (Q15 to Q23)
Questions designed to understand extent of RM tool utilization	Annex 1.2 - Section 5 (Q1-2 and Q9-Q10)
Questions designed to understand perceived utility of RM tools	Annex 1.2 - Section 5 (Q3 to Q7 and Q12 to Q14)
Questions designed to understand behaviors	Annex 1.2 - Section 4 (Case study 1 Q1 to Q3; Case study 2 Q1 and Q2; Case study 3 Q1 to Q3) Section 5 (Q8 and Q11)

9.4. Data Sources

This study involves primary data collection. A web-based, cross-sectional, structured self-administered questionnaire will be used to collect survey data from the HCPs. The questionnaires will have a disclaimer and consent at the beginning. They are designed to collect information on the eligibility and demographics of the HCPs. Depending on the answers to the screening questions, survey participation could either be terminated or continued. If ineligible, the respondent is immediately notified with a "thank you" message that survey participation has ended. If eligible, the respondent is allowed to continue survey participation.

9.4.1. Questionnaire description

The questionnaire will be comprised of closed-ended questions or statements with multiple response choices (ie, questions or statements asking the HCPs to choose from a defined list of responses). Additionally, the questionnaire will include some sections based on hypothetical, risk-based scenarios (specifically designed for each indication). The language of questionnaire will be English.

The questionnaire is designed to be nondirecting, to avoid inducement of social desirability bias, and without any self-evident answers. Also, to avoid information bias, the web questionnaires will be programmed in such a way that the participants cannot go back to the previous questions.

The questionnaire will collect data on HCP characteristics and their responses to the risk knowledge questions. The data collected from the surveys will be used to inform the evaluation of the effectiveness of the RM tools.

9.4.2. Questionnaire pilot testing

The objective of each questionnaire will be tested among 3 HCPs to make sure the right language and medical terms are used, and also to check the understandability of the language. In case any change needed, those 3 questionnaires will be excluded from the analysis.

9.4.3. Time to completion

HCP questionnaire is estimated to take 20 to 25 minutes to complete.

9.5. Study Size

At the time of protocol writing, approximately 85 HCPs were prescribing/dispensing Eliquis® in KSA, and around 73 of these received the RM tools in-person and 12 by email, per Pfizer Inc.'s Distribution List. Given this relatively small pool of HCPs, an empirical sample size of 20 HCPs is proposed. It is important to note that the final survey sample size will depend on HCPs' willingness to participate in the survey. All completed surveys received during the data collection period of approximately 4-6 months will be included in the final study report.

A threshold of 80% correct responses per risk question will be used to define the success of the program. However, this criterion will not be used for formal statistical testing. The selection of this threshold for success was regarded as being subjective and not based on prior knowledge, experience, or established scientific criteria.

9.6. Data Management

All the online survey data will be collected in a webtool (Decipher) via single data entry, directly entered by the enrolled HCP. Once all the HCPs complete the survey, data from the webtool (Decipher) will be extracted and stored on Redacte secure server. The data will be locked once inputs from all the HCPs are validated (see Section 9.8 for details on validation).

At the end of the study, the extracted HCP data from Decipher will be securely transferred to the Pfizer. The data collected will not contain any names or other personal information that can be used for direct identification of the individuals. The data collection period will last for approximately 4-6 months and the data related to the variables listed in Section 9.3 will be collected from the HCP questionnaire. The HCP questionnaire will be a separate stand alone document included in Annex 1.2, *see* Section 16.1.

9.6.1. Case Report Forms (CRFs)/Data Collection Tools (DCTs)/Electronic Data Record

As used in this protocol, the term DCTs should be understood to refer to either a paper form or an electronic data record or both, depending on the data collection method used in this study.

A completed DCT is required for each included participant. The completed original DCTs are the sole property of Pfizer and should not be made available in any form to third parties, except for authorized representatives of Pfizer or appropriate regulatory authorities, without written permission from Pfizer. Redac shall ensure that the DCTs are securely stored at the Redac Decipher system in encrypted electronic form and will be password protected or secured in a locked room *to* prevent access by unauthorized third parties.

Redac has ultimate responsibility for the collection and reporting of all data entered on the DCTs as required and ensuring that they are accurate, authentic/original, attributable, complete, consistent, legible, timely (contemporaneous), enduring, and available when required. The DCT serves as the source document. Any corrections to entries made in the DCT must be dated, initialed, and explained (if necessary) and should not obscure the original entry.

9.6.2. Record Retention

To enable evaluations and/or inspections/audits from regulatory authorities or Pfizer, Redac agrees to keep all study-related records. The records should be retained by Redac according to local regulations or for the period specified by the Pfizer, whichever is longer. Redac must ensure that the records continue to be stored securely for so long as they are retained.

If Redac becomes unable for any reason to continue to retain study records for the required period, Pfizer should be prospectively notified. The study records must be transferred to a designee acceptable to Pfizer.

Study records must be kept for a minimum of 15 years after completion or discontinuation of the study, unless Redac and Pfizer have expressly agreed to a different period of retention via a separate written agreement. Record must be retained for longer than 15 years if required by applicable local regulations.

Redac must obtain Pfizer's written permission before disposing of any records, even if retention requirements have been met.

9.7. Data Analysis

General statistical considerations

The statistical analysis will be conducted using the SAS® software V9.4 (SAS Institute North Carolina, USA), or R version 3.6 or higher on Windows™. All the analyses will be descriptive. Continuous variables will be described by their number (of valid cases, of missing values), mean, standard deviation, and median, Q1, Q3, minimum and maximum. Categorical variables will be described as the total number and relative percentage per category.

In case of multiple-choice questions, the frequency of each option provided by the HCPs will be reported as the total number and relative percentage per category. Different combinations of the answers provided (if any) will not be considered.

Wilson CIs of 95% will be evaluated on the overall result.

The participation rate will be analyzsed overall for HCPs.

The proportion of correct and desirable answers to the selected questions asked in the questionnaire will be expressed for HCPs who provide answers to those questions (the missing data will not be counted as a denominator in proportions). Success indicators by objectives will be presented for HCPs.

9.7.1. Primary analysis

The general statistical considerations described above will be applied to quantitative and qualitative variables. The number of missing data will be indicated. Missing values are expected to be few and distributed at random. Since there is no applicable method unanimously accepted, there will be no replacement or imputation of missing data.[9] Confidence interval of 95% will be evaluated for endpoint variables.

For each question associated with an outcome included in the objectives, a criterion will be applied to separate participants with the correct and desirable answers (or at least one correct and desirable answer as a response if the corresponding question allows multiple answers/true-false or is an open-ended question). These proportions of correct and desirable answers to each question will be expressed for HCPs who answer that question. Analysis for the survey will be performed for HCPs for the endpoints described below:

Primary endpoints

- HCPs' knowledge of RM tools (ie, Prescriber Guide and Patient Alert Card) with regards to the bleeding risk associated with Eliquis® treatment, will be assessed by the proportion of targeted HCPs' who respond to the knowledge-related questions in agreement with the RM tools for Eliquis®

Secondary endpoints

- Utilization of Eliquis® RM tools (ie, Prescriber Guide and Patient Alert Card) by HCPs will be assessed by the proportion of targeted HCPs using Eliquis® for any approved indication who have utilized the RM tools**.**
- HCPs' self-declared behavior with regards to the specific guidance related to the prevention and management of bleeding associated with Eliquis® treatment will be assessed by the proportion of targeted HCPs whose responses to the practice-related questions, self-declared behavior are in agreement with the RM tools**.**

In the survey, the proportion of correct or desirable responses across all questions related to the evaluation of the primary objectives of the surveys will be considered to assess the success.

- The questions considered as complementary will not be included in the assessment of success. The details of the assessment of the success for each survey and each objective is described in Annex 1.3, *see* Section 16.2.
- Success will be defined for each primary objective based on the number of sub-questions related to that objective being completed with correct/desirable responses. An HCP will be successful for knowledge and comprehension, if at least 80% of the related questions, including sub-questions, are completed with correct responses. An HCP will be successful in each of the secondary objectives if 80% of the related questions, including sub-questions, will be completed with desirable responses.
- A threshold of 80% successful HCPs on the primary outcome would be considered appropriate for assessing the effectiveness of an RM tools.
- It should be noted that the selection of this threshold for success is subjective and not based on *a priori* knowledge, experience, or established scientific criteria in the education or risk communication or evaluation literature. If additional information from published literature becomes available at the time of reporting, then the results will be discussed in the context of this new information.

Description of characteristics of HCPs with desirable/undesirable responses

The charactertistics of HCPs with desirable and undesirable responses to questions related to each outcome will be described using all available and relevant participant information collected in the survey (ie, region, HCP profession, gender, age range, duration of practice, type of setting, years of professional experience and experience with Eliquis®).

Detailed methodology for summary and statistical analyses of data collected in this study will be documented in a statistical analysis plan (SAP), which will be dated, filed, and maintained by the Pfizer. The SAP may modify the plans outlined in the protocol; any major modifications of primary endpoint definitions or their analyses would be reflected in a protocol amendment.

9.7.2. Analysis of participation rate

9.7.2.1. HCP survey

The following different cases will be distinguished:

- HCPs who do not participate (R): HCPs who do not respond or that explicitly indicate their refusal to participate.
- HCPs with partially answered questionnaires (P): HCPs click on the link provided in the invitation email, and who begin answering the questionnaire but never submit it.
- Failed screening (F): HCPs who will not be eligible for the survey (HCPs who will not meet inclusion criteria and/or who will meet any of the exclusion criteria).
- HCPs with completed questionnaire (C): HCPs who complete the entire questionnaire and submit it.
- Contacted HCPs: HCPs who are contacted by phone or who receive a web link to the online survey via email = C+P+R+F.
- HCPs who agree to participate: HCPs willing to participate in the survey (eg, by clicking on the link provided in the invitation email) = P+C.

The HCPs participation in the survey will be examined as follows:[10]

- Response rate $= \frac{C}{C+P+R}$
- Refusal rate $= \frac{R}{C+P+R}$

For HCPs, R, P, F, C and response and refusal rates criteria will be presented overall.

9.8. Quality Control

All surveys are programmed internally using Redac Decipher system, a secure online data collection software. Redac guarantees senior-level programming support on all research engagements, with programmers who have been trained using a stringent quality control process to ensure that the surveys are programmed error-free. Redac utilizes a rigorous quality assurance process which includes the following:

- Programmer and researcher manual testing: Manual testing process which includes several members of the research and programming team (Operations) testing each survey path thoroughly to ensure accuracy in both the text and all survey logic (skip and jump patterns). Each survey is tested on stimulator associated with the web browsers.
- Random Data Generation (RDG) and Data Check Edits (DCE): Once testing is completed by both the Redac operations and research teams, a member of the operations team runs a set of randomly generated data (“dummy” data) to fill all possible paths and quotas, then writes a programmatic check designed to test the validity of the survey. Each question is tested for the correct number and coding of responses, that respondents answering the questions meet the base criteria as well as duplicate any calculated or algorithmic variables and compared for accuracy. An independent member of the operations team then writes the DCE. The data are also run through the DCE one again with soft launch data, full field data (data from the day after full fielding has begun) and the final data set.

- Soft launching: Once the DCE is approved, Redac begins fielding with a limited amount of sample designed to recruit 10% of the total quota. The soft launch data is then thoroughly checked utilizing the DCE to ensure programming accuracy.
- In-field data checks: A core member of the Redac research team monitors the data at regular intervals (eg, 10%, 25%, 50%, 75% of data collection). The data are examined for the following, and considered together to identify and exclude respondents for whom the data are suspected to be of poor quality:
    - Length of survey – survey length is estimated prior to fielding; any surveys completed substantially below a lower threshold are flagged with the help of hidden variables.
    - Quality control questions – each survey includes a few questions for the sole purpose of being a quality control check (eg, "For quality control purposes, please select No" with response options of "Yes, No, Maybe"). These questions help to evaluate a respondent's level of attention to the survey.

9.9. Strengths and Limitations of the Research Methods

9.9.1. Strengths

1. Web-based surveys

Web-based surveys have been selected as the preferred research approach because:

- The HCP survey includes behavioral scenario-based questions that might be difficult to implement using other approaches.
- Web-based surveys can be answered at the participant's convenience so that an interview does not need arranging – this can increase a participant's motivation to do the survey (improving response rates), thus resulting in more consistent completion of surveys.
- Web-based surveys are programmed to ask standardized questions and should elicit more consistent and reliable results than questions asked by telephone interviewers.[11, 12]
- Web-based techniques allow for a degree of interactivity to be introduced into the survey (eg, logic to ask follow-on questions or not ask irrelevant questions), which strengthen the validity of the behavioral scenarios.

2. Questionnaire design and testing

- The web questionnaires include general questions followed by specific ones. They include both open and closed questions. As the HCPs may understand the right answer in subsequent questions, it will not be possible to go back in the questionnaire and edit answers in former questions.
- The questionnaires will be tested for their clarity. It will also be checked whether there are questions which would suggest a specific answer for any reason, for example social desirability.

3. Experience in drug safety and the evaluation of risk minimization measures

The study will be conducted by an experienced team specialized in the design and conduct of such surveys. It follows Redac SOPs, as well as the methodological guidelines from SFDA Guideline on Good Pharmacovigilance Practices (GVP) and Guidelines for Good Pharmacoepidemiology Practices (GPP).

4. Quality control and compliance

Quality controls are implemented on a regular basis by Redac team.

9.9.2. Limitations

1. Bias

Selection bias

a. HCPs survey

The potential for selection bias of HCPs participating in a survey is an inherent limitation to any study based on volunteer participation. For instance, it is possible that HCPs willing to participate in the study will have the highest awareness of risks associated with use of Eliquis®.

Non-response bias may also be introduced into the study if targeted HCPs have activated filters in their mailbox that block spam and unsolicited emails. If a very strict degree of message filtering is set, they may not even see the invitation to participate in the survey. Having multiple email addresses could also be a critical situation. If the one used is not the primary address or if the HCPs do not check their emails frequently, they will not receive the invitation during the recruitment period. Some HCPs who are sent a letter may not receive it. This is one of the reasons why the HCPs will also be contacted by phone.

Penetration and use of Eliquis® may be low for an indication compared to other anticoagulants eg, warfarin, potentially resulting in limited recruitment and potential sampling bias.

Information bias

Recall bias may lead to an underestimation of the HCP recalling having received aRMMs. To mitigate the risk of recall bias for HCPs, they will be recruited in the survey if they have provided prescribed or dispensed Eliquis® in the past 12 months.
Moreover, web surveys may promote social desirability bias, which refers to the tendency of HCP to give socially desirable/expected responses instead of choosing those reflecting their current knowledge or behavior, eg, physicians can copy-paste information gathered online instead of giving their own opinions.[11] Social desirability can affect the validity of survey research findings, but the use of prepopulated items in the questionnaire could/tends to reduce this bias. The access to the web questionnaire interface will be strictly limited to the invited participants, with the possibility to participate only once, and a traceability system will be in place. Thus, stakeholder bias (multiple answers of people who have a personal interest in survey results and/or who incite peers to fulfill the survey in order to influence the results) or unverified respondents (when it is not possible to verify who responds) are not applicable.

2. Generalization of the survey results to the overall target population

In such surveys, the generalization and external validity of the results is restricted to HCPs who can be reached and are willing (and able) to answer a questionnaire online. These HCPs may not be fully representative of the whole target population.[11]

The study report will discuss the results in the light of the limitations described above including variability and uncertainty of the data and methods.

9.10. Other Aspects

Not applicable.

10. PROTECTION OF HUMAN PARTICIPANTS

10.1. Study Participant Information

All parties will comply with all applicable laws, including laws regarding the implementation of organizational and technical measures to ensure protection of participant personal data. Such measures will include omitting HCP names or other directly identifiable data in any reports, publications, or other disclosures, except where required by applicable laws.

HCP personal data will be stored at Redac Decipher system in encrypted electronic form and will be password protected to ensure that only authorized study staff have access. Redac will implement appropriate technical and organizational measures to ensure that the personal data can be recovered in the event of disaster. In the event of a potential personal data breach, Redac shall be responsible for determining whether a personal data breach has in fact occurred and, if so, providing breach notifications as required by law.

To protect the rights and freedoms of natural persons with regard to the processing of personal data, when study data are compiled for transfer to Pfizer and other authorized parties, any HCP names will be removed and will be replaced by a single, specific, numerical code. All other identifiable data transferred to Pfizer or other authorized parties will be identified by this single, study-specific code. In case of data transfer, Pfizer will maintain high standards of confidentiality and protection of HCPs' personal data consistent with the master research service agreement and applicable privacy laws.

10.2. HCP Consent

Participants need to go to the survey website in order to complete the survey. Consent is implied by these actions. Additionally, at the beginning of the survey, the respondent is asked if he/she agrees to take part in the survey. If yes, the respondent continues with the survey questions. If no, then the survey is terminated.

10.3. Participant Withdrawal

Not applicable.

10.4. Institutional Review Board (IRB)/ Ethics Committee (EC)

IRB/EC is not required.

10.5. Ethical Conduct of the Study

The study will be conducted in accordance with legal and regulatory requirements, as well as with scientific purpose, value, and rigor and follow generally accepted research practices described in Guideline for Good Pharmacovigilance Practice (GVP) Version 3.1 30 January 2023 - Drug Sector, Saudi Food and Drug Authority (SFDA) and Guidelines for Good Pharmacoepidemiology Practices (GPP) issued by the International Society for Pharmacoepidemiology (ISPE).

11. MANAGEMENT AND REPORTING OF ADVERSE EVENTS/ADVERSE REACTIONS

This study does not involve treating healthcare professionals collecting data on individual patients and the online questionnaire/survey used in this study does not intend to identify product safety information. The online questionnaire/survey for this study will be completed online via a secure website. The online questionnaire/survey does not provide a free text field where study participants could specify information that may constitute product safety information. Further, routine communication with study participants via email or phone with Redac is not expected during the conduct of the study. However, it is possible that a study participant may volunteer product safety information to Redac while in

conversation about the online questionnaire/survey for any other reason (eg, seeking information about the purpose of the study); this information must be reported as described below.

The following must be reported on the "Non-Interventional Study Adverse Event Report Form For Protocols Without Stipulated Active Collection of Adverse Events" (hereinafter referred to as the NIS AEM Report Form): safety events (serious and non-serious adverse events, when associated with the use of a Pfizer product), and scenarios involving exposure during breastfeeding, medication error, overdose, misuse, extravasation, lack of efficacy, occupational exposure and off-label use **(all reportable, regardless of whether associated with a safety event)**, when associated with the use of a Pfizer product.

Exposure during pregnancy (EDP) reports are reportable using the NIS AEM Report Form and the EDP Supplemental Form, irrespective of the presence of an associated safety event.

EDP are not reportable for the following scenarios:

- A Pfizer product approved to terminate pregnancy is administered to terminate pregnancy and termination is successful;
- A Pfizer product approved to evacuate uterine contents is administered to evacuate uterine contents following an intrauterine death;
- A Pfizer product approved to induce labor is correctly administered to induce labor.

If the mother or the fetus experiences a safety event during administration of such drugs, the safety event must be reported without the event EDP reported.

For EDP in studies exclusively of pregnant people, data on the exposure to the Pfizer product during pregnancy, are not reportable. However, if the mother or the fetus experiences any adverse events (either serious or non-serious), the event must be reported without the event EDP.

If a study participant volunteers any of the above product safety information, Redac team must complete the NIS AEM Report Form and submit to Pfizer DSU within 24 hours of becoming aware of the safety event. Included in the completion of the NIS AEM Report Form is the study participant's contact information; if contact information is available or is provided by the study participant and consent allows this; complete contact information should be obtained so that once the NIS AEM Report Form is sent to Pfizer, the NIS AEM Report Form can be assessed and processed according to Pfizer's standard operating procedures, including requests for follow-up to the study participant.

Redac team who will serve to be available to study participants to answer questions during study participant completion of the data collection tool, and address any query from participants about the study must complete the following Pfizer training requirements:

- *"Your Reporting Responsibilities (YRR) with Supplemental Topics".*

This training must be completed by Redac team prior to the start of data collection. The training includes a "Confirmation of Training Statement" (for signature by the trainee) as a record of completion of the training, which must be kept in a retrievable format. The study vendor will also provide copies of all signed training statements to Pfizer.

12. PLANS FOR DISSEMINATING AND COMMUNICATING STUDY RESULTS

A final report describing the survey objectives, detailed methods, results, discussion, and conclusions will be developed at the end of the survey for submission to SFDA within the timeframe specified in 'Section 6 Milestones.'

In the event of any prohibition or restriction imposed (eg, clinical hold) by an applicable Competent Authority in any area of the world, or if Redac is aware of any new information which might influence the evaluation of the benefits and risks of a Pfizer product, Pfizer should be informed immediately.

In addition, Redac will inform Pfizer immediately of any serious breaches of this NI study protocol that Redac becomes aware of.

13. REFERENCES

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14. LIST OF TABLES

15. LIST OF FIGURES

None

16. ANNEX 1. LIST OF STAND-ALONE DOCUMENTS

Number	Document Reference Number	Date	Title
1.1	Section 4	16 May 2025	Abstract
1.2		03 December 2024	HCP Questionnaire
1.3		03 December 2024	Assessment of success

16.1. Annex 1.2 HCP Survey questionnaire

SURVEY LEGEND

- **[[[PROGRAMMER]]]** is used to indicate directions to the programmer and is set in bold, red, uppercase letters between square brackets.
- [[[**START OF HCP SURVEY**]]] and **[END OF HCP SURVEY]** are used to indicate to the programmer the type of survey administration and the beginning and end of the survey.
- **[TERMINATE]** is displayed next to responses that should cause the survey to end. The following termination language will be programmed into the survey or read by the interviewer.

  Thank you for your time today. Based on your answer, you are not eligible to take part in this survey.

SURVEY LEGEND

- **[GO TO Qx]** (skip logic) is inserted after a response to indicate to the programmer that the survey should skip to the indicated question (for example, **[GO TO Q17]** skips to question 17). If no skip logic is indicated the survey continues to the next question in the sequence.

- **[FREE TEXT]** indicates to the programmer that one line should be provided for data entry.

[[[START OF HCP SURVEY]]]

SECTION 1: INTRODUCTION

[[[Start of Section 1]]]

Disclaimer

This research is sponsored by Pfizer Inc. The aim of this research is to assess knowledge about the key safety messages as referred to in the risk management tools that includes the Prescriber Guide and Patient Alert Card for Eliquis®. Taking part in this survey is voluntary; you are under no obligation to participate. You may refuse to take the survey or stop taking the survey at any time.

How We Use Your Information

Your answers to the survey questions will be combined with those from other respondents and reported in anonymous form to Sponsor "Pfizer Inc. or any Pfizer affiliate" and Saudi FDA (SFDA). Your name will not be used in any report. If you are eligible to take the questionnaire, kindly complete all the questionnaire.

How We Protect Your Privacy

We respect that the privacy of your personal information is important to you. All the information you provide will be kept strictly confidential. You will not be contacted for marketing purposes based on your personal information or your answers to the survey. Your answers will be kept strictly confidential. Your privacy will be protected; however, research survey records may be inspected by the SFDA or local country Ethics Committees. Your choice to allow Pfizer to use your information is entirely voluntary but necessary to take part in this survey.

How to Learn More about the Online Survey

If you have questions about or problems with the survey, please contact the Help Desk Youssef M Talaat at: youssefm.talaat@iqvia.com your questions will be answered.

Screening questions for the HCPs:

Please provide a response to all questions and statements.

1. Do you agree to take part in this survey? [[[Single punch]]]

   ☐ Yes

   ☐ No **[TERMINATE]**

2. Have you prescribed or dispensed Eliquis® (Apixaban) within the past 12 months? [[[Single punch]]]

   ☐ Yes

   ☐ No, **[TERMINATE]** In case of Terminate this sentence will display : *Thank you for your interest in participating, but unfortunately you cannot proceed with the survey*

3. Are you currently employed by Pfizer, or any research organization//vendor contracted by Pfizer to administer the survey? [[[Single punch]]]

   ☐ Yes, **[TERMINATE]** In case of Terminate this sentence will display: *Thank you for your interest in participating, but unfortunately you cannot proceed with the survey*

   ☐ No

[[[End of Section 1]]]

SECTION 2: YOU AND YOUR HEALTHCARE PRACTICE

[[[Start of Section 2]]]

In the next section, please tell us a little about yourself and your professional involvement in Eliquis®.

1. Please indicate your gender [[[Radio button option- Single punch]]]

   ☐ Male

   ☐ Female

   ☐ I do not wish to answer

2. Please indicate your age range [[[Radio button option- Single punch]]]

   ☐ <30 years

   ☐ 30-39 years

   ☐ 49 years

   ☐ 50-59 years

   ☐ ≥60 years

3. Which location (city) of KSA are you associated as an HCP where you prescribe or dispense Eliquis®? [[[Radio button option- Single punch]]]

☐

☐

☐

4. What is your occupation? [[[Radio button option- Single punch]]]

☐ Physician [A]

☐ Other HCPs, eg, Pharmacist [B]

☐ If 'Other,' please specify:
[[[Free text field]]]

[[[LOGIC FLOW: If answer is B is selected then go to Question 6]]]

5. What is your main specialty area? [[[Radio button option- Single punch]]]

☐ Cardiology or allied specialty (eg, electrophysiology, angiology)

☐ General (internal) medicine/internist

☐ Other medical specialty

☐ If 'Other,' please specify:
[[[Free text field]]]

6. How long have you been in professional practice as a healthcare professional (HCP)? [[[Radio button option- Single punch]]]

- ☐ Less than 5 years
- ☐ 5 to 10 years
- ☐ 11 to 15 years
- ☐ 16 to 20 years
- ☐ 21 to 25 years
- ☐ More than 25 years

7. In what type of treatment center do you primarily see patients whose Eliquis® treatment you are involved in? [[[Radio button option- Single punch]]]

- ☐ University teaching hospital
- ☐ Community hospital
- ☐ Other secondary care center (eg, clinic/office)
- ☐ Primary care center (general practice)
- ☐ Tertiary care center
- ☐ Community pharmacy
- ☐ Other
- ☐ If 'Other,' please specify:
  [[[Free text field]]]

8. What role(s) have you performed during Eliquis® treatment? (Please select all that apply) [[[Radio button option- Multi punch]]]

- ☐ Initiating Eliquis® prescribing [A]
- ☐ Continuing/ongoing Eliquis® prescribing [B]
- ☐ Dispensing/administering Eliquis® [C]

[[[LOGIC FLOW:

- If Answer includes A or B, go to Question 10.
- If Answer C is selected (ie, the respondent is a non-prescriber), go to Question 9, and exclude the questions- Q15-17 from Section 3 of the survey,; and all case study questions from Section 4]]]

9. Since you do not prescribe Eliquis®, who is the main prescriber of Eliquis® for patients whose treatment you are involved in? [[[Radio button option- Single punch]]]

- ☐ General practice/primary care
- ☐ General (internal) medicine/internist
- ☐ Cardiology or allied specialty (eg, electrophysiology, angiology)
- ☐ Geriatrics/care of the elderly
- ☐ Hematology
- ☐ Neurology/Stroke medicine
- ☐ Surgical Specialty
- ☐ Other medical specialty
- ☐ Other, Please Specify [[[Free text field]]]

10. For which indication you prescribed or dispensed Eliquis®? [[[Radio button option- Single punch]]]

- ☐ Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation (NVAF) with one or more risk factors [A]
- ☐ Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults [B]
- ☐ Prevention of venous thromboembolic events (VTE) in adult patients who have undergone elective hip or knee replacement surgery [C]

[[[LOGIC FLOW:

- If Answer A is selected then go to Question 11a, 12a, 13a and 14
- If Answer B is selected then go to Question 11b, 12b, 13b and 14
- If Answer C is selected then go to Question 11c, 12c, 13c and 14]]]

11a. In total, how many patients have you been involved in treating with Eliquis® for the prevention of stroke and systemic embolism in adult patients with NVAF, with one or more risk factors? [[[Radio button option- Single punch]]]

- ☐ 1-5
- ☐ 6-10
- ☐ 11-20
- ☐ 21-50
- ☐ More than 50
- ☐ I don’t know/I’m not sure

b. In total, how many patients have you been involved in treating with Eliquis® for the treatment of DVT and PE, and prevention of recurrent DVT and PE in adults?
[[[Radio button option- Single punch]]]

- ☐ 1-5
- ☐ 6-10
- ☐ 11-20
- ☐ 21-50
- ☐ More than 50
- ☐ I don't know/I'm not sure

11c. In total, how many patients have you been involved in treating with Eliquis® for prevention of venous thromboembolic events (VTE) in adult patients who have undergone elective hip or knee replacement surgery?
[[[Radio button option- Single punch]]]

- ☐ 1-5
- ☐ 6-10
- ☐ 11-20
- ☐ 21-50
- ☐ More than 50
- ☐ I don't know/I'm not sure

12a. On average, how many patients per month have you been involved in treating with Eliquis® for this indication (prevention of stroke and systemic embolism in adult patients with NVAF, with one or more risk factors) during the last six months? [[[Radio button option- Single punch]]]

- ☐ Less than one patient per month
- ☐ 1-5 patients per month
- ☐ 6-10 patients per month
- ☐ More than 10 patients per month
- ☐ I don't know/I'm not sure

12b. On average, how many patients per month have you been involved in treating with Eliquis® for this indication (treatment of DVT and PE, and prevention of recurrent DVT and PE in adults) during the last six months? [[[Radio button option- Single punch]]]

- ☐ Less than one patient per month
- ☐ 1-5 patients per month
- ☐ 6-10 patients per month
- ☐ More than 10 patients per month
- ☐ I don't know/I'm not sure

12c. On average, how many patients per month have you been involved in treating with Eliquis® for this indication (prevention of venous thromboembolic events (VTE) in adult patients who have undergone elective hip or knee replacement surgery) during the last six months? [[[Radio button option- Single punch]]]

- ☐ Less than one patient per month
- ☐ 1-5 patients per month

- ☐ 6-10 patients per month
- ☐ More than 10 patients per month
- ☐ I don't know/I'm not sure

13a. When were you most recently involved in the treatment of a patient with Eliquis® for the prevention of stroke and systemic embolism in adult patients with NVAF, with one or more risk factors? [[[Radio button option- Single punch]]]

- ☐ Within the last month
- ☐ 1-3 months ago
- ☐ 4-6 months ago
- ☐ More than 6 months ago
- ☐ I'm not sure/I can't remember

13b. When were you most recently involved in the treatment of a patient with Eliquis® for the treatment of DVT and PE, and prevention of recurrent DVT and PE in adults? [[[Radio button option- Single punch]]]

- ☐ Within the last month
- ☐ 1-3 months ago
- ☐ 4-6 months ago
- ☐ More than 6 months ago
- ☐ I'm not sure/I can't remember

13c. When were you most recently involved in the treatment of a patient with Eliquis® for the prevention of venous thromboembolic events (VTE) in adult patients who have undergone elective hip or knee replacement surgery? [[[Radio button option- Single punch]]]

- ☐ Within the last month
- ☐ 1-3 months ago
- ☐ 4-6 months ago
- ☐ More than 6 months ago
- ☐ I'm not sure/I can't remember

14. Have you participated in a clinical trial for an anti-coagulation treatment in the last twelve months? [[[Radio button option- Single punch]]]

- ☐ Yes
- ☐ No

[[[End of Section 2]]]

SECTION 3: TREATING PATIENTS USING ELIQUIS®

[[[Start of Section 3]]]

15. While being treated with Eliquis®, it is important that early recognition and immediate contact with an HCP is made for signs and symptoms of what associated risk? [[[Radio button option- Single punch]]]

- ☐ Increased blood pressure
- ☐ Bleeding which does not stop on its own*
- ☐ Suppressed immunity over an extended period

☐ Neutropenia (low neutrophil count)

☐ I don't know/I'm not sure

[[[LOGIC FLOW:

- If Answer is A for Question 10 of Section 2 then go to Question 16a, then 17a and then 18
- If Answer is B for Question 10 of Section 2 then go to Question 16b, then 17b and then 18
- If Answer is C for Question 10 of Section 2 then go to Question 16c, then 17c and then 18]]]

16a When Eliquis® is used for the prevention of stroke and systemic embolism in adult patients with NVAF, what is the standard recommended dosing? [[[Radio button option- Single punch]]]

☐ 10 mg twice daily

☐ 5 mg twice daily*

☐ 2.5 mg twice daily

☐ 2.5 mg once daily

☐ I don't know/I'm not sure

16b When Eliquis® is used for the treatment and prevention of DVT and PE in adults, what is the standard recommended dosing? [[[Radio button option- Single punch]]]

☐ 10 mg twice daily for at least 3 months for treatment; and 2.5 mg twice daily following 6 months of anticoagulant treatment for prevention

☐ 10 mg twice daily for 7 days, followed by 5 mg twice daily for at least 3 months for treatment; and 2.5 mg twice daily following 6 months of anticoagulant treatment for prevention*

☐ 5 mg twice daily for 7 days, followed by 2.5 mg twice daily for at least 3 months for treatment; and 2.5 mg once daily following 6 months of anticoagulant treatment for prevention

☐ None of the above

☐ I don't know/I'm not sure

16c When Eliquis® is used for the prevention of venous thromboembolic events (VTE) in adult patients who have undergone elective hip or knee replacement surgery, what is the standard recommended dosing? [[[Radio button option- Single punch]]]

☐ 10 mg twice daily

☐ 5 mg twice daily

☐ 2.5 mg twice daily*

☐ 2.5 mg once daily

☐ I don't know/I'm not sure

17a For which type of renal impairment can Eliquis® be used at a reduced dose for the prevention of stroke and systemic embolism in adult patients with NVAF? [[[Radio button option- Single punch]]]

☐ Severe renal impairment (CrCl 15-29 mL/min)*

☐ Renal failure (CrCl < 15 mL/min)

☐ Dialysis

☐ None of the above

☐ I don't know/I'm not sure

17b For which type of renal impairment can Eliquis® be used with caution for treatment of DVT and PE, and prevention of recurrent DVT and PE in adults? [[[Radio button option- Single punch]]]

☐ Severe renal impairment (CrCl 15-29 mL/min)*

☐ Renal failure (CrCl < 15 mL/min)

☐ Dialysis

☐ None of the above

☐ I don't know/I'm not sure

17c For which type of renal impairment can Eliquis® be used with caution for prevention of venous thromboembolic events (VTE) in adult patients who have undergone elective hip or knee replacement surgery? [[[Radio button option- Single punch]]]

☐ Severe renal impairment (CrCl 15-29 mL/min)*

☐ Renal failure (CrCl < 15 mL/min)

☐ Dialysis

☐ None of the above

☐ I don't know/I'm not sure

18. Which of these groups of patients are at increased risk of bleeding complications when treated with Eliquis®? (Please select Yes, No, or I don't know/I'm not sure for each patient population)
[[[Radio buttons – 3 for each option following the caption- Single punch]]]

Patients:	Yes, at increased risk	No, not at increased risk	I don't know/I'm not sure
With severe renal impairment (CrCl 15-29 ml/min)	*		
Taking strong inhibitors of both CYP3A4 and P-gp	*		
Taking oral contraception		*	
Who have recently undergone brain, ophthalmic or spinal surgery	*		

Taking Non-steroidal anti-inflammatory drugs (NSAIDs), including acetylsalicylic acid (ASA)	*		
With recent gastrointestinal (GI) ulceration	*		
With significant dyspepsia, gastro-oesophageal reflux disease (GORD), or other upper GI disorders		*	

19. In which one of the following patient groups is the prescribing of Eliquis® not contraindicated? [[[Radio button option- Single punch]]]

- ☐ First-degree relative family history of haemorrhagic stroke*
- ☐ Current or recent gastrointestinal ulceration
- ☐ Patients with cancers at high-risk of bleeding
- ☐ Recent brain or spinal injury
- ☐ I don't know/I'm not sure

20. How should Eliquis® be taken? [[[Radio button option- Single punch]]]

- ☐ With water, and can be taken with or without food*
- ☐ With water, one hour before eating
- ☐ With water, one hour after eating
- ☐ None of the above
- ☐ I don't know/I'm not sure

21. Is routine coagulation monitoring required in patients taking Eliquis®? [[[Radio button option- Single punch]]]

- ☐ Yes, for all patients
- ☐ Yes, for high-risk patients only
- ☐ No*
- ☐ I don't know/I'm not sure

22. Is the International Normalized Ratio (INR) appropriate for measuring the anticoagulant activity of Eliquis®? [[[Radio button option]]]

- ☐ Yes
- ☐ No*
- ☐ I don't know/I'm not sure

23. What discussion, if any, do you have with your patients being treated with Eliquis® about what to do if they experience a bleeding event?
[[[Radio button option- Single punch]]]

- ☐ To immediately seek medical attention for a bleeding event which does not stop on its own*
- ☐ To seek medical attention for all bleeding events
- ☐ I do not discuss this with my patients being treated with Eliquis®

[[[End of section 3]]]

SECTION 4: PATIENT CASE STUDIES

[[[Start of Section 4]]]

In the following section, you will be presented with three case studies relevant to the treatment of patients with Eliquis®.

When answering the related questions, please consider what you would do in normal practice.

[[[START OF CASE STUDY 1]]]

[[[LOGIC FLOW:

- If Answer is A for Question 10 of Section 2 then go to Case Study 1a, then 2a and then 3a
- If Answer is B for Question 10 of Section 2 then go to Case Study 1b, then 2b and then 3b
- If Answer is C for Question 10 of Section 2 then go to Case Study 1c, then 2c and then 3c]]]

1a. CASE STUDY 1: A 67-year-old male patient with NVAF has been receiving the anticoagulant, warfarin, a Vitamin K antagonist (VKA), for the prevention of stroke and systemic embolism. Due to problems regularly monitoring his INR on warfarin, a decision has now been taken to switch him from warfarin to Eliquis®.

OR

1b. CASE STUDY 1: A 67 year-old male patient has been receiving the anticoagulant, warfarin, a Vitamin K antagonist (VKA), for prevention of recurrent DVT. Due to problems regularly monitoring his INR on warfarin, a decision has now been taken to switch him from warfarin to Eliquis®.

1. How would you manage the switch from warfarin to Eliquis®? [[[Radio button option- Single punch]]]

   ☐ Stop warfarin, and start Eliquis® immediately

   ☐ Stop warfarin, and start Eliquis® when the INR is less than 2.0*

   ☐ Stop warfarin, and start Eliquis® when the INR is less than 3.0

   ☐ I don't know/I am not sure

2. Some months after starting Eliquis®, the patient is scheduled for minor skin surgery associated with a low risk of bleeding. What course of action would you take leading up to the day of the surgery? [[[Radio button option- Single punch]]]

   ☐ Stop Eliquis® at least 2 weeks before the surgery

   ☐ Stop Eliquis® at least 48 hours before the surgery

   ☐ Stop Eliquis® at least 24 hours before the surgery*

   ☐ Continue Eliquis® at the currently prescribed dose

☐ I don't know/I am not sure

3. Following minor surgery, when is the earliest time that you would restart Eliquis®? [[[Radio button option- Single punch]]]

☐ As soon as possible provided the clinical situation allows and adequate haemostasis has been established*

☐ At least 24 hours after surgery, and once any clinically significant bleeding present has stopped

☐ At least 48 hours after surgery, and once any clinically significant bleeding present has stopped

☐ I don't know/I'm not sure

OR

1c. CASE STUDY 1: A 67 year-old male patient who has recently undergone elective hip replacement surgery is prescribed Eliquis® for the prevention of venous thromboembolic events (VTE).

1. When would you recommend that the initial Eliquis® dose be taken? [[[Radio button option- Single punch]]]

☐ Before surgery

☐ Immediately after surgery

☐ 6 to 12 hours after surgery

☐ 12 to 24 hours after surgery*

☐ None of the above

☐ I don't know/I'm not sure

2. What duration of Eliquis® treatment would you recommend in this case? [[[Radio button option- Single punch]]]

☐ 10 to 14 days

- ☐ 32 to 38 days*
- ☐ 56 to 72 days
- ☐ None of the above
- ☐ I don't know/I am not sure

3. The patient suffers a minor nosebleed while taking Eliquis®. What action would you take for the minor nosebleed? [[[Radio button option- Single punch]]]

- ☐ Symptomatic treatment and continue Eliquis® treatment as the bleeding is minor*
- ☐ Symptomatic treatment and stop Eliquis® treatment until the bleeding stops
- ☐ Symptomatic treatment and reduce Eliquis® dose until the bleeding stops
- ☐ None of the above
- ☐ I don't know/I'm not sure

[[[END OF CASE STUDY 1]]]

[[[START OF CASE STUDY 2]]]

2a. CASE STUDY 2: A 45 year-old male patient presents with new onset of NVAF, for which he is taking Eliquis® 5 mg twice daily for the prevention of stroke and systemic embolism. He is scheduled to undergo electrical cardioversion in an attempt to return him to normal sinus rhythm.

Two weeks prior to the cardioversion, the patient suffers a minor nosebleed while taking Eliquis®.

OR

2b.CASE STUDY 2: A 45 year-old male patient is taking Eliquis® as treatment for DVT and PE following recent lower limb trauma and immobilization. He recovers fully and returns to normal mobility a month after the trauma.

The patient suffers a minor nosebleed while taking Eliquis®

1. What action would you take for the minor nosebleed? [[[Radio button option- Single punch]]]

- ☐ Symptomatic treatment and continue Eliquis® treatment as the bleeding is minor*
- ☐ Symptomatic treatment and stop Eliquis® treatment until the bleeding stops
- ☐ Symptomatic treatment and reduce Eliquis® dose until the bleeding stops
- ☐ None of the above
- ☐ I don't know/I'm not sure

[[[LOGIC FLOW:

- For those who select Case Study 2a go to Question 2a
- For those who select Case Study 2b go to Question 2b]]]

2a. The minor nosebleed resolves completely. When would you stop Eliquis® before the cardioversion? [[[Radio button option- Single punch]]]

- ☐ Stop Eliquis® 5 hours before the cardioversion
- ☐ Stop Eliquis® 24 hours before the cardioversion
- ☐ Stop Eliquis® 48 hours before the cardioversion
- ☐ Eliquis® does not need to be stopped before cardioversion*
- ☐ I don't know/I am not sure

OR

2b. The minor nosebleed resolves completely. In the absence of any other risk factors for DVT and/or PE, how long would you continue Eliquis® at a treatment dose for? [[[Radio button option- Single punch]]]

- ☐ 12 months

- ☐ 6 months
- ☐ 3 months*
- ☐ None of the above

OR

2c. CASE STUDY 2: A 55 year-old female patient, who has just undergone elective knee replacement surgery, is prescribed Eliquis® for the prevention of venous thromboembolic events (VTE).

1. When would you recommend that the initial Eliquis® dose be taken? [[[Radio button option- Single punch]]]

- ☐ Before surgery
- ☐ Immediately after surgery
- ☐ 6 to 12 hours after surgery
- ☐ 12 to 24 hours after surgery*
- ☐ None of the above
- ☐ I don't know/I'm not sure

2. What duration of Eliquis® treatment would you recommend in this case? [[[Radio button option- Single punch]]]

- ☐ 10 to 14 days*
- ☐ 32 to 38 days
- ☐ 56 to 72 days
- ☐ None of the above
- ☐ I don't know/I am not sure

[[[END OF CASE STUDY 2]]]

[[[START OF CASE STUDY 3]]]

3a. CASE STUDY 3: A 73 year-old female patient with NVAF, taking Eliquis® for the prevention of stroke and systemic embolism, presents with a serious upper gastrointestinal bleed that is associated with melaena (bloody, tar-colored stool).

OR

3b. A 73 year-old female patient, taking Eliquis® for the prevention of recurrent DVT and PE, presents with a serious upper gastrointestinal bleed that is associated with melaena (bloody, tar-colored stool).

OR

3c. A 73 year-old female patient, taking Eliquis® for the prevention of venous thromboembolic events (VTE) following elective hip replacement surgery, develops a serious upper gastrointestinal bleed, associated with melaena (bloody, tar-colored stool).

1. Aside from appropriate investigation and intervention (eg, surgical), what urgent action would you take here in relation to Eliquis® therapy?
[[[Radio button option- Single punch]]]

- ☐ Continue Eliquis®, but at a lower dose
- ☐ Stop Eliquis® immediately*
- ☐ Neither of the above
- ☐ I don't know/I'm not sure

2. It becomes apparent that the patient may have taken an accidental overdose of Eliquis®. Which one of the following treatment options is unlikely to be appropriate? [[[Radio button option- Single punch]]]

- ☐ Activated charcoal at 2- and 6-hour intervals after the last dose of Eliquis®
- ☐ Surgical haemostasis

- ☐ Transfusion of fresh frozen plasma
- ☐ Hemodialysis*
- ☐ I don't know/I'm not sure

3. The patient recovers and eventually restarts Eliquis® treatment. A decision is then made to switch the patient from Eliquis® to warfarin (a VKA).
How would you switch the patient from Eliquis® to warfarin? [[[Radio button option- Single punch]]]

- ☐ Stop Eliquis®, and start warfarin after a gap of at least 2 days
- ☐ Give Eliquis® along with warfarin for at least 2 days, then stop Eliquis® once the INR is 2.0 or higher*
- ☐ Give Eliquis® along with warfarin for at least 2 weeks, then stop Eliquis® once the INR is 2.0 or higher
- ☐ None of the above
- ☐ I don't know/I'm not sure

[[[END OF CASE STUDY 3]]]

[[[End of Section 4]]]

SECTION 5: UTILIZATION OF RM TOOLS

[[[Start of Section 5]]]

1. Have you read the Eliquis® Prescriber Guide? [[[Radio button option- Single punch]]]

- ☐ I have read part of or the entire guide more than once [A]
- ☐ I have read the entire guide once [B]

☐ I have read part of the guide once [C]

☐ No, I have not read the guide [D]

☐ I cannot remember [E]

2. Do you use the Prescriber Guide to assist you in discussing Eliquis® with the patient? [[[Radio button option- Single punch]]]

☐ Yes, at all patient visits [A]

☐ Yes, at most patient visits [B]

☐ Yes, at all new patient visits [C]

☐ Yes, at most new patient visits [D]

☐ Yes, occasionally [E]

☐ No, I do not use the Prescriber Guide for discussing Eliquis® with patients [F]

☐ I can't remember [G]

3. Have you found the Prescriber Guide useful? [[[Radio button option- Single punch]]]

☐ Yes, it has been very useful [A]

☐ Yes, it has been quite useful [B]

☐ No, I have not found it useful [C]

[[[LOGIC FLOW: If C is selected, go to Question 4; if A or B is selected go to Question 5]]]

4. Why have you not found the Prescriber Guide very useful? (Please select all that apply) [[[Radio button option- Multi punch]]]

- ☐ Inadequate/not enough information
- ☐ Too detailed/complicated
- ☐ Information is unclear/not easily understood
- ☐ I am already sufficiently aware of the risks
- ☐ Information is not relevant
- ☐ None of the above

5. How useful did you find the following sections in the Eliquis® Prescriber Guide? [[[Radio buttons – one per caption- Single punch]]]

	Not useful	**Quite useful**	**Very useful**
Patient Alert Card information	o	o	o
Eliquis® therapeutic indications/ Dosing	o	o	o
Switching to and from Eliquis®	o	o	o
Populations potentially at higher risk of bleeding	o	o	o
Surgery and invasive procedures	o	o	o
Temporary discontinuation	o	o	o
Spinal/epidural anesthesia or puncture	o	o	o
Management of overdose and haemorrhage	o	o	o
Use of coagulation tests	o	o	o

6. Which sections of the Eliquis® Prescriber Guide provided you with information that you did not know before? (Please select all that apply) [[[Radio button option- Multi punch]]]

- ☐ Patient Alert Card information

- ☐ Eliquis® therapeutic indications/dosing
- ☐ Switching to and from Eliquis®
- ☐ Populations potentially at higher risk of bleeding
- ☐ Surgery and invasive procedures
- ☐ Temporary discontinuation
- ☐ Spinal/epidural anesthesia or puncture
- ☐ Management of overdose and haemorrhage
- ☐ Use of coagulation tests
- ☐ None of the above

7. Do you have any suggestions for improving the Eliquis® Prescriber Guide? [[[Radio button option- Single punch]]]

- ☐ [[[Free text field]]]

8. What proportion of the patients who you have been involved in treating with Eliquis® has been provided with a Patient Alert Card? [[[Radio button option- Single punch]]]

- ☐ None of the patients were given a Patient Alert Card [A]
- ☐ Less than 25% [B]
- ☐ 26-50% [C]
- ☐ 51-75% [D]
- ☐ More than 75% [E]

☐ All the patients were given a Patient Alert Card [F]

☐ I cannot remember/I don't know [G]

[[[LOGIC FLOW: If A selected go to Question 12]]]

9. In which situations, if any, do you refer to the information on the Patient Alert Card with your patients taking Eliquis®? (Please select all that apply) [[[Radio button option- Multi punch]]]

☐ When a patient is first prescribed the drug [A]

☐ When a patient is scheduled to have an invasive procedure [B]

☐ When a patient has bleeding complications [C]

☐ When a patient experiences a suspected Eliquis®-related adverse event [D]

☐ I do not refer to the Patient Alert Card [E]

☐ I don't know/I'm not sure [F]

[[[LOGIC FLOW: If E selected go to Question 12]]]

10. How is the Patient Alert Card used by you to assist the patient? [[[Radio button option- Single punch]]]

☐ I/We commonly discuss the content in detail with the patient [A]

☐ I/We advise the patient to read the Patient Alert Card [B]

☐ I/We commonly discuss the content in detail with the patient and advise the patient to read the Patient Alert Card [C]

☐ None of the above [D]

11. Which aspects covered by the Patient Alert Card do you usually discuss with a patient? (Please select all that apply) [[[Radio button option- Multi punch]]]

- ☐ The importance of treatment compliance [A]
- ☐ The signs or symptoms of bleeding [B]
- ☐ When to seek attention from a HCP [C]
- ☐ The need to carry the Patient Alert Card at all times [D]
- ☐ The need to inform HCPs that they are taking Eliquis® if the patient requires surgery or invasive procedures [E]
- ☐ None of the above [F]

12. In your opinion, is the Patient Alert Card useful for patients?
[[[Radio button option- Single punch]]]

- ☐ Yes, it is very useful [A]
- ☐ Yes, it is quite useful [B]
- ☐ No, it is not useful [C]

[[[LOGIC FLOW: If C not selected, go to Question 14]]]

13. Why do you think the Patient Alert Card is not very useful for patients? (Please select all that apply) [[[Radio button option- Multi punch]]]

- ☐ Inadequate/not enough information
- ☐ Too detailed/complicated
- ☐ Information is unclear/not easily understood
- ☐ Patient is already sufficiently aware of the risks
- ☐ Information is not relevant
- ☐ None of the above

14. Do you have any suggestions for improving the Patient Alert Card? [[[Radio button option- Single punch]]]

☐ [[[Free text field]]]

[[[End of Section 5]]]

You have completed the survey. Thank you for your help.

You may now close your browser.

[[[END OF HCP SURVEY]]]

16.2. Annex 1.3 Assessment of Success

Objectives	Questions	Is the question included in the assessment of success? (Yes/No)	Definition of desirably/correctly answered question	Assessment of success
Knowledge about the RM tools	***Annex 1.2 - Section 3***			An HCP is considered successful for Knowledge when he/she provides at least 7 out of 9 (~80%) provide correct responses. Success for Knowledge: if ≥80% of HCPs are successful
	15. While being treated with Eliquis®, it is important that early recognition and immediate contact with an HCP is made for signs and symptoms of what associated risk?	Yes	Question completed correctly (Correct answer- Bleeding which does not stop on its own)	
	16a When Eliquis® is used for the prevention of stroke and systemic embolism in adult patients with NVAF, what is the standard recommended dosing?	Yes	Question completed correctly (Correct answer- 5 mg twice daily)	

Objectives	Questions	Is the question included in the assessment of success? (Yes/No)	Definition of desirably/correctly answered question	Assessment of success
	16b When Eliquis® is used for the treatment and prevention of DVT and PE in adults, what is the standard recommended dosing?	Yes	Question completed correctly (Correct answer- 10 mg twice daily for 7 days, followed by 5 mg twice daily for at least 3 months for treatment; and 2.5 mg twice daily following 6 months of anticoagulant treatment for prevention)	
	16c When Eliquis® is used for the prevention of venous thromboembolic events (VTE) in adult patients who have undergone elective hip or knee replacement surgery, what is the standard recommended dosing?	Yes	Question completed correctly (Correct answer- 2.5 mg twice daily)	
	17a For which type of renal impairment can Eliquis® be used at a reduced dose for the prevention of stroke and systemic embolism in adult patients with NVAF?	Yes	Question completed Correctly (Correct answer- Severe renal impairment (CrCl 15-29 mL/min))	
	17b For which type of renal impairment can Eliquis® be used with caution for treatment of DVT and PE, and prevention of recurrent DVT and PE in adults?	Yes	Question completed Correctly (Correct answer- Severe renal impairment (CrCl 15-29 mL/min))	
	17c For which type of renal impairment can Eliquis® be used with caution for prevention of venous thromboembolic events (VTE) in adult patients who have undergone elective hip or knee replacement surgery?	Yes	Question completed Correctly (Correct answer- Severe renal impairment (CrCl 15-29 mL/min))	

Objectives	Questions	Is the question included in the assessment of success? (Yes/No)	Definition of desirably/correctly answered question	Assessment of success
	18 Which of these groups of patients are at increased risk of bleeding complications when treated with Eliquis®? (Please select Yes, No, or I don't know/I'm not sure for each patient population)	Yes	Question completed Correctly (Correct answer- ***Yes,* at increased risk** for ● With severe renal impairment (CrCl 15-29 ml/min), ● Taking strong inhibitors of both CYP3A4 and P-gp ●Who have recently undergone brain, ophthalmic or spinal surgery ● Taking Non-steroidal anti-inflammatory drugs (NSAIDs), including acetylsalicylic acid (ASA) ● With recent gastrointestinal (GI) ulceration ***No,* at increased risk** for ● Taking oral contraception ● With significant dyspepsia, gastro-oesophageal reflux disease (GORD), or other upper GI disorders	
	19 In which one of the following patient groups is the prescribing of Eliquis® not contraindicated?	Yes	Question completed correctly (correct answer- First-degree relative family history of haemorrhagic stroke)	
	20 How should Eliquis® be taken?	Yes	Question completed correctly (correct answer- With water, and can be taken with or without food)	

Objectives	Questions	Is the question included in the assessment of success? (Yes/No)	Definition of desirably/correctly answered question	Assessment of success
	21 Is routine coagulation monitoring required in patients taking Eliquis®?	Yes	Question completed correctly (correct answer- No)	
	22 Is the International Normalized Ratio (INR) appropriate for measuring the anticoagulant activity of Eliquis®?	Yes	Question completed correctly (correct answer- No)	
	23 What discussion, if any, do you have with your patients being treated with Eliquis® about what to do if they experience a bleeding event?	Yes	Question completed correctly (correct answer- To immediately seek medical attention for a bleeding event which does not stop on its own)	
Self-declared behavior/ Practice	***Annex 1.2 - Section 4***			An HCP is considered successful for self-reported behaviour when he/she provides desirable responses to 9 out of 11 questions or 8 out of 10 questions. Success for self-reported practices if ≥80% of HCPs are successful
	Case Study 1 (a or b)			
	1 How would you manage the switch from warfarin to Eliquis®?	Yes	Question completed desirably (desirable answer- Stop warfarin, and start Eliquis® when the INR is less than 2.0)	
	2 Some months after starting Eliquis®, the patient is scheduled for minor skin surgery associated with a low risk of bleeding. What course of action would you take leading up to the day of the surgery?	Yes	Question completed desirably (desirable answer- Stop Eliquis® at least 24 hours before the surgery	
	3 Following minor surgery, when is the earliest time that you would restart Eliquis®?	Yes	Question completed desirably (desirable answer- As soon as possible provided the clinical situation allows and adequate haemostasis has been established)	
	Case Study 1c			
	1 When would you recommend that the initial Eliquis® dose be taken?	Yes	Question completed desirably (desirable answer- 12 to 24 hours after surgery)	

Objectives	Questions	Is the question included in the assessment of success? (Yes/No)	Definition of desirably/correctly answered question	Assessment of success
	2 What duration of Eliquis® treatment would you recommend in this case?	Yes	Question completed desirably (desirable answer- 32 to 38 days)	
	3 The patient suffers a minor nosebleed while taking Eliquis®. What action would you take for the minor nosebleed?	Yes	Question completed desirably (desirable answer- Symptomatic treatment and continue Eliquis® treatment as the bleeding is minor)	
	Case Study 2 (a or b)			
	1 What action would you take for the minor nosebleed?	Yes	Question completed desirably (desirable answer- Symptomatic treatment and continue Eliquis® treatment as the bleeding is minor)	
	2a The minor nosebleed resolves completely. When would you stop Eliquis® before the cardioversion?	Yes	Question completed desirably (desirable answer- Eliquis® does not need to be stopped before cardioversion)	
	2b The minor nosebleed resolves completely. In the absence of any other risk factors for DVT and/or PE, how long would you continue Eliquis® at a treatment dose for?	Yes	Question completed desirably (desirable answer-3 months)	
	Case Study 2c			
	1 When would you recommend that the initial Eliquis® dose be taken?	Yes	Question completed desirably (desirable answer-12 to 24 hours after surgery)	
	2 What duration of Eliquis® treatment would you recommend in this case?	Yes	Question completed desirably (desirable answer-10 to 14 days)	
	Case Study 3 (a, b, or c)			

Objectives	Questions	Is the question included in the assessment of success? (Yes/No)	Definition of desirably/correctly answered question	Assessment of success
	1 Aside from appropriate investigation and intervention (eg, surgical), what urgent action would you take here in relation to Eliquis® therapy?	Yes	Question completed desirably (desirable answer- Stop Eliquis® immediately)	
	2 It becomes apparent that the patient may have taken an accidental overdose of Eliquis®. Which one of the following treatment options is unlikely to be appropriate?	Yes	Question completed desirably (desirable answer- Hemodialysis)	
	3 The patient recovers and eventually restarts Eliquis® treatment. A decision is then made to switch the patient from Eliquis® to warfarin (a VKA). How would you switch the patient from Eliquis® to warfarin?	Yes	Question completed desirably (desirable answer- Give Eliquis® along with warfarin for at least 2 days, then stop Eliquis® once the INR is 2.0 or higher)	
	Annex 1.2 - Section 5			
	8 What proportion of the patients who you have been involved in treating with Eliquis® has been provided with a Patient Alert Card?	Yes	Question completed desirably (desirable answer- D, E or F)	
	11 Which aspects covered by the Patient Alert Card do you usually discuss with a patient? (Please select all that apply)	Yes	Question completed desirably (desirable answer- A,B,C, D and E)	
Utilization of RM tools and perceived utility of RM tools	***Annex 1.2 - Section 5***			An HCP is considered successful for utilization when he/she reports utilizing all/some of all RM tools and always/sometimes using them
	1 Have you read the Eliquis® Prescriber Guide?	Yes	Question completed desirably (desirable answer- A, B and C)	
	2 Do you use the Prescriber Guide to assist you in discussing Eliquis® with the patient?	Yes	Question completed desirably (desirable answer- A, B, C and D)	
	3 Have you found the Prescriber Guide useful?	No	Complementary question	

Objectives	Questions	Is the question included in the assessment of success? (Yes/No)	Definition of desirably/correctly answered question	Assessment of success
	4 Why have you not found the Prescriber Guide very useful? (Please select all that apply)	No	Complementary question	Success for utilization: if ≥80% of HCPs are successful
	5 How useful did you find the following sections in the Eliquis® Prescriber Guide?	No	Complementary question	
	6 Which sections of the Eliquis® Prescriber Guide provided you with information that you did not know before? (Please select all that apply)	No	Complementary question	
	7 Do you have any suggestions for improving the Eliquis® Prescriber Guide?	No	Complementary question	
	9 In which situations, if any, do you refer to the information on the Patient Alert Card with your patients taking Eliquis®? (Please select all that apply)	No	Complementary question	
	10 How is the Patient Alert Card used by you to assist the patient?	Yes	Question completed desirably (desirable answer- C)	
	12 In your opinion, is the Patient Alert Card useful for patients?	No	Complementary question	
	13 Why do you think the Patient Alert Card is not very useful for patients? (Please select all that apply)	No	Complementary question	
	14 Do you have any suggestions for improving the Patient Alert Card?	No	Complementary question	

17. ANNEX 3. ADDITIONAL INFORMATION

3.1	Prescriber Guide	aRMMS_PRx Guide
3.2	Patient Alert Card	aRMMS_PT Card_English
3.3	Eliquis® SmPC	Saudi Eliqius_FCT_LPD

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