NON-INTERVENTIONAL (NI) STUDY PROTOCOL

PASS NIGERIA

Study information

Title	Evaluation of the Effectiveness of Implementation of Additional Risk Minimization Measures (aRMM) Materials for Xeljanz® (Tofacitinib) / Rheumatoid Arthritis (RA) indication in Nigeria via a Survey among Prescribers: A Non-Interventional Post Authorization Safety Study (PASS).
Protocol number	A3921450
Protocol version identifier	2.0
Date	23 March 2026
EU Post Authorisation Study (PAS) register number	EUPAS1000000900
Active substance	L04AA29 – Tofacitinib citrate
Medicinal product	Xeljanz® (Tofacitinib)
Marketing Authorisation Holder(s) (MAH)	Pfizer Specialties Limited
Joint PASS	No
Research question and objectives	The research question is: Is there evidence that implementation of the Xeljanz® additional risk minimisation measures (aRMMs) in Nigeria results in prescriber behaviours and decision-making practices that are expected to reduce identified and potential safety risks associated with Xeljanz® use in rheumatoid arthritis? (RA)? The primary objectives is to: To evaluate whether implementation of the Xeljanz® aRMM materials (Patient Alert Card, Prescriber Brochure, and Prescriber Treatment Maintenance Checklist) in Nigeria results in prescriber risk-mitigation behaviours and

	decision-making practices that are expected to reduce identified and potential safety risks associated with Xeljanz® use in RA (including serious infections/TB, malignancy/NMSC, VTE, MACE, and laboratory abnormalities).
Country of study	Nigeria
Author	Redacted [redacted]

Redacted [redacted]

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2. LIST OF ABBREVIATIONS

Abbreviation	Definition
AEM	Adverse Event Monitoring
aRMM	Additional risk minimisation measures
BID	Bis in die (Latin: twice a day)
cells/L	cells per liter
CSA	Clinical Study Agreement
CV	Cardiovascular
DCT	Data Collection Tool
DVT	Deep Vein Thrombosis
DMARD	Disease-modifying antirheumatic drug
DSU	Drug Safety Unit
EDP	Exposure During Pregnancy
EC	Ethics Committee
EMA	European Medicines Agency
EU	European Union
FRCP	Fellow of the Royal College of Physicians
GERD	Gastroesophageal Reflux Disease
HCP	Healthcare Professional
HMA-EMA	Heads of Medicines Agencies-European Medicines Agency
i.e.	id est (Latin: for “that is” or "in other words)
IEC	Independent Ethics Committee
IQR	Interquartile Range
Redacted	[redacted]
IRB	Institutional Review Board
MACE	Major Adverse Cardiovascular Events
MAH	Marketing Authorisation Holder
JAK	Janus kinase inhibitors
M.D.	Doctor of Medicine
MACR	Master of the American College of Rheumatology
M.B.A.	Master of Business Administration
MTX	Methotrexate
NAFDAC	National Agency for Food and Drug Administration and Control
NI	Non-Interventional
NMSC	Non-melanoma skin cancer
PASS	Post-Authorisation Safety Study
PE	Pulmonary Embolism
Prof.	Professor
QPPV	Qualified Person Responsible for Pharmacovigilance
QC	Quality Control
RA	Rheumatoid Arthritis

Abbreviation	Definition
RMP	Risk Management Plan
RWD	Real World Data
SAP	Statistical Analysis Plan
SD	Standard Deviation
SMS	Short Message Service
SOP	Standard Operating Procedures
TNF	Tumour Necrosis Factor
TB	Tuberculosis
VTE	Venous thromboembolism
YRR	Your Reporting Responsibilities

3. RESPONSIBLE PARTIES

Principal Investigator(s) of the Protocol

Redacted			

4. ABSTRACT

Title: Evaluation of the Effectiveness of Implementation of Additional Risk Minimization Measures (aRMM) Materials for Xeljanz® (Tofacitinib) / Rheumatoid Arthritis (RA) indication in Nigeria via a Survey among Prescribers: A Non-Interventional Post Authorization Safety Study (PASS).

Protocol Version 2.0, 23 March 2026

Main author: Redacted

Local Qualified Person Responsible for Pharmacovigilance (QPPV) responsible: Redacted

Rationale and background: Tofacitinib citrate (Xeljanz®) is an oral Janus kinase (JAK) inhibitor approved by the Nigerian National Agency for Food and Drug Administration and Control (NAFDAC) for the treatment of adults with active rheumatoid arthritis (RA). To minimise important potential and identified risks associated with the use of tofacitinib, the Marketing Authorisation Holder (MAH) implemented additional risk minimisation measures (aRMM). This protocol assesses the effectiveness of the Xeljanz® additional risk-minimisation measures (aRMMs) by evaluating prescriber behaviours and clinical decision-making practices related to screening, risk assessment, monitoring, and treatment management. These behaviours represent necessary and proximal determinants of risk minimisation and are assessed regardless of whether prescribers have already initiated treatment with Xeljanz®."

Research question and objectives:

The research question is:

Is there evidence that implementation of the Xeljanz® additional risk minimisation measures (aRMMs) in Nigeria results in prescriber behaviours and clinical decision-making practices aligned with the aRMM recommendations that are expected to reduce identified and potential safety risks associated with Xeljanz® use in rheumatoid arthritis (RA)?

The primary objective of this study is:

To evaluate whether implementation of the Xeljanz® aRMM materials (Patient Alert Card, Prescriber Brochure, and Prescriber Treatment Maintenance Checklist) in Nigeria results in prescriber risk-mitigation behaviours and decision-making practices that are expected to reduce identified and potential safety risks associated with Xeljanz® use in RA (including serious infections/TB, malignancy/NMSC, VTE, MACE, and laboratory abnormalities).

Secondary objectives:

- Evaluate prescriber awareness (receipt) and utilisation of each aRMM component.
- Evaluate prescriber knowledge and comprehension of key contraindications, risks, and risk-minimisation instructions.
- Describe prescriber practice characteristics and barriers/facilitators to implementation.
- Explore descriptive associations between receipt/knowledge and implementation of risk-mitigation behaviours.

Study design: This study will be a non-interventional cross-sectional survey. It will involve the collection of data on additional risk minimisation measures through a structured questionnaire administered to Nigerian physicians who have received Xeljanz® aRMM materials. The study will be conducted via a paper-based survey.

Population: The study population is limited to physicians authorised to prescribe Xeljanz® who have received the additional risk-minimisation measure (aRMM) materials.
Therefore, the study population consists of Rheumatologists and other prescribers of Xeljanz® in Nigeria, (e.g. Internists).

Variables
Exposure variables include receipt and utilisation of Xeljanz® additional risk minimisation measures (aRMMs), including the Prescriber Brochure, Prescriber Treatment Maintenance Checklist, and Patient Alert Card.

Primary outcomes assess prescriber implementation of risk minimisation behaviours and clinical decision-making practices aligned with aRMM recommendations, including screening, risk assessment, decision-rule application, preventive counselling and Patient Alert Card use. These outcomes will be measured using prescriber responses to predefined behaviour-based and clinical scenario-based questions in a structured, paper-based questionnaire administered face to face, with responses classified according to prespecified criteria aligned with approved aRMM recommendations.

Secondary outcomes include prescriber awareness (receipt) and utilisation of aRMM materials and knowledge of key contraindications and safety risks, measured through structured questionnaire items assessing recall, use, and correct responses to predefined knowledge questions. Key covariates include prescriber professional background and practice characteristics (e.g., specialty, years of practice, practice setting), experience with Xeljanz®, and perceived barriers to implementation of aRMM recommendations, collected via self-reported questionnaire data.

Table 1. List of Variables, Role, Data Source and Operational Definition

Variable	Role	Data Source	Operational Definition
Pre-initiation risk-mitigation behaviours	Primary outcome	Annex 1 – Section D (Q11–Q12)	Performance of TB screening, baseline labs, and VTE/CV/malignancy risk assessment prior to initiation
Decision-rule application in high-risk scenarios	Primary outcome	Annex 1 – Section D (Q13)	Selection of predefined desirable action aligned with aRMM guidance
Preventive counselling and Patient Alert Card use	Primary outcome	Annex 1 – Section D (Q14)	Frequency of counselling and Patient Alert Card provision
Behaviour-based implementation indicators	Primary outcome	Annex 1 – Section F	Additional behaviour-based measures of checklist use and mandatory actions
Awareness (receipt) of aRMM materials	Secondary outcome	Annex 1 – Section E	Self-reported receipt of each aRMM component
Utilisation of aRMM materials	Secondary outcome	Annex 1 – Section E	Self-reported use of each aRMM component in practice
Knowledge of contraindications and risks	Secondary outcome	Annex 1 – Section C	Proportion of correct responses to predefined knowledge questions
Prescriber specialty	Descriptive	Annex 1 -Section A	Rheumatology / Internal Medicine / Other
Years in clinical practice	Descriptive	Annex 1 -Section A	Categorised (<5, 5–10, 11–20, >20 years)
Location of practice	Descriptive	Annex 1 -Section A	State of practice
Practice setting	Descriptive	Annex 1 – Section A	Public or private practice
Experience with Xeljanz®	Descriptive	Annex 1 – Section B	Time since last prescription and approximate prescribing volume
Treatment approach / involvement	Descriptive	Annex 1 Section B (Q8)	Initiate only / Initiate +monitor / Monitor only
Perceived barriers to implementation	Exploratory	Annex 1 – Section F	Self-reported barriers affecting aRMM implementation

Table 1. List of Variables, Role, Data Source and Operational Definition

Variable	Role	Data Source	Operational Definition
Perceived usefulness of aRMM materials	Exploratory	Annex 1 Section E	Proportion rating each material as Very useful / Somewhat useful / Not useful

Data sources:
The survey will collect primary data through paper questionnaires distributed to the identified Physicians. Responses from the respondents will be transcribed into a web platform for analysis.

Study size:

A target sample size of 30–35 completed questionnaires is proposed to support descriptive evaluation of the primary and secondary study outcomes. This sample size is based on the number of Nigerian Physicians (n=46) with confirmed receipt of the additional risk-minimisation measure (aRMM) materials, consistent with the study inclusion criteria, which restrict participation to Physicians who have received the materials.

Data analysis:

Physicians' responses will be presented descriptively using frequencies and proportions. As the objective of this study is to evaluate the effectiveness of the aRMM, material the predefined benchmark is for ≥80% of Physicians answer Knowledge of Contraindications & Risks questions correctly.

Implementation will be assessed using prespecified desirable responses for each behaviour-based item and summarised as the proportion of prescribers meeting each criterion.

Methodology:

An established questionnaire has been developed and previously implemented in other settings such as the European Union (EU) and Canada. This similar questionnaire adopted for Nigeria will be used to assess:

- Professional background (e.g., years of practice, practice setting and medical specialty).
- Experience with Xeljanz®
- Knowledge of Xeljanz®'s contraindications and risks as per Nigerian label

Implementation of risk-minimization behaviours aligned with the aRMM recommendations Awareness and use of the risk minimization materials.
The questionnaire will be available in paper format and will be implemented in paper format. To assess the effectiveness of the additional risk minimization measures, the initiation of the questionnaire will commence no sooner than six months following conclusion of the distribution of the aRMM materials. This interval is intended to provide prescribers with sufficient time to familiarize with the aRMM materials. The minimum six-month period also ensures that both the product and the associated risk messages are fully embedded in clinical practice prior to initiating data collection.

This approach supports the sustained availability of Xeljanz® in the Nigerian market and enables an accurate capture of established usage patterns.

Milestones:

Survey questionnaire distribution planned to start in June 2026 (pending Regulatory Agency and any other required approvals) and completion of data collection expected to end September 2026. Completion of Study Report is expected to be completed by January 2027.

Milestone dates are indicative and contingent upon receipt of regulatory and/or IRB/IEC approvals. Data collection will commence upon initiation of survey distribution following approval and will conclude approximately four months thereafter, defined as completion of the final questionnaire.

5. AMENDMENTS AND UPDATES

Version Identifier	Date	Amendment Type	Protocol Section(s) Changed	Summary of Amendment(s)	Reason
2.0	23 March 2026	Substantial	Sections 4.0, 7.0, 8.0	Revised rationale, research question, and primary objective to focus on behaviour-based and decision-making outcomes linked to risk minimisation rather than prescriber perception or utilisation.	To address NAFDAC feedback and align objectives with GVP Chapter 7 requirements.
2.0	23 March 2026	Substantial	Sections 9.1, 9.2, 9.2.1, 9.2.2	Updated study design and population description; clarified setting, representativeness, and sampling approach; expanded inclusion criteria to include Physicians who received aRMM materials regardless of prior prescribing experience.	To ensure consistency between objectives, survey design, and the low-utilisation context in Nigeria.
2.0	23 March 2026	Substantial	Section 9.3	Revised and expanded variables to clearly define primary behaviour-based outcomes, secondary awareness and knowledge outcomes, and descriptive/exploratory covariates aligned with Annex 1.	To eliminate orphan variables and ensure traceability across objectives, questionnaire, and analyses.
2.0	23 March 2026	Substantial	Section 4 and Section 9.5	Revised the target sample size from 42–50 to 30–35 completed questionnaires to reflect the number of Nigerian Physicians with confirmed receipt of the additional risk-minimisation measure (aRMM) materials, consistent with the study inclusion criteria.	To align the study sample size with confirmed exposure to the aRMM materials and ensure feasibility and proportionality in the Nigerian low-utilisation context while maintaining descriptive assessment of prescriber

Version Identifier	Date	Amendment Type	Protocol Section(s) Changed	Summary of Amendment(s)	Reason
					awareness, knowledge, and implementation of risk-minimisation behaviours.
2.0	23 March 2026	Substantial	Sections 9.7, 9.7.1–9.7.5	Re-structured analysis plan to include primary behaviour-based effectiveness analyses, secondary analyses for awareness/utilisation and knowledge, prespecified effectiveness thresholds, and comprehensive exploratory analyses.	To provide a transparent and regulator-relevant analysis and interpretation framework.
2.0	23 March 2026	Substantial	Section 9.7.4	Introduced predefined effectiveness benchmarks for receipt/utilisation, knowledge, and implementation of risk-minimisation behaviours, with a structured interpretation framework.	To support consistent interpretation of aRMM effectiveness in the absence of validated thresholds in the literature.
2.0	23 March 2026	Substantial	Sections 10.3.1, 10.4	Added clarification that, given the non-interventional Physicians only survey design with no patient-level data, an IRB/IEC waiver or exemption from full review may be applicable, subject to local determination.	To align ethical oversight with study risk level and avoid unnecessary review burden.
2.0	23 March 2026	Substantial	Annex 1	Revised the Xeljanz Prescribers Survey Questionnaire to strengthen behaviour- and scenario-based items and align with updated objectives, variables, and analyses.	To ensure the instrument directly measures aRMM implementation mechanisms.
2.0	23 March 2026	Substantial	Section 6.0	Updated planned study milestone dates, including timelines for survey initiation,	To ensure that milestone timelines accurately reflect

Version Identifier	Date	Amendment Type	Protocol Section(s) Changed	Summary of Amendment(s)	Reason
				completion of data collection, and final study report, to reflect refined operational planning following alignment on Protocol Version 2.0.	the revised protocol, operational feasibility, and anticipated regulatory and ethics approval timelines.
2.0	23 March 2026	Administrative	All relevant sections	Standardised terminology by consistently using the term “physicians” to describe the study population, in alignment with the inclusion criteria and the prescriber-focused nature of the additional risk-minimisation measures (aRMMs).	To ensure consistent and precise terminology throughout the protocol and avoid ambiguity regarding the eligible prescriber population.
2.0	23 March 2026	Administrative	Section 2 (List of Abbreviations)	Updated the list of abbreviations to include newly referenced terms introduced in the revised protocol.	To improve clarity and completeness for regulatory review.
2.0	23 March 2026	Administrative	Section 3.0	Added two additional individuals to the list of Responsible Parties.	To ensure that all contributors are listed.

6. MILESTONES

Milestone	Planned Date
Start of data collection	01 June 2026
End of data collection	30 September 2026
Registration in the HMA-EMA Catalogues of RWD Studies	15 May 2026
Final study report	31 January 2027

Milestone dates are indicative and contingent upon receipt of regulatory and/or IRB/IEC approvals. Data collection will commence upon initiation of survey distribution following approval and will conclude approximately four months thereafter, defined as completion of the final questionnaire.

7. RATIONALE AND BACKGROUND

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Tofacitinib citrate (Xeljanz®) is an oral Janus kinase (JAK) inhibitor approved by the Nigerian National Agency for Food and Drug Administration and Control (NAFDAC) Agency in 2018 as an immediate-release film-coated tablet (5 mg), taken twice a day (BID), for the treatment of adults with moderate-to-severe active rheumatoid arthritis (RA) who have had inadequate response or intolerance to one or more disease-modifying antirheumatic drugs (DMARDs).[1] Despite a number of treatment options available, many patients do not reach and/ or sustain remission..[2] In clinical trials, patients treated with 5 mg of tofacitinib BID, in combination with methotrexate (MTX), showed significantly reduced disease activity scores and improved physical functioning and general health status as compared to patients on placebo.[3] The approved dose of tofacitinib for the treatment of moderate-to-severe active RA is 5 mg which should not be exceeded, in combination with MTX; it may also be given as monotherapy in the case of intolerance to MTX or when treatment with MTX is inappropriate.[4]

To minimise the safety concerns associated with the use of Xeljanz®, the Marketing Authorisation Holder (MAH) implemented additional risk minimisation measures (aRMM) materials in the form of a Patient Alert Card and for prescribers a Prescriber Treatment Maintenance Checklists & a Prescriber Brochure.

On 24 March 2025, NAFDAC approved the additional risk minimisation measures (aRMMs) for Xeljanz®, including patient alert cards and prescriber materials, to enhance safety communication. According to NAFDAC's Good Pharmacovigilance Practice Guidelines, the effectiveness of these aRMM materials should be assessed. NAFDAC has therefore requested Pfizer to conduct a Regulatory Post-Authorisation Safety Study (PASS) in Nigeria. This study is a regulatory requirement and aims to measure the effectiveness of the aRMM materials of Xeljanz®. A physician survey will be implemented to measure the effectiveness of the aRMM materials for Xeljanz® in Nigeria[5]

This protocol assesses the effectiveness of the Xeljanz® additional risk-minimisation measures (aRMMs) by evaluating prescriber behaviours and clinical decision-making practices related to screening, risk assessment, monitoring, and treatment management. These behaviours represent necessary and proximal determinants of risk minimisation and are assessed regardless of whether prescribers have already initiated treatment with Xeljanz®.

This non-interventional study is designated as a post-authorization safety study (PASS) and is a commitment to National Agency for Food and Drug Administration and Control (NAFDAC) in Nigeria.

Summary of approved indications and dosages for tofacitinib[6]:

Therapeutic indications:

Rheumatoid Arthritis

XELJANZ® is indicated for the treatment of adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response to one or more disease modifying anti-rheumatic drugs (DMARDs).

Rheumatoid Arthritis Posology

XELJANZ® may be used as monotherapy or in combination with methotrexate (MTX) or other nonbiologic DMARDs.

The recommended dose of XELJANZ® is 5 mg administered twice a day. Some patients may benefit from an increase to XELJANZ® 10 mg administered twice a day based on clinical response.

Two XELJANZ® 5 mg tablets are bioequivalent to one XELJANZ® 10 mg tablet and may be used as an alternative to one XELJANZ® 10 mg tablet.

In general, use the lowest effective dose to maintain therapeutic benefit.

8. RESEARCH QUESTION AND OBJECTIVES

The research question is: Is there evidence that implementation of the Xeljanz® additional risk minimisation measures (aRMMs) in Nigeria results in prescriber behaviours and clinical decision-making practices aligned with the aRMM recommendations that are expected to reduce identified and potential safety risks associated with tofacitinib use in rheumatoid arthritis (RA)?

The primary objective is to evaluate whether implementation of the Xeljanz® aRMM materials (Patient Alert Card, Prescriber Brochure, and Prescriber Treatment Maintenance Checklist) in Nigeria results in prescriber risk-mitigation behaviours and decision-making

tofacitinib use in RA (including serious infections/TB, malignancy/NMSC, VTE, MACE, and laboratory abnormalities).

Secondary objectives:

- Evaluate prescriber awareness (receipt) and utilisation of each aRMM component.
- Evaluate prescriber knowledge and comprehension of key contraindications, risks, and risk-minimisation instructions.
- Describe prescriber practice characteristics and barriers/facilitators to implementation.
- Explore descriptive associations between receipt/knowledge and implementation of risk-mitigation behaviours.

Table 2. Safety Concerns and aRMM Risk-Minimisation Logic

Safety concern (RMP)	Key aRMM message	Behaviour measured	Risk-reduction mechanism
Serious infections / TB	Screen before initiation	TB screening performed	Prevents initiation in infected patients
VTE / PE	Assess risk & discontinue if suspected	Correct decision-rule application	Prevents thrombotic progression
MACE	CV risk assessment	Avoid initiation in high-risk patients	Reduces CV events
Malignancy / NMSC	Risk review	Pre-initiation risk checks	Avoids high-risk exposure
Lab abnormalities	Baseline & follow-up labs	Treatment interruption	Prevents severe cytopenias

9. RESEARCH METHODS

9.1 Study design

This study is designed as a cross-sectional, non-interventional survey targeting Physicians specializing in Rheumatology, Internal Medicine, and other relevant disciplines who have been identified by Pfizer as prescribers of Xeljanz®. The survey will be distributed in paper format and the completed questionnaire collected via face-to-face meetings with Physicians. Data from these completed questionnaires will be transcribed into a web platform for subsequent analysis.

Figure 1. Data Collection Process

An established questionnaire has been developed and used in other settings such as the EU and Canada.

This similar questionnaire adopted for Nigeria will be used to assess:

- Professional background (e.g., years of practice, practice setting).
- Experience with Xeljanz®.
- Knowledge of Xeljanz®'s contraindications and risks as per Nigerian label.
- Implementation of risk-minimisation behaviours aligned with the aRMM recommendations Awareness and use of the risk minimization materials.

The questionnaire will be available in paper format and will be implemented in paper format. To assess the effectiveness of the aRMMs materials the initiation of the questionnaire will commence no sooner than 6-months following conclusion of the distribution of the aRMM materials. This interval is intended to provide prescribers with sufficient time to get familiarized with the aRMMs materials information and ensure that both the product usage and the associated risk messages are fully embedded in clinical practice prior to initiating response collection. There follows an additional 4-month period of effective completion of the questionnaires. This approach supports the sustained availability of Xeljanz® in the Nigerian market and enables an accurate capture of established usage patterns.

9.2. Setting

This study will be conducted in Nigeria and will involve a non-interventional**,** cross-sectional survey of Physicians practising in outpatient clinical settings, including public and private healthcare facilities. The study will not involve direct patient contact, clinical interventions, or collection of patient-level data.

The study population consists of Physicians involved in the initiation, management, or clinical decision-making for patients with rheumatoid arthritis (RA) who are part of the target audience for the Xeljanz® additional risk-minimisation measures (aRMMs) in Nigeria. This

includes Physicians who have prescribed Xeljanz® as well as Physicians who have received the aRMM materials but have not yet prescribed Xeljanz®, reflecting the low utilisation of the product and the preventive intent of the aRMMs.

The survey will be conducted at Physicians practice locations across Nigeria. Data collection is planned to occur no earlier than six months after completion of aRMM material distribution, to allow sufficient time for Physicians to be exposed to, review, and integrate the aRMM recommendations into clinical practice. The data-collection period is expected to span approximately four months, as described in Section 6 (Milestones).

This study uses a targeted, non-probability sampling approach. Physicians eligible for participation will be identified based on records of aRMM material distribution and Pfizer-defined targeting lists for Xeljanz® safety communication in Nigeria.

All Physicians meeting the inclusion criteria will be invited to participate, and no formal sampling frame or stratified sampling will be applied. This approach is considered appropriate for a regulatory PASS conducted in a low-utilisation setting, where the primary objective is to assess implementation of risk-minimisation measures rather than to estimate population-level prescribing rates.

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Inclusion and exclusion criteria are described in Sections 9.2.1 and 9.2.2.

9.2.1 Inclusion criteria

Physicians invited to participate must meet all the following inclusion criteria to be eligible for inclusion in the study:

1. Physicians identified by Pfizer as part of the target audience for the Xeljanz® additional risk-minimisation measures (aRMMs) in Nigeria.

2. Physicians who have received the Xeljanz® aRMM materials, regardless of whether they have already prescribed Xeljanz®.

3. Physicians who provide consent to participate in the survey.

Physicians who have not yet prescribed Xeljanz® are included to allow assessment of decision-making practices and intended application of aRMM recommendations in a low utilisation setting.

9.2.2 Exclusion Criteria

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

1. Physicians identified by Pfizer as prescribers of Xeljanz® but have since left Nigeria after 04 July 2025 will be excluded.

9.3 Variables

The unit of assessment for all outcome variables is the **Prescriber**.

Table 1. List of Variables, Role, Data Source and Operational Definition

Variable	Role	Data Source	Operational Definition
Pre-initiation risk-mitigation behaviours	Primary outcome	Annex 1 – Section D (Q11–Q12)	Performance of TB screening, baseline labs, and VTE/CV/malignancy risk assessment prior to initiation
Decision-rule application in high-risk scenarios	Primary outcome	Annex 1 – Section D (Q13)	Selection of predefined desirable action aligned with aRMM guidance
Preventive counselling and Patient Alert Card use	Primary outcome	Annex 1 – Section D (Q14)	Frequency of counselling and Patient Alert Card provision
Behaviour-based implementation indicators	Primary outcome	Annex 1 – Section F	Additional behaviour-based measures of checklist use and mandatory actions
Awareness (receipt) of aRMM materials	Secondary outcome	Annex 1 – Section E	Self-reported receipt of each aRMM component
Utilisation of aRMM materials	Secondary outcome	Annex 1 – Section E	Self-reported use of each aRMM component in practice
Knowledge of contraindications and risks	Secondary outcome	Annex 1 – Section C	Proportion of correct responses to predefined knowledge questions
Prescriber specialty	Descriptive	Annex 1 -Section A	Rheumatology / Internal Medicine / Other
Years in clinical practice	Descriptive	Annex 1 -Section A	Categorised (<5, 5–10, 11–20, >20 years)
Location of practice	Descriptive	Annex 1 -Section A	State of practice
Practice setting	Descriptive	Annex 1 – Section A	Public or private practice

Table 1. List of Variables, Role, Data Source and Operational Definition

Experience with Xeljanz®	Descriptive	Annex 1 – Section B	Time since last prescription and approximate prescribing volume
Treatment approach / involvement	Descriptive	Annex 1 Section B (Q8)	Initiate only / Initiate+monitor / Monitor only
Perceived barriers to implementation	Exploratory	Annex 1 – Section F	Self-reported barriers affecting aRMM implementation
Perceived usefulness of aRMM materials	Exploratory	Annex 1 Section E	Proportion rating each material as Very useful / Somewhat useful / Not useful

For behaviour-based and scenario-based variables, a prescriber is considered to have implemented a risk minimisation measure when the predefined desirable response aligned with aRMM recommendations is selected. These variables represent prescriber behaviours and clinical decision-making practices that are expected to reduce identified and potential safety risks associated with Xeljanz®.

9.4 Data Sources

The survey will collect primary data through paper questionnaires distributed to the identified Physicians. Responses from the respondents will be transcribed into a web platform for analysis.

The responses will be collected via a vendor (selection and contracting finalized) and analysed locally. The datasets and analytic programs will be stored according to the third-party's procedures.

The recruitment of potential Physician participants will be done according to the following process:

- Physicians will be invited to participate through a phone call explaining the survey background, objectives and contact information for questions.
- If the Physician agrees to participate in the survey, Redacted will discuss with the Physicians and align on a suitable time for an in person visit for paper questionnaire distribution, at the Physicians convenience.
- A time will then be scheduled for the face-to-face meeting for questionnaire completion with one of our team members if it has not been completed by the Physician.

- Redacted will transcribe all paper-based responses into the web platform for analysis. If the questionnaire is not completed, Redacted will follow up with five reminder phone calls or Short Message Service (SMS) within four weeks of the initial contact.

Redacted will reach out in person to each of the targeted Physicians at the beginning and the end of the 4 months' time allocated for the completion of the questionnaires. Invitations will be issued primarily by postal mail, phone call and email, if available. Each contact attempt by Redacted of the targeted Physician will be recorded.

A targeted Physician will be considered contacted if they:

- Expressed refusal to participate in the survey study (i.e., did not provide their consent; "Refused Physicians")

- Partially completed the screening, demographic, or survey questions ("Partial Complete Physician"); or

- Submitted a completed survey ("Completed Survey Physician").

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A submitted and completed survey will be defined as a survey in which Questions in sections A to Section F of the survey were answered completely and collected from the Physician. If a Physicians completed only the screening questions or the demographic and screening questions (Sections A and B), it will not be considered a completed survey.

A Physicians will be considered unreachable if he or she cannot be reached after 3-5 attempts by any means (i.e., email, postal mail, and/or phone) or were unreachable for other reasons (i.e., wrong workplace, retired, or temporarily unavailable). However, Redacted maintains the flexibility to contact them more times if there is reason to believe that the additional contact will lead to participation.

Recruitment for this protocol will be stopped when all targeted Physicians have been either considered contacted or deemed unreachable *or* after the data collection period ends, whichever occurs first.

To the extent possible, reasons for nonresponse will be collected. This will help ensure that missing data are reported with enough details to strengthen the results' validity, as recommended by the Strengthening the Reporting of Observational Studies in Epidemiology guideline.[7,8]

9.5 Study Size

No formal hypothesis testing or statistical power calculation was performed for this study, as it is descriptive in nature and not designed to test comparative hypotheses or estimate effect sizes.

A target sample size of 30–35 completed questionnaires is proposed to support descriptive evaluation of the primary and secondary study outcomes. This sample size is based on the number of Nigerian Physicians (n=46) with confirmed receipt of the additional risk-minimisation measure (aRMM) materials, consistent with the study inclusion criteria, which restrict participation to Physicians who have received the materials.

Given the low utilisation of Xeljanz® in the Nigerian setting and the limited number of prescribers exposed to the aRMM materials, the proposed sample size is considered feasible and appropriate to characterise prescriber awareness, knowledge, and implementation of risk-minimisation behaviours, as described in Section 9.7 (Data Analysis).

9.6 Data Management:

9.6.1 Case Report Forms/Data Collection Tools/Electronic Data Record:

As used in this protocol, the term DCT 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. Redacted shall ensure that the DCTs are securely stored at the Redacted designated location in paper form and will be secured in a locked room to prevent access by unauthorized third parties.

Redacted 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 DCTs must be dated, initialled 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, Redacted agrees to keep all study-related records. The records should be retained by Redacted according to local regulations or as specified in the Clinical Study Agreement (CSA), whichever is longer. Redacted must ensure that the records continue to be stored securely for so long as they are retained.

If Redacted 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 Redacted and Pfizer have expressly agreed to a different period of retention via a separate written agreement. Records must be retained for longer than 15 years if required by applicable local regulations.

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

9.7 Data Analysis

All analyses will be descriptive and conducted at the prescriber level, which is the unit of assessment for this study. Categorical variables will be summarised using frequencies and proportions, and continuous variables will be summarised using mean, standard deviation, median, range, and interquartile range (IQR), as appropriate.

Analyses are structured to correspond directly to the study objectives and the variables defined in Section 9.3, and to the questionnaire sections provided in Annex 1.

Given the descriptive, threshold-based nature of the analysis and the number of prescribers exposed to the additional risk-minimisation measure (aRMM) materials, the proposed sample size is sufficient to determine whether predefined adequacy thresholds for awareness, knowledge, and implementation of risk-minimisation behaviours are met, without reliance on formal hypothesis testing.

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 sponsor. 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.

9.7.1 Primary Analysis – Implementation of Risk-Minimisation Behaviours

This primary analysis evaluates the effectiveness of the Xeljanz® additional risk-minimisation measures (aRMMs) through prescriber behaviours and clinical decision-making practices that are expected to reduce identified and potential safety risks.

The following primary effectiveness indicators, derived from Annex 1 Sections D and F, will be analysed:

a) Pre-initiation risk-mitigation behaviours, including screening for latent or active tuberculosis, baseline laboratory testing, and assessment of venous thromboembolism, cardiovascular, malignancy/non-melanoma skin cancer, and age-related risks prior to treatment initiation.

b) Decision-rule application in high-risk scenarios, assessed as the proportion of prescribers selecting the predefined desirable action aligned with aRMM recommendations (e.g., treatment interruption or discontinuation).

c) Preventive counselling and Patient Alert Card use, assessed as the frequency with which prescribers report providing counselling on key safety risks and issuing the Patient Alert Card.

For behaviour-based and scenario-based indicators, a prescriber will be considered to have implemented a risk-minimisation measure when the predefined desirable response aligned with the aRMM recommendations is selected. Results will be summarised descriptively and interpreted using the prespecified effectiveness thresholds described in Section 9.7.4.

9.7.2 Secondary Analysis – Awareness (Receipt) and Utilisation of aRMM Materials

This analysis assesses prescriber awareness (receipt) and utilisation of each aRMM component using data from Annex 1 Section E.

Per-item analyses will summarise the frequency and proportion of prescribers reporting receipt and utilisation of the Prescriber Brochure, Prescriber Treatment Maintenance Checklist, and Patient Alert Card.

Overall analyses will summarise the number of aRMM components received and utilised per prescriber using descriptive statistics.

9.7.3 Secondary Analysis – Knowledge of Key Risks and Contraindications

Prescriber knowledge of contraindications and key safety risks associated with Xeljanz® will be assessed using Annex 1 Section C.

Per-item analyses will summarise the frequency and proportion of prescribers providing correct responses to each knowledge question.

Overall analyses will summarise the proportion of prescribers meeting the prespecified knowledge success criterion (e.g., ≥80% correct responses), and knowledge scores per prescriber will be summarised descriptively.

9.7.4 Effectiveness Thresholds and Interpretation Framework

To ensure transparent, objective, and regulator-relevant interpretation of study results, predefined effectiveness thresholds are specified in this protocol prior to data collection and analysis.

These predefined thresholds describe how findings related to awareness, knowledge, and implementation of risk-minimisation behaviours will be interpreted to determine whether the Xeljanz® additional risk-minimisation measures (aRMMs) are considered effective, partially effective, or whether additional risk-minimisation actions may be warranted.

Specifically:

- Receipt and utilisation of each aRMM component will be considered adequate when ≥80% of prescribers report receipt and use of the component.

- Knowledge of key risk messages will be considered adequate when ≥80% of prescribers provide correct responses to predefined knowledge items.

• Implementation of critical risk-minimisation behaviours will be considered adequate when ≥70% of prescribers demonstrate each prespecified behaviour.

Interpretation of results will be based on the combined assessment of these predefined benchmarks, which are specified in advance to support transparent, consistent, and context-specific interpretation of study findings, and will be used to inform regulatory conclusions regarding the effectiveness of the aRMM.

The thresholds are established to ensure that a clear majority of prescribers are consistently aware of, knowledgeable about, and applying critical risk-minimisation measures, thereby supporting patient safety and regulatory objectives. Lower thresholds may limit confidence in the consistency and robustness of risk-minimisation implementation and reduce the interpretability of study findings in relation to the intended impact of the aRMMs. This approach is consistent with guidance from the European Medicines Agency (EMA), which emphasises that effectiveness indicators for risk-minimisation measures should be defined in advance, be appropriate to the measures implemented, and support optimal patient protection[9]

9.7.5 Exploratory Analysis

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Exploratory analyses will describe prescriber practice characteristics (including professional background and experience with Xeljanz®) and perceived barriers to implementation of aRMM recommendations using data from Annex 1 Sections A, B, and F. Results will be summarised descriptively to provide context for interpretation of the primary and secondary effectiveness analyses.

Exploratory descriptive associations between (i) receipt and utilisation of aRMM materials and (ii) knowledge outcomes, and implementation of risk-minimisation behaviours will be assessed using descriptive cross-tabulations and comparisons of proportions (with confidence intervals where appropriate).

Perceived usefulness of each aRMM material will be summarised descriptively (Very useful / Somewhat useful / Not useful).

9.8 Quality Control

QC will be conducted according to Pfizer's Non-Interventional Integrated Quality Control Plan and the standard operating procedures (SOPs) of Redacted

All aspects of the study, from protocol development to the reporting of the results, will be conducted within the framework of theRedacted Quality Management System.

A QC plan for the study will be developed and executed, which will include QC on the study methodology, data management and analysis, study results, conclusions, and final study report. Furthermore:

The study QC plan will establish ownership for the execution of the individual QC steps.

The Principal in Charge of the study will ensure that individuals responsible for the execution of specific QC steps will have the knowledge, capability, and experience necessary to perform the assigned tasks.

The result of the execution of the individual steps of the QC plan will be documented, and will include the required corrective actions, if any. The execution of any required corrective action will also be documented.

The QC plan will be subjected to a final review and approval for sufficiency and completeness from the Principal in Charge of the study. Redacted will have a qualified individual external to the writing team conduct QC reviews of all final deliverables, which will include the following:

- Confirming that the source of the data and/or results has been documented and that the reported data and/or results have been verified against the source.
- Checking the internal consistency of the results presented in the deliverable.
- Confirming that the conclusions are accurate, objective, balanced; and
- Confirming that the format and content of the deliverable are aligned with applicable external requirements.

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The survey was developed (for a similar previous project) jointly by Pfizer and Redacted based on the final approved aRMM materials and is included in Annex 1 (Physician Questionnaire). The survey instrument will be delivered in English (local physicians are trained in English language).

9.9 Limitations of the Research Methods:

9.9.1 Absence of Baseline

The Sponsor's ability to measure the extent to which Physicians' knowledge or behaviours can be attributed to the aRMM program will be limited. No baseline measures of Physicians' knowledge or behaviour in the absence of the aRMM materials will be available.

9.9.2 Limitation of Human Recall

The Physicians will be asked if they recall having received the aRMM materials, that has been documented. This survey is commenced no sooner than 6 months after the aRMM material distribution to optimize recollection and allow adequate time for Physicians to familiarize themselves with the aRMM materials and safety measures.

9.9.3 Social Desirability

As in all surveys, this survey may promote a social desirability bias, which refers to the tendency of Physicians to give socially desirable/expected responses instead of choosing those reflecting their current knowledge or behavior. For example, Physicians can provide information gathered via other sources instead of giving their own opinions or declare a conforming prescribing practice when they are not adherent to the aRMM materials. Social desirability can affect the validity of survey research findings, but the use of pre-populated items (i.e., response options) in the survey could/tends to reduce this bias.[10]

9.9.4 Possible limitations related to local implementation (paper survey, aRMM)

To assess the effectiveness of the additional risk minimization measures, the initiation of the questionnaire will commence minimum six months following conclusion of the distribution of the aRMM materials. This interval is intended to provide prescribers sufficient time to prescribe and use the aRMM materials. The minimum six-month period also ensures that both the product and the associated risk messages are fully embedded in clinical practice prior to initiating response collection. There follows an additional 4-month period of effective completion of the questionnaires. This approach supports the sustained availability of Xeljanz® in the Nigerian market and enables the capture of established usage patterns.

9.9.5 Generalization of the survey results to the overall target population

In such surveys, the generalization and external validity of the results is restricted to Physicians who can be reached and are willing (and able) to answer the questionnaire. These Physicians may not be fully representative of the whole target population who received the materials.

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

9.9.6 Limitations Related to Low Product Utilisation and Feasibility of Patient-Level Outcomes

Given the limited utilisation of Xeljanz®, effectiveness is assessed using prescriber behaviours and clinical decision-making practices that represent necessary and proximal determinants of risk minimisation, in line with NAFDAC GVP Chapter 7 proportionality principles[9].

9.10 Other aspects

Not applicable.

10. PROTECTION OF HUMAN SUBJECTS

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 participant names or other directly identifiable data in any reports, publications, or other disclosures, except where required by applicable laws.

Participant personal data will be stored at Redacted designated location in encrypted electronic and/or paper form and will be password protected or secured in a locked room to ensure that only authorized study staff have access. Redacted 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, Redacted 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 othe

parties, participant 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, participant-specific code. Redacted will maintain a confidential list of participants who participated in the study, linking each participant's numerical code to his or her actual identity. In case of data transfer, Pfizer will maintain high standards of confidentiality and protection of participants' personal data consistent with the clinical study agreement and applicable privacy laws.

10.2 Study Participant Consent

The informed consent language and any Physicians recruitment materials must be in compliance with local regulatory requirements and legal requirements, including applicable privacy laws.

Participants in the survey will be informed via a study packet about the objectives of the investigation, the nature of the transmitted data, the intended use of data, recipients of these data, and their right of access and rectification to their personal data, as well as their right of objection to use their data or to Redacted keeping their data. Participants will be informed that as a part of the documentation they receive, by returning a completed survey questionnaire by mail or submitting responses electronically, the participant is agreeing that they have read and understood the informed consent statement and voluntarily agree to participate in this research study.

The informed consent language as incorporated within the survey and any Physicians recruitment materials must be reviewed and approved by Pfizer and by local Authorities, as locally required and made available for inspection.

10.3 Study Participant Withdrawal

Participation in the survey is entirely voluntary, and participants can withdraw from the survey at any time. Only completed and submitted surveys will be included in the analysis.

Participants may request that any survey or questionnaire responses provided as part of the study be withdrawn before the completion of the data collection period. Participants will be informed that once the responses have been analysed, it may not be possible to remove them from the study.

Complete survey/questionnaires withdrawn before the end of the data collection period will be destroyed, however survey/questionnaires which responses have already been analysed will not be destroyed but they will be kept in a secure location for the time required by applicable local regulations.

10.3.1 Ethical Considerations

- The study will adhere to ethical guidelines.
- If required, the study will be approved by local Ethics Committee

10.4 Institutional review board (IRB) / Independent ethics committee (IEC)

It is the responsibility of Redacted to have prospective approval of the study protocol, protocol amendments, materials describing the consent process (e.g., statement regarding agreement to participate), and other relevant documents, (e.g., recruitment advertisements), if applicable, from the IRB/EC. All correspondence with the IRB/EC should be retained by Redacted.

For this questionnaire-based study involving healthcare professionals only, the IRB/IEC may determine that a waiver of ethical approval or an exemption from full review is appropriate. Any such determination will be obtained in writing and retained in the study records prior to study initiation.

Copies of IRB/EC approvals/waiver should be forwarded to Pfizer.

There must be prospective approval/waiver of the study protocol, protocol amendments, and other relevant documents (e.g., informed consent forms, if applicable from the local Regulatory Body (National Agency for Food and Drug Administration and Control, NAFDAC). All correspondence with NAFDAC must be retained.

10.5 Ethical conduct of the study

The study will be conducted in accordance with applicable local legal and regulatory requirements, as well as with scientific purpose, value, and rigor and follow generally accepted research practices as applicable for non-interventional studies described in:

- NAFDAC Good Pharmacovigilance Practice Guidelines (Revision) – (21 January 2021).
- NAFDAC Good Pharmacovigilance Practice Regulations (08 September 2021).
- NAFDAC Good Clinical Practice Guidelines (05 May 2025).
- NAFDAC Clinical Trial Regulations (30 August 2021).
- Guidelines for Qualified Person for Pharmacovigilance (15 October 2024).

11. MANAGEMENT AND REPORTING OF ADVERSE EVENTS/ADVERSE REACTIONS REQUIREMENTS

This study does not involve treating healthcare professionals (HCP) collecting data on individual patients, and the survey/questionnaire used in this study does not intend to identify product safety information. However, the survey/questionnaire will be completed by participants on paper, and the participant could volunteer product safety information to the Redacted representative or in the blank margins or the survey. Any safety information that is volunteered, for example by the patient him/herself, health care professional, lay person, during the course of this research must be reported as described below.

The following must be reported on the "Non-Interventional Study (NIS) Adverse Event Monitoring (AEM) 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-

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:

Depending upon the design of the non-interventional study, add the appropriate examples of situations where an EDP report would not be created and remove what is not applicable.

- 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, Redacted study staff must complete the NIS AEM Report Form and submit it to the Pfizer Drug Safety Unit (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.

Redacted Study staff who will fill in with appropriate research activities (e.g., review the data collection tool for the study) must complete the following Pfizer training:

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

This training must be completed by Redacted study staff 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, which must be kept in a retrievable format. The study vendor will also provide copies of all signed training statements to Pfizer.

Retraining must be completed on an annual basis using the most current *"Your Reporting Responsibilities (YRR) with Supplemental Topics"*

shall ensure all vendor personnel complete the updated safety training within sixty (60) calendar days of issuance by Pfizer.

12. PLANS FOR DISSEMINATING AND COMMUNICATING STUDY RESULTS

Final Study Report describing the study results will be written in English and submitted to the local Regulatory Agency (ie, NAFDAC) no later than 4 months after the end of data collection; it will also be shared with Pfizer product team and risk management committee and possibly developed into a manuscript.

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 the party responsible for collecting data from the participant (Redacted) 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, the party responsible for collecting data from the participant will inform Pfizer immediately of any urgent safety measures taken by them to protect the study participants against any immediate hazard, and of any serious breaches of this NIS protocol that the party responsible for collecting data becomes aware of.

Redacted

13. REFERENCES

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7. Von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. *International Journal of Surgery.* 2014;12(12):1495-1499.
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10. Nederhof AJ. Methods of coping with social desirability bias: A review. European Journal of Social Psychology. 1985;15(3):263-280.

14. LIST OF TABLES

15. LIST OF FIGURES

ANNEX 1: XELJANZ PRESCRIBERS SURVEY QUESTIONNAIRE

Number	Document Reference Number	Date	Title
1	Version 2.0	23 March - 2026	**XELJANZ PRESCRIBERS SURVEY QUESTIONNAIRE Version 2.0 dated 23-March-2026**

Please note: This questionnaire applies only to your experiences with Pfizer branded Xeljanz® for rheumatoid arthritis (RA).
This does not apply to generic tofacitinib

This survey takes approximately 20 to 25 minutes and consists of 6 sections.

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SECTION A: Professional Background

1. Specialty: ☐ Rheumatology ☐ Internal Medicine ☐ Other: _____
2. Years in Clinical Practice as a Specialist: ☐ <5 ☐ 5–10 ☐ 11–20 ☐ >20
3. Practice Setting: ☐ Public hospital ☐ Private hospital ☐ Other: (Please indicate) _____`
4. State of Practice: _____

SECTION B: Experience with Xeljanz® for RA

5. When did you last prescribe Xeljanz® for RA?

☐ Within the past 6 months
☐ More than 6 months ago

☐ I have not yet prescribed Xeljanz®

6. Since January 2024, how many prescriptions (new + repeat) for RA have you written for Xeljanz®?

☐ Fewer than 10
☐ 10–20

☐ 21–50
☐ More than 50

☐ I have not yet prescribed Xeljanz®

7. How many individual RA patients have you treated with Xeljanz® since January 2024?

☐ Fewer than 5
☐ 5–10
☐ 11–20
☐ More than 20

☐ I have not yet prescribed Xeljanz®

8. Which best describes your treatment approach for RA patients who qualify for treatment with Xeljanz®? (Please answer this question even if you have not yet prescribed Xeljanz)

☐ I initiate treatment only
☐ I initiate, follow up, and monitor
☐ I monitor patients prescribed Xeljanz® by other Physicians

SECTION C: Knowledge of Contraindications & Risks

9. Please select the best response (True, False, I don't know) for each of the following statements about **contraindications** of Xeljanz®.

		True	False	I don't know
A	Xeljanz® may be administered to patients with severe hepatic impairment.	○	●	○
B	Xeljanz is contraindicated in patients who are pregnant or lactating®.	●	○	○
C	Xeljanz® is contraindicated in patients with moderate renal impairment.	○	●	○
D	Patients should be evaluated and tested for latent or active tuberculosis (TB) infection prior to administration of Xeljanz® and periodically (e.g., annually) while taking Xeljanz®.	●	○	○

		True	False	I don't know
E	Xeljanz® treatment should be interrupted if patient develops serious infection, an opportunistic infection, or sepsis.	●	○	○
F	Xeljanz® should not be given to patients with active TB or other active infections.	●	○	○

● = *desired answers*
Data: Single punch per row

10. Please select the best response (True, False, I don't know) for each of the following statements about the **risks** associated with the use of Xeljanz®.

		True	False	I don't know
A	Xeljanz® can be used in combination with other Janus kinase (JAK) inhibitors, immunomodulating biologics (e.g., biologic DMARDs), or with potent immunosuppressants such as azathioprine and cyclosporine.	○	●	○
B	Lymphoma and other malignancies have been observed in patients treated with Xeljanz®. An increase in malignancies, including lung cancer, were observed in rheumatoid arthritis patients 50 years or older with at least one additional cardiovascular (CV) risk factor who were taking Xeljanz® compared with TNF inhibitors.	●	○	○
C	Live vaccines should not be given concurrently with Xeljanz®.	●	○	○
D	Prior to administering Xeljanz®, it is NOT necessary to check patients' laboratory parameters including lymphocytes, neutrophils, and haemoglobin.	○	●	○
E	Xeljanz® should be used with caution in patients who may be at increased risk for gastrointestinal perforation.	●	○	○
F	Initiation of treatment with Xeljanz® should be avoided in patients with a low lymphocyte count (i.e., less than 0.5 x 10^9cells/L).	●	○	○

		True	False	I don't know
G	Caution should be applied when using Xeljanz® in geriatric patients (>65 years of age), patients who are current or past smokers, and patients with other CV risk factors.	●	○	○
H	Among rheumatoid arthritis patients 50 years or older with at least one CV risk factor, a dose dependent increase in frequency of pulmonary embolism was observed with Xeljanz® 5 mg BID and 10 mg BID compared to those treated with TNF blockers.	●	○	○
I	Major adverse cardiovascular events, including non-fatal myocardial infarction, were observed more frequently with Xeljanz® compared to TNF inhibitors in rheumatoid arthritis patients who were 50 years or older with at least one additional CV risk factor.	●	○	○

Answer: points a and d are wrong answers
Data: Single punch per row

SECTION D: QUESTIONS ABOUT IMPLEMENTATION OF BEHAVIOURS INTENDED TO REDUCE IDENTIFIED AND POTENTIAL SAFETY RISK.

11. In your clinical practice, before starting a patient on Xeljanz®, which of the following do you check or ask? Each question has a predefined desirable response aligned with aRMM recommendations.

		Yes	No
A	Does this patient have gastroesophageal reflux disease (GERD)?	○	●
B	Is the patient at an increased risk for non-melanoma skin cancer (NMSC)?	●	○
C	Are this patient's immunizations up to date?	●	○
D	Does this patient have a history of hyperthyroidism?	○	●
E	Is this patient at an increased risk for venous thromboembolism (VTE), including pulmonary embolism (PE) and deep vein thrombosis (DVT), and/or arterial thromboembolism?	●	○
F	Is the patient 65 years of age or older?	●	○

		Yes	No
G	Does the patient have a current malignancy or a past history of malignancy?	●	○
H	Does the patient have CV risk factors?	●	○
I	Is the patient a current or past smoker?	●	○

Desired responses: b, c, e, f, g, h, I *Data: Single punch per row*

12. In your clinical practice, which of the following tests do you perform prior to initiating a patient on Xeljanz®? Each question has a predefined desirable response aligned with aRMM recommendations

		Yes	No
a	Screen for viral hepatitis	●	○
b	Perform a urinalysis	○	●
c	Screen for latent or active tuberculosis (TB)	●	○
d	Check lymphocyte count	●	○
e	Check absolute neutrophil count	●	○
f	Check haemoglobin level	●	○
g	Check blood glucose level	○	●

Desired responses: a, c, d, e, f
Data: Single punch per row

13. In your clinical practice, which actions would you take when faced with the following scenarios during treatment follow-up and monitoring? Each question has a predefined desirable response aligned with aRMM recommendations.

		I would discontinue	I would interrupt dosing	I would lower the dose	I would take no action
A	The patient's neutrophil count <0.5 x 10^9cells/L. This is confirmed by repeat testing.	●	○	○	○
B	The patient's lymphocyte count is <0. 5 x 10^9 cells/L. This is confirmed by repeat testing.	●	○	○	○
C	The patient develops a serious infection, an opportunistic infection or sepsis.	○	●	○	○
D	The patient develops severe hepatic impairment (Child Pugh C).	●		○	○
E	The patient's haemoglobin level is less than <80 g/L or there is ≥20 g/L decrease. This is confirmed by repeat testing.	○	●	○	○
F	The patient has a suspected venous thromboembolism (VTE).	●	○	○	○

Answer: The black circles indicate a desired response *Data: Single punch per row*

14. In your clinical practice, how frequently do you perform each of these activities when initiating treatment with Xeljanz®? Please select the best response: "Always," "Sometimes," or "Never".

		Always	Sometimes	Never
a	Give the Xeljanz® patient safety card to the patient.	●	●	○
b	Advise the patient to inform you immediately if they experience any of the symptoms on the Xeljanz® patient safety card.	●	●	○

		Always	Sometimes	Never
c	Advise patients to carry the Xeljanz® patient safety card with them, particularly when they visit a doctor, a hospital, or Emergency Room.	●	●	○
d	Discuss the signs and symptoms of venous thromboembolism (VTE) with the patient.	●	●	○
e	Discuss the signs and symptoms of major adverse cardiovascular events with the patient	●	●	○

Data: Multiple punch per row
Answer: The black circles indicate a desired response

SECTION E: QUESTIONS ABOUT AWARENESS (RECEIPT) AND UTILISATION OF XELJANZ® aRMM MATERIALS

Redacted

15.1. Have you ever received a Prescriber Brochure for Xeljanz®? Please select one.

□ Yes □ No □ I don't remember

15.2. If yes, have you read the Prescriber Brochure for Xeljanz®? (*Answer only if Yes in 15.1)*

□ Yes, all of it □ Yes, some of it □ No, I did not read it □ I don't remember

15.3. How useful or not useful have you found the Prescriber Brochure for Xeljanz® in your clinical practice? (*Answer only if Yes in 15.2)*

□ Very useful □ Somewhat useful □ Not useful

16.1. Have you ever received a Prescriber Treatment Maintenance Checklist for Xeljanz®? Please select one.

□ Yes □ No □ I don't remember

16.2. If yes, have you used the Prescriber Treatment Maintenance Checklist for Xeljanz® in your clinical practice? (*Answer only if Yes in 16.1)*

□ Yes □ No, I did not read it □ I don't remember

16.3. How useful or not useful have you found the Prescriber Treatment Maintenance Checklist for Xeljanz® in your clinical practice? (*Anwers only if Yes in 16.2)*

□ Very useful □ Somewhat useful □ Not useful

17.1. Have you ever received a supply of Xeljanz® Patient Alert Card? This is a card which is designed to be given to patients. Please select one.

□ Yes □ No □ I don't remember

17.2. How useful or not useful have you found the Xeljanz® Patient Alert Card in your clinical practice? *(Answer only if Yes in 17.1).*

□ Very useful □ Somewhat useful □ Not useful

SECTION F: IMPLEMENTATION OF RISK-MINIMISATION BEHAVIOURS

Instruction: Please answer the following questions based on **your current clinical practice** or, where applicable, **how you would manage** patients if initiating or managing treatment with Xeljanz® in accordance with the aRMM recommendations.

F1. Prior to initiating Xeljanz®, which information sources do you routinely consult? (Select all that apply)

☐ Xeljanz® Prescriber Brochure

☐ Xeljanz® Prescriber Treatment Maintenance Checklist

☐ Nigerian Xeljanz® Product Label

☐ Xeljanz® Patient Alert Card

☐ Institutional or national treatment guidelines

☐ Other (please specify): _____

F2. When initiating Xeljanz®, how consistently do you apply the Prescriber Treatment Maintenance Checklist?

☐ Always

☐ Often

☐ Sometimes

☐ Rarely

☐ Never

☐ Not applicable (I have not yet prescribed Xeljanz®)

F3. Which of the following actions do you consider mandatory before initiating Xeljanz®? (Select all that apply)

☐ Confirm TB screening results

☐ Assess venous thromboembolism (VTE) risk factors

☐ Assess cardiovascular risk factors

☐ Review history of malignancy or non-melanoma skin cancer

☐ Review baseline laboratory parameters (e.g., haemoglobin, neutrophils, lymphocytes)

☐ None of the above

F4. If a patient treated with Xeljanz® develops symptoms suggestive of a serious infection, your usual immediate action would be:

☐ Interrupt treatment until the infection is resolved

☐ Discontinue treatment permanently

☐ Continue treatment with closer monitoring

☐ No specific action

F5. How frequently do you provide counselling to patients on the following topics when initiating Xeljanz®?

Signs and symptoms of serious infection: ☐ Always ☐ Often ☐ Sometimes ☐ Never

Signs and symptoms of venous thromboembolism (VTE): ☐ Always ☐ Often ☐ Sometimes ☐ Never

Signs and symptoms of major adverse cardiovascular events: ☐ Always ☐ Often ☐ Sometimes ☐ Never

Importance of carrying the Xeljanz® Patient Alert Card: ☐ Always ☐ Often ☐ Sometimes ☐ Never

F6. In your opinion, what are the main barriers to fully implementing the Xeljanz® aRMM recommendations in your practice?

☐ Low number of Xeljanz®-treated patients

☐ Limited time during consultations

☐ Limited access to diagnostic testing or laboratory services

☐ Complexity of patient risk profiles

☐ Lack of familiarity with aRMM materials

☐ No significant barriers

☐ Other (please specify): _____

Thank you for your participation in this survey!

ANNEX 2. ADDITIONAL INFORMATION

Not Applicable

Document Approval Record

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