# **PATIENT INFORMATION SHEET AND INFORMED CONSENT FORM**

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| **Study Title:** | **A** **Phase 4, Randomized, Double-blind, Placebo-Controlled, Efficacy and Tolerability Trial of Rimegepant for the Acute Treatment of Migraine in Adults Unsuitable for Triptan Use** |
| **Study Number:** | **BHV3000-406 (C4951004)** |
| **EudraCT Number:** | **2022-001175-14** |
| **Sponsor** | **Pfizer, Inc.**  **66 Hudson Boulevard East, New York,**  **NY 10001, USA** |
| **Investigator:**  **(Study Doctor)** | **Dr Conor Clerkin-Oliver** |
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## Introduction

You are invited to participate as a subject in a clinical research study. The Sponsor is providing funding to the study site to conduct the study. Your participation in this study is voluntary. This research study is studying the effects of an oral medication called "rimegepant" in a group of adults living with migraine. Rimegepant has been previously studied at the dose being used in the current trial (75 mg once daily, as needed), and has been approved by the U.K. Medicines and Healthcare products Regulatory Agency (MHRA) for the treatment of migraine attacks in adults.

Recently, the UKs National Institute for Health and Care Excellence (NICE) has issued final draft guidance recommending the use of rimegepant for acute migraine attacks

The current study is investigating the potential benefit of rimegepant in a group of adults who are not able to take "triptan" medications (a class of medication commonly prescribed to treat migraine attacks) due to prior lack of benefit, intolerable side effects, or other safety concerns.

The study is being conducted for Pfizer, Inc (a pharmaceutical company based in New York, U.S.A.). The study doctors and staff conducting this trial are being paid by Pfizer.

**Please note** where ‘**we**’ is mentioned in this document, this will refer to the sponsor Pfizer and not the study site.

Please read this form carefully. Take your time to ask the study doctor or study staff as many questions about the study as you would like. The study doctor or study staff can explain words or information that you do not understand. Reading this form and talking to the study doctor or study staff may help you decide whether to take part or not. If you decide to take part in this study, you must sign your name at the end of this form and date it.

During this study, you will receive either placebo (no medication) or Rimegepant (study medication). Rimegepant (approved in some countries as Nurtec ODT or Vydura) is a medication for the acute and preventive treatment of migraine in adults.

As of 26 August 2022, more than 8,900 people have taken part in the rimegepant clinical trial. It is estimated that approximately 6,036 people have been administered rimegepant across the clinical trials.

You may experience risks or discomforts when taking part in this study, and a summary of possible risks and discomforts will be provided to you. The summary is based on information collected in studies with rimegepant that have been completed in people and in animals.

The most common adverse effect possibly related to the use of rimegepant is nausea, which occurred in 1.2% of participants in trials for the acute treatment of migraine and 1.4% of participants in migraine prevention studies.

Most cases of nausea have been considered as mild or moderate in severity. Allergic reactions (also called, “hypersensitivity reactions”), including those causing shortness of breath and/or severe rash, have occurred uncommonly (less than 1%). You may also experience risks or discomforts that are unknown at this time.

*Thank you for reading this Information Sheet.*

**2. What is the purpose of the study?**

You are being asked to take part in this research study because you have episodic migraines and have tried at least two triptans unsuccessfully or triptan medications are not an option for you to take.

Migraine is a debilitating disorder that affects approximately 15% of the population. Migraines are characterised by recurrent attacks lasting 4 to 72 hours with multiple symptoms, including pulsating (throbbing) headaches of moderate to severe pain that could be associated with nausea or vomiting, and/or sensitivity to sound (phonophobia) and sensitivity to light (photophobia).

The purpose of this research study is to:

* Test the effectiveness of rimegepant compared with placebo in the acute treatment of migraine with subjects who:
  + Are at least 18 years old.
  + Have at least 1 year of migraines before the age of 50
  + Migraine attacks that last about 4-72 hours if untreated
  + Have 4-14 migraine days a month.
  + Have less than 15 headache days (migraine or non-migraine) per month
  + Have been unsuccessful with at least 2 triptan medications (for example, triptans did not improve your migraine symptoms, or you had prior intolerance to triptans, or you could not use triptans due to a safety concern)

This is a double-blind study, which means neither you nor the study doctor will know if you were given rimegepant or placebo. In the event of an emergency, the study doctor can get this information.

1. **Why am I being asked to take part in the study?**

You are being invited to take part in this research study because you have migraines and have tried at least two triptans unsuccessfully. This research study will be for a new medicinal product.

This research study is looking at Rimegepant as a possible therapy for the acute treatment of migraine in adults unsuitable for triptan use

Your participation in this study will last approximately 24 weeks and will include approximately8 study visits to the study centre.

* The Screening Phase can last up to 28 days.
* The double-blind study treatment phase (2 site visits) will last up to 45 days or until you have a migraine of moderate or severe intensity that is recorded in the electronic diary (eDiary, study-provided).
* The continued eligibility confirmation phone visit will occur after the double-blind study treatment phase. This visit is a phone call from the study site.
* The second 12 weeks is called the open-label extension phase (4 site visits).
* The last 2 weeks are called the follow-up phase (1 site visit).

This study will use competitive enrollment. This means that when a target number of subjects begins the study, all further enrollments will be closed. Therefore, it is possible that you could be in the screening phase, ready to begin the study, and be dropped without your consent if the target number of subjects has already begun the study.

About 900 subjects will participate in this study and approximately 600 subjects will receive Rimegepant or matching placebo.

**Washout Period**: If you are taking a medication that is not allowed while on this study, you may be asked to stop taking that medication. This is called a washout period, during which the effects of these medications leave your body.

**Use of the following migraine medications must be stopped for the pre-specified amount of time prior to your Screening Visit.**

* Atogepant and ubrogepant must be stopped at least 10-days prior to the Screening Visit
* Eptinezumab, erenumab, femanezumab, and galcanezumab must be stopped at least 6-months prior to the Screening Visit
* Botox (onabotulinumtoxinA) and CefalyTM (an external nerve stimulation device or devices like this) must be stopped at least 3-months prior to the Screening Visit

In addition, the use of other investigational medications (medications not yet approved by government agencies) must be stopped at least 30-days to 6-months prior to your Screening Visit, depending on the nature of the drug. Please inform your Study Doctor of all medicines you have taken over the 6 months prior to entering this study.

It is important that you discuss with your Study Doctor the benefits and risks of your participation in this study, in part to ensure that you are not deprived of the usual standard of care medications.

Before you stop any of your medications, it is important that you consult with the clinician who is prescribing the medication to you and your General Practitioner (GP)

**A full list of all the prohibited medications can be found in Section 8 of this document.**

1. **Do I have to take part?**

Your participation in this study is voluntary and the decision whether to take part or not is entirely yours. This decision will not affect your relationship with your doctor or affect your current or future medical treatment. If you want to, please discuss this study with your friends and family. Ask the investigator (the study doctor) about anything that is not clear or for additional information you may require.

Before agreeing to take part in this research study, it is important that you read and understand the following explanation of the proposed research study. This consent document describes the purpose, procedures, benefits, risks, discomforts, and precautions of the study. It also describes the alternative procedures that are available to you and your right to withdraw from the study at any time. No guarantees or assurances can be made as to the results of the study.

1. **What is the design of the study?**

This is a multicenter, phase 4, randomised, double-blind placebo-controlled study, with an open label extension (OLE) phase to assess the efficacy and tolerability of rimegepant for the acute treatment of migraine in a population of adult subjects that are unsuitable for the use of triptan medications due to previous intolerance, lack of efficacy, or contraindication (including a history of clinically significant cardiovascular disease). The total study duration for each subject will be up to 24 weeks.

1. **What will happen to me if I take part?**

If you agree to take part, you will participate in the study and will expect to take part in this study for 24 months and attend approximately 8 study visits to the clinic or hospital.

The information below describes what will happen to you during the study.

If the study doctor thinks you are suitable for the study, and you agree to take part, you will first be asked to sign and date the Informed Consent Form. You will then enter the Screening Period.This study will be conducted in 4 phases: Pretreatment Phase (including Screening Period and Baseline Period), Treatment Phase, Open-label extension phase and Follow-Up Phase (after the end of treatment).

**Screening Phase**

Screening Visit:

Before any study-related tests and procedures are performed, you will be asked to read, sign, and date this consent document. The following screening tests and procedures will then be performed to decide if you qualify to take part in this study:

Once the screening is complete, results may show that some participants do not qualify to be part of the study following screening, and therefore would be excluded. **A second screening would not be available.**

* Review of your medical history and past and current medications.
* You will be asked about your typical migraine symptoms, frequency, severity and how your migraines are treated monthly.
* You will be asked about all medications and (including those over the counter and vitamins) you are currently taking or have previously taken.
* A physical examination will be performed.
* Your vital signs and weight will be measured (blood pressure, heart rate, breathing rate and temperature), and height (only assessed at the Screening Visit).
* You will have blood samples collected (approximately 15 ml) for laboratory tests.
  + You should not eat at least 8 hours prior to these blood tests.
  + This will include a pregnancy test if you are a woman who may be able to become pregnant. The result of the pregnancy test must show that you are not pregnant for you to qualify to take part in this study.
  + Additional diagnostic testing will be completed including blood tests to assess your general health and the health of your kidneys and liver.
* A urine sample will be collected for:
  + A drug screen to test for drug abuse. The result of the test must meet study entry criteria evaluated by the study doctor for you to take part in this study.
* Your heart function will be assessed with an electrocardiogram (ECG – a test that measures and records the electrical activity of your heart).
* You will be asked to complete a questionnaire about any thoughts about suicide you may have had and any suicidal actions (Columbia-Suicide Severity Rating Scale).
* You will be asked how you are feeling.
* You will be given a concomitant medication paper log (sometimes referred to as a paper diary) to complete at home.
* You will not receive study drug at this visit.

**Double-Blind Study** **Treatment Phase**

The double-blind study treatment phase will have two (2) scheduled study visits, Baseline (Randomisation) and Double-Blind End of Study Treatment. **These visits must be completed in person**. Eligible subjects will be dispensed a single dose of double-blind study medication at the Baseline Visit.

At the Baseline (Randomisation) Visit, eligible subjects will be given a single tablet of study medication. The tablet will be either rimegepant or placebo. You have a 1 in 2 (50%) chance of receiving rimegepant or placebo. The look, feel, and taste of the blinded rimegepant and placebo tablets will be the same so study staff and subjects cannot tell which treatment they are receiving during this phase of the trial.

Baseline (Randomisation) Visit:

After your initial screening visit, you will be scheduled to return to the study site in approximately 3-28 days for the Baseline Visit. The following tests and procedures will be performed:

* Review of any changes in your health since your last visit.
* Review of the medications and vitamins you are currently taking or have previously taken.
* Your vital signs and weight will be measured.
* If you are a woman of childbearing potential: A urine sample will be collected for a pregnancy test. The result of the pregnancy test must show that you are not pregnant for you to continue to take part in this study.
* You will be asked about how you have been feeling and if you have had any important medical events since your last visit.
* You will be provided an electronic diary (eDiary) and will be trained on how to use the eDiary by the study staff. Your use of the handheld device is required for you to be part of this study. Your data will be securely, accurately, and dependably transmitted from the handheld device to the study servers. All transmissions will be concealed to help protect the confidentiality of your data.
* You will be asked to complete the Migraine-Specific Quality-of-Life Questionnaire (MSQ) 24 hours after you have taken the study medication.
* You will be asked to complete a questionnaire about any thoughts about suicide you may have had and any suicidal actions (Columbia-Suicide Severity Rating Scale).
* You will be asked to complete a questionnaire about how having migraines affects your life in-between attacks (Migraine Interictal Burden Scale; MIBS).
* If you are eligible, you will be given a rescue medication paper log (sometimes referred to as a paper diary) to complete at home.
* If you are eligible, the study doctor or study staff will give you a single tablet of blinded study medication (either rimegepant or matching placebo) and dosing instructions (you will be told when and how to take the drug).

Study Treatment Period:

During the study treatment period at any time you experience a migraine, you should use the eDiary to report your migraine.

**Once a migraine reaches moderate to severe intensity you must answer the questions in your eDiary before taking study medication**.

Upon completion of all questions, the eDiary will prompt you to take study medication, without further delay.

The eDiary will ask you questions:

* Every day, before being treated with study medication, the eDiary will send timed reminders to complete a daily check-in. In the daily check-in, there will be questions on whether you have a migraine. If you confirm you have a moderate to severe migraine headache pain, then you will be asked to provide information indicating whether you have taken any other migraine medications. If this is not the case, then you will be asked whether you are ready to take the study medication.
* You will be instructed to only take the study medication when your migraine reaches moderate to severe headache pain intensity and **after** you have answered some questions about your current migraine.
  + In the event you experience migraine symptoms (such as visual aura) which prevent you from being able to complete the eDiary questionnaires, you will be allowed to take permitted medication, as needed, to treat those symptoms. Under such circumstances, you should not take blinded study medication. Once able, you should return to the eDiary to complete all questions and to follow related instructions.
* You will be asked to answer the following specific questions using the handheld device:
  + **Assessment of Migraine Pain** – (indicate if you have no migraine pain, mild, moderate or severe pain) just prior to taking your study medication, and then 15, 30, 45, 60 and 90 minutes, and 2, 3, 4, 6, 8, 24 and 48 hours after taking study medication
  + **Assessment of Migraine Symptoms** (photophobia, phonophobia and nausea) – just prior to taking your study medication and then 15, 30, 45, 60 and 90 minutes and 2, 3, 4, 6, 8, 24 and 48 hours after taking study medication
  + **Functional Disability Scale** (how the current migraine headache is affecting your health) – just prior to taking your study medication, 15, 30, 45, 60 and 90 minutes and 2, 3, 4, 6, 8, 24 and 48 hours after taking study medication.
  + **Health-related quality of life impairments (difficulties)** caused by the migraine headache (MQoL - Migraine Quality of Life Questionnaire, 16 questions) - to be completed 24 hours after taking study medication.

**If you are a woman who may be able to become pregnant, you will need to complete an at-home (urine) pregnancy test, to confirm you are not pregnant, before taking study medication for the very first time**.

While at-home pregnancy test kits will be made available to you, upon request, throughout the conduct of the trial, you will only be required to perform at-home (urine) pregnancy testing prior to taking study medication for the very first time.

Once home pregnancy testing results show you are not pregnant, and all diary entries are complete, you may take study medication, as directed by the eDiary, without further delay.

* **If you do not have a migraine within the 45-day study treatment period, you should not take the study medication.** You will be scheduled to return to the study site for an end of study treatment visit with your unused study medication, eDiary, rescue and concomitant medication log.
* You will complete two paper diaries; your rescue medication paper diary (**a diary used for recording all non-study medications taken for the purpose of treating unresolved migraine symptoms**) and your concomitant medication paper diary (**a diary used for recording** **all non-rescue and non-study medications for e.g., vitamins or supplements)** if you take any medication that is not your study medication.

End of Double-Blind Study Treatment Visit:

* A physical examination will be performed.
* Your vital signs and weight will be measured.
* You will have blood samples collected (approximately 15 ml):
* Including a pregnancy test (blood or urine test is acceptable) if you are a woman who may be able to become pregnant.

* These laboratory tests will be used as one of the factors to figure out if you are eligible for the Open-Label Extension Phase.
* You will have an electrocardiogram (ECG) at this visit, only if you are not continuing into the Open-Label Extension Phase
* You will also be asked about any medications that you have taken since your last study visit.
* You will be asked about how you have been feeling and if you have had any important medical events since your last visit.
* Your eDiary will be reviewed for completeness.
* You will be asked to complete a questionnaire about any thoughts about suicide you may have had and any suicidal actions (Columbia-Suicide Severity Rating Scale).
* You will return the used or unused study medication wallet, even if this is empty.
* You will return your two paper diaries, the rescue medication paper diary and the concomitant medication paper diary for review.
* At this visit you will also be evaluated for entry into the 12-week Open-label Extension Phase following laboratory results within acceptable ranges per protocol.

**Open-label Extension Phase**

If you are still on study treatment or in the follow up at the time the study has a data cut off, you may be able to continue to receive the same study treatment as part of the Extension phase.

**If you did not complete the double-blind study treatment phase or if you did not continue to meet the study requirements, then would not be eligible for this part of the study.**

Participation entrance into the open-label extension phase is assessed at the double-blind end of study treatment visit. If you continue to qualify for the open-label extension phase at the double-blind end of study treatment visit, you will be given study medication for the open-label phase. Study medication in the open-label extension phase is Rimegepant. There is no placebo in this phase.

Eligibility Confirmation Phone Visit

**You must wait to take the first dose of open-label study drug until the study staff contacts you to confirm that you are eligible for this phase of the study, based on your laboratory test results.** This contact will be made through a Telephone visit call.

You will be required to report information about your headaches and migraines you experience during the open-label extension phase (12 weeks) using the eDiary.

The eDiary will ask you questions such as:

* If you took your medication drug as directed.
* The intensity of the migraine (mild, moderate, or severe), the time of and/ or duration of the migraine.
* If you took any standard of care medications to treat the migraines, you will record this information on a paper diary which will be provided to you by the study staff.
  + In the event you experience migraine symptoms (such as visual aura) which prevent you from being able to complete the eDiary questionnaires, you will be allowed to take permitted medication, as needed, to treat those symptoms. Under such circumstances, you should not take open-label study medication. Once able, you should return to the eDiary to complete all questions and to follow related instructions.
* 24 hours after the **first five (5)** qualifying migraines (must be of moderate or severe headache pain intensity) are reported and study drug has been taken, you will be required to complete the Migraine Quality of Life Questionnaire (MQoL). This questionnaire has 16 questions.

During the open-label extension phase, you, the study doctor, study staff and the Sponsor will know the study medication (r1imegepant) and the dose (75 mg) that you are given; there is no placebo during this part of the study.

In the open-label extension phase, you will be instructed to take open-label study medication (r1imegepant 75 mg) once daily as needed to treat migraines of moderate to severe headache pain intensity, consistent with dosing in the double-blind phase.

Notably, throughout the study, you are **not** permitted to take study medication more than once daily and are **not** permitted to use study medication on more than 18 calendar days per month (a month is considered as a 28-day period of time).

If you require medication for the management of migraine headaches beyond once daily or on >18 days per month, you will be allowed to use other migraine medications that are permitted by the study protocol. In such circumstances, you should inform your study doctor or study site.

If you stop the open-label extension phase early (before Week 12), you will have an early termination visit to complete the open-label end of study treatment assessments. You will also need to return for the Follow-up Week 2 Safety Visits after the Early Termination Visit.

Week 2, Week 4, and Week 8 Visits:

The following tests and procedures will be performed at Weeks 2, 4 and 8:

* Review of any changes in your health since your last visit.
* Review of the medications and vitamins you are currently taking or have previously taken.
* Your vital signs and weight will be measured.
* If you are a woman of childbearing potential: A urine sample will be collected for a pregnancy test. The result of the pregnancy test must show that you are not pregnant for you to continue to take part in this study.
* You will be asked about how you have been feeling and if you have had any important medical events since your last visit.
* Blood sample collection for laboratory tests (approximately 15 ml) ***– week 4 only.***
* At every visit, you must bring:
  + Your eDiary for review of completeness.
  + Paper Diaries for review of completeness.
  + Study medication (used and unused wallets).
* You will be asked to complete a questionnaire about any thoughts about suicide you may have had and any suicidal actions (Columbia-Suicide Severity Rating Scale) ***– week 4 only.***
* You will be asked to complete a questionnaire about how having migraines affects your life in-between attacks (Migraine Interictal Burden Scale; MIBS) ***– week 4 and week 8 only.***
* If needed, additional study medication will be dispensed.

Week 12 or Open-Label Extension End of Study Treatment Visit:

The following tests and procedures will be performed at Week 12 or if you end your participation early in the open-label extension phase for any reason:

* A physical examination will be performed.
* Your vital signs and weight will be measured.
* You will have blood samples collected (approximately 15 ml):
* Including a pregnancy test if you are a woman who may be able to become pregnant.
* You will be asked about how you have been feeling and if you have had any important medical events since your last visit.
* You will also be asked about any medications that you have taken since your last study visit.
* Your eDiary will be reviewed and returned.
* You will return the used and unused study medication wallets.
* You will return your two paper diaries, the rescue medication paper diary and the concomitant medication paper diary for review.
* Your heart function will be assessed with an electrocardiogram (ECG - a test that measures and records the electrical activity of your heart).
* You will be asked to complete a questionnaire about any thoughts about suicide you may have had and any suicidal actions (Columbia-Suicide Severity Rating Scale).
* You will be asked to complete a questionnaire about how having migraines affects your life in-between attacks (Migraine Interictal Burden Scale (MIBS)).
* You will be asked to complete the Migraine-Specific Quality-of-Life Questionnaire (MSQ).

**Follow-Up Phase (after the end of treatment):**

**Follow-up Visit (Week 2)**

* Review of any changes in your health and if you have had any important medical events occur since your last visit.
* Review of the medications and vitamins you currently are taking or have previously taken.
* Your vital signs and weight will be measured.
* If you are a woman of childbearing potential: A urine sample will be collected for a pregnancy test.
* You will be asked how you have been feeling since your last visit.
* Your paper diary will be reviewed by study staff.

Study Treatment:

The study medication is rimegepant or matching placebo. Rimegepant is an oral disintegrating tablet (a tablet that is taken by and dissolves in the mouth), 75 mg, taken orally.

During the **double-blind study treatment phase**, you will be randomly assigned by chance (like the flip of a coin) to receive either rimegepant or placebo (inactive medication which looks like rimegepant but does not have a medicinal effect).

You will have a 50%chance (1 in 2)of receivingrimegepantand a 50% chance (1 in 2) of receiving placebo. This is a double-blind study, which means neither you nor your study doctor (Investigator) will know which of the study medication groups you are assigned to. In case of an emergency, however, the study doctor can get this information.

All subjects who enter the **open-label extension phase**, will receive open label rimegepant.

After Study Treatment:

Because this is a research study, the study medicationwill be given to you only during this study and not once the study is over. This study medicationmay be available by prescription for acute treatment of migraine and migraine prevention.

1. **What are my responsibilities while I am in the study?**

As a patient in this study, you will have responsibilities while taking part. These responsibilities are listed below.

* Attend each scheduled visit.
* Tell the study doctor and study staff about any change in your health and medications (including over-the-counter medications and supplements).
* Take the study medication as instructed by the study doctor and study staff.
* Store the study drug as instructed by the study doctor and study staff.
* Return all unused study medication (including empty wallets) to the study staff. Bring the unused study medication (including empty wallets) with you to every site visit.
* Complete the questionnaires using your handheld device at **all** the appropriate time points.
* Complete the paper diaries as per instruction. Bring the paper diaries with you to every site visit for review.
* Complete the eDiary as per instruction.

**8. Is there any medication I am not allowed to take whilst on this study?**

**Prohibited and Restricted Medications and Devices Taken During the Study**

**The following medications and devices should not be taken during the study (i.e., starting from the screening visit and through the Follow-up Week 2 Visit), unless otherwise specified.**

**If you would like to understand more about why these medications are restricted, then please speak to your study team or study doctor.**

1. Acetaminophen or paracetamol containing products for the treatment of pain that is not a migraine or a headache. If it is used for migraine or a headache during the study, cannot be taken more than 1000 mg per day or over two (2) consecutive days at a time.
   1. Non-narcotic analgesics such as ibuprofen or naproxen, of the class nonsteroidal anti-inflammatory drugs [NSAIDs], or gabapentin, cannot be taken more than fifteen (15) -days per month for non-migraine pain.
   2. Triptans (e.g., almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan, zolmitriptan, etc.)
   3. Other CGRP antagonists (beyond rimegepant), including:

-Oral CGRP antagonists such as atogepant and ubrogepant must be stopped at least ten (10) -days prior to the Screening Visit and are prohibited throughout the study.

-CGRP antagonist monoclonal antibodies such as eptinezumab, erenumab, femanezumab, and galcanezumab must be stopped at least six (6)-months prior to the Screening Visit and are prohibited throughout the study.

-The use of non-study Rimegepant is prohibited throughout the study.

* 1. Botox (onabotulinumtoxinA) must be stopped at least three (3)-months (12 weeks) prior to the Screening Visit and not taken throughout the study.
  2. All devices and/or procedures used for the acute and preventive treatment of migraine (e.g., nerve blocks, nerve stimulators such as Cefaly), must be stopped within three (3)-months (12 weeks) of the Screening Visit and throughout the study.
  3. Ergotamine taken  ten (10) days per month on a regular basis for  three (3) months ( 12 weeks) in the year prior to the Screening Visit and is prohibited throughout the study.
  4. Lamotrigine is prohibited.
  5. All forms of marijuana and inhaled cannabidiol (CBD) and THC-containing products are prohibited.
  6. Narcotics, such as opioids (e.g., morphine, codeine, oxycodone, hydrocodone) or barbiturates (e.g., butalbital) taken  four (4) days per month during the three (3) months (12 weeks) prior to the Screening Visit and are prohibited throughout the study
  7. Participation in any other investigational clinical trial while taking part in this clinical trial.
  8. Use of an investigational agent, other than r1imegepant, for the purpose if this clinical study.

Other prohibited medications during the study:

* Moderate to strong inducers of the CYP3A4 enzyme (non-exhaustive list) such as apalutamide, avasimibe, bosentan, carbamazepine, dexamethasone, mitotane, modafinil, nafcillin, phenobarbital, phenytoin, primidone, rifabutin, rifampin, rifapentine, St. John’s wort, etc.
* Moderate to strong inhibitors of the CYP3A4 enzyme (non-exhaustive list) such as aprepitant, boceprevir, casopitant, cimetidine, ciprofloxacin, clarithromycin, cobicistat, crizotinib, cyclosporine, diltiazem, dronedarone, erythromycin, fluconazole, fluvoxamine, imatinib, isavuconazole, itraconazole, ketoconazole, lefamulin, letermovir, mibefradil, mifepristone, nefazodone, netupitant, posaconazole, ravuconazole, ritonavir, telaprevir, telithromycin, tofisopam, troleandomycin, verapamil, voriconazole, etc.
* Strong inhibitors of the P-gp (P-glycoprotein) transporter (non-exhaustive list) such as amiodarone, clarithromycin, cyclosporine, dronedarone, itraconazole, ketoconazole, lapatinib, lasmiditan, propafenone, quinidine, ritonavir, verapamil, etc.

**9. What are the potential side effects, risks and discomforts if I take part in the study?**

Taking part in this study has some risks. The study medication(s) or procedure(s) may make you feel unwell or uncomfortable.

Side effects might be mild or serious. The study doctor may determine that you need additional procedures or medicines to help manage the side effects.

**It is important that you report all symptoms and side effects to the study team as soon as they happen, even if you feel the study medication or procedure was not the cause.**

**SIDE EFFECTS OF RIMEGEPANT**

**Like all medicines, this medicine can cause side effects, although not everybody may experience them.**

**The most common adverse reaction was nausea for acute treatment (1.2%) and for migraine prevention (1.4%). Most of the cases of nausea were mild or moderate in severity.**

**Allergic reactions (also called, “hypersensitivity reactions”), including those causing shortness of breath and/or severe rash, have occurred uncommonly (less than 1%). In some cases, hypersensitivity reactions can be delayed and can occur days after starting rimegepant.**

**Other Risks**

**There may be other risks that are currently unknown.**

**All drugs have the potential to cause an allergic reaction, which (if not treated quickly) could become life-threatening. You should get medical help right away or call your local emergency number and contact the study doctor if you think you have any of the following symptoms of**

**a serious allergic reaction: trouble breathing or swelling of the face, mouth, lips, gums, tongue, or neck. Other allergic reactions may include rash, hives, or blisters.**

**Risks of Study Procedures**

You may feel discomfort during some of the tests and there are some risks, such as:

* Blood samples: Possible side effects from blood drawing include faintness, inflammation of the vein, pain, bruising, or bleeding at the site of puncture. There is also a slight possibility of infection.
* Electrocardiogram (ECG): Skin irritation is rare but could occur during an ECG from the electrodes or gel that is used.
* Questionnaires: The questionnaires used in this study may be upsetting. You do not need to answer any questions that you are not comfortable with. If you decide not to complete certain questionnaires, you may not be eligible to continue participation in this study.
* If you are having suicidal thoughts, you can call 999 and or The Samaritans on 116 123 that is answered 24 hours a day with a skilled, trained counselor. If you receive placebo (the inactive substance) as part of this study, your symptoms may not improve.

**Unforeseen Risks**

The study medication (rimegepant) and dosing regimen (75 mg once daily as needed) being used in this study has been previously investigated in clinical trials of adults living with migraine.

Rimegepant (brand names, “*Vydura*” and “*Nurtec ODT*”) has been previously approved by the U.K. Medicines and Healthcare products Regulatory Agency (MHRA) as well as other global regulatory authorities (e.g., U.S. FDA and European Medicines Agency [EMA]) for the treatment of migraine in adults.

While the medication has been shown to be generally well-tolerated by adults using rimegepant for the treatment of migraine attacks, there is the potential that you could experience an adverse effect(s) or serious adverse effect(s), following dosing with rimegepant.

Throughout the study, your wellbeing will be regularly monitored (by physical examination, blood tests, questionnaires, and other testing). If you were to experience any change in your health status during the course of the trial, you are to inform your study doctor or study staff using the details provided at the front of this document.

If you were to experience a serious or life-threatening medical event, you are to access standard emergency care and later notify your study doctor or study team as soon as it is safely feasible for you.

In addition, there may be unknown risks to a pregnancy, or to the embryo, fetus, and/or child were you (or your pregnant partner) to become pregnant while taking study medication.

**If you suspect you (or your sexual partner) may be pregnant, you should not take any additional doses of study medication and should contact your study doctor or study team immediately.**

If you are a female who can become pregnant, or a male with a sexual partner(s) who can become pregnant, you will be required to use contraception to prevent pregnancy (further details are provided below).

If, at any time during your participation in the clinical trial, you were to develop suicidal thoughts or any consideration of self-harm, you are to immediately stop any further dosing of study medication and contact your study doctor or study team as soon as it is safe to do so. Site contact information can be found at the front of this document.

In such an occurrence, your study site will perform a first assessment and discuss a care plan with you.

The study investigator may recommend that you permanently discontinue from the trial and/or may refer you to an Accident and Emergency Centre (A&E) for further psychiatric evaluation and treatment.

The study investigator is to urgently inform your General Practitioner (GP) of the event and appropriately document the occurrence in the study record.

As needed, psychiatric services are available to you:

* Help and support is available 24-hours-a-day from the Samaritans by calling 116 123
* Mental health advice and possible referral are available by calling the NHS non-emergency hotline on 111 or by going online and entering “111.nhs.uk”
* In the case of a psychiatric emergency, which requires immediate intervention to prevent significant danger to yourself or another, dial “999” on your phone to access an emergency operator or go to the nearest A&E

Electronic Devices:

At the Baseline (Randomisation) Visit, you will be supplied an electronic diary (eDiary). When you use this eDiary some of your personal information will be transferred electronically via the Internet.

While every effort will be made to protect the confidentiality of your information, electronic transmissions via the Internet are not necessarily secure from interception, and absolute

confidentiality cannot be guaranteed. A complete description of the data collection and sharing for the eDiary can commonly be found in the Terms of Use, End User License Agreement, or

Privacy Policy associated with the device. If you would like to read these documents, request a copy or instructions about how to access this information from the study doctor.

We, as the Sponsor of the trial, and our contracted partners should not be collecting nor sharing any personal identifying information (such as name, address, telephone number, or government-issued identification number) throughout the conduct of this trial.

##### Birth Control Requirements:

* If you are currently pregnant, plan to become pregnant, or are breastfeeding a child, you should not join this study.
* If you are able to become pregnant and you join this study, you must take appropriate

precautions to prevent pregnancy during the study and for 28 days after the last dose of the

study drug.

**Use of Birth Control**

* If you are able to have children and you are sexually active, you must use contraception consistently and correctly during the study and for 28 days after you have stopped taking the study medication.
* The study doctor will discuss with you the methods of contraception that you should use while you are in this study. The study doctor will help you select the method that is appropriate for you. At each of your study visits, the study doctor may review contraception methods with you and make sure you understand how to use your selected contraception method.
* If abstinence (not having sexual intercourse at all) is your usual and preferred lifestyle, and both you and the study doctor agree that it is your selected method of contraception, you must continue not to have sexual intercourse or you or your partner may become pregnant.
* The study doctor or designee will discuss with you regarding the need to use effective contraception consistently and correctly. You will need to affirm your consistent and correct use of the selected methods of contraception. You are asked to immediately notify the site if the selected contraception method is discontinued.

**Pregnancy Follow-Up**

If you or your partner become pregnant during the study or within 28 days after you have stopped taking the study medication, tell the study doctor immediately. Also tell the health care provider(s) taking care of you or your partner during the pregnancy that you took part in this study.

The study doctor will ask if you or your partner or your health care provider(s) are willing to

provide updates on the progress of the pregnancy and its outcome. If you or your partner agree, this information will be provided to the sponsor for safety follow-up.

**10.What are the alternatives for treatment?**

**Alternatives to Participation**

You do not have to be in this study to receive treatment for your migraines. Your options may include:

* Prescription and non-prescription medications such as aspirin, acetaminophen, non-steroidal anti-inflammatory medication (NSAIDs) such as ibuprofen and naproxen, combination pain relievers with aspirin, acetaminophen and caffeine, opioids, triptans, and ergotamine and Botox. Some of these medications are approved by the FDA specifically for the treatment of migraine.

Please talk to the study doctor about your options before you decide whether or not you will take part in this study.

**New Findings**

Any new important information that is discovered during the study and which may influence your willingness to continue participation in the study will be provided to you.

**11. Will I receive any benefits or payments for being on this study?**

###### Benefits

There is no guarantee that you will benefit from your participation in this study. Information learned from the study may help other people in the future.

# **Compensation for participation**

You will not have to pay to take part in this study. Any travel and accommodation costs will be reimbursed up to the amount of £150.00. Any expenses over this amount will need to be approved by the sponsor or sponsor delegate. You will not receive any other payments for taking part in this study.

Pfizer will reimburse the clinic or hospital for the cost of including you in the study, but no payment will be made to the study doctor or to you for taking part. Reasonable travel expenses for attending the clinic or hospital for the study visits will be reimbursed.

You should keep the receipts of travel expenses where available and discuss with the study doctor or staff to arrange reimbursement of travel costs.

# **Ethics and Regulations of the Study**

This study was given a favourable ethical opinion by the South Central – Oxford B Research Ethics Committee Research Ethics Committee.

**12. What will happen to my Personal Data, and will it be safe?**

**Processing of Personal Data for the Study**

### How will we use information about you?

We will need to use information from your medical records for this research project.

This information will include:

* Some of your background information, such as your gender, your age, your ethnicity and
* All the medical information relevant for the study, including your medical history, your medical condition, and the results of your examinations performed during the study.

People will use this information to do the research or to check your records to make sure that the research is being done properly.

People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead.

We will keep all information about you safe and secure.

Some of your information will be sent to **countries** **such as the United States of America and other countries**. They must follow our rules about keeping your information safe.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

Your personal information will be collected, used, and shared (together called “processing”) in compliance with applicable privacy laws. The use and disclosure of your study records will be done in accordance with the Authorisation to Use and Disclosure your Protected Health Information.. Outside of the clinical site, you will be identified at all times by a number. The records and information labelled with this code are called “Coded Information.” The study site will keep the link between the code and your name confidential. Your information will be transferred to the Sponsor using the unique code assigned to you. The Sponsor’s employees and those with whom your Coded Information is shared are required to protect your Coded Information and will not attempt to re-identify you. If the results of this study are published or presented at meetings, you will not be identified.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

The sponsor may use and has a legitimate interest in using your coded information in the future to support and advance other scientific research projects, including improving the quality, design and safety of other research studies, research supporting public health aims and developing medicines, vaccines, diagnostic products and tools.

At this time, we do not know the specific details of these research projects; however, your coded information could be used in combination with data from other sources, not related to you or this study. Reasonable safeguards will be used to protect your coded information used in any future research and may include: (a) limiting access to individuals bound by duties of confidentiality; (b) taking steps to minimize the risk that you could be re-identified; and (c) obtaining approval of ethical review boards. Furthermore, if your coded information is anonymised such that they can no longer be identified with you, they may be used for future research purposes.

### What are your choices about how your information is used?

* You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.
* If you choose to stop taking part in the study, we would like to continue collecting information about your health from central NHS records/ your hospital/ your GP. If you do not want this to happen, tell us and we will stop.
* We need to manage your records in specific ways for the research to be reliable. This means that we won’t be able to let you see or change the data we hold about you.

### Where can you find out more about how your information is used?

You can find out more about how we use your information

* At [www.hra.nhs.uk/information-about-patients/](https://url.avanan.click/v2/___http:/www.hra.nhs.uk/information-about-patients/___.YXAzOmxpbmljYWxncm91cDphOm86YTc2NWM0NTQ4ZWMxZmMwNjk4YTk3N2U1MDE4MGVjNzU6NjpiMDkzOmFhZGRjOTdjMzI1MWEwMzliNTdlNGMwZjI1YmE3Y2VkMDFiZDk4ZDVkOGJhYTQ0ODgxZDI2YWQ0MGIxODNkZWI6cDpU)
* our leaflet available from [**www.hra.nhs.uk/patientdataandresearch**](https://url.avanan.click/v2/___http:/www.hra.nhs.uk/patientdataandresearch___.YXAzOmxpbmljYWxncm91cDphOm86YTc2NWM0NTQ4ZWMxZmMwNjk4YTk3N2U1MDE4MGVjNzU6NjoxOThiOmNjMDJkMTkwOGQyMDU2ZTkzZWMyZDk1NTZiNDU4YWEwZmNhOGZhOGI3NWY4NGE2ZTMzOGI0ZjYzMGM1M2JlMWY6cDpU)
* by asking one of the research team
* At www/dpo.pfizer

**13. What happens if I am injured whilst taking part in the study?**

**Compensation for Injury**

You should inform the General Practitioner (GP) treating you that you are taking part in this study. If you tell the study staff that you think you have been injured, then they will help you get the care you need.

If you are injured as a result of taking the study medication(s) or from procedures done for the purpose of this study, the sponsor will pay for any medical expenses necessary to treat your injury.

The sponsor of this study has taken out an insurance policy with the company

**Policy number UKCAID35629 issued by Chubb European Group SE, London, in the name of Pfizer Inc. provides Clinical Trials Liability Insurance to cover all patients who take part in this study.**

By signing and dating this informed consent document, you will not lose any of your legal rights or release anyone involved in the research from responsibility for mistakes.

**Costs**

There will be no charge to you for your participation in this study. The study medication, study-related procedures, and study visits will be provided at no charge to you.

**Whom to contact about this study**

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study such as:

* Whom to contact in the case of a research-related injury or illness;
* Payment or compensation for being in the study, if any;
* Your responsibilities as a research subject;
* Eligibility to take part in the study;
* The study doctor’s or study site’s decision to exclude you from participation;
* Results of tests and/or procedures;

**Please contact the Study Doctor at the telephone number listed on the first page of this consent document.**

If you seek emergency care, or hospitalisation is needed, alert the treating clinician that you are participating in this research study.

**Complaints**

If you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, you should contact Dr Conor Clerkin-Oliver, 012 655 0166, [cclerkin@re-cognitionhealth.com](mailto:cclerkin@re-cognitionhealth.com)

To find out about how to make a complaint, please ask a member of staff or contact PALS for more information.

If you’re not happy with the care or treatment you’ve received and your concerns have not been resolved with input from PALS, you may wish to make a formal complaint.

You can do this by writing to our Compliance Team, or you can email them] via [compliance@re-cognitionhealth.com Compliance Team Address: 77 Wimpole Street, London, W1G 9RU, United Kingdom.

**14. What happens if I want to leave the study?**

Voluntary Participation/Withdrawal

Your decision to take part in this study is voluntary. You may choose to not take part, or you may withdraw from the study for any reason without penalty or loss of benefits to which you are otherwise entitled and without any effect on your future medical care. **However, please note that any information collected up to the point of your withdrawal cannot be removed from the study.**

The study doctor or the Sponsor can stop your participation at any time without your consent for the following reasons:

* If it appears to be medically harmful to you;
* If you do not follow directions for taking part in the study, including failure to complete the electronic diary (and paper diaries) or failure to show up at the site for study visits.
* If it is discovered that you do not meet the study requirements;
* If the study is canceled; or
* For administrative reasons, including competitive enrollment - the target number of subjects has entered the study.

If you leave the study for any reason, the study doctor may ask you to have some end-of-study tests for your safety.

You may request that any samples that have been collected from you as part of the study be destroyed, and in some countries, local laws or regulations may require that your samples be

destroyed regardless of whether you specifically make such a request. However, we cannot guarantee the destruction of samples because, for example, the samples may no longer be traceable to you or the samples may have been used up.

General Practitioner **Notification**

By signing this consent form, you are agreeing to the study site informing your general practitioner (GP) of your participation in this trial.

|  |  |
| --- | --- |
| Name and address of family doctor or primary health care provider: | Name: |
| Address: |
|  |
| Telephone and Fax Number: | Tel: |
| Fax: |

### **CONSENT FORM**

|  |  |
| --- | --- |
| **Study Title:** | **A** **Phase 4, Randomized, Double-blind, Placebo-Controlled, Efficacy and Tolerability Trial of Rimegepant for the Acute Treatment of Migraine in Adults Unsuitable for Triptan Use** |
| **Subject Number for this Study:** | \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ |
| **Sponsor:** | **Pfizer, Inc.**  **66 Hudson Boulevard East, New York,**  **NY 10001, USA** |
| **Name of Investigator:** |  |

**Please initial the ‘Yes’ column if you agree or initial the ‘No’ column if you do not agree**:

|  |  |  |
| --- | --- | --- |
| 1. I confirm that I have read and understand the Information Sheet specific for UK V4.0 dated 28Dec2023 for the above study and have had the opportunity before today to discuss the study and ask questions. My questions have been answered to my satisfaction and I have had time to decide whether I wish to take part. | **Yes** | **No** |
| 1. I understand that my taking part is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. | **Yes** | **No** |
| 1. I understand that sections of any of my medical notes may be looked at by responsible individuals from the Sponsor, its affiliates and their associates or legitimate third-party contractors, consultants, health/regulatory authorities or other approving bodies, or ethics committees where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. | **Yes** | **No** |
| 1. I agree to my personal data being used for the purposes of the study, and to my data being shared with the Sponsor, third party contractors and consultants, and heath/regulatory authorities and other authorised entities both within and outside this country, as described in the Information Sheet. I acknowledge that this may involve my data being transferred to countries outside the European Union and the European Economic Area which may not provide the same standard of legal protection for my data as in this country. | **Yes** | **No** |
| 1. I agree to take part in the above study. | **Yes** | **No** |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  |
| Name of patient |  | Date |  | Signature |  |

***For the Principal/Site investigator***

|  |
| --- |
| I confirm that I will provide the patient with a copy of the signed Patient Information Sheet and Consent Form, at the time of signing. |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  |
| Name of person taking consent (if different from Investigator) |  | Date |  | Signature |  |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  |
| Name of Investigator |  | Date |  | Signature |  |

*\*1copy for participant; 1 copy for researcher site file; 1 (original) to be kept in medical notes or subject source file.*