# Medicines Management Programme

# Managed Access Protocol – Medicines for the management of episodic and chronic migraine

| Medicine | Date of addition to Managed Access Protocol |
|---|---|
| **Erenumab (Aimovig®)** | 01/09/2021 |
| **Fremanezumab (Ajovy®)** | 01/10/2021 |
| **Galcanezumab (Emgality®)** | 01/04/2022 |
| **Eptinezumab (Vyepti®)** | 28/06/2023 |
| **Atogepant (Aquipta®)** | 01/02/2025 |
| **Rimegepant (Vydura®)** | 01/02/2025 |

| **Approved by** | **Professor Michael Barry, Clinical Lead, MMP** | |
|---|---|---|
| **Date approved** | Version 1.0 | 11/08/2021 |
| **Date updated** | Version 1.1 | 01/09/2021 |
| | Version 1.2 | 05/10/2021 |
| | Version 1.3 | 01/04/2022 |
| | Version 1.4 | 28/07/2023 |
| | Version 2.0 | 31/01/2025 |

# Table of Contents

# List of Tables



# List of Abbreviations

| | |
|---|---|
| CGRP | Calcitonin gene-related peptide |
| CHO | Chinese hamster ovary |
| CYP | Cytochrome P450 |
| HSE | Health Service Executive |
| HTH | High Tech Hub |
| ICHD | International Classification of Headache Disorders |
| MAB | Monoclonal antibody |
| MAP | Managed Access Protocol |
| MMD | Monthly migraine days |
| MMP | Medicines Management Programme |
| OATP | Organic anion transporting polypeptide |
| PCRS | Primary Care Reimbursement Service |
| PFP | Pre-filled pen |
| PFS | Pre-filled syringe |
| SmPC | Summary of Product Characteristics |

## 1. Medicines for the management of episodic and chronic migraine

There are currently five medicines referenced in this Managed Access Protocol (MAP) for the management of episodic and chronic migraine that are available under the High Tech Arrangement; atogepant (Aquipta®), erenumab (Aimovig®), fremanezumab (Ajovy®), galcanezumab (Emgality®) and rimegepant (Vydura®), and one medicine available under Hospital Pricing Approval; eptinezumab (Vyepti®).

Aquipta® contains atogepant. Atogepant shows affinity to several receptors of the calcitonin/ calcitonin gene-related peptide (CGRP)-receptor family. The precise mechanism of action of atogepant in the prophylaxis of migraine remains to be established.

From February 2025, two presentations of atogepant are available on the High Tech Arrangement:

- Aquipta® 10 mg tablet
- Aquipta® 60 mg tablet.

Vyepti® contains eptinezumab. Eptinezumab is a recombinant humanised IgG1 monoclonal antibody (MAB) produced in Pichia pastoris yeast cells. Eptinezumab binds to α- and βforms of human CGRP ligand. Eptinezumab prevents the activation of the CGRP receptors and hence the downstream cascade of physiological events linked to initiation of migraine attacks.

From 28 June 2023, one presentation of Vyepti® (eptinezumab) is available under Hospital Pricing Approval:

- Vyepti® 100 mg concentrate for solution for infusion.

Aimovig® contains erenumab. Erenumab is a fully human IgG2 MAB produced using recombinant DNA technology in Chinese hamster ovary (CHO) cells. Erenumab binds to the CGRP receptor. Erenumab potently and specifically competes with the binding of CGRP and inhibits its function at the CGRP receptor.

From September 2021, two presentations of erenumab are available on the High Tech Arrangement:

- Aimovig® 70 mg solution for injection in pre-filled pen (PFP)
- Aimovig® 140 mg solution for injection in PFP.

Ajovy® contains fremanezumab. Fremanezumab is a humanised MAB produced in CHO cells by recombinant DNA technology. Fremanezumab selectively binds the CGRP ligand and blocks both CGRP isoforms (α-and β-CGRP) from binding to the CGRP receptor.

From October 2021, two presentations of fremanezumab are available on the High Tech Arrangement:

- Ajovy® 225 mg solution for injection in PFP
- Ajovy® 225 mg solution for injection in pre-filled syringe (PFS).

Emgality® contains galcanezumab. Galcanezumab is a recombinant humanised IgG4 MAB produced in CHO cells. Galcanezumab binds CGRP thus preventing its biological activity.

From April 2022, one presentation of galcanezumab is available on the High Tech Arrangement:

- Emgality® 120 mg solution for injection in PFP.

Vydura® contains rimegepant. Rimegepant selectively binds with high affinity to the human CGRP receptor and antagonises CGRP receptor function.

From February 2025, one presentation of rimegepant is available on the High Tech Arrangement:

- Vydura® 75 mg oral lyophilisate.

## 1.1 Licensed indications

Atogepant (Aquipta®), eptinezumab (Vyepti®), erenumab (Aimovig®), fremanezumab (Ajovy®) and galcanezumab (Emgality®) are indicated for the prophylaxis of migraine in adults who have at least four migraine days per month.

Rimegepant (Vydura®) is indicated for the preventive treatment of episodic migraine in adults who have at least four migraine attacks per month.

In addition, rimegepant (Vydura®) is indicated for the acute treatment of migraine with or without aura in adults, which is outside the scope of this MAP.

## 1.2 Reimbursement

Reimbursement of atogepant, erenumab, fremanezumab, galcanezumab and rimegepant on the High Tech Arrangement, and eptinezumab under Hospital Pricing Approval, is supported only for the following subgroups of the licensed population, who meet the criteria outlined in this MAP:

- prophylaxis of episodic migraine in adults who have failed three or more prophylactic treatments (atogepant, rimegepant)
- prophylaxis of chronic migraine in adults who have failed three or more prophylactic treatments (atogepant, eptinezumab, erenumab, fremanezumab, galcanezumab).

All criteria must be satisfied in order for reimbursement to be supported. An application for reimbursement approval is required to be submitted on an individual patient basis through the online application system.

Table 1 outlines the licensed therapeutic dosages of atogepant, eptinezumab, erenumab, fremanezumab, galcanezumab and rimegepant for the prophylaxis of migraine available on the High Tech Arrangement/ Hospital Pricing Approval. Please refer to the relevant Summary of Product Characteristics (SmPC) for further prescribing information.

**Table 1: Licensed therapeutic dosage of atogepant, eptinezumab, erenumab, fremanezumab, galcanezumab and rimegepant**

| Medicine | Reimbursed patient population | Route of administration | Dosage |
|---|---|---|---|
| **Atogepant** | Episodic migraine/ Chronic migraine | Oral | 60 mg once daily<br><br>Dose modification required for concomitant use with strong CYP34A inhibitors and strong OATP inhibitors*: 10 mg once daily |
| **Eptinezumab** | Chronic migraine | Intravenous infusion | 100 mg every 12 weeks<br><br>Some patients may benefit from a dose of 300 mg every 12 weeks |
| **Erenumab** | Chronic migraine | Subcutaneous | 70 mg every 4 weeks<br><br>Some patients may benefit from a dose of 140 mg every 4 weeks |
| **Fremanezumab** | Chronic migraine | Subcutaneous | 225 mg once monthly (monthly dosing) or<br>675 mg every three months (quarterly dosing) |
| **Galcanezumab** | Chronic migraine | Subcutaneous | 120 mg once monthly with a 240 mg loading dose as the initial dose |
| **Rimegepant** | Episodic migraine | Oral | 75 mg every other day |

CYP: cytochrome P450; mg: milligrams; OATP: organic anion transporting polypeptide; PFP: pre-filled pen, PFS: pre-filled syringe

* Refer to SmPC for prescribing information

If a patient is recommended for reimbursement of atogepant, eptinezumab, erenumab, fremanezumab, galcanezumab, or rimegepant, reimbursement is supported up to the relevant maximum licensed dosage specified in Table 1. Reimbursement of dosages in excess of the licensed therapeutic dosages (as outlined in Table 1) is not supported.

Reimbursement is not supported for:

- rimegepant for the acute treatment of migraine or the prophylaxis of chronic migraine,
- eptinezumab, erenumab, fremanezumab or galcanezumab for the prophylaxis of episodic migraine,
- concomitant use of any of the medicines reimbursed under this MAP.

See Section 3 for further details on Reimbursement criteria – Treatment continuation.

## 1.3 Reimbursement prices

The reimbursement prices of the presentations of atogepant, erenumab, fremanezumab, galcanezumab and rimegepant available on the High Tech Arrangement are outlined in Table 2. The ex-factory price of the presentation of eptinezumab available under Hospital Pricing Approval is outlined in Table 3. Commercial-in-confidence arrangements are in place with the marketing authorisation holders to reduce the net acquisition cost of these medicines to the Health Service Executive (HSE).

**Table 2: Reimbursement codes and prices for the presentations of atogepant, erenumab, fremanezumab, galcanezumab and rimegepant available on the High Tech Arrangement**

| Medicine (pack size) | Code | Reimbursement price* |
|---|---|---|
| **Aimovig® 70 mg PFP (1)** | 89090 | €436.11 |
| **Aimovig® 140 mg PFP (1)** | 89091 | €441.88 |
| **Ajovy® 225 mg PFP (1)** | 89109 | €432.00 |
| **Ajovy® 225 mg PFS (1)** | 89094 | €432.00 |
| **Aquipta® 10 mg tablet (28)** | 89382 | €392.16 |
| **Aquipta® 60 mg tablet (28)** | 89383 | €392.16 |
| **Emgality® 120 mg PFP (1)** | 89169 | €414.03 |
| **Vydura® 75 mg oral lyophilisate (2)** | 89391 | €38.88 |
| **Vydura® 75 mg oral lyophilisate (8)** | 89392 | €177.11 |

mg: milligrams; PFP: pre-filled pen; PFS: pre-filled syringe
*Correct as at 01/02/2025

**Table 3: Ex-factory price for available presentation of eptinezumab under Hospital Pricing Approval**

| Strength (pack size) | Ex-factory price* |
|---|---|
| **Vyepti® 100 mg concentrate for solution for infusion (1 ml vial x 1)** | € 1,296.00 |

mg: milligrams; ml: millilitre
*Correct as at 01/02/2025

## 2. Reimbursement criteria - Initiation

This section outlines the criteria that must be satisfied in order for patients to be recommended for:

- reimbursement of atogepant and rimegepant for prophylaxis of episodic migraine under the High Tech Arrangement.
- reimbursement of atogepant, eptinezumab, erenumab, fremanezumab and galcanezumab for prophylaxis of chronic migraine under the High Tech Arrangement/ Hospital Pricing Approval.

### 2.1 Prescribers

Applications for reimbursement approval for atogepant, eptinezumab, erenumab, fremanezumab, galcanezumab and rimegepant for the management of episodic and chronic migraine under the High Tech Arrangement/ Hospital Pricing Approval will only be considered from consultants with specialist registration with the Irish Medical Council in a specialism relevant to the management of migraine (i.e. neurology), who have agreed to the terms of this MAP and been approved by the HSE ('approved consultants').

Approved consultants are responsible for ensuring that the patient or their representative/guardian is aware that the application for reimbursement approval is being made on their behalf.

The prescribing of Aimovig®, Ajovy®, Aquipta®, Emgality® and Vydura® for approved patients for the management of episodic and chronic migraine under the High Tech Arrangement will be confined to the approved consultants and their teams. The governance of the team on the High Tech Hub, including access, rests with the approved consultant.

### 2.2 Patient age

Applications for reimbursement approval will only be considered for individuals aged 18 years and older at time of application.

### 2.3 Patient diagnosis

Clinicians will be required to confirm the diagnosis of episodic migraine or chronic migraine at the time of application.

Episodic migraine is defined as the occurrence of headache on 14 or less days per month.

Chronic migraine is defined as the occurrence of headache on 15 or more days per month for more than three months, which on at least eight days per month, has the features of migraine headache. The diagnosis of chronic migraine should be made in line with the 3rd edition of the International Classification of Headache Disorders (ICHD-3) diagnostic criteria.

### 2.3.1 Number of monthly migraine days

For patients with a diagnosis of episodic migraine, clinicians will be required to confirm that the number of monthly migraine days (MMD)[i] the patient experienced in the one month period prior to the date of application is greater than or equal to four.

For patients with a diagnosis of chronic migraine, clinicians will be required to confirm that the number of MMD the patient experienced in the three months prior to the date of application is greater than or equal to eight.

## 2.4 Patient clinical history

In line with SmPCs for Aimovig®, Ajovy®, Aquipta®, Emgality®, Vydura® and Vyepti®, applications for reimbursement approval will not be considered for individuals who meet any of the contraindications for treatment as outlined in the relevant SmPC.

Clinicians should consider persistent medication overuse, in particular with codeine containing analgesics or other opioid analgesics, as a relative contraindication to prescribing any of the medicines reimbursed under this MAP.

## 2.5 Patient's medical treatment

Evidence of treatment failure with at least three prophylactic treatments outlined in Table 4 must be included in the application for reimbursement approval.

Treatment failure for oral prophylactic treatments is defined as:

- an inadequate response after confirmed adherence to treatment for a period of at least three consecutive months at the maximum tolerated dose, or
- discontinuation of treatment due to a clinically significant adverse reaction prior to completion of a period of at least three consecutive months at the maximum tolerated dose.

[i] Clinicians should note that rimegepant is indicated for the preventive treatment of episodic migraine in adults who have at least four migraine attacks per month, rather than at least four MMD.

**Table 4: Prophylactic treatments for which treatment failure with three must be demonstrated prior to an application for reimbursement approval of a medicine for episodic and chronic migraine under the High Tech Arrangement/ Hospital Pricing Approval**

| Prophylactic treatment | |
|---|---|
| **Oral** | Acetazolamide |
| | Amitriptyline/ Dosulepin/ Nortriptyline |
| | Atenolol/ Metoprolol/ Propranolol |
| | Candesartan |
| | Flunarizine |
| | Pizotifen |
| | Sodium valproate |
| | Topiramate |
| | Venlafaxine |
| **Intramuscular** | Botulinum Toxin Type A (Botox®) |
| **Intravenous** | Dihydroergotamine |

Not all treatments in Table 4 are licensed for the prophylaxis of migraine. Please refer to individual SmPCs for further information. In the case of Botulinum Toxin Type A (Botox®), an adequate trial is considered to be two cycles of Botox® injections administered 12 weeks apart.

In cases where a patient experienced a clinically significant adverse reaction to a prophylactic treatment in Table 4 which led to discontinuation of treatment prior to completion of a period of at least three consecutive months at the maximum tolerated dose, information in relation to the adverse reaction experienced should be provided in the application.

When reviewing applications, the HSE-Medicines Management Programme (MMP) may request evidence to validate the patient's current or prior treatment with prophylactic treatments outlined in Table 4, e.g. pharmacy printout of dispensed medicinal products.

## 3. Reimbursement criteria- Treatment continuation

In chronic migraine, a 30% reduction in migraine frequency is considered a clinically meaningful response to treatment. A 50% reduction is considered a clinically meaningful response in episodic migraine.

Ongoing reimbursement approval is conditional on a reduction in the frequency of migraine of at least 50% in episodic migraine and at least 30% in chronic migraine. Patients not showing this reduction in migraine frequency would be considered non-responders, or non-adherent to treatment; reimbursement support may not continue for these patients.

Follow-up data may be requested by the MMP for audit purposes and provision of same is a condition of ongoing reimbursement. It is the responsibility of the approved consultant to ensure that the patient or their representative/guardian is aware that the provision of follow-up data is a condition of reimbursement, and that audits may occur during which their personal data will be reviewed.

## 4. Prescribing of atogepant, eptinezumab, erenumab, fremanezumab, galcanezumab and rimegepant for approved patients

Please refer to the relevant SmPCs for Aquipta®, Vyepti®, Aimovig®, Ajovy®, Emgality® and Vydura® for full prescribing information including monitoring and patient counselling requirements.

If a patient is recommended for reimbursement of a medicine for the management of episodic and chronic migraine, and the prescriber wishes to prescribe atogepant, erenumab, fremanezumab, galcanezumab or rimegepant, the High Tech prescription for the required medicine should be generated on the High Tech Hub (HTH). High Tech prescriptions which are not hub generated for atogepant, erenumab, fremanezumab, galcanezumab or rimegepant will not be eligible for reimbursement by the HSE-Primary Care Reimbursement Service (PCRS). Only approved consultants and their teams will have access to generate prescriptions.