NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Rimegepant for treating or preventing migraine

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of rimegepant within its marketing authorisation for treating or preventing migraine.

Background

Migraine is primarily a headache disorder manifesting as recurring attacks usually lasting between 4 and 72 hours involving throbbing head pain of moderate to severe intensity. It is often accompanied by nausea, sometimes vomiting, sensitivity to light, sensitivity to sounds, and/or other sensory stimuli. Migraine can have significant impacts on quality of life and ability to carry out normal activities. Some people can have warning symptoms called an aura, before the start of a headache. Factors that can trigger attacks in people susceptible to migraines include stress, change in sleep pattern, overtiredness, menstruation, consumption of caffeine or alcohol, climatic conditions and use of visual display units.

Migraine is on a continuum, and it is possible for people to move between episodic and chronic migraine:

- Episodic migraine is defined as the occurrence of headaches on less than 15 days per month

- Chronic migraine is defined by the International Classification of Headache Disorders 3rd edition (ICHD-3)[1]. It is described as headache occurring on 15 or more days a month, which, on at least 8 days a month, has the features of migraine headache.

It is estimated that there are 190,000 migraine attacks experienced every day in England[2]. Prevalence has been reported to be 5-25% in women and 2-10% in men[2]. There are 3 broad approaches to managing migraine: lifestyle and trigger management, acute treatments and preventive treatments.

Treatments for acute migraine attacks include analgesics, triptans and anti-emetics. NICE clinical guideline 150 and the NICE pathway on the management of migraine (with or without aura) recommend an oral triptan with either a nonsteroidal anti-inflammatory drug (NSAID) or paracetamol, taking into account patient preferences, comorbidities and the risk of adverse events. For people who prefer to take only one drug, monotherapy with an oral triptan, NSAID, high-dose aspirin or paracetamol should be considered. Anti-emetics should be considered in addition to other acute migraine treatment even in the absence of nausea and vomiting.

Preventive treatment of migraines can take many forms including nutritional supplements, lifestyle alterations such as increased exercise and avoidance of migraine triggers. It can also include medications, which are generally considered for people depending on their disease burden and frequency of attacks. NICE clinical guideline 150 recommends offering topiramate or propranolol, and considering

amitriptyline, for preventing migraine according to the person's preference, comorbidities and risk of adverse events.

NICE technology appraisal guidance 682 recommends erenumab for preventing migraine in adults who experience 4 or more migraines per month and at least 3 preventive drug treatments have failed. NICE technology appraisal guidance 659 recommends galcanezumab for preventing migraine in adults who experience 4 or more migraines per month and at least 3 preventive drug treatments have failed. NICE technology appraisal guidance 631 recommends fremanezumab for preventing migraine in adults if the migraine is chronic and at least 3 preventive drug treatments have failed. NICE technology appraisal guidance 260 recommends botulinum toxin type A for preventing headaches in adults with chronic migraine that has not responded to at least 3 prior pharmacological prophylaxis therapies and whose condition is appropriately managed for medication overuse.

The technology

Rimegepant (Vydura, BioHaven Pharmaceuticals) is a calcitonin gene-related peptide receptor antagonist. It inhibits the action of calcitonin gene related peptide, which is believed to transmit signals that can cause severe pain. Rimegepant is administered orally.

Rimegepant does not currently have a marketing authorisation in the UK for treating or preventing migraine. As a treatment for migraine, it has been studied in placebo-controlled trials in adults who have 2 to 8 acute migraine attacks with or without aura per month and who have had at least a 1-year history of migraine. As a preventative treatment, it has been studied in a placebo-controlled trial in adults who have 4 to 18 migraine attacks of moderate to severe intensity per month and who have had at least a 1-year history of migraine.

Intervention(s)	Rimegepant
Population(s)	Adults with migraine
Comparators	For acute migraine: • Paracetamol, with or without an anti-emetic • An NSAID (such as aspirin, ibuprofen, diclofenac or naproxen), with or without an anti-emetic • An oral or non-oral triptan (such as sumatriptan, zolmitriptan, rizatriptan, almotriptan or eletriptan), with or without an anti-emetic • Paracetamol with an oral or non-oral triptan, with or without an anti-emetic • An NSAID with a triptan, with or without an anti-emetic • Best supportive care For migraine prevention: • Oral preventive treatments (such as topiramate, propranolol, amitriptyline)

	• Erenumab (4 or more migraines per month and after at least 3 preventive drug treatments have failed) • Galcanezumab (4 or more migraines per month and after at least 3 preventive drug treatments have failed) • Fremanezumab (in chronic migraine and after at least 3 preventive drug treatments have failed) • Botulinum toxin type A (in chronic migraine that has not responded to at least 3 prior pharmacological prophylaxis therapies) • Best supportive care
Outcomes	The outcome measures to be considered include: For acute migraine: • reduction in headache pain (including freedom from pain) • speed of onset • freedom from most bothersome symptom • reduction in nausea and vomiting • reduction in hypersensitivity (e.g. light, sound, smell) • regain of normal functioning • prevention of recurrence • use of rescue medication • adverse effects of treatment • health-related quality of life For migraine prevention: • frequency of headache days per month • frequency of migraine days per month • severity of headaches and migraines • number of cumulative hours of headache or migraine on headache or migraine days • reduction in acute pharmacological medication • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for

	estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.
Other considerations	If the evidence allows, the following subgroups will be considered: For migraine prevention: • people with chronic or episodic migraine • subgroups defined by the number of previous preventive treatments • subgroups defined by the frequency of episodic migraine For acute migraine: • subgroups defined by migraine severity • people currently having treatment for the prevention of migraine • people with or at risk of developing medication overuse • people for whom triptans are contraindicated or not tolerated • subgroups defined by the number of headache days per month. Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	**Related Technology Appraisals:** 'Erenumab for preventing migraine' NICE technology appraisal 682 (2021). 'Galcanezumab for preventing migraine' (2020). NICE technology appraisal 659. Review date 2023. 'Fremanezumab for preventing migraine' NICE technology appraisal 631 (2020). 'Botulinum toxin type A for the prevention of headaches in adults with chronic migraine' (2012). NICE Technology Appraisal 260

	Related Guidelines: 'Headaches in over 12s: diagnosis and management' (2012). NICE guideline CG150. Updated 2015. Reviewed 2016. **Related Interventional Procedures:** 'Transcranial magnetic stimulation for treating and preventing migraine' (2014). NICE interventional procedures guidance 477. 'Transcutaneous stimulation of the cervical branch of the vagus nerve for cluster headache and migraine' (2016). NICE interventional procedures guidance 552. 'Transcutaneous electrical stimulation of the supraorbital nerve for treating and preventing migraine' (2016). NICE interventional procedures guidance 559. **Related Quality Standards:** 'Headaches in over 12s' (2013). NICE quality standard 42. **Related NICE Pathways:** Headaches (2020) NICE Pathway
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2019) Adult Highly Specialist Pain Management Service. Reference 170135S Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 2 and 3. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017 NHS England (2019) Headache & Migraine Toolkit

Questions for consultation

Have all relevant comparators for rimegepant been included in the scope?

Which treatments are considered to be established clinical practice in the NHS for acute migraine or preventing migraine?

How should best supportive care be defined? Should best supportive care be considered as a comparator?

Are the outcomes listed appropriate?

Are the subgroups suggested in 'other considerations appropriate? Are there any other subgroups of people in whom rimegepant is expected to be more clinically effective and cost effective or other groups that should be examined separately?

- Would rimegepant be used in combination with existing treatments for the prevention of migraine?
- If used for the prevention of migraines, would additional treatment be used in event of acute migraine or would treatment continue with rimegepant?

- Would rimegepant be used in combination with existing treatments for acute migraine attacks?

Where do you consider rimegepant will fit into the existing NICE pathway, Headaches?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which rimegepant will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider rimegepant to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of rimegepant can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

References

1. The International Headache Society. International Classification of Headache Disorders 3rd edition (ICHD-3). Accessed November 2020.

2. Steiner TJ et al. The prevalence and disability burden of adult migraine in England and their relationships to age, gender and ethnicity. Cephalalgia. 2003;23(7):519-527.