Surrey Heartlands Integrated Care System
Area Prescribing Committee (APC)

Integrated Care Partnership - Surrey Downs, Guildford & Waverley, North-West Surrey, and East Surrey Places & associated partner organisations.

NICE Technology Appraisals (TA) briefing paper for local implementation

NICE TA Guidance name and number	Rimegepant for preventing migraine Technology appraisal guidance 906		
Available at	https://www.nice.org.uk/guidance/ta906		
Date of issue	5 July 2023	**Implementation deadline**	5 Oct 2023

Medicine details[1]	
Name and brand name	Rimegepant (Vydura)
Manufacturer	Pfizer
Mode of action	Rimegepant selectively binds with high affinity to the human calcitonin gene-related peptide (CGRP) receptor and antagonizes CGRP receptor function.
Licensed indication	VYDURA is indicated for the • Acute treatment of migraine with or without aura in adults; • Preventive treatment of episodic migraine in adults who have at least 4 migraine attacks per month.
Formulation	Each oral lyophilisate contains rimegepant sulfate, equivalent to 75 mg rimegepant. The oral lyophilisate should be placed on the tongue or under the tongue. It will disintegrate in the mouth and can be taken without liquid.
Dosage	Acute treatment of migraine: The recommended dose is 75 mg rimegepant, as needed, once daily. Prophylaxis of migraine: The recommended dose is 75 mg rimegepant every other day. The maximum dose per day is 75 mg rimegepant. VYDURA can be taken with or without meals.
Comparison of NICE TA with Summary of Product Characteristics (SmPC)[2]	Please note: Rimegepant is licensed for both the treatment of acute migraine and the prophylaxis of episodic migraine. This NICE TA however, is ***only*** for rimegepant for preventing episodic migraine. Preventing chronic migraine was not considered because it is not

	within rimegepant's marketing authorisation. Migraine can be classified as episodic or chronic, based on the frequency of headaches. Episodic migraine is defined as fewer than 15 headache days a month. Chronic migraine is defined as 15 or more headache days a month with at least 8 of those having features of migraine. In addition, the licensed indication of the comparators is for *migraine days per month*. This differs slightly from the rimegepant indication, which is for the *number of migraine attacks per month*. This is because a migraine attack can last more than 1 day a person can have more than 4 monthly migraine days (MMDs) but could still have fewer than 4 attacks per month. This is the current dose considered by NICE as part of this NICE evaluation. Subsequent changes in the license following NICE publication will need to be considered by the Area Prescribing Committee and will not be routinely funded by local commissioners, as the incremental cost per QALY would not have been considered.

NICE TA recommendations[2]

Recommendations

1.1 Rimegepant is recommended as an option for preventing episodic migraine in adults who have at least 4 and fewer than 15 migraine attacks per month, only if at least 3 preventative treatments have not worked.

1.2 Stop rimegepant after 12 weeks of treatment if the frequency of migraine attacks does not reduce by at least 50%.

1.3 If people with the condition and their clinicians consider rimegepant to be 1 of a range of suitable treatments, after discussing the advantages and disadvantages of all the options, use the least expensive. Take account of administration costs, dosage, price per dose and commercial arrangements.

1.4 These recommendations are not intended to affect treatment with rimegepant that was started in the NHS before this guidance was published. People having treatment outside these recommendations may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

Decision-making framework (DMF)

National guidance and priorities

The ICS has a legal obligation to commission this medicine in line with the NICE TA.

- This NICE TA has been assigned an implementation deadline of 3 months.
- The implementation deadline is 5 October 2023.

Clinical effectiveness

The company proposed rimegepant for preventing episodic migraine after 3 or more treatments have not worked, which is narrower than the marketing authorisation. Usual treatments at this point include erenumab, fremanezumab or galcanezumab, which are injections. Rimegepant is an oral treatment, which may be preferred by some people.

Clinical trial evidence shows that rimegepant reduces monthly migraine days more than placebo. It has not been directly compared in a trial with erenumab, fremanezumab or galcanezumab, but indirect comparisons suggest that it is likely to be similar to or less effective than these.

Rimegepant is cost-effective compared with 2 of the 3 usual treatments. So rimegepant is recommended for preventing migraine after 3 or more preventative treatments have not worked.

Patient safety

- The product should be used within its product license.
- Rimegepant is a Black Triangle drug – all suspected adverse reactions should be reported in order to identify rare adverse effects.

Patient factors

- An additional treatment option would be valued by patients.
- This is the first oral alternative to injectable preventative options, with the potential for primary care prescription.
- The recommended dosage for the prophylaxis of migraine is unusual – one 75mg tablet every other day. This may lead to issues with compliance.
- Patients may be seen in specific migraine clinics outside of secondary care where rimegepant may be prescribed.

Environmental impact

No statement from NICE.

As an oral treatment there should be less packaging and easier disposal when compared to the other sub-cutaneous injection comparators.

Equality & diversity

The following equality considerations were taken into account by NICE. NICE decided no adjustments were needed to their methods and that the factors raised did not affect their conclusions:

'The company, clinical and patient experts, and consultation comments highlighted that migraine can be considered a disability under the Equality Act 2010. The committee noted that all relevant benefits associated with migraine as a disability were likely captured in the model. It noted that the decision making took into account any obligations related to the Equality Act 2010.

Comments also said that migraine is more common in people of working age and affects more women than men. But it was agreed that issues relating to differences in prevalence or incidence of a condition cannot be addressed in a technology evaluation. Also, one comment said that some existing treatments cannot be used in pregnancy because of gestational and maternal safety considerations around continuous dosing. The company responded that there is no available data on rimegepant's use in pregnancy. The summary of product characteristics for rimegepant states that as a precautionary measure, it is preferable to avoid taking rimegepant during pregnancy (see section 2.3).

The clinical experts said that there are a limited number of headache centres in the UK and there are long waiting lists. So, there may be unequal access to specialist headache clinics in England. The committee considered these issues and noted that unequal access was not associated with a protected characteristic.

Consultation comments noted that people in more deprived areas of the country are at greater risk of becoming disabled by migraine and of losing their jobs and experiencing severe financial hardship. The committee considered whether its recommendations could affect health inequalities associated with socioeconomic factors. It considered that it had not been presented with evidence that people in more deprived areas are at greater risk of becoming disabled by migraine. It also considered that NICE's methods do not include productivity costs in its analyses.

In response to consultation, some comments highlighted that rimegepant is available in the US, Europe, United Arab Emirates and Israel. The committee noted that the decision to recommend rimegepant in those places is independent from NICE decision making because they have different health systems to the NHS.

The committee said that they had read all consultation comments and acknowledged the equality considerations raised. It factored these considerations into its decision making. The committee decided that these factors did not affect the conclusions reached in this appraisal and that no specific adjustments were needed to NICE's methods in this situation.'

Note: Drugs approved by NICE for adult conditions will be commissioned in children at specialised paediatric centres if the patient meets the NICE criteria and there is evidence to suggest that the drug is safe and clinically appropriate to use in children as per the NHS England Medicines for Children Policy (see https://www.england.nhs.uk/publication/commissioning-medicines-for-children-specialised-services/ and a Blueteq form is available.

Place in therapy relative to available treatments

There is a range of oral preventative treatments that people with at least 4 migraine days per month would try before moving onto a different type of treatment. These include topiramate, propranolol and amitriptyline.

The clinical experts noted that rimegepant would usually be offered after 3 preventative oral treatments had not worked, or the person cannot tolerate them.

Other available treatments on the NHS for the NICE indication of episodic migraine are the injectable monoclonal antibodies erenumab, fremanezumab, and galcanezumab, and also eptinezumab which is given by iv injection. However, there is not sufficient evidence to currently recommend sequential use.

The committee acknowledged that rimegepant could eventually be used in primary care but recognised that it would need specialist involvement.

Erenumab, fremanezumab and galcanezumab are the most appropriate comparators. There was no direct evidence comparing rimegepant with erenumab, fremanezumab and galcanezumab. The company's network meta-analysis (NMA) using data from separate clinical trials of rimegepant, erenumab, galcanezumab and fremanezumab.

The results of the NMA numerically favoured erenumab, fremanezumab and galcanezumab in both outcomes (the results are academic in confidence and cannot be reported here). The committee concluded that rimegepant is likely to be similar to or less effective than erenumab, fremanezumab and galcanezumab at reducing MMDs.

Stakeholder views

The paper was sent out for consultation and comments are listed on the front sheet.

Cost-effectiveness

The drug cost per Place according to NICE resources does not exceed £100,000.

Section 1: cost of the technology

a. Annual cost per patient (or complete course if shorter)

The proposed price of rimegepant is £12.90 per 75 mg tablet (excluding VAT). The recommended dose is 75 mg rimegepant every *other* day.

The total cost of treatment incl. VAT in primary care is:

Year 1:

Initiation (12 weeks, 28-day cycle) 75mg every other day*	£743
Maintenance (33 weeks, 28-day cycle) 75mg every other day	£1,858
Total first year	**£2,601**

The prices in secondary care will be presented at the meeting.

Because there is no commercial arrangement for rimegepant it can be used in all applicable settings. NICE's health technology evaluation manual 2013 states that for medicines mainly prescribed in primary care, prices are based on the drugs tariff.

b. Availability of CAP/PAS price:
No - there is no commercial arrangement for rimegepant which means that it can be used in all applicable settings.

Also, there is no contract or PAS price for rimegepant with the trusts.

c. Price relative to comparable medicines:

Table 1: Costs of all anti-CGRP technologies with a NICE TA for preventing migraine.

Technology	NICE TA	Administration frequency	Cost (as per TA)	Annual cost*
Erenumab	TA682 March 2021	4-weekly	£386.50 per 70 mg or 140 mg injection	£5,025
Fremanezumab	TA764 Feb 2022	Monthly	£450.00 per 225-mg injection (£1,350 per 675 mg)	£5,400
Galcanezumab	TA659 Nov 2020	Monthly or 3-monthly	£450.00 per 120-mg injection	£5,850
Eptinezumab	TA871 Mar 2023	12-weekly	£1,350 for a 100 mg per ml vial	£5,400

*Commercial arrangements and administration costs associated are NOT included.

The most cost-effective currently available anti-CGRP is erenumab.

NICE have also stated that if rimegepant is one of a range of suitable treatments, after discussing the advantages and disadvantages of all the options, use the least expensive. Take account of administration costs, dosage, price per dose and commercial arrangements.

The cost-effectiveness estimates after including the comparators' confidential commercial discounts showed that rimegepant is less expensive and less effective than some of the standard treatments.

Section 2: NICE resource impact statement and template

a. NICE resource impact statement
'We expect the resource impact of implementing the recommendations in England will be less than £5 million per year (or approximately £8,800 per 100,000 population, based on a population for England of 56.6 million people).

This is because rimegepant is a further treatment option. Uptake of rimegepant would displace other calcitonin gene-related peptide (CGRP) receptor antagonists, and the overall cost of treatment for this patient group will be similar.

Rimegepant is an oral tablet which may be preferrable when compared with other CGRP receptor antagonists which are administered by subcutaneous injection. There are likely to be resource benefits for the NHS because no training is required to administer the treatment and injection site reactions would be avoided. As there are no commercial arrangements in place for rimegepant, the medicine can be procured and dispensed in primary care and reimbursed at the Drug Tariff price.

Rimegepant is commissioned by integrated care boards. Providers are NHS hospital trusts or primary care practitioners, possibly with specialist involvement through shared care

agreements or advice and guidance (please see primary care approach section in the guidance). In NHS hospital trusts, the payment mechanism is determined by the responsible commissioner and depends on the technology being classified as high cost. In primary care, rimegepant can be procured by community pharmacies and reimbursed at the Drug Tariff price. Pricing of rimegepant does not differ across healthcare settings.'

Please note:
The Drug Tariff price is applicable across all healthcare settings. There is no contract price at the trusts.

NICE resource impact template

The NICE resource template states that for the SH population, there would be 88 people who have episodic migraine, have access to a neurologist/pain specialist and have had 3 or more prior treatments.

According to Blueteq reports, there are currently 122 patients receiving CGRP inhibitor treatment in SH. If it is assumed that 13% are treated for episodic migraine as per the assumptions input in the NICE resource impact template, then this would be 16 patients.

Of the 122 patients, 39 (32%) were initiated at SH trusts as highlighted in below:

As NICE have stated that if rimegepant is one of a range of suitable treatments, after discussing the advantages and disadvantages of all the options, to use the least expensive, taking account of administration costs, dosage, price per dose and commercial arrangements.

The cost-effectiveness estimates after including the comparators' confidential commercial discounts showed that rimegepant is less expensive and less effective than some of the standard treatments.

As rimegepant is a further treatment option, uptake of rimegepant would displace other calcitonin gene-related peptide (CGRP) receptor antagonists, and the overall cost of treatment for this patient group will be similar.

Drug costs for Surrey Heartlands:
The cost is not anticipated to exceed the £100,000 per Place threshold and may yield a saving in terms of medicines cost and trust attendance costs (and administration costs if eptinezumab would have been used).

Traffic light recommendation to APC

a. NHS Payment Scheme (NHSPS) excluded high-cost drug:
No – not listed as HCD on the NHS payment system.

b. Recommended traffic light status and rationale:
The NICE TA states:

'The committee concluded that rimegepant could eventually be used in primary care. But it recognised that specialist referral and treatment management would likely be needed before rimegepant could be used in primary care.'

Therefore, the TLS proposal is:
BLUE – for initiation at the trust. Prescribing period to be at least 12 weeks with a request for continuation in primary care if patient meets the NICE TA criteria for continuation.

A Blueteq form should be completed at the trust as for other CGRP inhibitors, to avoid inadvertent sequential use which is not currently allowed.

PAD definitions, available at: Traffic Light Status (res-systems.net)

Implementation

NICE TA implementation must be within three months of publication.

Actions to implement:
Providers are NHS hospital trusts or primary care practitioners, possibly with specialist involvement through shared care agreements or advice and guidance

a. Primary care

- This is the first CGRP inhibitor which is available in primary care. Primary care prescribers should adhere to the GMC 'Good practice in prescribing and managing medicines and devices' guidelines, available at: Good practice in prescribing and managing medicines and devices - professional standards - GMC (gmc-uk.org)

b. Secondary care

- Providers are NHS hospital trusts or primary care practitioners
- Trusts to follow internal governance procedures to add to their formulary and initiate homecare.
- The initiation, administration and on-going treatment with requests for continuation in primary care is managed by secondary care.
- Specialists will be required to notify the high-cost drugs teams of initiation and response to treatment using the Blueteq® system.
- Homecare arrangements should not be required at the trust.

c. ICS

- This technology is commissioned by integrated care systems.
- Pathway is based on the NHS Kent and Medway guidelines which are in the process of being reviewed.

d. PAD and Joint Formulary

- Addition to PAD as per decisions of the APC.

Proposed tick box forms

Blueteq® forms to be developed.

References:

1 Summary of Product Characteristics. emc. VYDURA 75 mg oral lyophilisate. Available at: VYDURA 75 mg oral lyophilisate - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk) Accessed <11.7.23>

2 NICE Technology Appraisal Guidance: Rimegepant for preventing migraine. Available at: https://www.nice.org.uk/guidance/ta906 Accessed <10.7.23>

3 NICE Resource Impact Report: Rimegepant for preventing migraine. Available at: https://www.nice.org.uk/guidance/ta906/resources Accessed <10.7.23>

4 NICE Resource Impact Template: Rimegepant for preventing migraine. Available at: https://www.nice.org.uk/guidance/ta906/resources Accessed <10.7.23>

Declaration of interest:

	Name	Role	Date	Declaration of interests (please give details below)
Prepared by	Tejinder Bahra	Lead Pharmacist	17.8.23	Yes

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Supported by				
Reviewed by	Sarah Watkin	AD	7.9.23	

Explanation of declaration of interest:
Tejinder Bahra – as per SH ICS declaration of interest.

Version control sheet:

Version	Date	Author	Status	Comment
1		Tejinder Bahra	Draft	Out for consultation
			Final	Out for clinical comment