Rimegepant for treating acute migraine NICE TA919

NHS
Bath and North East Somerset, Swindon and Wiltshire
Integrated Care Board

NICE TA919 recommendation:

Rimegepant (Vydura®) is recommended as an option for the **acute treatment** of migraine with or without aura in adults, only if for previous migraines:

- at least 2 triptans were tried and they did not work well enough or
- triptans were contraindicated or not tolerated, and nonsteroidal anti-inflammatory drugs (NSAIDs) and paracetamol were tried but did not work well enough.

- The list price for the 75mg oral lyophilisate tablets is £25.80 per pack of 2 tablets.
- Local BSW traffic light status: **GREEN**
- Note that NICE have also approved rimegepant for **prevention** of episodic migraine (NICE TA906) 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. This currently has a **RED** Traffic Light Status in BSW for prevention indication while commissioners consider a business case. Note that the frequency of use for prevention is different to use in acute migraine.

Migraine *Acute* Treatment Pathway
PRN, not normally more than 2 x per week

1. Simple analgesic + antiemetics
NSAIDS or aspirin 900mg AND paracetamol AND antiemetic
(Do not use Opioids)

2.Triptan + NSAID + antiemetic
Try lower cost triptans first e.g. oral sumatriptan.
Not effective at 2 hours on at least 3 occasions, or not tolerated.

3. Second line triptan + NSAID + antiemetic
Consider alternative delivery method e.g. spray, S/C
Consider longer acting NSAIDS e.g. naproxen

Failed 2 triptan or triptans contraindicated:

4. Rimegepant 75mg orodispersible

For all patients:
- Lifestyle triggers addressed (depression, poor sleep, poor diet, weight loss, caffeine)
- No medication overuse

Rimegepant mode of action:

Rimegepant is a first in class *oral* calcitonin gene-related peptide (CGRP) receptor antagonist and selectively binds with high affinity to the human CGRP receptor. It is thought to relieve migraine by blocking CGRP-induced neurogenic vasodilation, returning dilated intracranial arteries to normal by halting the cascade of CGRP-induced neurogenic inflammation which leads to peripheral and central sensitisation and / or by inhibiting the central relay of pain signals from the trigeminal nerve to the caudal trigeminal nucleus.

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Rimegepant prescribing information (see SPC for full details):

- Rimegepant is an oral lyophilisate. 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.
- The recommended dose is 75 mg, as needed, once daily taken with or without food.
- The max dose per day is 75 mg. Another dose of rimegepant should be avoided within 48 hours when concomitantly administered with certain interacting medicines, see section below.
- The SPC mentions medication overuse headaches in the special warnings section, however, local specialist consensus is that this drug is unlikely to cause this problem.
- **Review number of prescriptions issued regularly as patients might need prophylaxis to reduce the number of acute migraines.**
- Elderly: There is limited experience with rimegepant in patients aged 65 years or older. No dose adjustment is required as the pharmacokinetics of rimegepant are not affected by age.
- It should be noted that patients with significant CV risk were excluded from the clinical trials, hence there is a lack of data upon use in such patients, therefore caution is advised.
- No dose adjustment is required in patients with mild, moderate, or severe renal impairment.
- No dose adjustment required in patients with mild or moderate (Child-Pugh A&B) hepatic impairment.

Contra-indications:

- Hypersensitivity to the active substance or to any of the excipients

Notable side-effects [for acute treatment] (see SPC for full details):

- Nausea (1.2%).
- Hypersensitivity, reactions (mostly mild or moderate in severity) including dyspnoea and severe rash (<1%).
- Hypersensitivity reactions include dyspnoea and rash as well as serious hypersensitivity and can occur days after administration. If a hypersensitivity reaction occurs, rimegepant should be discontinued and appropriate therapy should be initiated.

Notable drug interactions (see SPC for full details):

Rimegepant is a substrate of CYP3A4, P-glycoprotein (P-gp) and breast cancer resistance protein (BCRP) efflux transporters. Rimegepant has clinically significant interactions that may influence frequency of doses. A summary is given below but prescribers should consult the BNF or SPC for full information.

Inhibitors of CYP3A4 increase plasma concentrations of rimegepant.

- Concomitant administration of rimegepant with strong CYP3A4 inhibitors (e.g., **clarithromycin, itraconazole, ritonavir**) is not recommended. Concomitant administration of rimegepant with drugs that moderately inhibit CYP3A4 (e.g., **diltiazem, erythromycin, fluconazole**) may increase exposure to rimegepant. Another dose of rimegepant within 48 hours should be avoided when concomitantly administered with moderate CYP3A4 inhibitors.

Inducers of CYP3A4 decrease plasma concentrations of rimegepant and loss of efficacy.

- Concomitant administration of rimegepant with strong CYP3A4 inducers (e.g., **phenobarbital, rifampicin, St John's wort**) or moderate CYP3A4 inducers (e.g., **bosentan, efavirenz, modafinil**) is not recommended. The effect of CYP3A4 induction may last for up to 2 weeks after discontinuation of the strong or moderate CYP3A4 inducer.

Inhibitors of P gp and BRCP efflux transporters may increase plasma concentrations of rimegepant.

- Another dose of rimegepant within 48 hours should be avoided when concomitantly administered with strong inhibitors of P gp (e.g., **ciclosporin, verapamil, quinidine**).

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Pregnancy & breastfeeding (see SPC for full details):

- The SPC states that there are limited data from the use of rimegepant in pregnant women. Animal studies demonstrate that rimegepant is not embryocidal, and no teratogenic potential has been observed at clinically relevant exposures.
- Local specialist view is that although there is no known teratogenic risk, CGRP is widely expressed in the placenta/blood vessels and therefore caution is required if prescribing for a woman of childbearing potential not on effective contraception.
- The SPC states that the relative percentage of a maternal dose estimated to reach the infant is less than 1%. There are no data on the effects on milk production. The developmental and health benefits of breast-feeding should be considered along with the mother's clinical need for rimegepant and any potential adverse reactions on the breastfed infant from rimegepant or from the underlying maternal condition.

Advice for the patient:

Rimegepant has no or negligible influence on the ability to drive and use machines.
Encourage use of a **headache diary** and stress management. Use a diary to record the frequency, duration and severity of headaches, to monitor effectiveness of headache interventions and to use as a basis for discussion with the patient. The Migraine Trust have diaries: **Home - The Migraine Trust**

Further information:

- CKS: Migraine in adults (Sept 22): Scenario: Adults | Management | Migraine | CKS | NICE (Accessed 12/1/24)
- Headaches in over 12s: diagnosis and management. NICE CG150 (updated dec 2021): Overview | Headaches in over 12s: diagnosis and management | Guidance | NICE (Accessed 12/1/24)
- NHS Scotland Acute treatment of migraine in primary care Oct 2023: **national-headache-pathway-acute-treatment-of-migraine-in-primary-care.pdf (nhscfsd.co.uk)** (Accessed 12/1/24)
- Headache UK for clinicians (links to BASH guidance 2019): For Clinicians - Headache UK (Accessed 12/1/24)
- SIGN 155, March 2023 Pharmacological management of migraine Pharmacological management of migraine (sign.ac.uk) (Accessed 12/1/24)