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	Atogepant for preventing migraine Technology appraisal guidance TA973		
Available at	https://www.nice.org.uk/guidance/ta973		
Date of issue	15 May 2024	**Implementation deadline**	15 Aug 2024

Medicine details[1]	
Name and brand name	Atogepant (Aquipta)
Manufacturer	Abbvie
Mode of action	Atogepant is an orally administered, small molecule, selective calcitonin gene-related peptide (CGRP) receptor antagonist that blocks the binding of the CGRP to the receptor and antagonizes CGRP receptor function. CGRP is a neuropeptide that has been associated with migraine pathophysiology. In the trigeminovascular system, CGRP modulates nociceptive signalling and inflammation, and also functions as a vasodilator.
Licensed indication	AQUIPTA is indicated for prophylaxis of migraine in adults who have at least 4 migraine days per month.
Formulation	10mg & 60 mg tablets. Please note; the 10mg tablet is not subject to the NICE TA
Dosage	The recommended dose for AQUIPTA is 60 mg taken orally once daily with or without food. A missed dose should be taken right away. If it is almost time for the next dose, patients should be instructed to skip the missed dose and take the next dose as scheduled. Dose modifications Dosing modifications for concomitant use of specific drugs are provided in Table 1 **Table 1: Dose modifications for drug interactions**

Dosage modifications	**Recommended once daily dose**
Strong CYP3A4 inhibitors	10 mg
Strong OATP inhibitors	10 mg

Comparison of NICE TA with Summary of Product	Atogepant is recommended as an option for preventing migraine in adults who have at least 4 migraine days per month, only if at least 3 preventive medicines have failed.

Characteristics (SmPC)[2]	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. Please note; the licensed indication is for migraine days per month. This is because as 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. NICE recommends atogepant to be used only after 3 preventative medicines have failed, whereas the product licence does not. This is the current dose considered by NICE as part of this NICE evaluation. Subsequent changes in the licence 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 Atogepant is recommended as an option for preventing migraine in adults who have at least 4 migraine days per month, only if at least 3 preventive medicines have failed.

1.2 Stop atogepant after 12 weeks if the frequency of migraines does not reduce by:

- at least 50% in episodic migraine (defined as fewer than 15 headache days per month)
- at least 30% in chronic migraine (defined as 15 or more headache days per month, with at least 8 of those having features of migraine).

1.3 If people with the condition and their healthcare professional consider atogepant 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 This recommendation is not intended to affect treatment with atogepant that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS healthcare professional 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 15 August 2024.

Clinical effectiveness

For this evaluation, the company asked for atogepant to be considered only for people who have already had at least 3 preventive medicines that have not worked. **This does not include everyone who atogepant is licensed for.**
Usual alternative medicines at this point include erenumab, fremanezumab, galcanezumab, eptinezumab, rimegepant (for episodic migraine only) or botulinum toxin type A (for chronic migraine only).

Clinical trial evidence shows that atogepant reduces monthly migraine days more than

placebo, but there is no clinical trial evidence directly comparing it with other preventive medicines. The results from indirect comparisons are uncertain and it is unclear how well atogepant works compared with other alternative medicines for episodic or chronic migraine.

Patient safety

- The product should be used within its product licence.
- This medicinal product is subject to reporting of all suspected adverse drug reactions to the MHRA. This will allow timely identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.
- AQUIPTA 60 mg tablets contain 31.5 mg sodium per dose; this is equivalent to 1.6% of the WHO recommended maximum daily intake of 2 g sodium for an adult.
- Atogepant has a shorter half life than injectable medicines, which may be beneficial if treatment needs to be stopped quickly e.g. high vascular risk, or considering conception.

Patient factors

- An additional treatment option would be valued by patients.
- This is another alternative to injectable preventative options, with the potential for primary care prescription.
- Atogepant dosing is once daily which many patients will find easier to follow than for Rimegepant, reducing compliance issues.
- Patients may be seen in specific migraine clinics outside of secondary care where Rimegepant or atogepant 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

- An oral medicine would benefit people who cannot self-administer an injectable medicine because of disability.
- As a non-biologic medicine, this treatment would be valued by patients who cannot use biologic medicines due to their religious or ethical beliefs.

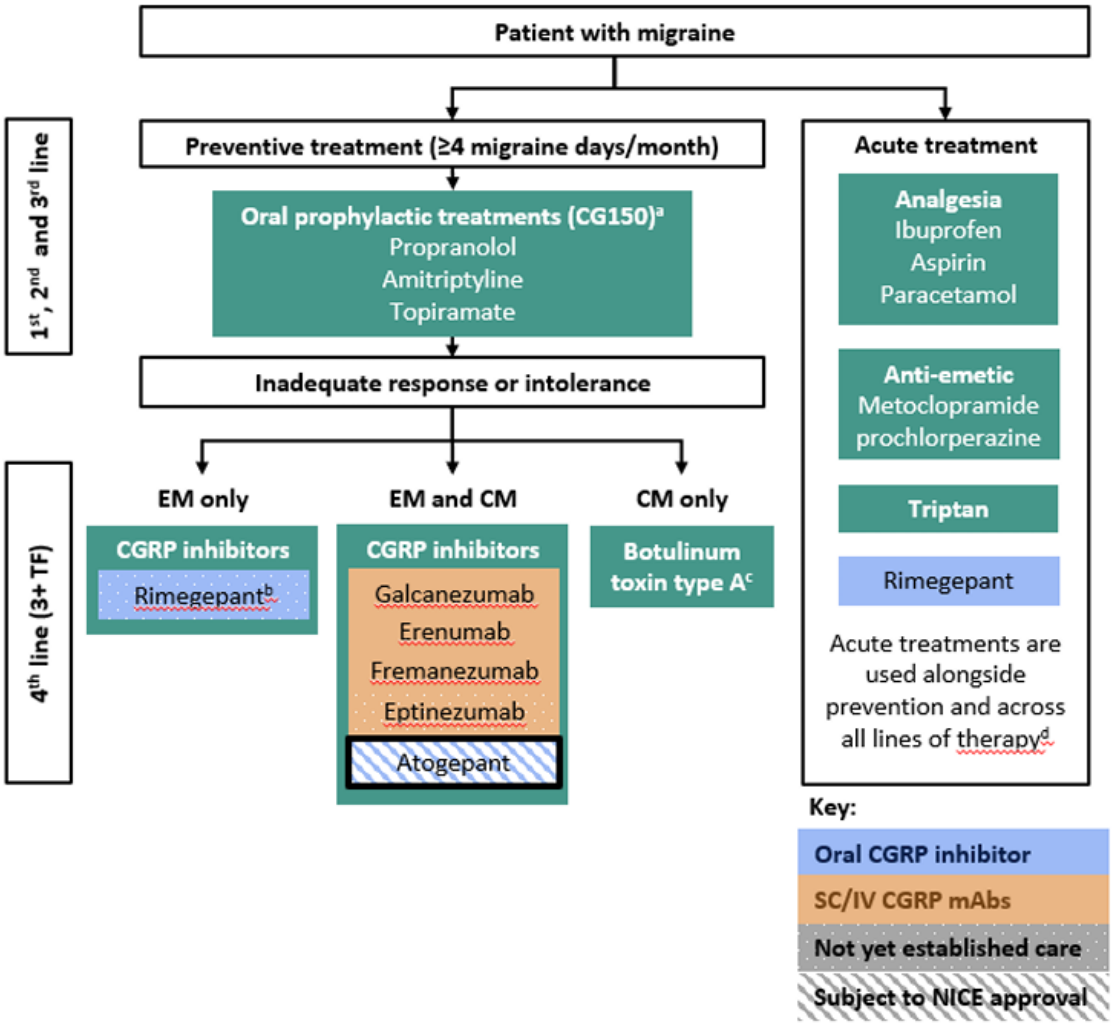
Place in therapy relative to available treatments

- Preventive treatments are key in reducing the frequency, severity, and duration of migraine attacks, in patients with ≥4 migraine days a month. They also reduce the development of medication overuse headaches.
- Available oral prophylactic treatment options (beta-blockers, antiepileptics and antidepressants) are not migraine-specific. Adherence and persistence to these medications is poor among patients due to suboptimal efficacy and poor tolerability.
- NICE recommend the CGRP monoclonal antibodies (mAbs), galcanezumab, erenumab and fremanezumab for migraine prophylaxis in EM and CM for patients for whom ≥3 preventive treatments have failed.
    - However, there are limitations associated with these treatments including slow rates of drug clearance, variable treatment effect between doses, observed rates of discontinuation and restricted access
    - Furthermore, these CGRP mAbs are only available via subcutaneous (SC) injection, which may be seen as an inconvenient, intrusive, and painful mode of administration by patients.
- Botulinum toxin type A is approved by NICE for migraine prevention in a subset of patients with CM only, for whom ≥3 preventive treatments have failed.
    - There are also limitations associated with botulinum toxin type A, which are administered via up to 39 intramuscular (IM) injections. The need for specialist clinicians with the necessary training to administer this treatment can lead to capacity constraints and extensive waiting times. Therefore clinicians would not consider atogepant as an alternative to botulinum toxin type A.
- Recently, a further two therapies have been recommended by NICE in the same indication, eptinezumab (1 March 2023) and rimegepant (5 July 2023). However, neither

eptinezumab nor rimegepant are considered established clinical practice.

- In line with the anticipated place in the treatment pathway, galcanezumab, erenumab and fremanezumab represent relevant comparators to atogepant in this submission.

Figure 3: Anticipated clinical pathway of care for migraine patients



- ref. NICE committee papers

Stakeholder views

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

Cost-effectiveness

For episodic migraine, the most relevant comparator is rimegepant because it is also an oral preventive medicine. The most likely cost-effectiveness estimate for atogepant compared with rimegepant is within the range that NICE normally considers an acceptable use of NHS resources.

For chronic migraine, it is not clear whether atogepant is better or worse than the other preventive medicines, but it has lower costs. So, atogepant is recommended for preventing episodic and chronic migraine after 3 or more preventive medicines.

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

Total resource impact	Current practice	year 1	year 2	year 3	year 4	year 5
	£'000	£'000	£'000	£'000	£'000	£'000

Cash items and financial impact of capacity items	£799	£805	£838	£850	£862	£870
		£5	**£39**	**£51**	**£63**	**£71**
		£5	**£34**	**£12**	**£12**	**£8**

Section 1: cost of the technology

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

The proposed price of atogepant is £182.16 for 28 tablets (excluding VAT). The recommended dose is 60mg once daily.

Year 1:

Atogepant, oral, 60mg daily	£2,375
Total first year	**£2,375**

Because there is no commercial arrangement for atogepant 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 Drug Tariff?

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

Also, there is no contract or PAS price for atogepant 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
Rimegepant	TA906 July 2023	Every other day	£103.20 for 8 tablets	£2,167

*Commercial arrangements and administration costs associated are NOT included.

The most cost-effective currently available anti-CGRP are rimegepant / erenumab. The most cost-effective oral treatment for EM prevention is rimegepant. The most cost-effective treatment for CM prevention in erenumab (followed by atogepant. Please note that rimegepant does not have a NICE TA for CM prevention).

NICE have also stated that if atogepant 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 atogepant 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 atogepant is a further treatment option. Uptake of atogepant would displace other calcitonin gene-related peptide (CGRP) receptor antagonists, and the overall cost of treatment for this patient group will be similar.

Atogepant is an oral tablet, which may be preferrable when compared with other CGRP receptor antagonists that are administered by subcutaneous injection or intravenous infusion.

The list price of atogepant is £182.16 for 28 tablets (excluding VAT; company information). An updated resource impact template is provided for completion at a local level. This is because there are five other CGRP receptor antagonists recommended by NICE for migraine. These are eptinezumab (TA871) fremanezumab (TA764) erenumab (TA682) galcanezumab (TA659) and rimegepant (TA906). TA871, TA764, TA682 and TA659 have discounts that are commercial in confidence.

The price of each option can be input into the template to assess the resource impact. The prices for atogepant and rimegepant are included in the template because they do not have a confidential commercial arrangement.

To improve usability, the template has been simplified using average treatment durations for each treatment option, which can be amended locally. This is possible because CGRP receptor antagonists have been in use for some time (since 2020), therefore the number of people with migraine who are starting, stopping and continuing treatment can be assumed to have reached a steady state each year. The resource impact template covers all treatment options and updates and replaces the previous NICE resource impact templates that were published for these topics.

The local resource impact template allows users to model local service arrangements.
In NHS hospital trusts, the payment mechanism is determined by the responsible commissioner and depends on the technology being classified as high cost. Both atogepant and rimegepant have a list price that allows flexibility for prescribing. Please see the table below for the commissioners, providers and prescribing setting of each treatment.

Treatment	**Comissioner**	**Provider**	**Prescribing setting**
Atogepant (oral tablet)	ICBs	NHS hospital trusts – neurology or primary care GP services	Secondary care acute hospital trusts (headache clinic) or primary care GP
Rimegepant (oral tablet)	ICBs	NHS hospital trusts – neurology or primary care GP services	Secondary care acute hospital trusts (headache clinic) or primary care GP
Eptinezumab (IV infusions)	ICBs	NHS Hospital trusts – neurology	Secondary care acute hospital trusts (headache clinic)
Fremanezumab (subcutaneous injection prefilled	ICBs	NHS Hospital trusts – neurology (homecare	Secondary care acute hospital trusts (headache

pen)		services)	clinic)
Erenumab (subcutaneous injection prefilled pen)	ICBs	NHS Hospital trusts – neurology (homecare services)	Secondary care – acute hospital trusts (headache clinic)

Abbreviations: ICB, integrated care board.

The committee concluded that both atogepant and rimegepant could eventually be prescribed in primary care. There is also potential for people receiving both treatments to be monitored in primary care and for follow-up appointments to be done by GPs. But it recognised that specialist referral and treatment management would likely be needed before atogepant or rimegepant could be used in primary care.

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

NICE resource impact template

As NICE have stated that if atogepant 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 atogepant is less expensive and less effective than some of the standard treatments.

As atogepant is a further treatment option, uptake of atogepant 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:
Yes – listed as HCD on the NHS payment system.

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

'The committee concluded that both atogepant and rimegepant could eventually be prescribed in primary care. There is also potential for people receiving both treatments to be monitored in primary care and for follow-up appointments to be done by GPs. But it recognised that specialist referral and treatment management would likely be needed before atogepant or 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 commissioned.

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
- 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 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 as agreed at SWL Collaborative Neurology guidelines which are in the process of being updated following this guidance release (and may be discussed / reviewed during meeting).

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: AQUIPTA 60 mg tablets - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk) Accessed <14.06.24>

2 NICE Technology Appraisal Guidance: Rimegepant for preventing migraine. Available at: https://www.nice.org.uk/guidance/ta973 Accessed <14.06.24>

3 NICE Resource Impact Statement: Available at: https://www.nice.org.uk/guidance/ta973/resources Accessed <14.06.24>

4 NICE Resource Impact Template: Available at: https://www.nice.org.uk/guidance/ta973/resources Accessed <14.06.24>

Declaration of interest:

	Name	Role	Date	Declaration of interests (please give details below)

Prepared by	Georgina Randall	Senior Pharmacy Technician	14.06.24	Yes
Supported by	Tejinder Bahra	Lead Pharmacist – MRU	3.7.24	No
Reviewed by				

Explanation of declaration of interest:
Georgina Randall – as per SH ICS declaration of interest.

Version control sheet:

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

Blueteq® form:

Please indicate whether patient meets the following NICE criteria:	Please tick
1. The patient has at least 4 migraine attacks per month? Please provide number of migraines per month (insert number)?:	○ Yes ○ No
2. At least 3 preventative drug treatments have not worked. Please provide details below:	○ Yes ○ No
3. Treatment with atogepant will be stopped after 12 weeks if the frequency of migraines does not reduce by: - at least 50% in episodic migraine (defined as fewer than 15 headache days per month) - at least 30% in chronic migraine (defined as 15 or more headache days per month, with at least 8 of those having features of migraine)	○ Yes ○ No