NHS
Cheshire and Merseyside

ATOGEPANT for preventing migraine

The Cheshire and Merseyside Area Prescribing Group recommends the prescribing of ATOGEPANT following specialist initiation, for preventing migraine in accordance with NICE TA973.

AMBER patient retained by specialist

NICE technology appraisal (TA973)[1] recommends atogepant as an option for preventing migraine in adults who have at least 4 migraine days per month, only if, at least 3 preventative treatments have failed.

Treatment should be stopped after 12 weeks if the frequency of migraine attacks 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)

Prescribing is to be initiated by the specialist and treatment efficacy reviewed at week 12. If adequate response is achieved, the specialist may then request the patient's GP to take over prescribing responsibility. It is the responsibility of the specialist to undertake the 12 month review of treatment. The decision to stop or continue treatment should be clearly communicated to the patient's GP after each annual review.
The specialist should submit a Blueteq form for initiation and first assessment of treatment efficacy where Blueteq is implemented across Cheshire and Merseyside.

If people with the condition and their clinicians 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].

For further information on the management of migraine, please refer to the following national and local guidance:

> NICE Clinical Guideline [CG150] Headaches in over 12s: diagnosis and management, last updated 17 December 2021.
> British Association for the Study of Headache National Headache Management System for Adults National Headache Management System for Adults, 2019
> Legacy Merseyside: Pan Mersey Area Prescribing Committee Headache pathway (adults), last updated 28 September 2022.
> Legacy Cheshire: Cheshire Area Prescribing Group Headache Pathway (Adults), last updated December 2020.

Note: Patients who are not eligible for treatment under this statement may be considered on an individual basis where their GP or consultant believes exceptional circumstances exist that warrant deviation from the rule of this policy. In this situation, follow locally defined processes.

ATOGEPANT for preventing migraine

Effectiveness

Atogepant is an orally administered, selective calcitonin gene-related peptide (CGRP) receptor antagonist that blocks the binding of the CGRP to the receptor and antagonizes CGRP receptor function[2].
The efficacy of atogepant has been investigated in three Phase III clinical studies:
including two trials investigating patients with episodic migraine (EM) [2,3,4] and one trial investigating with patients with chronic migraine (CM) [2,5]

Episodic migraine (4 to 14 migraine days per month)

The ADVANCE trial enrolled 910 eligible patients with EM with a ≥1 year history of migraine (with or without aura). A total of 680 patients were randomised 1:1:1 to receive atogepant 60 mg (n=235), atogepant 10 mg (n=222) or placebo (n=223) once daily for 12 weeks[3]. The licensed dose of atogepant 60 mg met the primary endpoint of change from baseline in mean monthly migraine days across the 12-week treatment period. The results showed a significant reduction in mean monthly migraine days (MMD) from baseline with atogepant 60mg (-4.2) compared to placebo (-2.5) [3]
Some secondary endpoints included change from baseline in mean number of headache days per month across 12 weeks and mean number of days of acute medication use across 12 weeks.

Chronic migraine (15 or more migraine days per month)

The PROGRESS trial enrolled 778 eligible adult patients with history of CM who had 15 or more headache days per month in the three months prior to visit 1, and 15 or more headache days of which eight or more were migraine days during the 4-week screening/baseline period.[5] A total of 521 patients were randomised 1:1 to receive atogepant 60 mg (n=262) or placebo (n=259) once daily for 12 weeks. A subset of patients (11%) was allowed to use one concomitant migraine prophylaxis medication (e.g., amitriptyline, propranolol, topiramate). Patients were allowed to use acute headache treatments (i.e., triptans, ergotamine derivatives, NSAIDs, acetaminophen and opioids) as needed. Patients with acute medication overuse and medication overuse headache also were enrolled[2]. The primary efficacy endpoint was change from baseline in mean monthly migraine days across the 12-week treatment period. The results showed a significantly significant reduction in mean monthly migraine days (MMD) from baseline with atogepant 60mg (-6.9) compared to placebo (-5.1)[5].
Some additional endpoints included change from baseline in mean monthly headache days across 12 weeks and monthly acute medication use days across 12 weeks[5].

Safety

The most commonly reported adverse drug reactions were nausea (7%), constipation (7%), and fatigue/somnolence (5%). The majority of these cases were mild, and none were serious. The adverse reaction that most commonly led to discontinuation was nausea (0.6%)[2].

Atogepant is contraindicated in patients with hypersensitivity to the active substance or to any of the following excipients: polyvinylpyrrolidone/vinyl acetate copolymer, vitamin E polyethylene glycol succinate, mannitol, microcrystalline cellulose, sodium chloride, croscarmellose sodium, colloidal silicon dioxide and sodium stearyl fumarate[2]. Refer to SPC for full safety information.

Cost

The annual cost of atogepant based on the UK list price is £2368.08 (both for the 60mg and the 10mg presentations).
NICE expect the overall costs of treatment for this patient group to remain similar. This is because atogepant is a further treatment option and will displace other calcotonin gene-related peptide (CGRP) receptor antagonists and is available at a similar or lower cost.

Patient factors

Elderly (>65 years)

There is limited data available in the elderly with no data available in patients over 80 years of age.
There are no clinically significant pharmacokinetic differences observed in population pharmacokinetic modelling between elderly and younger subjects. No dose adjustment of atogepant is needed in elderly patients[2].

Hepatic impairment

Use of atogepant should be avoided in patients with severe hepatic impairment. No dose adjustment is recommended in patients with mild or moderate hepatic impairment[2].

Renal impairment

- the recommended dose of atogepant is 10 mg once daily in patients with severe renal impairment (creatinine clearance [CLcr] 15–29 mL/min), and in patients with end-stage renal disease (ESRD) (CLcr <15 mL/min).
- For patients with ESRD undergoing intermittent dialysis, atogepant should preferably be taken after dialysis.
- No dose adjustment is recommended for patients with mild or moderate renal impairment[2].

Interactions with other medicinal products

Dose modifications are recommended for concomitant use of strong CYP3A4 inhibitors and strong OATP inhibitors. Refer to SPC [2].

Pregnancy and breastfeeding

Atogepant is not recommended during pregnancy or breastfeeding[2].

Prescribing information

> The recommended dose for atogepant is 60 mg taken orally once daily with or without food.
> See **Patient factors** section above for dose modifications in renal impairment and concomitant use of specific drugs.
> Atogepant is recommended for prophylaxis of episodic and chronic migraine. It is not recommended for treatment of acute migraine, therefore patients will be advised to use alternative treatment.
> Patients should be on one CGRP inhibitor at a time for the prevention of migraine.

Implementation notes

> Atogepant requires specialist initiation within secondary or tertiary care.
> Patients will be counselled by the specialist centre and advised to keep headache diaries whilst on atogepant treatment, as the diaries are required for further reviews. The specialist will inform the patient about the possibility of pausing treatment at the 12 month review.
> Prescribing is to be continued by the specialist until treatment efficacy is assessed at week 12.
> The specialist should submit a Blueteq form for initiation and first assessment of treatment efficacy where Blueteq is implemented across Cheshire and Merseyside.
> If adequate response achieved, the specialist may then request the patient's GP to take over prescribing responsibility.
> All atogepant patients will be retained and reviewed annually by the specialist and will not be discharged.
> The decision to stop or continue treatment should be clearly communicated to the patient's GP after each annual review.

References

1. National Institute for Health and Care Excellence. Technology Appraisal 973 Atogepant for preventing migraine, 15 May 2024. Accessed 15 May 2024.
2. AbbVie Ltd. Summary of Product Characteristics, AQUIPTA 60 mg tablets, 30 August 2023. Accesssed 01 May 2024.
3. Ailani J, Lipton RB, Goadsby PJ, et al. Atogepant for the Preventive Treatment of Migraine. N Engl J Med. 2021;385(8):695–706.
4. Ashina M, et al. Once-daily oral atogepant for the long-term preventive treatment of migraine: Findings from a multicenter, randomized, open-label, phase 3 trial. Headache. 2023;63(1):79–88
5. Pozo-Rosich P, Ailani J, Ashina M et al. Atogepant for the preventive treatment of chronic migraine (PROGRESS): a randomised, double blind, placebo-controlled, phase 3 trial. Lancet. 2023 Jul 26:S0140-6736(23)01049-8.