Hertfordshire and West Essex Integrated Care System

NHS Hertfordshire and West Essex Integrated Care Board

Atogepant (Aquipta®) for preventing migraine

PRESCRIBING CRITERIA:

In line with NICE TA973, 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.

Prescribing of atogepant for preventing migraine is to be initiated by a neurology specialist.
Atogepant must only be initiated after unsuccessful trials of at least 3 standard preventatives at sufficient dose and duration.

Atogepant should 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).

Prescribing will be maintained by the specialists until the patient is reviewed at 3 months and it is confirmed that the patient is responding and meets the continuation criteria outlined above.

Neurology specialist

Patient reviewed in specialist clinic.
History confirmed and patient meets the prescribing criteria.
Drug history confirmed to establish if they are on any interacting drugs (dose reduce if indicated).

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Atogepant initiated within secondary care by specialist team & Blueteq form completed.

If rimegepant is being taken for treatment of acute migraine advise patient & GP on any changes to recommendations for acute treatment.

Provide counselling to the patient to improve adherence and manage any adverse effects, emphasise the importance of keeping a headache diary.

Advise patient to read the patient information leaflet inside the medicine pack

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Review at 3 months to confirm efficacy and tolerability.

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Primary Care

TRANSFER OF CARE:

- Specialist provides GP with the baseline investigations and monitoring results (i.e. pre- and post-treatment migraine frequency & confirmation of at least a 30% or 50% reduction dependent on migraine type), rationale of treatment choice, dose to be prescribed and any other information deemed necessary to ensure safe transfer of prescribing responsibility.
- GP takes over prescribing responsibility and review of ongoing treatment. Patients should be reviewed within 9 to 12 months of starting treatment and then annually.

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Problems in Primary Care:

- Seek advice and discuss management plan with the specialist team if concerns arise around adherence, tolerability issues and/or new contra-indications, drug interactions, loss of response, adverse drug events, or if the patient's clinical condition has changed.

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Prescribing Support Document

The aim of this prescribing support document is to ensure sufficient information is provided to enable GPs to be confident to take on the clinical and legal responsibility for prescribing atogepant in stable patients.

This information does not replace the Summary of Product Characteristics (SPC) and should be read in conjunction with it. Please see BNF & SPC for comprehensive information.

BACKGROUND AND INDICATION(S) FOR USE

Atogepant is a calcitonin gene-related peptide (CGRP) receptor antagonist which inhibits the function of CGRP, thereby preventing migraine attacks.

Migraine can be classed as chronic (defined as 15 or more headache days per month, with at least 8 of those having features of migraine, over at least a 3 month period) or episodic (defined as more than 4 migraine days per month but less than 15 headache days [including migraine] per month).

Atogepant is licensed for the prophylaxis of migraine in adults who have at least 4 migraine days per month[1], and can be used for prevention of both chronic and episodic migraine.

SUPPORTING INFORMATION

Criteria for patient selection in line with NICE and local recommendations

NICE TA 973[2] states that 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.

Atogepant should 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).

Atogepant must only be initiated after unsuccessful trials of at least 3 standard preventatives at sufficient dose and duration, unless there have been issues with intolerance (refer to Treatment of migraine in adults guideline[3] for details)

RESPONSIBILITIES

Specialist Responsibilities	
1	Confirm patient adherence with trials of at least 3 standard oral preventative therapy prior to considering atogepant.
2	Assess the clinical need and suitability of the patient for atogepant and ensure recommendation is in line with local recommendations and criteria recommended in NICE TA973.
3	Complete baseline investigations.
4	Initiate and prescribe atogepant for the initial 3 month trial period. Ensure patient is on the correct starting dose by reviewing drug history (including OTC and herbal items) to check for any interactions which may require dose modification.
5	Prescribe atogepant using the generic name so any concomitant prescribing of additional gepant therapy is more easily identified.
6	Inform the GP at initiation of 3-month trial of therapy, prescribing retained by the specialist. The correspondence should include clinical details such as the monthly headache/migraine days at baseline. If patient is currently receiving rimegepant for treatment of acute migraine advise the patient and GP on any changes to recommendations for acute treatment.
7	Ensure the patient/carer has agreed to treatment and has been counselled at initiation. Advise the patient to read the patient information leaflet inside the pack when they receive the medication. To contact the specialist if any issues/concerns following initiation.
8	Review the patient after 3 months of treatment to assess efficacy and tolerability of atogepant. If adequate response has been achieved (i.e. at least a 30% or a 50% reduction in migraine frequency dependent on migraine type) and the treatment is to continue, provide the GP with the baseline investigations and efficacy results, rationale of treatment choice, dose to be prescribed and any other information deemed necessary to ensure safe transfer of prescribing responsibility for the patient to the GP. Ensure the patient has sufficient supply of medication to allow the transfer of care to take place.
9	Be available to the GP for advice if the patient's clinical condition changes, (e.g. sustained loss of response/worsening of symptoms, patient develops a new contra-indication to atogepant), if there are concerns around adherence, tolerability or adverse drug events.

General Practitioner Responsibilities	
1	Prescribe atogepant at the dose specified by the neurology service, using the generic name so any concomitant prescribing of additional gepant therapy is more readily identified.
2	If the patient is currently on rimegepant for acute treatment of migraine the specialist will advise on whether any changes to therapy are needed.
3	Review on going treatment as specified below, seeking support from the specialist team where appropriate.
4	Seek advice and discuss management plan with the specialist team if concerns arise about adherence, tolerability issues and/or contra-indications, efficacy monitoring results, adverse drug events or if the patient's clinical condition has changed.
5	Monitor adherence with therapy and raise concerns with the specialist team as required.
6	Review the patient after 9 to 12 months of starting treatment to include assessment of ongoing response (use headache diaries), tolerance/adverse events, new cautions/contraindications, adherence, drug interactions and need for continued therapy.
7	For patients remaining on treatment continue to review annually to include assessment of ongoing response (use headache diaries), tolerance/adverse events, new cautions/contraindications, adherence, drug interactions and need for continued therapy.

CONTRAINDICATIONS[1]

- Hypersensitivity to the active substance or to any of the excipients
- Pregnancy and/or breastfeeding (local specialists have advised that treatment should be stopped for at least 4 weeks before trying to conceive)
- Severe hepatic impairment
- Children (under 18 years of age)

CAUTIONS[1]

- Renal impairment – CL_{cr} below 30ml/min (see recommended dose adjustments below)
- Drug interactions (see recommended dose adjustments & notable drug interactions sections below)
- CGRP is a potent vasodilator and blocking its vasodilatory action may have other effects within the body. Whilst there are no specific cautions or contraindications listed in the SmPC, patients with clinically significant cardiovascular or cerebrovascular disease were excluded from trials (e.g. Myocardial Infarction (MI), Acute Coronary Syndrome (ACS), Percutaneous Coronary Intervention (PCI), cardiac surgery, stroke or Transient Ischemic Attack (TIA) during the 6 months prior to enrolment in the trial). The potential risk of use in these cohorts is therefore uncertain and specialist advice should be sought if needed**.**
    - If the patient develops a new vascular condition whilst on treatment the risk/benefit should be reassessed, and specialist advice sought if needed.

DOSAGE

- The recommended dose of atogepant is one 60mg tablet once daily with or without food.

Dosage modifications for drug interactions

Concomitant drug	Recommended once daily dose
Strong CYP3A4 inhibitors	10mg
Strong OATP inhibitors	10mg
Telmisartan	10mg

Dosage modifications in renal impairment

Renal function	Recommended once daily dose
Mild or moderate renal impairment	60mg (no adjustment required)
Severe renal impairment (CL_{cr} 12-29ml/min) or end stage renal disease (ESRD)* (CL_{cr}<15ml/min)	10mg

*ESRD with intermittent dialysis - Preferable to take atogepant after dialysis

Dosage modification in hepatic impairment

Atogepant should be avoided in patients with severe hepatic impairment. No dose adjustment is recommended for patients with mild or moderate hepatic impairment.

FOLLOW UP/REVIEW IN PRIMARY CARE

In primary care patients should be reviewed within 9 to 12 months of starting treatment and then annually. Patients should be encouraged to contact their GP if they experience issues between review appointments.

At the appointments:

- Review headache diary and discuss frequency of attacks, effectiveness of treatment, adherence, adverse effects, new cautions/contra-indication, drug interactions and lifestyle improvements. It is important to also evaluate the most bothersome symptom of migraine as this may not be well captured on a pain diary and can sometimes reflect the mismatch between reporting of significant benefit but pain diaries seemingly not reflecting this.
- Reassess lifestyle advice, check correct usage of treatment and reiterate advice on avoidance of MOH (i.e. restriction of use of acute medications to a max of 2 days per week)
- While preventative migraine therapies aim to achieve a clinically meaningful reduction in migraine attacks, the majority of patients will use acute medications to manage breakthrough events.
    - a 30% reduction in severity and frequency of attacks is considered a good response in chronic migraine
    - a 50% reduction in severity and frequency of attacks is considered a good response in episodic migraine
- If atogepant has been effective and the patient is now experiencing fewer than 4 migraine days per month consider a trial withdrawal, (the medication can just be stopped there is no need to taper).
- If atogepant has been effective but the patient is still having more than 4 migraine days a month, continue atogepant (with appropriate medication reviews).
- Ask the patient to reconsult if they experience problems in the future (for example increasing severity or frequency of migraine or side effects of medication).

Patient reports worsening of symptoms outside of annual reviews:

- Review headache diaries, treatment history and any lifestyle factors that could be contributing.
- Check correct usage of atogepant.
- If there has been a sustained loss of response over a 3-month period seek advice from the specialist.

SIDE EFFECTS

The most commonly reported adverse drug reactions were nausea (7%), constipation (7%), and fatigue/somnolence (5%). The majority of the cases were mild, and none were serious. The adverse reaction that most commonly led to discontinuation was nausea (0.6%). Decreased appetite and decreased weight were also commonly seen.
Atogepant has no or negligible influence on the ability to drive and use machines. However, it may cause somnolence in some patients. Patients should exercise caution before driving or using machinery until they are reasonably certain that atogepant does not adversely affect performance.

For a detailed list of side effects, please refer to the summary of product characteristics (SmPC)

Atogepant is a ▼ drug - report adverse effects directly to the MHRA via the Yellow Card Scheme

NOTABLE DRUG INTERACTIONS (for a comprehensive list, please see BNF or SmPC)

Drug / Drug class	Examples	Recommendation
Strong CYP3A4 inhibitors	• Ketoconazole • Itraconazole • Voriconazole • Clarithromycin • Telithromycin • Indinavir • Nelfinavir • Ritonavir • Saquinavir	• Reduce daily dose to 10mg. [no dose adjustment is needed with concomitant use of moderate or weak CYP3A4 inhibitors]
Strong OATP inhibitors	• Rifampicin • Atazanavir • Ritonavir • Tipranavir • Ciclosporin • Telmisartan	• Reduce daily dose to 10mg.
Grapefruit/grapefruit juice		• Regular consumption may increase atogepant levels and increase the risk of side effects

HEADACHE DIARIES

Patients should be asked to keep a headache diary to record details of their migraine attacks or headache. This can help to confirm the diagnosis and can be used to assess whether acute or preventative medication is working. It can also help the patient to recognise any triggers and warning signs and to show any patterns to attacks.

A headache diary should be simple and record basic information which should include:
Date / day of the week / duration (how long the attack lasted) / severity (how bad the attack was using a severity scale of 0-10 where 0 is no pain and 10 is the worst possible and patient is bed-bound) / other symptoms (e.g., dizziness, vertigo, sensitivity to light, sound, smells) / medication taken / any side effects from medication / any potential triggers.

Example headache diary template: Keeping a headache diary - The Migraine Trust

INFORMATION FOR PATIENTS

- Migraine from Patient Info UK: Migraine leaflet
- Treatment of migraine from Patient Info UK: Migraine treatment-medication and prevention
- NHS Health A-Z: Migraine
- The Migraine Trust: Migraine
- British Association for the Study of Headache Guidelines (BASH): For headache sufferers

VERSION CONTROL

Version	1.0
Prepared by	Pharmacy and Medicines Optimisation Team, Hertfordshire and West Essex (HWE) ICB with relevant HWE ICS stakeholders
Approved by	HWE Area Prescribing committee, November 2024
Review date	The recommendation is based upon the evidence available at the time of publication. This recommendation will be reviewed upon request in the light of new evidence becoming available.

REFERENCES

1. Aquipta 60mg tablets. Summary of medicinal Product characteristics. Last updated August 2023 https://www.medicines.org.uk/emc/product/15049/smpc Accessed 23/07/24
2. NICE TA 973 Atogepant for preventing migraine. Published date 15th May 2024. https://www.nice.org.uk/guidance/ta973 Accessed 23/07/24
3. HWE ICS Treatment of migraine in adults in primary care. November 2024.