National Institute for Health and Care Excellence

Health Technology Evaluation

Atogepant for preventing migraine [ID5090]
Response to stakeholder organisation comments on the draft remit and draft scope

Please note: Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Comment 1: the draft remit and proposed process

Section	Stakeholder	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	BASH	Appropriate	Thank you for your comment. No action required
	TEVA UK	This appears an appropriate topic for appraisal	Thank you for your comment. No action required
	Novartis	We consider it appropriate to refer this topic to NICE for appraisal. The proposed evaluation route (single technology appraisal) seems appropriate.	Thank you for your comment. No action required
	Abbvie	Yes, it is appropriate to refer this topic for a single technology appraisal.	Thank you for your comment. No action required

Section	Stakeholder	Comments [sic]	Action
	Migraine Trust	This is appropriate evaluation route.	Thank you for your comment. No action required
	ABN	Appropriate for single technology appraisal	Thank you for your comment. No action required
Wording	BASH	Wordings are appropriate	None required
	TEVA UK	The wording appears appropriate	None required.
	Novartis	We consider the proposed wording of the remit appropriate.	None required.
	AbbVie	Yes, the wording of the remit is appropriate.	None required.
	Migraine Trust	Yes	None required
	ABN	Yes	None required
Timing Issues	BASH	Urgent	Thank you for your comment.
	TEVA UK	A number of other migraine preventive drugs have recently been made available in the NHS	Thank you for your comment.
	Novartis	No comments	Thank you for your comment.

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	AbbVie	The timing of this appraisal is appropriate. Migraine is a severely debilitating disease that remains an urgent area of high unmet need; particularly in patients whereby at least 3 prior oral preventive drug treatments have failed. In this line of therapy, patients are limited to only injectable therapy in the form of a monoclonal antibody (mAb) or botulinum toxin type A (in chronic migraine only). Access to injectable therapies is further limited by the need for specialist care, leading to inequities in the distribution of their use and capacity issues across the UK. For example, mAbs and botulinum toxin type A are largely dispensed by headache specialists; while access to botulinum toxin type A is dependent on the availability of skilled injectors. There is also currently no branded oral preventive treatment option available for both episodic and chronic migraine. Therefore, this appraisal remains a priority to the NHS, to provide non-responsive patients access to a targeted, daily, oral preventive therapy that is easily accessible and will alleviate disease burden.	Thank you for your comment. No action required
	Migraine Trust	We would say there is an urgency to this appraisal (within the next 6 months) as many people do not have appropriate acute treatment for migraine. This is due to lack of effects, side effects, medication overuse from current treatments or medical comorbidities that exclude or limit current acute treatments. This is exacerbated by the current issue around access to medication already on the market, making it even more important to have atogepant available as soon as possible to help alleviate this issue.	Thank you for your comment. No action required
	ABN	Migraine represents a huge burden to the UK population in terms of morbidity and days lost to employment	Thank you for your comment. Burden of employment not considered explicitly in

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			NICE remit. None required
Additional comments on the draft remit	BASH	No comments	None required
	TEVA UK	No comments	None required
	Novartis	No comments	None required
	AbbVie	No comments	None required
	Migraine trust	No comments	None required
	ABN	No comments	None required

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	BASH	Yes	None required
	TEVA UK	No comment	None required
	Novartis	The description of existing NICE guidance for galcanezumab (TA659), erenumab (TA682), and fremanezumab (TA764) has to be amended to correctly refer to adults with 4 or more migraine ***days*** a month.	Thank you for your comment. The scope has been updated to refer to “4 or more migraine days” for the previous appraisals.

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	AbbVie	We note that the following sentence may be misleading, as it may imply that visual disturbance is the only symptom of migraine aura: • "Some people experience visual disturbances known as aura, which precede the headache and other symptoms, but the most common type of migraine is without aura" Other forms of aura may include numbness or tingling sensations, muscle weakness, and/or a loss of balance. Also, the NICE recommendations listed under background information for erenumab (TA682), fremanezumab (TA764), and galcanezumab (TA659) are currently described for "adults who experience 4 or more migraines a month". However, the NICE recommendations refer to adults who experience 4 or more migraine days a month. The background information is otherwise appropriate and accurate.	Thank you for your comment. The definition of aura has been updated to clarify that it is not solely a visual phenomenon.
	Migraine trust	The background information is accurate and complete	Thank you for your comment. No Action required
	ABN	Yes: although there are existing acute and preventative treatments for migraine many patients have inadequate response to these, treatments may be contraindicated because of co-morbidities and patients may not tolerate side effects	Thank you for your comment. No Action required
Population	BASH	Yes	None required
	TEVA UK	No comment	None required

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	Novartis	Depending on the population studied in clinical trials and the expected marketing authorisation wording, defining the population as “Adults with migraine” may be more appropriate than “People with migraine”.	Thank you for your comment. The population in the scope has been changed to “adults with migraine”
	AbbVie	In accordance with the expected licensed indication, please update the population to ‘Adults with migraine’. Specifically, atogepant is intended for appraisal in adult patients after at least 3 oral preventive drug treatments have failed.	Thank you for your comment. The population in the scope has been changed to “adults with migraine”
	Migraine Trust	Yes	None required
	ABN	Yes	None required
Subgroups	BASH	We consider migraine sufferers into three groups: Chronic Migraine – more than 15 days of headaches per month for at least three months. High Frequency Episodic Migraine – those with 8-14 days of headaches per month for at least three months. Low Frequency Episodic Migraine – those that have 4-7 days of headaches per month for at least three months. These sub-groups are based on clinical consensus and the degree of disability it cause to the migraine sufferers.	Thank you for your comment. The draft scope states that subgroups will be considered for those with chronic or episodic migraine and, for those with episodic migraine, further subgroups are be defined by frequency of episodic migraine.

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		Considering NICE has previously recommended newer treatments on those that had failed at least three first line preventative, it is important to include this group.	
	TEVA UK	No comment	None required
	Novartis	The proposed subgroups are in line with previous appraisals of migraine treatments	Thank you for your comment. No Action required
	AbbVie	Subgroups defined by the number of previous prophylactic treatments are appropriate. However, we note that due to a lack of consensus on the definition of, and clinical distinctiveness of high frequency episodic migraine, the NICE committee have concluded that there is insufficient evidence that high frequency episodic migraine is a clinically distinct subgroup during the technology appraisal processes for erenumab (TA682), fremanezumab (TA764), and galcanezumab (TA659). Therefore, subgroups defined by the frequency of episodic migraine (in those with episodic migraine) may not be appropriate for the scope.	Thank you for your comment. The committee will consider the clinical evidence presented to it and make recommendations based on that. Therefore, subgroups may be considered if any new evidence allows it.
	Migraine Trust	No. It is appropriate to consider the treatment for all migraine types.	Thank you for your comment. No Action required
	ABN	Yes: episodic and chronic migraine should be considered separately, chronic migraine is generally considered more refractory. For those with episodic migraine, those with high frequency migraine should be considered separately to those with low frequency episodic migraine	Thank you for your comment. These subgroups may be

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		We agree that subgroups analysis should include those who have previously trailed at least 3 other preventive treatments	considered if the evidence allows it.
Comparators	BASH	Botox is only a comparator for chronic migraine patients. Others are for both episodic and chronic migraines. Candesartan is another preventive treatment not listed but recommended by SIGN guidelines and BASH National Headache Management Systems.	Thank you for your comment. The final scope has been updated to reflect that botulinum toxin type A is only a comparator for chronic migraine.
	TEVA UK	No comment	None required
	Novartis	We agree with the comparators included in the draft scope.	Thank you for your comment. No Action required
	AbbVie	Potentially relevant comparators are those which are "established practice in the NHS." We therefore do not consider rimegepant and eptinezumab as relevant comparators, as they are not recommended by NICE, nor are they established within current NHS practice. We also note that oral preventive treatments (such as topiramate, propranolol, and amitriptyline) are not considered to be standard of care in patients who have failed at least 3 preventive drug treatments. In this population, patients with episodic migraine typically receive an injectable therapy in the form of a calcitonin gene-related peptide (CGRP)-targeted mAb (galcanezumab, erenumab, fremanezumab), while patients with chronic migraine may receive either a CGRP-targeted mAb or botulinum toxin type A.	Thank you for your comment. The comparators listed in the scope aims to be inclusive. The rationale for excluding any comparators from the evidence submission will be considered by the appraisal committee.

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		However, there is increasing focus on the targeted treatment of chronic migraine since the recent introduction of CGRP-targeted mAbs.	
	Migraine Trust	Yes, the listed comparators are the treatments currently used, or are being evaluated for use, in the NHS.	Thank you for your comment. No Action required
	ABN	Yes: Botulinum toxin is a comparator for chronic migraine, the other treatments listed are comparators for episodic and chronic migraine. A comprehensive list of recommended preventive treatments is outlined in the BASH national headache management system guidelines https://www.bash.org.uk/downloads/guidelines2019/01_BASHNationalHeadache_Management_SystemforAdults_2019_guideline_versi.pdf	Thank you for your comment. The final scope has been amended to specify that botulinum toxin type A is a comparator for chronic migraine.
Outcomes	BASH	Agreed	Thank you for your comment. No Action required
	TEVA UK	'*Changes in acute pharmacological medication given*' should be more accurately described as '*Changes in acute pharmacological medication taken/used*'. Acute migraine medications in this setting would be used as a rescue therapy when a migraine (or headache) occurs. Therefore, the patient will take these treatments as needed (they will be pre-prescribed) and so the use of these therapies is the important measure. Whilst it seems that this was the intention from NICE, the wording is not felt to be totally accurate on this point.	Thank you for your comment. The scope has been updated to read "changes in acute pharmacological medication ***used***"

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	Novartis	We agree that the outcomes listed in the draft scope are relevant.	Thank you for your comment. No Action required
	AbbVie	Yes, the listed outcomes are appropriate and will capture the most important health related benefits and harms of the technology.	Thank you for your comment. No Action required
	Migraine Trust	Yes, the outcomes are appropriate and relevant for the technology appraisal.	Thank you for your comment. No Action required
	ABN	Yes: a combination of overall health related quality of life and a measure of reduction in migraine symptoms (e.g. 2 and 24 hrs pain freedom post-dose) should be used	Thank you for your comment. No Action required
Equality	BASH	Migraines affect women three times more than men and is more common in the fertile age range of 18-45.	Thank you for your comment. This has been acknowledged on the EIA form for this appraisal.
	TEVA UK	No comment	None required
	Novartis	No comments.	None required
	AbbVie	None identified	None required
	Migraine Trust	No Comments	None required

Section	Consultee/ Commentator	Comments [sic]	Action
	ABN	No other issues identified	None required
Other considerations	BASH	None	None required
	TEVA UK	No comment	None required
	Novartis	No comments.	None required
	AbbVie	No additional issues identified	None required
	Migraine Trust	It would be helpful to identify any potential drug interactions or treatments to avoid when using this treatment. For example, can it be used with other acute treatments, how many attacks do you need to treat before efficacy is clear.	Thank you for your comment. The committee will consider any contraindications or interactions with alternative products, as outlined in the marketing authorisation. No Action required
	ABN	Nil	None required
Questions for consultation	BASH	• Atogepant should be considered as a preventive treatment option in those who have failed three first line treatments. • We suggest to include the utilisation of healthcare resources both in primary and secondary care and cost of acute treatments without any preventive treatment. • Being a new preventive treatment option, the initiation should be in the secondary care.	Thank you for your comments. Please see the relevant sections of this document for responses. No Action required

Section	Consultee/ Commentator	Comments [sic]	Action
		• **Would it be appropriate to use the cost-comparison methodology for this topic?** YES • **Is Atogepant likely to be similar in its clinical efficacy and resource use to any of the comparators? Or in what way is it different to the comparators?** Considering this is an oral preventive treatment it will consume less healthcare resources compared to Botulinum Toxin that needs injecting at the clinic. In comparison to the CGRP MAB this will not require homecare services to deliver the injections. • **Will Atogepant be used in the same place in the treatment pathway as the comparators?** Atogepant will have to be placed following failure of three first line treatment. Patients will have to choose from Botulinum Toxin, CGRP MAB and Atogepant that are all offered after first line treatment failures. • **Overall, is Atogepant likely to offer similar or improved health benefits compared with the comparators**? It would be similar to Botulinum Toxin and CGRP MAB. • **Is the primary outcome that was measured in the trial or used to drive the model for the comparators still clinically relevant?** YES • **Is there any substantial new evidence for the comparator technology that has not been considered? Are there any important ongoing trials reporting in the next year? PROGRESS study is expected to be published next year which is a phase 3 trial of Atogepant for chronic migraine.** PROGRESS study is expected to be published next year which is a phase 3 trial of Atogepant for chronic migraine.	

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	TEVA UK	Teva cannot comment fully on the appropriateness of the cost-comparison methodology for this appraisal, due to Teva not having access to all relevant efficacy data. Teva would like to highlight that there are a number of differences in the delivery of atogepant and its mechanism of action compared to the relevant comparators. These differences should be fully considered in any economic analysis and potentially may limit the applicability of the cost comparison methodology. In regards to new data and ongoing trials, Teva would like to highlight the PEARL study of fremanezumab. This 24-month, pan-European, prospective, observational study is ongoing to gather real-world evidence on the efficacy and safety of fremanezumab. To date, data from two interim analyses have been presented at conferences (Presentation at EAN 2022 – Ashina M, Mitsikostas D, Amin F *et al*. Effectiveness of fremanezumab for preventive treatment of migraine: The observational PEARL study [EPR-035]. Eur J Neurol 2022; 29 (Suppl. 1): 192. Poster at MTIS 2022 – Ashina M, Mitsikostas DD, Amin FM *et al*. Effectiveness of fremanezumab for the preventive treatment of migraine: Second interim analysis of the observational PEARL study [MTIS22-PO-054.). These available data provide important additional evidence of the efficacy and safety of fremanezumab within real-world clinical practice.	Thank you for your comment. None needed.
	Novartis	No comments	None required
	AbbVie	**Where do you consider atogepant will fit into the existing care pathway for migraine prevention?**	Thank you for your responses. NICE will consider any indirect

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		Atogepant is expected to provide the first daily, oral, targeted treatment option specifically designed for the preventive treatment of migraine; to be used in adult patients with migraine who have 4 or more migraine days a month, whereby at least 3 oral preventive drug treatments have failed. **Do you consider that the use of atogepant can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?** • **Please identify the nature of the data *which* you understand to be available to enable the committee to take account of these benefits.** Indirect health-related benefits of treatment (such as the impact on work productivity/absenteeism) are unlikely to be included in the QALY calculation. However, the atogepant clinical trial programme assessed the impact of atogepant in terms of daily, social and work-related activities as well as headache-related disability using the Headache Impact Test-6 (HIT-6), the Migraine Specific Quality of Life Questionnaire (MSQ) v2.1, and the Activity Impairment in Migraine Diary (AIM-D) questionnaires, among other patient-reported outcome measures. Differential route of administration (i.e. oral therapy vs injectable therapies) is another health-related benefit of treatment which may not be included in the QALY calculation. As a daily oral preventive therapy, atogepant may be preferred by some patients as an alternative to currently available intravenous and subcutaneous injectable treatments. • ***Will atogepant be used in the same place in the treatment pathway as the comparators?***	health-related benefits during the appraisal.

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		Yes, atogepant is anticipated to be used in the same place in the treatment pathway as the CGRP-targeted mAbs (galcanezumab, erenumab, and fremanezumab).	
	Migraine Trust	1. Where do you consider atogepant will fit into the existing care pathway for migraine prevention? It's likely to depend on cost, access and long-term safety. However, it could come after simple analgesics, especially for people who can't tolerate other treatment options or are at risk of medication overuse. As atogepant is in tablet form we hope that this is more likely to be prescribed through primary care, speeding up the process of access to treatment and reducing blockages in secondary care. 2. Would atogepant be a candidate for managed access? Yes, because there is an urgent need for effective, better tolerated acute medicines.	Thank you for your responses. The company states that atogeoant will be used in the same place as other CGRP-targeted therapies, i.e. in secondary care. No Action required.
	ABN	• Would it be appropriate to use the cost-comparison methodology for this topic? Yes • Is atogepant likely to be similar in its clinical efficacy and resource use to any of the comparators? Or in what way is it different to the comparators? Similar to comparators • Will atogepant be used in the same place in the treatment pathway as the comparators? Same as comparators • Overall, is atogepant likely to offer similar or improved health benefits compared with the comparators? Same as	Thank you for your responses.

Section	Consultee/ Commentator	Comments [sic]	Action
		comparators • Is the primary outcome that was measured in the trial or used to drive the model for the comparators still clinically relevant? Yes • Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year? 'PROGRESS' trials – phase 3 trial of atogepant for chronic Migraine expected publication in next year	
Additional comments on the draft scope	BASH	None	None required
	TEVA UK	For the economic analysis, it is stated that '*The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared*'. Teva notes that a lifetime time horizon was preferred in recent appraisals of migraine drugs (TAs: 764, 659 and 682). Careful consideration should be given to the definition of 'lifetime' as this has varied between appraisals.	Thank you for your comment. The time horizon will be considered during the appraisal. No action required.
	Novartis	None	None required
	AbbVie	Within the section titled 'The technology', please remove the brand name 'Qulipta'. Qulipta is the brand name for atogepant in the United States, and the proposed European brand name awaits approval by the MHRA.	Thank you for you comment. This has been amended in the final scope to read "Brand name unknown".

Section	Consultee/ Commentator	Comments [sic]	Action
	Migraine Trust	A potential barrier is likely to be equity and ease of access. If the treatment is only available via a headache specialist that is likely to create issues with access or treatment delays. It would be crucial for patients to have access in primary care and not only from headache specialists. This will help to ensure equitable geographical access.	Thank you for your comment. This has been acknowledged in the EIA form.
	ABN	NIL	None required

The following stakeholders indicated that they had no comments on the draft remit and/or the draft scope