National Institute for Health and Care Excellence

Single Technology Appraisal

Eptinezumab for preventing migraine [ID3803]

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

Section	Consultee/ Commentator	Comments [sic]	Action
Appropriateness	Lundbeck	We consider it appropriate to refer this topic to NICE for appraisal	Thank you for your comment. No action required.
	The Migraine Trust	Yes	Thank you for your comment. No action required.
	Novartis	We consider it appropriate to refer this topic to NICE for appraisal.	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.
Wording	Lundbeck	Yes, it does; we have no comments on the wording of the remit other than those listed at the end of this table	Thank you for your comment. No action required.

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	The Migraine Trust	Yes	Thank you for your comment. No action required.
	Novartis	We consider the proposed wording of the remit appropriate.	Thank you for your comment. No action required.
	Teva UK	The wording appears appropriate	Thank you for your comment. No action required.
Timing Issues	Lundbeck	Eptinezumab offers an alternative route of administration for aCGRP monoclonal antibody treatment for the prevention of migraine in adults, thus providing additional treatment choice to patients with migraine, an area of high unmet need. Therefore, we believe eptinezumab should be appraised by NICE at the earliest opportunity	Thank you for your comments. NICE has scheduled this topic into its work programme and aims to provide draft guidance to the NHS as soon as possible after marketing authorisation. No action required.
	The Migraine Trust	We would say there is an urgency to this appraisal (within 2022) as many people with migraine do not have access to a medication of this type as well as some who have tried another mAb, have not had an adequate or beneficial response. A different mode of delivery and timing of the treatment (quarterly dosing), may suit others better.	Thank you for your comments. NICE has scheduled this topic into its work programme and aims to provide draft guidance to the NHS as soon as possible after marketing authorisation. No action required.

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	Novartis	Eptinezumab will likely be the fourth CGRP inhibitor on the market. Three other CGRP inhibitors are already recommended by NICE (TA682, TA659, TA764) and available to people with migraine.	Thank you for your comment. No action required.
	Teva UK	A number of other anti-calcitonin gene-related peptide (aCGRP) drugs have recently been made available in the NHS	Thank you for your comment. No action required.
Additional comments on the draft remit	Lundbeck	Please could you add that on 12 November 2021 eptinezumab received a positive CHMP opinion for the prophylaxis of migraine. Please could you also replace the sentence *'eptinezumab does not currently have a marketing authorisation in the UK for preventing migraine'* with a note that eptinezumab received Marketing Authorisations from the EMA and MHRA on 24 and 26 January 2022, respectively, for the prophylaxis of migraine in adults who have at least 4 migraine days per month.	Thank for your comments. The scope has been updated to reflect that eptinezumab has received its marketing authorisation for preventing migraine.
	The Migraine Trust	No comment	No action required.
	Novartis	No comment	No action required.
	Teva UK	None	No action required.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Lundbeck	The background information is correct and we have no amends to request.	Thank you for your comment. No action required.
	The Migraine Trust	The background information is accurate and complete, except the update to TA631 (fremanezumab) which has recently been approved for episodic treatment also to people with 4 or more migraine days a month.	Thank you for your comment. The scope has been amended throughout to reflect NICE's updated technology appraisal guidance on fremanezumab for preventing migraine.
	Novartis	The wording of the ICHD-3 definition of chronic migraine is "Headache occurring on 15 or more days/month *for more than 3 months*, which, on at least 8 days/month, has the features of migraine headache" [italicised emphasis added]. The draft scope description omits this italicised wording which should be added, to ensure the full ICHD-3 definition of chronic migraine is accurately reported. The NICE TA recommendation for fremanezumab (previously TA631) has to be updated to reflect the revised recommendation of TA764.	Thank you for your comments. The background section has been updated to include the omitted wording on the definition of chronic migraine by the International Classification of Headache Disorders 3rd edition (ICHD-3). The scope has also been amended throughout to reflect NICE's updated technology appraisal guidance on

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			fremanezumab for preventing migraine.
	Teva UK	Update the details of the fremanezumab TA to the recently published TA764, which has superseded TA631	Thank you for your comment. The scope has been amended throughout to reflect NICE's updated technology appraisal guidance on fremanezumab for preventing migraine.
The technology/ intervention	Lundbeck	Please clarify that eptinezumab administration is every 12 weeks; this will bring the text in line with the wording of the SmPC for eptinezumab. In addition, the approved regulatory status of eptinezumab is to be updated as per our notes in section 1.	Thank you for your comment. The description of how often eptinezumab is administered has been amended to every 12 weeks, as suggested. The scope has been updated to reflect that eptinezumab has received its marketing authorisation for preventing migraine
	The Migraine Trust	Yes	Thank you for your comment. No action required.

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	Novartis	No comments	No action required.
	Teva UK	No comment	No action required.
Population	Lundbeck	Yes, we believe the population is defined appropriately.	Thank you for your comment. The population in the scope has been updated to reflect the marketing authorisation for eptinezumab.
	The Migraine Trust	Yes, the population is appropriate defined	Thank you for your comment. The population in the scope has been updated to reflect the marketing authorisation for eptinezumab.
	Novartis	We consider the definition of the population appropriate. In line with previous appraisals, episodic and chronic migraine populations should be assessed as separate subgroups.	Thank you for your comment. The population in the scope has been updated to reflect the marketing authorisation for eptinezumab.
	Teva UK	No comment	No action required.
Comparators	Lundbeck	Please could you update the comparators to align with the new recommendation for fremanezumab following its rapid review? i.e.	Thank you for your comment. The scope

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		Fremanezumab (4 or more migraine days per month and after at least 3 preventive drug treatments have failed)	has been amended throughout to reflect NICE's updated technology appraisal guidance on fremanezumab for preventing migraine.
	The Migraine Trust	Yes, the listed comparators are the standard treatments currently used in the NHS.	Thank you for your comment. No action required.
	Novartis	We agree with the comparators listed in the draft scope. The description of the reimbursed population for fremanezumab (previously TA631) has to be updated to reflect the revised recommendation of TA764. Rimegepant should be added as a potential comparator, subject to the ongoing NICE appraisal (ID1539).	Thank you for your comments. The scope has been amended throughout to reflect NICE's updated technology appraisal guidance on fremanezumab for preventing migraine. Because of the timing of the ongoing NICE appraisal of rimegepant, it is not expected to be established clinical practice at the time of appraising eptinezumab. Therefore, rimegepant has not been added as

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			a comparator to the scope.
	Teva UK	Update fremanezumab details to match TA764: fremanezumab (4 or more migraine days per month and after at least 3 preventive drug treatments have failed)	Thank you for your comment. The scope has been amended throughout to reflect NICE's updated technology appraisal guidance on fremanezumab for preventing migraine.
Outcomes	Lundbeck	Yes, the listed outcomes are appropriate and capture the relevant health-related benefits of eptinezumab.	Thank you for your comment. No action required.
	The Migraine Trust	Yes, the outcomes are appropriate and relevant for the technology appraisal	Thank you for your comment. No action required.
	Novartis	We agree that the outcomes listed in the draft scope are relevant. A response rate outcome could be added, as defined by a ≥30% reduction in monthly migraine days (MMDs) and a ≥50% reduction in MMDs for chronic migraine and episodic migraine populations, respectively. These outcomes were considered a clinically meaningful response to treatment in previous appraisals of preventive migraine treatments (TA682, TA631, TA659).	Thank you for your comments. The list of outcomes is not exhaustive, therefore information on those specific outcome measures can be submitted. No action required.
	Teva UK	No comment	No action required.

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Economic analysis	Lundbeck	We plan to provide a cost-utility analysis. The model will be a patient-level simulation model to allow issues raised in previous migraine appraisals, such as natural history and positive discontinuation, to be addressed.	Thank you for your comment. No action required.
	The Migraine Trust	No comment	No action required.
	Novartis	No comments	No action required.
	Teva UK	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'. Also, it should be ensured that all costs from the i.v. administration of eptinezumab are included within the economic analysis	Thank you for your comments. No action required.
Equality and Diversity	Lundbeck	We do not envisage any equality issues arising from the proposed remit and scope	Thank you for your comment. No action required.
	The Migraine Trust	No comment	No action required.
	Novartis	No comments	No action required.
	Teva UK	No comment	No action required.
Other considerations	Lundbeck	No comment	No action required.
	The Migraine Trust	It would be helpful to identify whether there are any potential safety concerns and additional monitoring required for this intravenous administration route.	Thank you for your comments. The committee will consider all relevant issues on

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		Will there be medical contraindications that are different from the other CGRP mAbs. Will patients with medication overuse be able to use this treatment. Many people affected by migraine who have found inadequate or no benefit from preventives, have had to rely on additional painkillers.	the use of eptinezumab in its decision making. No action required.
	Novartis	We agree that the proposed subgroups are relevant. Several of the treatments listed in the 'Comparators' section are recommended only after at least 3 preventive drug treatments have failed and one comparator (botulinum toxin [TA260]) is only recommended by NICE for use in chronic migraine (i.e. excluding episodic migraine). Therefore, subgroup analyses by chronic/episodic migraine and by number of previous preventive treatment failures are appropriate.	Thank you for your comments. No action required.
	Teva UK	No comment	No action required.
Innovation	Lundbeck	Migraine patients represent a patient group who have a substantial clinical burden, with particularly disabling symptoms. Eptinezumab offers a step-change in the clinical management of these patients as it would be the first intravenous aCGRP introduced to the clinical pathway of care, offering migraine patients a rapid-onset treatment option that is also associated with reduced hospital visits due to its quarterly dosing, helping to provide greater choice to patients.	Thank you for your comments. The appraisal committee will consider the innovative nature of this technology during the appraisal. No action required.
	The Migraine Trust	It has the potential to have a substantial positive impact especially to those who have currently not found a successful preventive treatment.	Thank you for your comments. The appraisal committee will consider the innovative nature of this technology during the

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			appraisal. No action required.
	Novartis	Eptinezumab will likely be the fourth CGRP inhibitor on the market. Three other CGRP inhibitors are already recommended by NICE (TA682, TA659, TA764) and available to people with migraine.	Thank you for your comments. The appraisal committee will consider the innovative nature of this technology during the appraisal. No action required.
	Teva UK	The technology is of limited innovation as it has the same mechanism of action (inhibition of CGRP) as some established migraine preventive therapies	Thank you for your comments. The appraisal committee will consider the innovative nature of this technology during the appraisal. No action required.
Questions for consultation	Lundbeck	**Have all relevant comparators for eptinezumab been included in the scope?** Yes **Which treatments are considered to be established clinical practice in the NHS for preventing migraine?** Question answered as part of the comparator and background sections (no changes to NICE scope text)	Thank you for your comments. No action required.

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		How should best supportive care be defined? Question answered as part of the comparator section **Are the outcomes listed appropriate?** Yes, the outcomes listed are appropriate **Are the subgroups suggested in 'other considerations appropriate? Are there any other subgroups of people in whom eptinezumab is expected to be more clinically effective and cost effective or other groups that should be examined separately?** Yes, the subgroups suggested are appropriate **Where do you consider eptinezumab will fit into the existing NICE pathway Headaches?** We anticipate that eptinezumab will be used for the prevention of migraine in adult patients with four or migraine days per month who have failed prior oral preventative treatment. **NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:** • ***could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which eptinezumab will be licensed;*** • ***could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;***	

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		• ***could have any adverse impact on people with a particular disability or disabilities.*** **Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.** We have not identified any issues that would lead to inequality **Do you consider eptinezumab to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?** Yes, we believe eptinezumab will be a step-change in the clinical management of migraine; please refer to our response in the innovation section for details **Do you consider that the use of eptinezumab can result in any potential significant and 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 Appraisal Committee to take account of these benefits.** **To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.** We don't anticipate any barriers to adoption. **NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).**	

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		We believe that the STA process is the appropriate appraisal route; we also consider that cost comparison methodology may also be appropriate for the appraisal of eptinezumab **NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made.** **Would it be appropriate to use the cost comparison methodology for this topic?** It would be appropriate to use a cost comparison methodology for this topic if comparators that are recommended for the same indication have similar health benefits to eptinezumab. **Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?** Analyses are currently ongoing to assess the comparative clinical efficacy and safety of eptinezumab vs its comparators and we anticipate that eptinezumab will be similar in clinical efficacy and resource use to erenumab, fremanezumab and galcanezumab. **Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) 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?**	

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		We are not aware of any significant new data that is expected to become available in the next year.	
	The Migraine Trust	**How should best supportive care be defined? Should best supportive care be considered as a comparator?** • Best supportive care usually refers to treatment for the migraine symptoms which is appropriate. It should be considered a comparator. • The outcomes listed are appropriate. • There are people with chronic migraine for whom botulinumtoxin A and other CGRP mAbs are not effective treatments. At this point in time there are limited options available to this patient group in terms of treatment. Eptinezumab could be considered an option for these people. Although it's important eptinezumab is considered in the same way as other CGRP mAbs and not necessarily just as the option that follows a failure of effect with another CGRP mAb, but as an option after a few preventives (of any treatment class) have failed and people continue to be debilitated by migraine. • Eptinezumab should be considered at the same stage of treatment as other CGRP mAbs. • Other factors that may impact include the severity of migraine and any co-morbidities the person has (as these may limit treatments that can be offered safely).	Thank you for your comments. No action required.
	Novartis	Regarding comparators, outcomes, and subgroups, please refer to our responses in previous sections.	Thank you for your comments. No action required.

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	Teva UK	"*Which treatments are considered to be established clinical practice in the NHS for preventing migraine?*" All of the treatments described in the scope should be considered as established clinical practice "*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?*" There are a number of studies that can provide additional evidence for fremanezumab (this includes completed studies and those in progress). The FOCUS open-label extension has reported results. This study provides clinical trial evidence for fremanezumab in a population with inadequate response to 2-4 classes of previous preventive therapies over 6 months of treatment (3 months of double-blind phase of FOCUS plus 3 months open-label extension). This study is the open-label extension of the FOCUS trial that was utilised as evidence during the fremanezumab appraisal. In addition, real-world evidence (RWE) for fremanezumab is being collected. Currently available RWE in Europe includes data from the experiences in Hull, and the FINESSE data from Austria & Germany. The pan-European PEARL RWE study is ongoing and an interim analysis is due later this year. Teva would be happy to provide additional details and relevant data to NICE in relation to any of these studies. No comment on other questions	Thank you for your comments. No action required.
Additional comments on the draft scope	Lundbeck	No additional comments.	Thank you for your comment. No action required.

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	The Migraine Trust	No comment	No action required.
	Novartis	No comment	No action required.
	Teva UK	Related NICE recommendations section to be updated with recently published guidance for fremanezumab (TA764)	Thank you for your comment. The scope has been amended throughout to reflect NICE's updated technology appraisal guidance on fremanezumab for preventing migraine.

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

None