NICE National Institute for Health and Care Excellence

NICE guidance

Galcanezumab for preventing migraine

Technology appraisal guidance
Published: 18 November 2020

www.nice.org.uk/guidance/ta659

Your responsibility

The recommendations in this guidance represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Contents

1 Recommendations

1.1 Galcanezumab is recommended as an option for preventing migraine in adults, only if:

- they have 4 or more migraine days a month
- at least 3 preventive drug treatments have failed and
- the company provides it according to the commercial arrangement.

1.2 Stop galcanezumab after 12 weeks of treatment if:

- in episodic migraine (less than 15 headache days a month) the frequency does not reduce by at least 50%
- in chronic migraine (15 headache days a month or more with at least 8 of those having features of migraine) the frequency does not reduce by at least 30%.

1.3 This recommendation is not intended to affect treatment with galcanezumab 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 clinician consider it appropriate to stop.

Why the committee made these recommendations

Treatment options for preventing episodic or chronic migraine include beta-blockers, antidepressants and anticonvulsant drugs. If episodic migraine does not respond to at least 3 oral preventive drug treatments, best supportive care (treatment for the migraine symptoms) is offered. If chronic migraine does not respond to at least 3 oral preventive drug treatments, botulinum toxin type A or best supportive care is offered.

For migraine that has not responded to at least 3 preventive treatments, clinical trial evidence shows that galcanezumab works better than best supportive care in both episodic and chronic migraine. It is plausible that galcanezumab may work better than botulinum toxin type A.

For episodic and chronic migraine, the most likely cost-effectiveness estimates are within what NICE normally considers an acceptable use of NHS resources. So galcanezumab is recommended for episodic and chronic migraine.

2 Information about galcanezumab

Marketing authorisation indication

2.1 Galcanezumab (Emgality, Eli Lilly) is 'indicated for the prophylaxis of migraine in adults who have at least 4 migraine days per month'.

Dosage in the marketing authorisation

2.2 The dosage schedule is available in the summary of product characteristics.

Price

2.3 The list price of galcanezumab is £450.00 per 120-mg injection (excluding VAT; Monthly Index of Medical Specialities online, accessed October 2020). The company has a commercial arrangement. This makes galcanezumab available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

3 Committee discussion

The appraisal committee considered evidence submitted by Eli Lilly, a review of this submission by the evidence review group (ERG), NICE's technical report, and responses from stakeholders. See the committee papers for full details of the evidence.

The appraisal committee was aware that several issues were resolved during the technical engagement stage, and agreed that:

- the time horizon in the model is 45 years to represent lifetime treatment (issue 1, see technical report page 9)
- the response rate differs between treatments and the change from baseline in migraine headache days differs for 'responders' based on results from the indirect treatment comparison (issue 4, see technical report page 13)
- treatment-effect waning periods are equal for galcanezumab and botulinum toxin A (issue 5, see technical report page 16)
- treatment-effect waning periods are equal for episodic and chronic migraine populations (issue 5, see technical report page 16)
- utility values are based on relevant utility data from all trials (issue 6, see technical report page 17)
- age-related disutility is applied in the model (issue 6, see technical report page 17)
- an additional cost for administering galcanezumab is applied for 10% of people (issue 7, see technical report page 19)

- resource costs are generated from the National Health and Wellness Survey (issue 7, see technical report page 19).

  It recognised that there were remaining areas of uncertainty associated with the analyses presented (see technical report, table 2, page 25), and took these into account in its decision making. It discussed the following issues that were outstanding after the technical engagement stage: the high-frequency episodic migraine subgroup (issue 2), the position of galcanezumab in the treatment pathway (issue 3), the indirect treatment comparison for chronic migraine (issue 4), the utility values applied to treatments (issue 6) and additional monitoring costs (issue 7).

The condition

Migraine substantially affects health-related quality of life

3.1 Migraine is a headache disorder with recurring attacks usually lasting between 4 and 72 hours. The patient expert explained the debilitating effect of migraine on their daily life with symptoms including fatigue, severe head pain, sensitivity to light, difficulty concentrating, nausea, stiff neck or back, feeling down, and sensitivity to sound. These symptoms were noted to adversely affect someone's ability to do their usual activities, including work, and to negatively affect their family. Chronic migraine is defined as 15 or more headache days a month with at least 8 of those having features of migraine. Episodic migraine is defined as less than 15 headache days a month. The clinical and patient experts explained that the severity and frequency can fluctuate over time and that recovery from a migraine can take a few days. The committee concluded that migraine, particularly chronic migraine, is a debilitating condition that substantially affects both physical and psychological aspects of health-related quality of life.

Treatment pathway and comparators

There is an unmet need for migraine-specific treatments

3.2 The committee understood that current oral treatment options for

preventing migraine include drugs that are used to treat other conditions including beta-blockers, antidepressants and anticonvulsant medications. The patient expert explained that these treatments can have significant side effects and any beneficial effects do not last or may not work at all for some people. This leads many people to try different medications to find one that works. The clinical expert stated that there is a risk of medication overuse with some of the current treatments for migraine such as triptans, which needs to be managed. The committee noted that NICE's technology appraisal guidance on botulinum toxin type A for the prevention of headaches recommends botulinum toxin type A for people with chronic migraine that has not responded to at least 3 previous oral preventive drugs. The clinical expert stated that some people who are eligible for botulinum toxin type A are unable to have it because there is no local specialist centre to administer it, or they have to wait a long time for it. The committee acknowledged that there may be an increase in the number of specialist centres, which may increase treatment access. A clinical expert also noted that face-to-face appointments are currently restricted in the NHS because of the COVID-19 pandemic, so there is a greater demand for virtual appointments. The committee understood that this has reduced the availability of botulinum toxin type A and increased the need for a migraine-specific self-administered treatment that could be managed with virtual appointments. The committee concluded that effective and well-tolerated migraine-specific treatment options are needed.

At least 3 oral preventive treatments are tried before specialist treatment is considered

3.3 The company's submission focused on people with migraine for whom at least 3 previous oral preventive treatments had failed (defined as lack of a clinically meaningful response, intolerance to the treatment or the treatment was contraindicated or unsuitable). The company considered this group to reflect people most in need of treatment options, who would likely be offered galcanezumab in NHS clinical practice. The clinical expert explained that the aim of treatment is to reduce the frequency, severity or duration of migraine and improve quality of life. The committee noted that, in chronic migraine, a 30% reduction in migraine frequency is considered a clinically meaningful response to

treatment. In episodic migraine, a 50% reduction is considered a clinically meaningful response. If clinical response is less than this, or the person is not able to have an adequate dosage for long enough or has adverse events, treatment is stopped and another oral preventive treatment is tried. The clinical expert explained that it is important for people to try a range of oral preventive treatments before considering more specialist treatment, such as botulinum toxin type A (for chronic migraine) or galcanezumab. The committee concluded that an insufficient response to an adequate trial of at least 3 oral preventive treatments represents usual NHS practice before more specialist treatment is considered. It also concluded that a clinically meaningful response is a 30% reduction in migraine frequency for chronic migraine and a 50% reduction for episodic migraine.

The most relevant comparators are best supportive care for episodic migraine, and botulinum toxin type A and best supportive care for chronic migraine

3.4 The company presented clinical-effectiveness evidence for galcanezumab, compared with placebo for episodic migraine and compared with placebo and botulinum toxin type A for chronic migraine. It considered that placebo was representative of best supportive care, because people were allowed to use the acute treatments they would usually take when preventive treatments failed. The clinical experts agreed that it is most likely that people would have best supportive care for episodic migraine, and botulinum toxin type A or best supportive care for chronic migraine, after 3 preventive oral treatments had failed. The committee was aware of NICE's recently published technology appraisal guidance recommending fremanezumab for chronic migraine but noted that fremanezumab treatment was not routine clinical practice in the NHS at the time of its decision making, so it is not considered a comparator for galcanezumab. The committee concluded that best supportive care is the most appropriate comparator in episodic migraine, and that botulinum toxin type A and best supportive care are both relevant comparators in chronic migraine.

Clinical evidence

High-frequency episodic migraine is not a clinically distinct subgroup

3.5 The company defined high-frequency episodic migraine as between 8 and 14 migraine headache days a month. The clinical expert explained that there is no internationally recognised classification of high-frequency episodic migraine and that it is not a clearly defined clinical subgroup. They also noted that the definition of high-frequency episodic migraine is arbitrary, and a person's quality of life is negatively affected irrespective of which type of migraine they have. The nature of the condition means that some people's migraine can be episodic one month and chronic the next, according to the definitions. The committee concluded that high-frequency episodic migraine is not a distinct subgroup and agreed not to consider it further.

The trials provide the most relevant clinical evidence for this appraisal

3.6 The company's systematic literature review identified 4 randomised controlled trials evaluating galcanezumab:

- CONQUER for episodic or chronic migraine that had inadequately responded to 2 to 4 previous classes of preventive treatment
- REGAIN for chronic migraine
- EVOLVE-1 for episodic migraine

- EVOLVE-2 for episodic migraine.

  All the trials compared galcanezumab (120 mg monthly dose after a 240 mg initial loading dose) with placebo in adults. The placebo-controlled period was 3 months for CONQUER and REGAIN and 6 months for EVOLVE. The company's submission focused on a subgroup of people from all the trials who had an inadequate response to 3 or more previous preventive medications. The committee concluded that the subgroup of people for whom 3 preventive treatments had failed provided the most relevant data for the population of interest.

Galcanezumab is clinically effective compared with placebo for episodic and chronic migraine

3.7 The company presented clinical-effectiveness results for the subgroup of people for whom 3 or 4 preventive migraine therapies failed to produce clinically meaningful improvement from CONQUER, REGAIN, EVOLVE-1 and EVOLVE-2. The results showed:

- galcanezumab reduced the number of monthly migraine days more than placebo for episodic and chronic migraine
- galcanezumab reduced the number of monthly headache days more than placebo for episodic and chronic migraine
- more people having galcanezumab had a reduction of at least 50% in the average monthly number of migraine days compared with placebo for episodic migraine

- more people having galcanezumab had a reduction of at least 30% in the average monthly number of migraine days compared with placebo for chronic migraine.

  The ERG noted that some people in CONQUER had botulinum toxin type A as 1 of the 3 prior failed treatments, which does not reflect standard NHS clinical practice. However, the company provided additional analyses that excluded people who had botulinum toxin type A as 1 of 3 or more prior preventive treatments. The results of this subgroup were similar, although the mean differences were slightly lower than the subgroup that included botulinum toxin type A. The results were considered academic in confidence by the company and cannot be reported here. The committee concluded that galcanezumab is an effective treatment compared with placebo for people with episodic or chronic migraine when 3 or 4 preventive treatments have failed.

The long-term effectiveness of galcanezumab is unknown

3.8 The duration of the blinded placebo-controlled phase was 3 months for CONQUER and REGAIN and 6 months for EVOLVE. The ERG noted the uncertainty about the long-term benefits of galcanezumab for extrapolating beyond these phases to an assumption of lifetime treatment. The committee concluded that the long-term benefits of galcanezumab compared with best supportive care remained uncertain.

Galcanezumab may be clinically effective for chronic migraine after failure of 3 preventive treatments and botulinum toxin type A

3.9 The committee acknowledged that there is a high unmet need in the group of people for whom 3 preventive treatments and botulinum toxin type A have failed, because they have a high disease burden and no further treatment options. The clinical expert stated that galcanezumab has a potential role as a treatment option when botulinum toxin type A has failed. However, considering that access to botulinum toxin type A varies within the NHS and it is more burdensome to administer than galcanezumab, the clinical expert agreed that the preferred position for galcanezumab would be after 3 oral preventive treatments have failed. This is the same position as other drugs in the same class as

galcanezumab; that is, anti-calcitonin gene-related peptides (CGRPs). At technical engagement, the company provided the patient numbers from CONQUER for people with chronic migraine who had galcanezumab after 3 oral preventive treatments and botulinum toxin type A. The company explained that the patient numbers are too small to provide meaningful results from any analysis. The company presented a post-hoc analysis for galcanezumab as a fourth-line treatment after botulinum toxin type A has failed. The results showed a significant decrease in migraine frequency for galcanezumab compared with placebo. The company considered these results to be representative of the effect of galcanezumab after 3 oral treatments and botulinum toxin type A have failed. The ERG agreed that the company's model did not consider this potential sequence and that there is no clinical evidence to support the use of galcanezumab as a fifth-line treatment after botulinum toxin type A. The committee acknowledged the results from the trials, which showed the clinical effectiveness of galcanezumab treatment after failure of botulinum toxin type A (see section 3.7). It concluded that while there is uncertainty in the evidence, galcanezumab may be clinically effective as a fifth-line treatment after 3 oral treatments and botulinum toxin type A.

Treatment with a second anti-CGRP drug is not recommended

3.10 The committee was not presented with any evidence to support subsequent treatment with other anti-CGRPs, if the initial clinically meaningful response to treatment with galcanezumab is subsequently lost. The committee was aware although the scope included 2 medicines in this class as potential comparators, neither was established practice in the NHS at the time of the decision-making and therefore did not formally compare galcanezumab with them. However, the committee heard from the clinical expert that there is no clinical evidence to support any difference in efficacy between the different anti-CGRP drugs. The committee noted that treatment preferences are not outlined in the British Association for the Study of Headache's guidelines, and therefore considered it reasonable that the least expensive drug would be used unless an alternative was more suitable for the patient. The committee concluded that treatment with another anti-CGRP drug, after failure of a previous anti-CGRP drug, is not supported by evidence and is not

recommended.

It is appropriate to apply a negative stopping rule

3.11 The company's model assumed that people stopped galcanezumab treatment at 3 months if their symptoms had not responded. This 'negative' stopping rule was applied to people having less than a 50% reduction in monthly migraine days for episodic migraine, and less than a 30% reduction in monthly migraine days for chronic migraine. The committee considered the 30% and 50% thresholds. It agreed these are appropriate measures of treatment response and are consistent with NICE's technology appraisal guidance on botulinum toxin type A for preventing chronic migraine and the British Association for the Study of Headache's guidelines. The committee concluded that it was appropriate to include a negative stopping rule at 3 months if there was insufficient response to treatment based on the agreed thresholds.

Indirect treatment comparison

It is appropriate to use clinical-effectiveness estimates from the indirect treatment comparison for chronic migraine

3.12 There was no direct evidence comparing galcanezumab with botulinum toxin type A for chronic migraine so the company did an indirect comparison, using data from:

- 2 trials of galcanezumab (CONQUER and REGAIN)

- 2 trials comparing botulinum toxin type A with placebo (PREEMPT-1 and PREEMPT-2).

  The comparison was in the subgroup of people for whom 3 or more preventive treatments had failed. It compared galcanezumab with botulinum toxin type A for the reduction in monthly migraine days, reduction in monthly headache days and 3 domains of the Migraine-Specific Quality of Life Questionnaire. The company acknowledged that there were limitations with the indirect treatment comparison including small sample sizes, differences in placebo response rates, differences in measuring and defining key outcome measures and missing data. To account for some of these limitations, the company did additional analyses that included a population with less than 3 prior failed preventative treatments, termed 'all-comers'. Most of the results of the indirect treatment comparison were not statistically significant for the all-comers population or the population with 3 or more prior treatment failures, but they did numerically favour galcanezumab. The only statistically significant result was the change in migraine headache days for the population with 3 or more prior treatment failures (results are academic in confidence and cannot be reported here). The company and the ERG noted that because of the limitations of the indirect treatment comparison, these results should be interpreted with caution. Despite this, the ERG advised that the indirect treatment comparison was sufficiently robust for use in the economic model. Given the concerns with the indirect treatment comparison and the low number of statistically significant results, the committee noted that there was a high degree of uncertainty about whether galcanezumab is more clinically effective than botulinum toxin type A for chronic migraine. It agreed it was appropriate to consider a scenario in which equivalent efficacy was assumed and another scenario that included the results of the indirect treatment comparison. It noted 2 surveys done by the Migraine Trust, which showed that most patient and clinical experts consider anti-CGRPs to be more effective than botulinum toxin type A. The ERG acknowledged that there is some statistical uncertainty in the indirect treatment comparison for galcanezumab but that this uncertainty had been addressed in the model. The committee noted that there were other sources of uncertainty such as small sample sizes, differences in placebo response rates and differences in outcome measures that were not quantified in the model. It concluded that although there is uncertainty it is plausible that galcanezumab may be more clinically effective than botulinum toxin type A, and that it was appropriate to use the clinical-effectiveness

estimates from the indirect treatment comparison for decision making.

Utilities

There is evidence for using differential utility values for treatments

3.13 The utility values used in the model were generated from mapping the Migraine Specific Questionnaire results to the EQ-5D-3L using the Gillard et al. (2012) algorithm. The committee understood that the company used estimated utility values for the population of patients who had a history of 3 or more failed prior preventatives from the relevant clinical trials (CONQUER, EVOLVE-1, EVOLVE-2 and REGAIN). The company presented evidence for a treatment-related difference in utility values. This demonstrated that utility values for galcanezumab were higher across all mean migraine headache day values compared with placebo. Also a regression analysis showed a large, statistically significant benefit of galcanezumab compared with placebo. The ERG considered this evidence to be of high quality and explained that the use of differential utilities applied to galcanezumab and comparators would allow for improvements in migraine severity to be captured beyond the number of migraine headache days. The committee noted that using differential utilities is not consistent with the approach used in NICE's technology appraisal of fremanezumab for preventing migraine. However, the ERG explained that compelling evidence for differential utilities has been presented by the company, which has not been presented in previous appraisals. The company provided the results of a correlation study as further evidence to support the use of differential utilities, and it demonstrated that galcanezumab reduced the levels of impairment and burden between migraine attacks. The ERG considered that the correlation study results provided evidence that galcanezumab improves the burden of migraine beyond that captured by the Migraine Specific Questionnaire. The patient expert described how galcanezumab reduced the impact of migraine attacks and improved recovery between attacks. The ERG noted that any differences in baseline (before treatment) utility values between treatment arms are accounted for in the applied statistical model and there is a statistically significant difference in utility

values after treatment. The committee acknowledged that there may be important aspects of the burden of migraine that are missed if only considering the frequency of migraine headache days. It acknowledged the uncertainties in using differential utility values, so it also considered a scenario of equal utility values. However, the committee concluded that there is evidence for the use of differential utility values between treatments.

Costs

Some people will not be able to self-administer galcanezumab

3.14 The company assumed that galcanezumab could be self-administered by subcutaneous injection. At the technical engagement stage, the clinical experts suggested that most people would be capable of self-administering galcanezumab. However, they noted that some disabled people, people who have a learning disability, are older or who have a phobia of needles may need help. They also noted that additional services may be needed to train people how to self-administer treatment. The committee noted that NICE's guidance on fremanezumab for preventing migraine concluded that it was unlikely that everyone will be able to self-administer treatment. It agreed that applying administration costs for 10% of people having galcanezumab was reasonable but acknowledged that this had little effect on the model results.

It is appropriate to include additional monitoring costs for galcanezumab

3.15 The company submission did not include costs associated with monitoring galcanezumab treatment. The clinical expert explained that people having galcanezumab are likely to need monitoring at regular intervals, and the committee acknowledged that monitoring is important for new treatments. The company and the ERG did not consider it appropriate to include the costs of monitoring without also including the benefits of positive discontinuation associated with it (that is, stopping treatment because it has been successful). However, the committee did

not consider it appropriate to include positive discontinuation because there are no clear criteria for when people should stop treatment. It also understood that positive discontinuation could be challenging to implement in clinical practice. The committee concluded that additional monitoring costs for galcanezumab should be included in the model to account for an appointment with a consultant every 6 months.

Cost-effectiveness estimates

Because of the uncertainty an acceptable ICER will be towards the lower end of what is normally considered cost effective for episodic migraine

3.16 NICE's guide to the methods of technology appraisal notes that above a most plausible incremental cost-effectiveness ratio (ICER) of £20,000 per quality-adjusted life year (QALY) gained, judgements about the acceptability of a technology as an effective use of NHS resources will take into account the degree of certainty around the ICER. The committee is more cautious about recommending a technology if it is less certain about the ICERs presented. The committee considered that the impact on NHS resources of introducing galcanezumab may be higher for episodic migraine than for chronic migraine. This is because episodic migraine is more common than chronic migraine. Because of the uncertainty in the clinical and economic evidence, the committee agreed that an acceptable ICER would be towards the lower end of the range normally considered a cost-effective use of NHS resources (£20,000 to £30,000 per QALY gained) for episodic migraine.

Galcanezumab is cost effective compared with best supportive care for episodic migraine after 3 oral preventive treatments have failed

3.17 The company's revised base-case ICER for galcanezumab compared with best supportive care for episodic migraine was within the range NICE normally considers an acceptable use of NHS resources. The company's revised base case included the committee's preferred

assumptions:

- including the ERG's corrections to model
- applying a lifetime (45 years) model time horizon
- using a consistent waning period for episodic and chronic migraine
- using data from all the trials to generate utility values
- using differential utilities for galcanezumab and the comparator
- applying age-related disutility
- including an administration cost for 10% of people having galcanezumab
- using resource consumption rates from the National Health and Wellness Survey.

  However, the revised base case did not include the committee's preferred assumption of:

- applying additional monitoring costs to galcanezumab treatment for a consultant appointment every 6 months.

  Taking its preferences into account, the committee agreed that the most plausible ICER for galcanezumab compared with best supportive care for episodic migraine was towards the lower end of the range NICE normally considers an acceptable use of NHS resources. Therefore, it concluded that galcanezumab is a cost-effective use of NHS resources for preventing episodic migraine after 3 oral preventive treatments have failed.

Galcanezumab is cost effective compared with best supportive care for chronic migraine after 3 oral preventive treatments have failed

3.18 The company's revised base-case ICER for galcanezumab compared with best supportive care for chronic migraine was below the range NICE normally considers an acceptable use of NHS resources. The company's revised base case included the committee's preferred assumptions:

- including the ERG's corrections in the model
- applying a lifetime (45 years) model time horizon
- using a consistent waning period for episodic and chronic migraine
- using data from all the trials to generate utility values
- using differential utilities for galcanezumab and the comparator
- applying age-related disutility
- including an administration cost for 10% of people having galcanezumab
- using resource consumption rates from the National Health and Wellness Survey.

However, the revised base case did not include the committee's preferred assumption of:

- applying additional monitoring costs to galcanezumab treatment for a consultant appointment every 6 months.

Taking its preferences into account, the committee agreed that the most plausible ICER for galcanezumab compared with best supportive care for chronic migraine was below the lower end of the range NICE normally considers an acceptable use of NHS resources. Therefore, it concluded that galcanezumab is a cost-effective use of NHS resources for preventing chronic migraine after 3 oral preventive treatments have failed.

Galcanezumab is cost effective compared with botulinum toxin type A for chronic migraine after 3 oral preventive treatments have failed

3.19 The company's revised base-case ICER for galcanezumab compared with botulinum toxin type A for chronic migraine was below the range NICE normally considers an acceptable use of NHS resources. The company's revised base case included the committee's preferred assumptions:

- including the ERG's corrections in the model
- applying a lifetime (45 years) model time horizon
- using a consistent waning period for episodic and chronic migraine
- using a consistent waning period for different treatments
- discontinuers wane back from responder migraine headache days (MHDs)
- using equivalent discontinuation rates for different treatments
- differing the response rate and the change from baseline in MHD based on results from the indirect treatment comparison
- using data from all the trials to generate utility values
- using differential utilities for galcanezumab and the comparator
- applying age-related disutility
- including an administration cost for 10% of people having galcanezumab
- using resource consumption rates from the National Health and Wellness Survey

However, the revised base case did not include the committee's preferred assumption of:

- applying additional monitoring costs to galcanezumab treatment for a consultant appointment every 6 months.

  The committee acknowledged that botulinum toxin type A could be administered by a nurse rather than a neurology consultant and this could reduce costs. However, it noted that the proportion of people having botulinum toxin type A administered by a nurse was unknown. Taking its preferences into account and including the confidential commercial medicine unit price for botulinum toxin type A, the committee agreed that the most plausible ICER for galcanezumab compared with botulinum toxin type A for chronic migraine was below what NICE normally considers an acceptable use of NHS resources. Therefore, it concluded that galcanezumab is a cost-effective use of NHS resources for preventing chronic migraine after 3 oral preventive treatments have failed.

Galcanezumab is cost effective for chronic migraine after botulinum toxin type A has failed

3.20 The committee noted that clinical evidence was not available for galcanezumab as a fifth-line treatment after botulinum toxin type A has failed (see section 3.9), and that no cost-effectiveness evidence had been provided. However, it acknowledged the post-hoc analysis showing the effect of galcanezumab as a fourth-line treatment after botulinum toxin type A had failed. It noted that the company considered these results to be representative of the effect of galcanezumab as a fifth-line treatment. The committee considered the uncertainty in the evidence for galcanezumab when used as a fifth-line treatment after botulinum toxin type A. However, it acknowledged that galcanezumab was clinically effective and cost effective as a fourth-line treatment after botulinum toxin type A and accepted this as a proxy for fifth-line use. It concluded that galcanezumab is cost effective compared with best supportive care for chronic migraine after botulinum toxin type A has failed.

Other factors

There are no additional equalities issues

3.21 No equalities issues were identified by the company. The clinical and patient submissions highlighted that migraine can be classed as a disability under the Equality Act 2010. Because migraine is most common in people of working age and affects more women than men, women may be further disadvantaged in the workplace. It was also noted that there may be unequal access to specialist headache clinics. The committee considered these issues and concluded that there were no specific adjustments needed to the NICE methods in this instance.

There are no health-related benefits that are not captured in the analyses

3.22 The committee acknowledged that galcanezumab administration may be considered more convenient and less unpleasant than administration of botulinum toxin type A. But it concluded that the modelling had adequately captured the benefits of galcanezumab.

Conclusion

Galcanezumab is recommended for episodic migraine

3.23 The committee noted that the most relevant comparator for episodic migraine was best supportive care. It considered that the evidence showed that galcanezumab is clinically effective compared with best supportive care. It also considered that high-frequency episodic migraine was not a clinically distinct subgroup and did not consider it further. At technical engagement, the company submitted a revised base case, which included a confidential simple discount patient access scheme for galcanezumab and most of the committee's preferred assumptions. Applying the additional committee assumption that monitoring costs for galcanezumab should be included, the most plausible ICER was likely to be towards the lower end of what NICE normally considers an acceptable

use of NHS resources. Therefore, galcanezumab is recommended for preventing episodic migraine in adults after at least 3 oral preventive treatments have failed. Treatment with galcanezumab should be stopped if migraine frequency does not reduce by at least 50% after 12 weeks of treatment.

Galcanezumab is recommended for chronic migraine

3.24 The committee recognised the high degree of burden that chronic migraine has on quality of life and daily functioning. It acknowledged that people with chronic migraine have the most severe form of the condition and that there is an unmet need for effective treatments. The committee noted that the most relevant comparators for chronic migraine were botulinum toxin type A and best supportive care. It considered that galcanezumab is a clinically effective treatment compared with placebo. However, the committee considered that there was uncertainty about whether galcanezumab is more clinically effective than botulinum toxin type A. At technical engagement the company submitted a revised base case, which included a confidential simple discount patient access scheme for galcanezumab and most of the committee's preferred assumptions. Applying the additional committee assumption that monitoring costs for galcanezumab should be included, the most plausible ICER is likely to be below what NICE normally considers an acceptable use of NHS resources compared with best supportive care and botulinum toxin type A. Therefore, galcanezumab is recommended for preventing chronic migraine in adults after at least 3 preventive treatments have failed. This includes the chronic migraine population for whom treatment with botulinum toxin type A has failed. Treatment with galcanezumab should be stopped if migraine frequency does not reduce by at least 30% after 12 weeks of treatment.

4 Implementation

4.1 Section 7(6) of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires clinical commissioning groups, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this appraisal within 3 months of its date of publication.

4.2 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 2 months of the first publication of the final appraisal document.

4.3 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has episodic or chronic migraine for which at least 3 oral preventive treatments have failed and the doctor responsible for their care thinks that galcanezumab is the right treatment, it should be available for use, in line with NICE's recommendations.

5 Appraisal committee members and NICE project team

Appraisal committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by committee D.

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

The minutes of each appraisal committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

NICE project team

Each technology appraisal is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the appraisal), a technical adviser and a project manager.

Omar Moreea
Technical lead

Caron Jones
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ISBN: 978-1-4731-3911-4

Accreditation