NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Appraisal consultation document

Mexiletine for treating myotonia in adults with non-dystrophic myotonic disorders

The Department of Health and Social Care has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using mexiletine in the NHS in England. The appraisal committee has considered the evidence submitted by the company and the views of non-company consultees and commentators, clinical experts and patient experts.

This document has been prepared for consultation with the consultees. It summarises the evidence and views that have been considered, and sets out the recommendations made by the committee. NICE invites comments from the consultees and commentators for this appraisal and the public. This document should be read along with the evidence (see the committee papers).

The appraisal committee is interested in receiving comments on the following:

- Has all of the relevant evidence been taken into account?
- Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?
- Are the recommendations sound and a suitable basis for guidance to the NHS?
- Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of race, gender, disability, religion or belief, sexual orientation, age, gender reassignment, pregnancy and maternity?

Issue date: February 2021

Note that this document is not NICE's final guidance on this technology. The recommendations in section 1 may change after consultation.

After consultation:

- The appraisal committee will meet again to consider the evidence, this appraisal consultation document and comments from the consultees.
- At that meeting, the committee will also consider comments made by people who are not consultees.
- After considering these comments, the committee will prepare the final appraisal document.
- Subject to any appeal by consultees, the final appraisal document may be used as the basis for NICE's guidance on using mexiletine in the NHS in England.

For further details, see NICE's guide to the processes of technology appraisal.

The key dates for this appraisal are:

Closing date for comments: 5 March 2021

Second appraisal committee meeting: TBC

Details of membership of the appraisal committee are given in section 5

This guidance is specifically for mexiletine (Namuscla). NICE's remit is to appraise the clinical and cost effectiveness of mexiletine within its marketing authorisation for the symptomatic treatment of myotonia in adults with non-dystrophic myotonic disorders. Unlicensed forms of mexiletine are not within this remit.

1 Recommendations

1.1 Mexiletine (Namuscla) is not recommended, within its marketing authorisation, for treating the symptoms of myotonia in adults with non-dystrophic myotonic disorders.

1.2 This guidance does not require that patients having treatment with mexiletine (Namuscla) that was started in the NHS through the interim agreement for use as a 'pass through' drug for patients within specialised neurosciences centres, which came into effect on 1st April 2019, should continue to receive treatment with Namuscla. Commissioners are not required to continue to fund that treatment. This is a departure from NICE's usual practice that negative guidance ought not to affect NHS treatment started before the guidance is published.

Why the committee made these recommendations

Treatments for the symptoms of myotonia in adults with non-dystrophic myotonic disorders already include imported mexiletine (that is not licensed in the UK). Other sodium channel blockers are used if mexiletine is not suitable. NICE's remit for this appraisal to appraise mexiletine (Namuscla) because it is the only product with a UK marketing authorisation.

Clinical trial evidence suggests that mexiletine is better than placebo at reducing the symptoms of myotonia. But the trial did not compare mexiletine with other sodium channel blockers and a higher dose of mexiletine was used in the clinical trial than people would normally have in the NHS.

The main problem with the economic model is that it does not compare mexiletine with other sodium channel blockers that are used in the NHS. The size of the clinical benefit is also uncertain. The cost-effectiveness estimates for mexiletine are much higher than what NICE considers a cost-effective use of NHS resources and would potentially be higher if compared with other sodium channel blockers rather than best supportive care. Therefore, mexiletine cannot be recommended.

2 Information about mexiletine

Marketing authorisation indication

2.1 Mexiletine (Namuscla, Lupin) is indicated 'for the symptomatic treatment of myotonia in adult patients with non-dystrophic myotonic disorders'.

Dosage in the marketing authorisation

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

Price

2.3 The price is £5,000 per 100 x 167 mg capsules (excluding VAT; BNF online, accessed October 2020). The company has a commercial arrangement, which would have applied if the technology had been recommended.

3 Committee discussion

The appraisal committee (section 5) considered evidence submitted by Lupin, 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.

Disease background and current clinical management

Non-dystrophic myotonia can affect the quality of life of patients and caregivers

3.1 Non-dystrophic myotonias (NDM) refers to a group of rare genetic disorders affecting skeletal muscle chloride or sodium ion channels. The most common symptom is myotonia, which is a delay in muscle relaxation and can lead to muscle locking and stiffness. The patient expert explained the constant effect of myotonia on quality of life for people with the condition and their caregivers. It can cause general muscular discomfort and pain, lack of sleep and major falls because muscle locking can cause falls and also limit the ability to break a fall. The patient expert highlighted that this leads to avoiding stairs where possible. It can also cause embarrassment for people with NDM because slurring speech and facial locking after sneezing can be misunderstood by other people. The patient organisation emphasised the invisible nature of the disease because of its rarity. The patient expert also noted constant worry about triggers that could affect myotonic episodes such as cold weather. The clinical experts explained that symptom severity varies between people, and can also vary over time for each individual (for example, it can affect different parts of the body). Some people need constant treatment and others choose episodic management, for instance during cold weather. If the disease is not managed, the patient expert explained that care is sometimes needed for tasks such as climbing stairs, lifting or bathing.

Current clinical management involves using mexiletine and other sodium channel blockers

3.2 Current clinical management of NDM includes muscle warming routines, specialist physiotherapy and avoidance of triggers. However, the clinical experts stated that pharmacological management should be offered to any person with NDM who is seeking treatment because it is affecting their daily lives. Sodium channel blockers (such as mexiletine,

carbamazepine, acetazolamide, flecainide and phenytoin) have been used off-label for many years to treat NDM. Off-label, imported mexiletine was used most because benefits can be seen very quickly. The clinical experts explained that a recent randomised controlled trial showed evidence of efficacy of another sodium channel blocker, lamotrigine, which is also sometimes used if mexiletine is contraindicated, not effective or not tolerated. The patient expert explained that using mexiletine addressed most of the symptoms of NDM with near normal muscle function and manageable side effects. The committee concluded that mexiletine is currently the preferred, established treatment for NDM and other options are available when mexiletine is not suitable.

The company should compare mexiletine with other sodium channel blockers

3.3 The committee was aware that the remit for this appraisal was to appraise mexiletine within its licensed indication for NDM and understood that it would make recommendations within the terms of the marketing authorisation, as published in the manufacturer's summary of product characteristics. It noted that the comparator in the scope for this appraisal was established clinical management without mexiletine, including but not limited to lamotrigine and best supportive care. The company considered that mexiletine (Namuscla) is now the only licensed treatment for NDM and therefore compared mexiletine with placebo to represent best supportive care. The company also indicated that lamotrigine is not established in clinical practice because few people take it. It also believed that pain and fatigue are influenced by the placebo effect and other sodium channel blockers would have no additional benefit to placebo as implemented in their comparison with best supportive care. The committee considered that established clinical management without mexiletine cannot currently be observed in the NHS because mexiletine is already established in clinical practice with off-label use and, more recently, an interim access agreement for the licensed treatment (Namuscla). Therefore, the committee deemed the most appropriate

comparison to be with what people currently taking mexiletine would have if mexiletine was not available. The clinical experts stated that patients would not remain untreated in the absence of mexiletine. Another sodium channel blocker would be used if mexiletine was not available. The patient organisation representative and patient expert also confirmed that they would expect people to be treated with another sodium channel blocker if mexiletine was not available. The committee concluded that the comparison of mexiletine with best supportive care was not appropriate because people would be offered other active treatments such as lamotrigine or other sodium channel blockers if mexiletine was not available and that other active treatments would likely be more effective than best supportive care.

Clinical evidence

The main clinical-effectiveness evidence comes from the MYOMEX trial, with supporting evidence from other studies

3.4 The main clinical evidence for mexiletine comes from MYOMEX, a randomised crossover trial of 26 patients with NDM comparing mexiletine with placebo. The primary outcome was muscle stiffness as measured by visual analogue scale but the efficacy evidence used in the economic model was a secondary outcome measure, the Individualised Neuromuscular Quality of Life (INQoL) questionnaire (see section 3.8). Supporting evidence came from 3 other studies:

- Suetterlin et al. (2015) – a retrospective review of 63 UK patients with NDM taking mexiletine for 6 months or more
- Statland et al. (2012) – a randomised crossover trial of 56 patients comparing mexiletine with placebo
- Stunnenberg et al. (2015) – an aggregated study of patients individually randomised to mexiletine or placebo in a crossover design for 30 patients with NDM in the Dutch neuromuscular database.

These trials were used as supporting clinical evidence and used to inform some economic model parameters and scenario analyses. The committee concluded that all the evidence, combined with the statements that mexiletine has been standard practice for over 15 years, suggest mexiletine is effective for relieving myotonia symptoms. However, the committee also noted that there were no comparisons of mexiletine with an active comparator.

MYOMEX is broadly generalisable to NHS clinical practice

3.5 MYOMEX included people aged between 18 and 65 with genetically confirmed NDM and with myotonic symptoms severe enough to justify treatment. The severity of symptoms was evaluated by whether it affected more than 1 segment of the body and if it impacted on 3 or more daily activities. The clinical experts explained that there are no formal methods of assessing severity of NDM because of the large amount of heterogeneity between patient symptoms and needs (see section 3.1). However, they considered that the severity inclusion criteria would be broadly generalisable to NHS clinical practice. The company noted that most people over 65 with NDM are on treatment with mexiletine and would not be treated differently, therefore do not consider the age criteria to be a limitation. The committee concluded that MYOMEX was broadly generalisable but noted the limitations of the inclusion criteria.

There are significant limitations with the design of the MYOMEX trial

3.6 A large proportion of patients in MYOMEX had previously had mexiletine. The clinical expert stated that this would be expected because there are few people with NDM who have not had mexiletine because it is a rare condition and mexiletine is routinely offered as a first treatment option. The ERG noted and the clinical expert agreed, that the recognisable side effects of mexiletine could have effectively unblinded patients to which treatment they had. This is supported by the Statland et al. study in which

around 80% of patients correctly guessed which treatment they had. The ERG considered that unblinding could potentially bias results because most of the outcomes are patient reported. Additionally, the ERG noted that there was potential for a carry-over effect between the 2 phases of the crossover trial if there was not enough time between the phases (the wash-out period). People in the MYOMEX trial had a 4 to 8 day wash-out period and the company presented analysis that there was no statistical evidence of a carry-over effect and the ERG noted that data from the first phase only also showed similar changes in muscle stiffness to both phases combined. However, the ERG noted the Statland et al. trial had at least a 7 day wash-out period and there was a statistically significant carry-over effect. The committee noted that MYOMEX included few patients and it was uncertain if the trial was powered to detect a carry-over effect. It also noted that MYOMEX had a short duration of only 18 days in each phase, so there is uncertainty in how effectiveness is maintained over a lifetime of treatment. The committee concluded that potential for unblinding and carry-over effects, short trial duration and few patients contribute substantial uncertainty to the MYOMEX results.

The dose and dosing schedule of MYOMEX does not match how it is used in clinical practice

3.7 Namuscla is a new formulation of mexiletine that uses different dose measurements to previous off-label use (a 167 mg capsule of Namuscla formulation [mexiletine base] is equivalent to 200 mg of imported mexiletine [mexiletine hydrochloride]). However, all the clinical evidence uses the imported formulation of mexiletine. The daily dose in MYOMEX started at 200 mg for 3 days, at which point all patients were titrated up to a 400 mg dose for a further 3 days and then a final titration to 600 mg for 12 days, at which point efficacy was assessed. The summary of product characteristics for Namuscla states that the dosing schedule is based on clinical response and can be increased after at least 1 week of treatment in 167 mg (200 mg imported mexiletine dose equivalent) increments to a maximum dose of 500 mg (600 mg equivalent). The clinical experts stated

that the rapid forced dose titration to 600 mg in MYOMEX does not represent current clinical management and is not in line with the summary of product characteristics. Currently, some people are titrated in smaller off-label 100 mg dose increments at a more cautious rate of titration to avoid gastric side effects of mexiletine. Some people who are experienced with mexiletine use could have a faster rate of titration but the clinical experts considered that this would not be as fast as in MYOMEX. The committee considered that because of the short duration of the MYOMEX trial, some adverse events might not have been reported. In clinical practice, such adverse events could take much longer than the MYOMEX trial duration to emerge. The clinical experts stated that most patients currently have between 300 mg to 400 mg of imported mexiletine but patients with more severe symptoms, or patients with specific subgroups of myotonia that need greater doses, can have 600 mg doses or greater. The company considered the average daily dose of 417 mg in the Suetterlin et al. retrospective review to be the most accurate dose for modelling, and therefore included 15 capsules a week (equivalent to a daily dose of 429 mg) in its base case. The committee noted the difference between this dose and the 600 mg dose that was used at the point of assessment of efficacy in MYOMEX. It considered that it is not appropriate to separate the costs and benefits of treatments and either the costs of the 600 mg dose should be included or the efficacy results should be adjusted to reflect a 429 mg dose. In the absence of effectiveness data based on the average dose given in clinical practice, the committee considered it appropriate to use the costs of the 600 mg dose in the economic modelling, as was seen in MYOMEX. The committee concluded that the dose and dosing schedule in MYOMEX does not reflect how mexiletine is currently used or would be used in clinical practice.

The company's economic model

The company's economic model does not represent clinical practice

3.8 The company's economic model has a simple structure with 3 states; 'alive on treatment', 'alive with no treatment' and 'death'. The transition between alive on treatment and alive with no treatment is based on the discontinuation rate of the Suetterlin et al. study and the transitions to death are based on general population mortality. The ERG considered that the model was simplistic and did not represent conventional health states such as disease severity or disease progression. However, in the absence of more data on the natural history of the disease, it was adequate for a comparison with best supportive care. The ERG also provided an indicative comparison with lamotrigine. It considered an indirect treatment comparison was not possible so provided analysis that varied the expected utility value of lamotrigine between best supportive care and mexiletine. The committee considered that 'alive with no treatment' would not happen in clinical practice because other treatments are available and would be used (see section 3.3). This would affect both how the comparator arm is created in the model and the subsequent treatments after stopping mexiletine. The committee also noted that not everyone in clinical practice would be expected to respond to treatment with mexiletine; MYOMEX and the Suetterlin et al. study selected patients that would be more likely to respond (see section 3.6). The committee concluded that the economic model does not reflect what would happen in clinical practice.

The natural history of the disease is not well characterised

3.9 The company considered that the disease progresses over time based on testimony that symptoms worsen after diagnosis. Therefore, it included a 15% reduction in quality of life after a modelled 'progression' event in the model. This event was modelled to happen at a faster rate for people who had not had treatment, the rate was estimated based on clinical opinion elicited through a Delphi panel. The clinical experts stated that there is no

long-term evidence on the natural history of the disease and that treatment is only aimed at relieving symptoms. It is not disease modifying. However, some patients may experience muscle weakening later in life which may be affected by treatment status. The ERG considered that the implementation of any disease progression in the model and its impact on quality of life was very uncertain. A single decrease in quality of life is not likely to reflect the natural history of the condition and the appropriateness of a 15% reduction in addition to differences seen in the trial was not justified by the evidence. The ERG removed this assumption in its base case with minimal effect on the incremental cost-effectiveness ratio (ICER). The committee considered that the natural history of the disease is uncertain and likely to be dependent on each patient's needs and preferences. It also considered that if an effect existed, the evidence for a differential rate of progression was not robust and the size of the effect on quality of life was not supported by any evidence. The committee concluded that there was no evidence of a worsening of disease for people having best supportive care and because mexiletine only treats the symptoms of the disease, it agreed with the ERG's removal of this assumption.

Health-related quality of life

Generic quality-of-life instruments can measure health-related quality of life in people with NDM

3.10 MYOMEX measured only the condition specific INQoL tool as a quality-of-life measurement. The company considered that generic quality-of-life measurement tools such as the Short Form 36 (SF-36) or EuroQoL 5 dimensions (EQ-5D-3L) are unable to effectively capture the quality-of-life implications of muscle locking in NDM. Therefore, the company used INQoL data conceptually mapped to EQ-5D-3L utility values using company valuation studies in its base case. The ERG considered that the company did not show that generic measures of quality of life are unable to measure health-related quality of life of people with NDM. It considers

generic instruments can be advantageous for capturing broader aspects of health, including comorbidities and adverse events. At the request of the NICE technical team, the ERG provided SF-36 data from the Statland et al. trial mapped to EQ-5D-3L utilities as a scenario analysis. The committee noted that generic quality-of-life instruments are included in the NICE reference case to achieve consistency in decision making across different diseases. The committee considered that domains such as physical function and activity in the SF-36 matched issues described by the patient expert. It considered that generic quality-of-life instruments can measure health-related quality of life of people with NDM, particularly through domains such as mobility, usual activities and pain. However, it recognised that some elements of muscle locking may be more difficult to capture. It concluded that the generic SF-36 data from the Statland et al. trial could be included in its considerations.

The utility values derived from the company's discrete choice valuation experiment are implausible

3.11 The company required a valuation study to map INQoL measurements from MYOMEX to EQ-5D-3L utility values (see section 3.10). The company commissioned a discrete choice experiment (DCE) which compared 2 hypothetical health states drawn from the INQoL questionnaire. The ERG noted several problems with the DCE valuation studies:

- A lack of clear ordering preference in the language used to describe health states (monotonicity), for example the difference between 'some' and 'moderate' problems may not be clear to people taking part.
- Many logical inconsistencies, some of which could not be explained by lack of clear ordering. This suggests lack of understanding or attention to the task.
- Lack of adequate quality control checks (other than whether the task was completed).

- 8 attributes of the INQoL were varied at the same time which may have been too complex for people taking part.
- Conceptual mapping to EQ-5D-3L introduces several problems including issues with anchoring the valuation model to the appropriate top and bottom EQ-5D-3L health state.

The company chose a scenario that assumed the worst health state in the INQoL was equivalent or 'anchored' to the worst state in the EQ-5D-3L but also provided a scenario with different anchoring assumptions. The ERG considered that the utility values derived from each of the scenarios were substantially different which showed considerable uncertainty with the conceptual mapping method. The committee saw the individual patient utility values for MYOMEX patients derived from the DCE study and considered the range of utility values to be implausible and some patients to have implausibly low utility. The clinical experts agreed that some of the utility values were implausibly low and did not represent the patient population seen in clinical practice. The committee concluded that the utility values and modelled treatment effect derived from the DCE were implausible and considered other valuation methods.

The utility values derived from the company's vignette valuation study and from the Statland et al. study are uncertain

3.12 The company also provided a vignette time trade-off study that asked people taking part to compare living in a hypothetical health state drawn from the INQoL for 10 years compared with 10 minus a given number of years in perfect health. The ERG considered that the vignette study had many of the same problems as the DCE study (see section 3.11) but also had potential issues with the study design such as lack of warm up exercises for the complex task and lack of explanation for some of the health states. The ERG preferred the vignette study because it avoided issues with conceptual mapping and produced a more plausible treatment effect. The committee agreed that the utility values derived from the

vignette study were more plausible. The ERG also presented utility values derived from SF-36 data in the Statland et al. trial (see section 3.10) which produced a treatment effect much lower than any of the company valuation studies. The ERG considered this to be validation that the vignette study should be considered but cautioned that the algorithm to map SF-36 to EQ-5D-3L utilities can underestimate severe health states. The ERG also considered the data from Statland et al. publication to be limited because only the reported mean values could be used and some data was missing for the crossover periods. The committee noted that NICE's guide to the methods of technology appraisal 2013 (section 5.3.9) states that when mapping to EQ-5D, the mapping function chosen should be based on data sets containing both health-related quality of life measures. The committee considered this was only available for the SF-36 data and it had not been justified that SF-36 instrument could not measure quality-of-life of people with NDM (see section 3.10). The committee noted that all utility values presented were not compared with other sodium channel blockers and were therefore not the comparison of interest (see section 3.3). However, for the comparison with best supportive care, it considered that both sets of utility data presented were highly uncertain. The committee concluded that both sets of utility values could be considered with caution, although the Statland et al. utility data is more methodologically appropriate.

The reduction in quality of life for carers of people with NDM should be removed as an assumption

3.13 At technical engagement, the company considered there to be a case for including carer disutility in the appraisal because caregivers would also expect to have a reduction in quality of life without treatment. The company included a carer disutility as published in NICE's highly specialised technology guidance on ataluren for treating Duchenne muscular dystrophy with a nonsense mutation in the dystrophin gene of 0.11 for an estimated 20% of patients with severe NDM. The ERG considered it could be appropriate to apply a carer disutility for patients

who had no treatment but it was uncertain how many people have severe enough symptoms to need care. It also noted that the disutility from NICE's guidance on ataluren for treating Duchenne muscular dystrophy is for non-ambulatory patients with progressive loss of motor function in the upper body, but no patients in MYOMEX needed to use wheelchairs or walking aids. The clinical expert stated that non-ambulatory patients with NDM are very rare, having only ever seen 1 patient that needed to use a wheelchair. The committee considered that patients not having mexiletine would have another treatment (see section 3.3) and therefore the carer disutility would have been overestimated. It concluded that it had not seen enough evidence to justify including consideration of carer quality of life, and that inclusion of this assumption is highly uncertain and should be removed.

Resource use

The costs of resource use for people with NDM who are not having treatment is likely to be overestimated

3.14 The company considers that people who do not have treatment would use 3 times the number of resources as somebody having mexiletine. This includes increased costs for admissions for falls, physiotherapy and other therapies. The company validates this multiplier using estimation from an advisory board. The ERG consider the justification behind the advisory board findings to be incorrect because it uses both the estimated frequency of resource use and the estimated number of people using the resource when only the frequency of resource use is needed for use in the model. The ERG therefore used only the frequency of resource use multiplier in its base case. The committee considered that this change had minimal effect on the ICER. It also noted that any comparison with best supportive care would overestimate the difference in resource use because many people would have other active treatments such as lamotrigine or other sodium channel blockers (see section 3.3). The committee concluded that the ERG amendments were likely to be

appropriate for any comparison with best supportive care but would not reflect what would happen in clinical practice.

Cost-effectiveness estimate

Mexiletine is not cost effective for people with NDM

3.15 The company's revised base case after technical engagement gave an ICER of £27,798 per quality-adjusted life year (QALY) gained for mexiletine compared with best supportive care. The ERG base case included removal of the disease progression assumptions (see section 3.9), use of the vignette valuation study (see section 3.12) and reduction of the resource use multiplier (see section 3.14). The ERG base case gave an ICER of £45,512 per QALY gained for mexiletine compared with best supportive care. The committee considered the ERG base-case assumptions were appropriate for the comparison with best supportive care and considered further scenarios:

- It is appropriate to remove the carer disutility because of the uncertainty around symptom severity and need for care (see section 3.13).
- It is appropriate to use the costs and benefits of the 600 mg equivalent dose from which the mexiletine efficacy data has been derived (see section 3.7).
- It is appropriate to explore scenarios using utilities derived from SF-36 data in the Statland et al. trial because it has the advantage of being a generic health-related quality-of-life measurement and there is substantial uncertainty in the utility values (see section 3.12).

The committee considered that the ICERs for mexiletine (Namuscla) compared with best supportive care using the ERG base case and committee assumptions were substantially higher than what NICE considers a cost-effective use of NHS resources (see NICE's guide to the methods of technology appraisal).

The committee also considered that comparison with best supportive care was not appropriate (see section 3.3) and the indicative ERG analysis comparison with lamotrigine (see section 3.8) suggests this would increase the ICER further if lamotrigine had any treatment effect greater than placebo, and would substantially increase the ICER at a plausible treatment effect (these analyses are commercial in confidence and cannot be included here). The committee considered that this analysis would likely also be indicative of any comparison with other sodium channel blockers because of the similar costs of treatment. The committee agreed that the ERG and committee preferred assumptions should also be applied to any comparison with an active treatment.

Equalities considerations

There are no equalities issues that can be addressed by the committee

3.16 The committee noted that disability is a protected characteristic and that people with NDM have a disability that could make travel to regional neurology centres for treatment more difficult. The committee noted that any equalities issue relating to geographical access to treatment with NDM would already be realised as mexiletine is current standard practice. However, the committee concluded that this potential equality issue could not be addressed in the guidance recommendations.

4 Implementation

4.1 If final guidance does not recommend mexiletine (Namuscla), commissioners are not required to continue to fund that medicine. This includes treatment via the interim agreement for mexiletine (Namuscla) for use as a ‘pass through’ drug for patients within specialised neurosciences centres, which came into effect on 1st April 2019.

4.2 This is a departure from NICE’s usual practice that negative guidance ought not to affect NHS treatment started before the guidance is published. The reason for this is that NICE typically appraises new

medicines that are not already established clinical practice. When NHS treatment that is outside the recommendation continues without change to the funding arrangements in place before the guidance was published, it does not commit the NHS to significant or prolonged costs.

5 Proposed date for review of guidance

5.1 NICE proposes that the guidance on this technology is considered for review by the guidance executive 3 years after publication of the guidance. NICE welcomes comment on this proposed date. The guidance executive will decide whether the technology should be reviewed based on information gathered by NICE, and in consultation with consultees and commentators.

Gary McVeigh
Chair, appraisal committee
November 2020

6 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.

Adam Brooke
Technical lead

Christian Griffiths
Technical adviser

Kate Moore
Project manager

ISBN: [to be added at publication]