NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

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

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of mexiletine within its marketing authorisation for treating myotonia in adults with non-dystrophic myotonic disorders.

Background

Myotonic disorders are a heterogeneous group of conditions which includes dystrophic and non-dystrophic myontonias. Myotonic disorders are linked by the presence of myotonia which is characterised by the slow relaxation (stiffness) of muscles after use.[1] Myotonic dystrophy typically affects skeletal muscles, but commonly has other systemic effects in the heart, breathing muscles, swallowing muscles, bowels, lens of the eyes, and the brain.[2] Non-dystrophic myotonias are caused by defects in either chloride channel or sodium channels.[3] Non-dystrophic myotonias typically causes painless muscle stiffness, but can lead to pain, weakness, and fatigue.[3,4] When myotonia is present in skeletal muscle mobility can be affected, interfering with daily activities.[5]

The prevalence of myotonic disorders varies depending on classification (dystrophic and non-dystrophic). Non-dystrophic myotonias are less common than dystrophic myotonias, with the prevalence in England estimated at 0.92 per 100,000 people.[6] Based on current population estimates the number of people with non-dystrophic myotonias in England is estimated to be 329.[7]

Currently there are no licensed treatments for myotonic disorders in the UK, however, antiarrhythmic and antiepileptic medicines are used off-label to manage the symptoms of myotonic disorders.[5] Non-pharmacological strategies for myotonic disorders include physiotherapy, lifestyle adaptations, mobility aids and occupational assistance.

The technology

Mexiletine (Namuscla, Lupin Healthcare limited) is an antiarrhythmic agent that blocks the sodium channels into muscle cells, reducing the prolonged muscle contractions.

Mexiletine does not currently have a marketing authorisation in the UK for the treatment of myotonic disorders. It has been studied in a phase 3 study of adults with non-dystrophic myotonic disorders. Mexiletine is administered orally.

Intervention(s)	Mexiletine
Population(s)	Adults with symptomatic myotonia and non-dystrophic myotonic disorders
Comparators	Established clinical management without mexiletine
Outcomes	The outcome measures to be considered include: • muscular symptoms (including stiffness, weakness and wasting) • exercise capacity • mortality • pain • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	None
Related National Policy	NHS England (2018) Manual for Prescribed Specialised Services 2018/19. (Chapters 4, 11, 48) NHS England (2017) Next steps on the five year forward view NHS England (2014) NHS Five year forward view NHS England (2013) 2013/14 NHS STANDARD CONTRACT FOR DIAGNOSTIC SERVICE FOR RARE

	NEUROMUSCULAR DISORDERS (ALL AGES) NHS England (2013) 2013/14 NHS STANDARD CONTRACT FOR NEUROSCIENCES: SPECIALISED NEUROLOGY (ADULT) Department of Health and Social Care, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1,2,4,5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Have all relevant comparators for mexiletine been included in the scope?

Which treatments are considered to be established clinical practice in the NHS for myotonia in adults with non-dystrophic myotonic disorders?

Are any antiarrhythmic or antiepileptic medicines used off-label to treat myotonia in adults with non-dystrophic myotonic disorders? If yes, which treatments are used in clinical practice?

Are the outcomes listed appropriate? Are there any other outcomes that should be included?

Are there any subgroups of people in whom mexiletine is expected to be more clinically effective and cost effective or other groups that should be examined separately?

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 mexiletine 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;
- 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.

Do you consider mexiletine 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)?

Do you consider that the use of mexiletine 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.

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).

References

1 Hahn, C., & Salajegheh, M. K. (2016). Myotonic disorders: A review article. Iranian Journal of Neurology, 15(1), 46–53.

2 The myotonic dystrophies. Muscular Dystrophy UK. Accessed: September 2018

3 Heatwole, Chad R., and Richard T. Moxley. (2007). The nondystrophic myotonias. Neurotherapeutics 4.2, 238-251.

4 Matthews, E., et al. (2009). The non-dystrophic myotonias: molecular pathogenesis, diagnosis and treatment. Brain 133.1, 9-22.

5 Trip J, Drost GG, van Engelen BGM, Faber CG. (2006) Drug treatment for myotonia. Cochrane Database of Systematic Reviews, Issue 1.

6 Horga A, Rayan DL, Matthews E, Sud R, Fialho D, Durran SC, Burge JA, Portaro S, Davis MB, Haworth A, Hanna MG. (2013) Prevalence study of genetically defined skeletal muscle channelopathies in England. Neurology.16;80(16):1472-5

7 Estimates of the population for the UK, England and Wales, Scotland and Northern Ireland: mid-2017. Office for National Statistics. Accessed: September 2018