NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

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

Final scope

Remit/appraisal objective

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.

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] Non-dystrophic myotonias are caused by defects in either chloride channel or sodium channels.[3] The absence of systemic features in brain, heart, and breathing and swallowing muscles in non-dystrophic myotonias distinguishes it from myotonic dystrophy. Non-dystrophic myotonias typically causes painless muscle stiffness, but can lead to pain, weakness, and fatigue.[2,3] Symptoms onset of non-dystrophic myotonias varies between types, but is normally during childhood, adolescence or early adulthood.[2] When myotonia is present in skeletal muscle mobility can be affected, interfering with daily activities.[4]

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.[5] Based on current population estimates the number of people with non-dystrophic myotonias in England is estimated to be 405.[6] However this may be an under-estimate of the prevalence because of the small sample size of the study where the estimate was derived, and the genetic testing required by the study.

Current practice includes using mexiletine used off-label for treating symptomatic myotonia. Lamotrigine is the most used alternative. Other antiarrhythmic and antiepileptic medicines have been used off-label to manage the symptoms of myotonic disorders.[4] However, this does not form part of standard care. Non-pharmacological strategies for myotonic disorders include physiotherapy, lifestyle adaptations, mobility aids and occupational assistance.

The technology

Mexiletine (Namuscla, Lupin Healthcare limited) blocks the sodium channels into muscle cells. It is most active on muscle fibres subject to repeated discharges (skeletal muscles), thereby reducing muscle stiffness.

Mexiletine has a marketing authorisation in the UK for the 'the symptomatic treatment of myotonia in adult patients with non-dystrophic myotonic disorders'. Mexiletine is administered orally.

Intervention(s)	Mexiletine
Population(s)	Adults with non-dystrophic myotonic disorders requiring treatment of symptomatic myotonia
Comparators	Established clinical management without mexiletine, including but not limited to: • lamotrigine • best support care.
Outcomes	The outcome measures to be considered include: • muscular symptoms (including stiffness and weakness) • fatigue • motor function • 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. The economic modelling should include the costs associated with genetic testing for mutations in CLCN-1 and SCN4A gene coding in people with myotonic disorders who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 5.9 of the Guide to the Methods of Technology Appraisals.

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	The NHS Long Term Plan (2019) NHS Long Term Plan NHS England (2018/2019) Manual for Prescribed Specialised Services 2018/19. (Chapters 4, 11, 48) NHS England (2017) Next steps on the 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

References

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

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

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

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

5 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

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