NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Recombinant human nerve growth factor for treating neurotrophic keratitis

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of recombinant human nerve growth factor (rhNGF) within its marketing authorisation for treating neurotrophic keratitis.

Background

Neurotrophic keratitis is a degenerative condition which affects the cornea (the clear layer covering the front of the eye). Damage to the nerve connected to the cornea causes a loss of sensation and impairment of healing, which leads to breakdown of the epithelium, ulceration and perforation. The most common causes of neurotrophic keratitis include viral infection (in particular, herpes), intracranial lesions (such as tumours or aneurisms) and injuries to the eye or nerves (for example, surgery, chemical or physical burns, or drug toxicity). It can also be caused by systemic diseases such as diabetes and multiple sclerosis.

Neurotrophic keratitis can be classified into 3 stages, based on the severity of corneal damage. Stage 1 disease is characterised by mild, non-specific symptoms and changes to the corneal epithelium, whereas in stage 2 disease the damage to the cornea is persistent and does not heal. Stage 3 neurotrophic keratitis is characterised by corneal ulcer, perforation and stromal melting.

Neurotrophic keratitis is a rare condition, with an estimated prevalence of less than 1.6 per 10,000 people (based on the prevalence of keratitis after herpes infection and after surgery for trigeminal neuralgia)[1]. This implies there may be fewer than 6800 adults with neurotrophic keratitis in England[2], although the precise number is unknown.

Management of neurotrophic keratitis aims to promote healing of the epithelium and prevent progression of corneal damage, and is based on the clinical stage of the disease. Management of early-stage disease focuses on addressing any underlying causes (such as topical medications) and providing artificial tears. For stages 2 and 3, options include therapeutic contact lenses, closure of the eyelid, collagenase inhibitors (for stromal melting) and surgery (for example, amniotic membrane transplant, corneal transplant and conjunctival flap surgery).

The technology

Recombinant human nerve growth factor (rhNGF; Sentinel, Dompé) is an artificial form of the naturally occurring signalling protein NGF. It aims to improve nerve function in the cornea and stimulate healing. It is administered as eye drops.

rhNGF does not have a marketing authorisation in the UK. It has been studied in clinical trials, compared with placebo, in adults with stage 2 or stage 3 neurotrophic keratitis that has not responded to at least 1 non-surgical treatment.

Intervention(s)	Recombinant human nerve growth factor (rhNGF)
Population(s)	Adults with stage 2 or 3 neurotrophic keratitis that has not responded to at least 1 non-surgical treatment
Comparators	Established clinical management without rhNGF (which may include treatment of any underlying causes, artificial tears, therapeutic contact lenses, eyelid closure, collagenase inhibitors and surgery)
Outcomes	The outcome measures to be considered include: • corneal healing • visual acuity (affected eye and both eyes) • corneal sensitivity • need for further treatment or hospitalisation for neurotrophic keratitis • 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. Cost effectiveness analysis should include consideration of the benefit in the best and worst seeing eye.

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	Related NICE Pathways: Eye conditions (2015) NICE pathway. http://pathways.nice.org.uk/pathways/eye-conditions
Related National Policy	Department of Health, NHS Outcomes Framework 2015-2016, Dec 2014. Domains 3, 4 and 5. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/385749/NHS_Outcomes_Framework.pdf NHS England (2014) Manual for prescribed specialised services 2013/14. Chapter 12 – Adult specialist ophthalmology services. NHS England (2013) NHS standard contract for specialised ophthalmology (adult). Schedule 2 - the services - A. the specifications.

Questions for consultation

How is rhNGF expected to be used in clinical practice?

- Will treatment be limited to people who have had previous non-surgical treatment?
- Will treatment be limited to people with specific stages of neurotrophic keratitis, or will it be used for all stages of disease?
- Will it be used for people with neurotrophic keratitis affecting 1 eye or both eyes (that is, unilateral or bilateral disease)?
- Will rhNGF be used in addition to established clinical management for neurotrophic keratitis, or will some treatments be displaced?
- Will people have a single course of treatment, or would further courses be given if the keratitis returned or progressed?
- How many people in England would be anticipated to have treatment with rhNGF for neurotrophic keratitis?

Have all relevant comparators for rhNGF been included in the scope? Which treatments are considered to be established clinical practice in the NHS for neurotrophic keratitis?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom rhNGF is expected to be more clinically effective and cost effective or other groups that should be examined separately? Should consideration be given to subgroups based on the stage or severity of neurotrophic keratitis or the underlying cause of the disease?

Where do you consider rhNGF will fit into the existing NICE pathway, Eye conditions?

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 rhNGF 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 rhNGF 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 rhNGF 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.

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. Sacchetti M and Lambiase A (2014) Diagnosis and management of neurotrophic keratitis. Clinical Ophthalmology 8:571–9.

2. Office for National Statistics (2015) Population estimates for UK, England and Wales, Scotland and Northern Ireland, mid-2014. Accessed December 2015.