

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Cenegermin for treating neurotrophic keratitis [ID946]

Final scope

**Remit/appraisal objective**

To appraise the clinical and cost effectiveness of cenegermin 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 aneurysms) 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 (mild) disease is characterised by mild, non-specific symptoms and changes to the corneal epithelium, whereas in stage 2 disease (moderate) the damage to the cornea is persistent and does not heal. Stage 3 (severe) neurotrophic keratitis is characterised by corneal ulcer, perforation and stromal melting.

Neurotrophic keratitis is a rare condition. The prevalence is estimated to be between 1.6 per 10,000 people (based on the prevalence of keratitis after herpes infection and after surgery for trigeminal neuralgia)<sup>1</sup> and 4.2 per 10,000,<sup>2</sup> of whom about one-third have stage 2 or 3 disease. This implies there may be fewer than 17,708 adults with neurotrophic keratitis in England,<sup>3</sup> 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. 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 and conjunctival flap surgery). Preservative free artificial tears may be used at all stages of the condition. Management should consider the underlying cause of the neurotrophic keratitis, in particular whether it is related to an ongoing

progressive condition (such as diabetes or multiple sclerosis) or an acute or non-progressive cause (such as surgery or an injury).

**The technology**

Cenegermin or recombinant human nerve growth factor (Oxervate, Dompé) is an artificial form of a naturally occurring signalling protein, nerve growth factor (NGF). It aims to improve nerve function in the cornea and stimulate healing. It is administered as eye drops.

Cenegermin has a marketing authorisation in the UK for treating ‘moderate (persistent epithelial defect) or severe (corneal ulcer) neurotrophic keratitis in adults’.

<b>Intervention(s)</b>	Cenegermin or recombinant human nerve growth factor
<b>Population(s)</b>	Adults with moderate (persistent epithelial defect) or severe (corneal ulcer) neurotrophic keratitis
<b>Comparators</b>	Established clinical management without cenegermin (which may include treatment of any underlying causes, preservative free artificial tears, collagenase inhibitors, medical or surgical eyelid closure, serum eye drops, therapeutic contact lenses and surgery)
<b>Outcomes</b>	The outcome measures to be considered include: <ul style="list-style-type: none"> <li>• corneal healing</li> <li>• visual acuity (affected eye and both eyes)</li> <li>• corneal sensitivity</li> <li>• need for further treatment or hospitalisation for neurotrophic keratitis</li> <li>• adverse effects of treatment</li> <li>• health-related quality of life.</li> </ul>

<b>Economic analysis</b>	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>Cost effectiveness analysis should include consideration of the benefit in the best and worst seeing eye.</p>
<b>Other considerations</b>	<p>If evidence allows separate consideration will be given to people with neurotrophic keratitis associated with progressive or non-progressive underlying causes.</p> <p>If evidence allows, consideration will be given to subgroups based on the stage or severity of the neurotrophic keratitis.</p> <p>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.</p>
<b>Related NICE recommendations and NICE Pathways</b>	<p>Related NICE Pathways:</p> <p>Eye conditions (2015) NICE pathway.  <a href="http://pathways.nice.org.uk/pathways/eye-conditions">http://pathways.nice.org.uk/pathways/eye-conditions</a></p>
<b>Related National Policy</b>	<p>Department of Health (2016) <a href="#">NHS Outcomes Framework 2016 to 2017</a>: Domains 3, 4 and 5.</p> <p>NHS England (2016) <a href="#">Manual for prescribed specialised services 2016/17</a>. Chapter 12 – Adult specialist ophthalmology services.</p> <p>NHS England (2013) <a href="#">NHS standard contract for specialised ophthalmology (adult). Schedule 2 - the services - A. the specifications</a>.</p>

## References

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

2. European Commission (2016) [Orphan drug designation \(EU/3/15/1586\) for recombinant human nerve growth factor for the treatment of neurotrophic keratitis](#). Accessed September 2017.
3. Office for National Statistics (2017) [Population estimates for UK, England and Wales, Scotland and Northern Ireland, mid-2016](#). Accessed September 2017.