

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Teprotumumab for treating thyroid eye disease

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of teprotumumab within its marketing authorisation for treating moderate to severe thyroid eye disease.

Background

Thyroid Eye Disease (TED) is a complex autoimmune condition characterised by inflammation and swelling of the muscles and tissues around the eyes. Symptoms of TED include bulging eyes (proptosis), swollen eyelids (eyelid oedema), and discomfort. Functional impairments such as dry eyes, sensitivity to light (photophobia), blurred or double vision (diplopia), eye pain, and difficulty moving the eyes are also prevalent. In severe cases, vision loss may occur. The symptoms can impact people's quality of life, and changes in appearance can lead to significant psychosocial distress.

TED often occurs alongside Graves' disease, an autoimmune disorder causing the immune system to overstimulate the thyroid gland, resulting in hyperthyroidism. Approximately 40% of individuals with Graves' disease are affected by TED.¹ In Graves' disease, antibodies called thyroid-stimulating immunoglobulins (TSIs) not only stimulate the thyroid gland to produce excessive thyroid hormones, but can also attack the tissues behind the eyes, leading to TED. One of the distinctive features of TED is its ability to occur independently of thyroid function. While many TED cases are seen in individuals with Graves' disease and hyperthyroidism, TED can also manifest in people with normal thyroid function (euthyroid) or even underactive thyroid (hypothyroid). Globally, the prevalence of hyperthyroidism, hypothyroidism, and euthyroidism among TED patients is 86.2%, 10.36%, and 7.9%, respectively.²

Genetic predisposition, combined with environmental factors like smoking and previous radioactive iodine therapy, contributes to the development and/or severity of TED. Concurrent endocrine disorders, such as type 1 diabetes, also play a role in its development.

While the prevalence is uncertain, estimates suggest that 50,000 to 204,000 people in the UK have TED.^{3,4} It primarily affects women (female-to-male ratio of 5:1). TED shows two age peaks: one around 40-44 years and another around 60-64 years for women (slightly later for men). Older individuals often experience more severe forms of TED, increasing the risk of complications like restrictive myopathy and dysthyroid optic neuropathy (DON). Management of TED involves a multidisciplinary approach to control inflammation, manage symptoms, and prevent complications like optic nerve compression. Disease activity for TED is typically assessed using the Clinical Activity Score (CAS). However, CAS has several limitations. For example, it relies on subjective, visual assessments which may be biased by the patient's skin colour and ethnicity. Treatment approaches typically follow the [European Group on Graves Orbitopathy \(EUGOGO, 2021\)](#) guidelines. The guidelines categorise cases into mild, moderate-to-severe, and sight-threatening. Mild cases are managed with supportive measures such as lubricating eye drops, sunglasses, and selenium supplementation.

For moderate to severe cases, first-line treatment is typically methylprednisolone, with or without mycophenolate. Where there is an inadequate response to first line treatment, clinicians may consider a repeat dose of methylprednisolone with the addition of mycophenolate (if not already given), immunosuppressants, radiotherapy (as recommended by [NICE Interventional procedures guidance 148](#)), or oral prednisolone with ciclosporin. Where systemic treatments are not suitable, TED may be treated with local steroid injections and radiotherapy. Sight-threatening cases may need urgent surgical intervention, such as orbital decompression, to relieve optic nerve pressure. Once the active stage of TED has passed, reconstructive surgery may be used to address residual proptosis or abnormal eyelid positions during the inactive phase.

The technology

Teprotumumab (Tepezza, Amgen Limited) does not currently have a marketing authorisation in the UK for TED. It has been assessed in clinical trials in adults with TED and with different levels of disease activity and severity.

Intervention(s)	Teprotumumab
Population(s)	People living with moderate to severe thyroid eye disease
Subgroups	<p>If evidence allows and where appropriate, the following may be considered:</p> <p>Subgroups by</p> <ul style="list-style-type: none"> - Disease activity <ul style="list-style-type: none"> • Active • Inactive - Duration of active symptom <ul style="list-style-type: none"> • More than 1 year • Less than 1 year - severe proptosis - severe diplopia - severe inflammation - treated vs untreated TED

<p>Comparators</p>	<p>Established clinical management without teprotumumab which may include:</p> <ul style="list-style-type: none"> • Corticosteroids <ul style="list-style-type: none"> ○ prednisolone ○ methylprednisolone ○ triamcinolone • Immunosuppressive agents <ul style="list-style-type: none"> ○ mycophenolate ○ rituximab ○ tocilizumab ○ ciclosporin • Orbital radiotherapy • Surgical interventions: <ul style="list-style-type: none"> ○ eyelid surgery ○ orbital decompression ○ strabismus surgery
<p>Outcomes</p>	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • disease activity • disease severity • proptosis response • diplopia response • adverse effects • health-related quality of life (including psychosocial impact) • duration of treatment response • retreatment • need for rehabilitation surgery • need for subsequent surgical intervention

<p>Economic analysis</p>	<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.</p> <p>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.</p> <p>The availability and cost of biosimilar and generic products should be taken into account.</p> <p>Cost effectiveness analysis should include consideration of the benefit in the best and worst seeing eyes' perspective.</p>
<p>Other considerations</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>
<p>Related NICE recommendations</p>	<p>Related NICE guidelines:</p> <p>Thyroid disease: assessment and management (2019, updated 2023) NICE guideline [NG145].</p> <p>Related interventional procedures:</p> <p>Retrobular irradiation for thyroid eye disease (2005) NICE interventional procedures guidance 148.</p>
<p>Related National Policy</p>	<p>NHS England (2019) The NHS long term plan</p> <p>NHS England (2013) NHS standard contract for ophthalmology (adult). D12/S/a.</p> <p>NHS England (2021) Policy book for eye health</p> <p>NHS England (2023) Prescribed specialised services manual (version 6) Chapter 12. Adult specialist ophthalmology services</p>

References

1 What is Thyroid Eye Disease? [Internet]. [cited 2024 Jun 28]. Available from: <https://stanfordhealthcare.org/medical-conditions/eyes-and-vision/thyroid-eye-disease.html>

2 Muñoz-Ortiz J, Sierra-Cote MC, Zapata-Bravo E, Valenzuela-Vallejo L, Marin-Noriega MA, Uribe-Reina P, et al. Prevalence of hyperthyroidism, hypothyroidism, and euthyroidism in thyroid eye disease: a systematic review of the literature. *Syst Rev*. 2020;9(1):201. Available from: <https://pubmed.ncbi.nlm.nih.gov/32873324/>

3 Thyroid eye disease (TED) [Internet]. [cited 2024 Jun 17]. Available from: <https://www.btf-thyroid.org/listing/category/thyroid-eye-disease-ted>

4 Lazarus JH. Epidemiology of Graves' orbitopathy (GO) and relationship with thyroid disease. *Best Pract Res Clin Endocrinol Metab*. 2012 Jun;26(3):273-9. doi: 10.1016/j.beem.2011.10.005. PMID: 22632364. [cited 2024 Sept 11].