Appendix B

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Teprotumumab for treating thyroid eye disease ID6432

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of teprotumumab within its marketing authorisation for treating 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, eye pain, and difficulty moving the eyes are also prevalent.

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 radiotherapy, contributes to the development of TED. Concurrent endocrine disorders, such as type 1 diabetes, also play a role in its development.

TED affects approximately 50,000 people in the UK, with about 2,500 new cases annually.[3,4] It primarily affects women (female-to-male ratio of 5:1) due to potential effects of oestrogen on immune responses via orbital tissue receptors. 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.

Management involves a multidisciplinary approach to control inflammation, manage symptoms, and prevent complications like optic nerve compression. Mild cases may require supportive measures such as lubricating eye drops and sunglasses. More severe cases often necessitate systemic corticosteroids and immunosuppressive therapies.

According to NICE Interventional Procedures guidance [IPG148]: retrobulbar irradiation for thyroid eye disease, radiation therapy is suggested for people with TED

who do not respond adequately to other therapies or experience significant side effects from them. Radiation therapy directed towards the tissues behind the eyeball aims to reduce inflammation in the orbit. It can be applied either independently or alongside corticosteroids. Surgical interventions, like orbital decompression, may be needed to relieve optic nerve pressure and correct proptosis. However, no pharmacological treatments are specifically approved for TED in the UK.

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 thyroid eye disease

Subgroups	If evidence allows and where appropriate, the following may be considered:
	Subgroups by
	- Disease activity
	  • Active
	  • Stable
	- Disease severity :
	  • Severe
	  • Moderate
	  • Mild
	- Associated underlying condition:
	  • Graves' disease only
	  • Graves' disease and others/not specified
	- Duration of active symptom
	  • More than 1 year
	  • Less than 1 year

Comparators	Established clinical management without teprotumumab which may include:
	• systemic corticosteroids
	  ○ prednisolone
	  ○ methylprednisolone
	  ○ triamcinolone
	  ○ dexamethasone
	• immunosuppressive agents
	  ○ mycophenolate
	  ○ rituximab
	• radiotherapy
	• surgical interventions
	  ○ eyelid surgery
	  ○ orbital decompression
	  ○ strabismus surgery
	• best supportive care

Outcomes	The outcome measures to be considered include: • change in disease activity • change in disease severity • proptosis response • change in proptosis • diplopia response • orbital pain • eyelid swelling • functional vision • adverse effects of treatment • health-related quality of life • retreatment time

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. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability and cost of biosimilar and generic products should be taken into account. Cost effectiveness analysis should include consideration of the benefit in the best and worst seeing eyes' 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	**Related technology appraisals:** None **Related highly specialised technology appraisals:** None **Related technology appraisals in development:** None **Related highly specialised technology appraisals in development:** None **Related NICE guidelines:** Thyroid disease: assessment and management (2019, updated 2023) NICE guideline [NG145]. **Related NICE guidelines in development:** None **Related interventional procedures:** Retrobulbar irradiation for thyroid eye disease (2005) NICE interventional procedures guidance 148. **Related quality standards:** None

Related National Policy	NHS England (2019) The NHS long term plan NHS England (2013) NHS standard contract for ophthalmology (adult). D12/S/a. NHS England (2021) Policy book for eye health NHS England (2023) Prescribed specialised services manual (version 6) Chapter 12. Adult specialist ophthalmology services

Questions for consultation

Is the population defined appropriately?

How is the activity of thyroid eye disease assessed and determined in the NHS? What criteria are currently used?

How is the severity of thyroid eye disease assessed and determined in the NHS? What criteria are currently used?

What is established clinical management for TED in the NHS?

Where do you consider teprotumumab will fit into the existing care pathway for TED?

What are the long-term monitoring and management practices for people with TED in the NHS?

Please select from the following, will teprotumumab be:

A. Prescribed in primary care with routine follow-up in primary care
B. Prescribed in secondary care with routine follow-up in primary care
C. Prescribed in secondary care with routine follow-up in secondary care
D. Other (please give details):

For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.

What are the most significant unmet needs in the treatment of TED?

Are there groups within the population that should be considered separately? For example, are there subgroups in which the technology is expected to be more clinically or cost effective?

Are the subgroups listed appropriate?

Would teprotumumab be a candidate for managed access?

Do you consider that the use of teprotumumab result in any potential 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 committee to take account of these benefits.

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 teprotumumab 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.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

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] New Guidelines for Thyroid Eye Disease | The Royal College of Ophthalmologists [Internet]. [cited 2024 Jun 17]. Available from: https://www.rcophth.ac.uk/news-views/guidelines-for-thyroid-eye-disease-2015/