NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Mepolizumab for treating hypereosinophilic syndrome

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of mepolizumab within its marketing authorisation for treating hypereosinophilic syndrome.

Background

Eosinophils are a type of white blood cell, usually involved in the body's immune response to some types of infection and allergies. Hypereosinophilic syndrome (HES) is an inflammatory condition where the body overproduces eosinophils, often with no known cause. The resulting high levels of eosinophils in the blood (typically defined as >1.5 x 10^9/L for more than 6 consecutive months) can cause eosinophil-associated organ damage.[1,2] High levels of circulating eosinophils can lead to inflammation in various tissue types and damage multiple organ systems including the lungs, skin, digestive tract and heart. If left untreated, HES can eventually be fatal in severe cases.

Symptoms of hypereosinophilic syndrome can vary depending on which systems in the body are affected. For example, people may experience lung problems (asthma, breathing difficulties, pleural effusion, recurring infections), fatigue, itching, rashes, vomiting and abdominal pain, pain in joints and muscles, arthritis, speech impairment, anaemia, deep vein thrombosis, vertigo, visual disturbances and a range of heart symptoms including congestive heart failure.[3] Some people have a specific form called lymphocytic hypereosinophilic syndrome with increased production of eosinophils and a protein called interleukin-5. People with lymphocytic HES are at risk of developing a type of cancer, T-cell lymphoma.[4]

HES has an estimated prevalence of 1.5 in every 100,000 people in the European Union,[5] with an estimated number of people with the condition in England between 800 and 900. The severity of hypereosinophilic syndrome may be defined by the number of flare ups within the previous 12 months. People with a flare up require emergency treatment which depends on the the severity of the condition and underlying cause. People without the FIP1L1/PDGFRA mutation are initially treated with high-dose corticosteroids and if the response to this treatment is not adequate (or where prolonged treatment is required, or corticosteroids are unsuitable for the specific patient), existing treatment options include immunomodulatory drugs, myelosuppressive therapy or imatinib (a tyrosine kinase inhibitor [TKI]). People with the FIP1L1/PDGFRA fusion gene are initially treated with imatinib. For severe hypereosinophilic syndrome of unknown cause which is unresponsive to other treatments, a monoclonal antibody, alemtuzumab, may be used.[6] Some people with HES that is refractory to drug therapy may receive an allogeneic hematopoietic cell transplant.

The technology

Mepolizumab (Nucala, GlaxoSmithKline) is an anti-interleukin-5 humanised

monoclonal antibody which reduces the number of circulating eosinophils. Mepolizumab is administered subcutaneously in addition to best standard care.

Mepolizumab does not currently have a marketing authorisation in the UK for treating hypereosinophilic syndrome. Mepolizumab has been studied in placebo controlled clinical trials as an add-on to standard of care in people with hypereosinophilic syndrome. One of the trials focused on severe hypereosinophilic syndrome (defined in the trial as a blood eosinophil count of ≥1000 cells/μL and at least 2 flare ups in the past 12 months).

Mepolizumab has a UK marketing authorisation as an add-on treatment for severe refractory eosinophilic asthma.

Intervention(s)	Mepolizumab (in addition to best standard care)
Population(s)	People aged 12 years and older with hypereosinophilic syndrome
Comparators	Current NHS best standard care, which may include: • corticosteroids such as prednisolone • imatinib (for people with FIP1L1/PDGFRA fusion gene) For people whose disease does not respond to corticosteroids, or who require prolonged corticosteroid therapy, or who are intolerant of corticosteroids, treatment may include: • imatinib • hydroxycarbamide (does not currently have a marketing authorisation in the UK for this indication) • interferon-alpha (does not currently have a marketing authorisation in the UK for this indication) • ciclosporin (does not currently have a marketing authorisation in the UK for this indication) • azathioprine (does not currently have a marketing authorisation in the UK for this indication) • alemtuzumab (does not currently have a marketing authorisation in the UK for this indication)
Outcomes	The outcome measures to be considered include: • number of HES flares • time to first HES flare • change in fatigue • 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 availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability of any managed access arrangement for the intervention will be taken into account.
Other considerations	If the evidence allows, the following subgroup will be considered: lymphocytic variant HES. The availability and cost of biosimilar and generic products should be taken into account. 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 Technology Appraisals: Mepolizumab for treating severe refractory eosinophilic asthma (2017). NICE Technology Appraisal 431. Review ongoing (2020). Appraisals in development (including suspended appraisals): Mepolizumab for treating severe eosinophilic asthma NICE technology appraisals guidance [ID3750]. Publication expected February 2021. Mepolizumab for treating chronic obstructive pulmonary disease NICE technology appraisals guidance [ID1237]. Publication date to be confirmed. Mepolizumab for treating eosinophilic granulomatosis with polyangiitis NICE technology appraisals guidance [ID1186]. Publication date to be confirmed (suspended). Proposed appraisals: Mepolizumab for treating severe chronic rhinosinusitis with nasal polyps Proposed NICE technology appraisal [ID3817]. Publication date to be confirmed.
Related National Policy	NHS England (2013) 2013/14 NHS Standard Contract For Specialised Allergy Services (all ages): section B part 1 - service specifications

	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019), chapter 59 Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1, 2, 3, 4. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Have all relevant comparators for mepolizumab been included in the scope? Which treatments are considered to be established clinical practice in the NHS for hypereosinophilic syndrome?

How should best standard care be defined?

Are the outcomes listed appropriate?

Is this treatment intended to be used in people with 'severe' hypereosinophilic syndrome? How should this be defined? Which treatments are considered to be established clinical practice in the NHS for severe hypereosinophilic syndrome?

Are the subgroups suggested in 'other considerations' appropriate? Are there any other subgroups of people in whom mepolizumab is expected to be more clinically effective and cost effective or other groups that should be examined separately?

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 mepolizumab 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 mepolizumab 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 mepolizumab 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.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

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 Roufosse FE, Goldman M, Cogan E (2007) Hypereosinophilic Syndromes. Orphanet Journal of Rare Diseases 2(37).

2 Tefferi A, Gotlib J, Pardanani A (2010) Hypereosinophilic Syndrome and Clonal Eosinophilia: Point-of-Care Diagnostic Algorithm and Treatment Update. Mayo Clinic Proceedings 85(2): 158-164.

3 National Institutes of Health (2017) Hypereosinophilic Syndrome. Accessed August 2020.

4 Boyer DF (2016) Blood and Bone Marrow Evaluation for Eosinophilia. Archives of Pathology & Laboratory Medicine 140(10): 1060-1067.

5 Orphanet Report Series, Rare Diseases Collection (2020) Prevalence of Rare Diseases: Bibliographic Data. Number 1: Diseases listed in alphabetical order.

6 Butt NM, Lambert J, Ali S et al. (2017) Guideline for the Investigation and Management of Eosinophilia. British Journal of Haematology 176: 553-572.

