NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Emapalumab for treating primary haemophagocytic lymphohistiocytosis

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of emapalumab within its marketing authorisation for treating primary haemophagocytic lymphohistiocytosis.

Background

Haemophagocytic lymphohistiocytosis (HLH) is a condition in which the body makes too many activated immune cells causing severe inflammation throughout the body. Excessive activation of specific white blood cells, including histiocytes (macrophages) and lymphocytes (specifically T cells, B cells and Natural Killer [NK] cells) and an associated increase in the level of interferon gamma (IFNγ) leads to overproduction of other pro-inflammatory cytokines and a hyperinflammatory syndrome.

The overactivation of the immune system causes fever, enlargement and damage to the liver and spleen; it also destroys blood-producing cells in the bone marrow. As a result, people have low numbers of red blood cells (anaemia), platelets (thrombocytopenia, which may cause abnormal bleeding) and neutrophils (neutropenia, which may cause susceptibility to infection). The central nervous system may also be affected by HLH which can cause impaired muscle coordination, paralysis, blindness, seizures and coma. HLH can also cause abnormalities of the heart, kidneys, and other organs and tissues. There is also an increased risk of developing cancers of blood-forming cells (leukaemia and lymphoma).[1] Without treatment the median survival time is less than 2 months.[2]

HLH primarily affects children and young people. Primary HLH is the inherited form of the disease. Several specific gene mutations have been identified but not all people with primary HLH have a recognised genetic mutation.

Published estimates for the incidence of confirmed primary HLH in people aged 15 and under range from 1.2 to 1.5 per million people per year,[3] suggesting there are approximately 13 to 15 people with confirmed primary HLH in England each year.[4]

Current treatment for HLH has a two-pronged approach: a short-term strategy to control the hyperinflammatory state including steroids, immunosuppressants and chemotherapy, and a long-term strategy aimed at curative approach by allogeneic haematopoietic stem cell transplantation

(HSCT). For people who do not respond to, or cannot tolerate treatment, best supportive care is given. Where appropriate, alemtuzumab may also be given.

The technology

Emapalumab (Gamifant, NovImmune) is a human monoclonal antibody that binds to and inhibits interferon gamma (IFNγ). IFNγ is a cytokine secreted by cells of the immune system, which is over-produced in HLH, leading to a hyperinflammatory state. Emapalumab is administered as an intravenous infusion.

Emapalumab does not currently have a marketing authorisation in the UK for treating primary HLH. It has been studied in clinical trials, in people 18 years and under.

Intervention(s)	Emapalumab
Population(s)	People with primary haemophagocytic lymphohistiocytosis
Comparators	Established clinical management without emapalumab
Outcomes	The outcome measures to be considered include: • overall response • survival, including survival to haematopoietic stem cell transplantation and post-transplant survival • time to response • durability of response • use of steroids • outcome of haematopoietic stem cell transplantation • long-term complications of HLH • duration of hospitalisation • 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. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	If evidence allows, consideration may be given to subgroups based on people who have not had previous treatment, people for whom previous treatment has failed or was not tolerated and people for whom a HSCT is unsuitable. 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 National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2017) Manual for prescribed specialised services 2018/19 Chapter 113. Children, Young People and Maternity Services - archived Department of Health and Social Care (2016) NHS outcomes framework 2016 to 2017

References

1) U.S. National Library of Medicine – Familial hemophagocytic lymphohistiocytosis https://ghr.nlm.nih.gov/condition/familial-hemophagocytic-lymphohistiocytosis Accessed August 2019.

2) Henter J et al. (2002) Treatment of hemophagocytic lymphohistiocytosis with HLH-94 immunochemotherapy and bone marrow transplantation. Blood 100:2367–73.

3) Meeths M et al. (2014) Incidence and clinical presentation of primary hemophagocytic lymphohistiocytosis in Sweden. Pediatric Blood & Cancer 62(2):346–52.

4) Population of England (2018) Population estimates - Office for National Statistics. Accessed August 2019.