Engagement Report

Topic details

Title of policy or policy statement:	Anakinra for Haemophagocytic Lymphohistiocytosis (HLH) for adults and children in all ages
Programme of Care:	Internal Medicine
Clinical Reference Group:	Specialised Rheumatology
URN:	1924

1. Summary

This report summarises the feedback NHS England received from engagement during the development of this policy proposition, and how this feedback has been considered in development of the policy.

Background

The policy proposition recommends that anakinra should be made routinely available as a bridging treatment for adults and children with haemophagocytic lymphohistiocytosis (HLH). Anakinra is not licensed for this indication.

HLH happens when the body's immune system responds abnormally to illness or some treatments which target the immune system. The illnesses include infection, cancer and some rheumatology conditions and treatments which can trigger HLH are some of those for blood cancers. Alternatively, HLH can be caused by an inherited genetic condition meaning the immune system cannot switch itself off once triggered. In HLH the body makes too many activated immune cells causing severe inflammation (known as hyperinflammation) throughout the body. This causes fever, damage to organs (including the liver, spleen brain and heart), and destroys blood-producing cells in the bone marrow. HLH can make people more at risk of infection. Without treatment many people die. With treatment, particularly if HLH is recognised and treated early, the outlook is much better. In addition to treating the HLH, the trigger needs to be found and treated too.

Anakinra is medicine which is given either by injection under the skin or as an infusion through a drip. It works by blocking the main driver of the hyperinflammation, interleukin1 (IL1). Anakinra is usually only needed for a short period in HLH, for 3-14 days on average.

This policy proposition has been developed by a Policy Working Group established in line with standard processes and involved clinical members, Public Health England and patient and public voice representatives.

2. Engagement

NHS England has a duty under Section 13Q of the NHS Act 2006 (as amended) to 'make arrangements' to involve the public in commissioning. Full guidance is available in the Statement of Arrangements and Guidance on Patient and Public Participation in Commissioning. In addition, NHS England has a legal duty to promote equality under the Equality Act (2010) and reduce health inequalities under the Health and Social Care Act (2012).

The policy proposition was shared for stakeholder testing for 3 weeks from 13th January 2021 to 3rd February 2021. The comments have then been discussed with the Policy Working Group to enable full consideration of feedback and to support a decision on whether any changes to the proposition might be recommended.

Respondents were asked the following questions:

- Do you support the proposition for anakinra for HLH to be available through routine commissioning based on the evidence review and within the criteria set out in this document?
- Do you believe that there is any additional information that we should have considered in the evidence review? If so, please give brief details.
- Do you believe that there are any potential positive and/or negative impacts on patient care as a result of making this treatment option available? If so, please give details.
- Do you have any further comments on the proposition? If Yes, please describe below, in no more than 500 words, any further comments on the proposed changes to the document as part of this initial 'sense check'.
- Do you support the Equality and Health Inequalities Impact Assessment?
- Does the Patient Impact Summary present a true reflection of the patient and carers lived experience of this condition?
- Please declare any conflict of interests relating to this document or service area.

A 13Q assessment has been completed following stakeholder testing.

The Programme of Care has decided that the proposition offers a clear and positive impact on patient treatment, by potentially making a new treatment available which widens the range of treatment options without disrupting current care or limiting patient choice, and therefore further public consultation was not recommended. This decision has been assured by the Patient Public Voice Advisory Group.

3 Engagement Results

There were twenty-two responses to engagement, of which two responses were from individual clinicians; four responses were from individual members of the public and sixteen responses were submitted by organisations.

Of the twenty-two responses received, twenty-one respondents fully supported the draft policy proposition. One individual respondent did not indicate if they did or did not support the draft policy proposition. Furthermore, twenty respondents supported the draft Equality and Health Inequalities Impact Assessment (EHIA) and agreed that the Patient Impact Assessment (PIA) represented a true reflection of the patient and carers lived experience of this condition. The other two responses felt that the PIA may underestimate the impact on patients and carers and may also need to highlight in the EHIA that predominantly children are affected, and that children of consanguineous families and cultures where English is a second language are affected too.

Respondents queried the following:

- If Ravelli HLH (MAS) criteria should be added when HLH is seen in the context of juvenile arthritis.
- The dosing, titration and intravenous (IV) off-label use needing clarification in the policy proposition
- It was suggested that the haemoglobinopathies Clinical Reference Group (CRG) was not relevant to this policy proposition; and instead there should be engagement with haematologists and the treatment made available directly for them to prescribe. This was also believed to apply to the funding route for the treatment.
- Covid-related HLH may have a role in the policy proposition.
- The Bone Marrow Transplant (BMT)/Haematopoietic Stem Cell Transplantation (HSCT), CAR-T and haemato-oncology aspects of inclusion criteria needs to be clearer.
- The licenced recommendation is for the subcutaneous use of anakinra, however many of the HLH trials using anakinra do so using the off-label IV route and with various dose regimes. Whilst this treatment approach appears to be well tolerated, it was suggested that further assessment will be needed to assess its safety.
- HLH occurring in pregnancy (now recorded in MBRACE) and the utility and safety of anakinra in this context needs to be explored further.
- The definition of a tertiary multi-disciplinary team (MDT) providing the service needs to be clarified.
- It was queried if the guidance regarding immunoglobulin (IVIG) prescribing fell under the remit of this policy.

The below articles included within the stakeholder consultation were selected for public health review by the Policy Clinical Lead.

i. Minoia F, Davì S, Horne A, et al. Clinical Features, Treatment, and Outcome of Macrophage Activation Syndrome Complicating Systemic Juvenile Idiopathic Arthritis: A Multinational, Multicenter Study of 362 Patients: Macrophage Activation Syndrome in Systemic JIA. Arthritis Rheumatol 2014; 66: 3160–9

ii. Miettunen PM, Narendran A, Jayanthan A, Behrens EM, Cron RQ. Successful treatment of severe paediatric rheumatic disease-associated macrophage activation syndrome with interleukin-1 inhibition following conventional immunosuppressive therapy: case series with 12 patients. Rheumatology 2011; 50: 417–9

Both articles fulfil the PICO criteria and time frame but were probably excluded because of one being a retrospective narrative review and the second included as a letter to the Editor. They complement and endorse the policy proposition but do not materially change it.

3. How has feedback been considered?

Responses to engagement have been reviewed by the Policy Working Group (PWG) and the Internal Medicine Programme of Care. The following themes were raised during engagement:

Key themes in feedback	NHS England Response
Relevant Evidence	
Off licence IV use	Anakinra is already delivered intravenously in clinical practice.
Use in pregnancy and breast feeding	The Electronic Medicines Compendiums allows for use in life-threatening situations.
Impact Assessment	
Long term effects of HLH on patients and carers	A patient representative has been recruited within the PWG; the Patient Impact Assessment has been amended in line with stakeholder comments.
Current Patient Pathway	
Ensuring equity of access to treatment via all relevant specialities	The policy has had input from relevant CRGs associated with the different relevant specialities.
Potential impact on equality and health inequalities	
This proposition will reduce health inequities by improving equitable access to treatment.	This is reflected in the EHIA.
Changes/addition to policy	
2 additional papers reviewed (see Engagement Results section)	The papers are consistent with the policy proposition.

4. Has anything been changed in the policy proposition as a result of the stakeholder testing and consultation?

The following change based on the engagement responses has been made to the policy proposition:

- The dosing guidance has been altered for clarification, as has the route for accessing expert advice.

5. Are there any remaining concerns outstanding following the consultation that have not been resolved in the final policy proposition?

There are no outstanding concerns.