Engagement Report

Topic details

Title of policy or policy statement:	Use of Adalimumab for refractory Chronic non-bacterial osteomyelitis / osteitis (CNO) (all ages)
Programme of Care:	Internal Medicine
Clinical Reference Group:	Specialised Rheumatology
URN:	1926

1. Summary

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

2. Background

Adalimumab is a biologic medicine which falls under the class of drugs called tumour necrosis factor blockers. It targets immune cells to reduce inflammation in the body. It is commonly used to treat multiple inflammatory conditions such as rheumatoid arthritis and psoriasis. In most cases, the medication is administered at home by the patient/parent under the skin (subcutaneously). Biosimilars for adalimumab are now available, these are newer versions of the original drug which are just as effective and safe to use but are often cheaper.

CNO is an auto-inflammatory condition that causes severe bone pain arising from inflammation of bone(s) without signs of an infection. CNO primarily affects children but can persist into adulthood. It covers a wide spectrum of disease ranging from time-limited mild inflammation affecting a single bone to severe chronically active or recurrent inflammation affecting multiple bones. Severe bone pain can result in functional impairment and CNO has a significant impact on quality of life (Zhao & Ferguson, 2018). In some cases, patients may continue to have impairment into adult life including bone deformity, disability and chronic pain resulting in significant morbidity (Roderick, Sen and Ramanan, 2018).

CNO is a rare disease, there are no current accurate data on incidence/prevalence in the UK. The incidence of CNO in Germany was reported to be 0.4 per 100,000 (= 4 per million) children (Jansson and Grote, 2011).

This policy statement proposition has been developed by a Policy Working Group consisting of Consultant Rheumatologists, Paediatric Rheumatologists, a Public Health Consultant, a Pharmacist and a Patient Representative.

3. Engagement

NHS England and NHS Improvement 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 and NHS Improvement 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 sent for stakeholder testing for 2 weeks from 11th to 25th June 2020. The comments have then been shared 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.

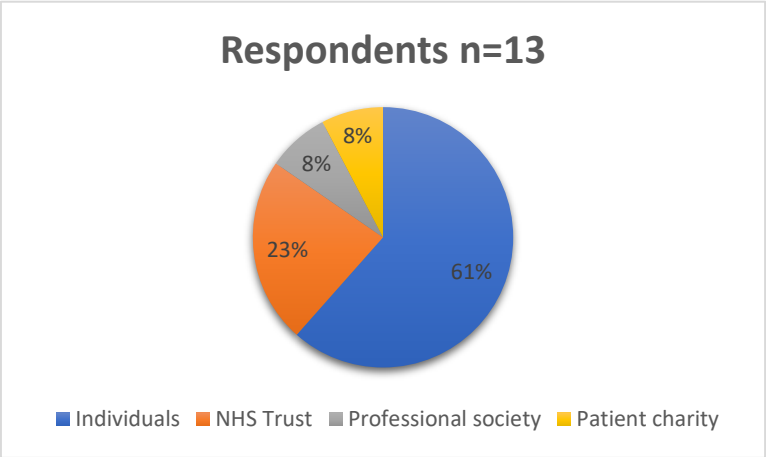
Respondents were asked the following questions:

- Do you support the proposal that Adalimumab for refractory Chronic non-bacterial osteomyelitis will not be routinely commissioned based on the evidence review and 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?
- Do you believe that there are any potential positive and/or negative impacts on patient care as a result of not making this treatment option available?
- Do you support the Equality and Health Inequalities Impact Assessment?
- Do you have any further comments on the proposal?
- Please declare any conflict of interests relating to this document or service area.

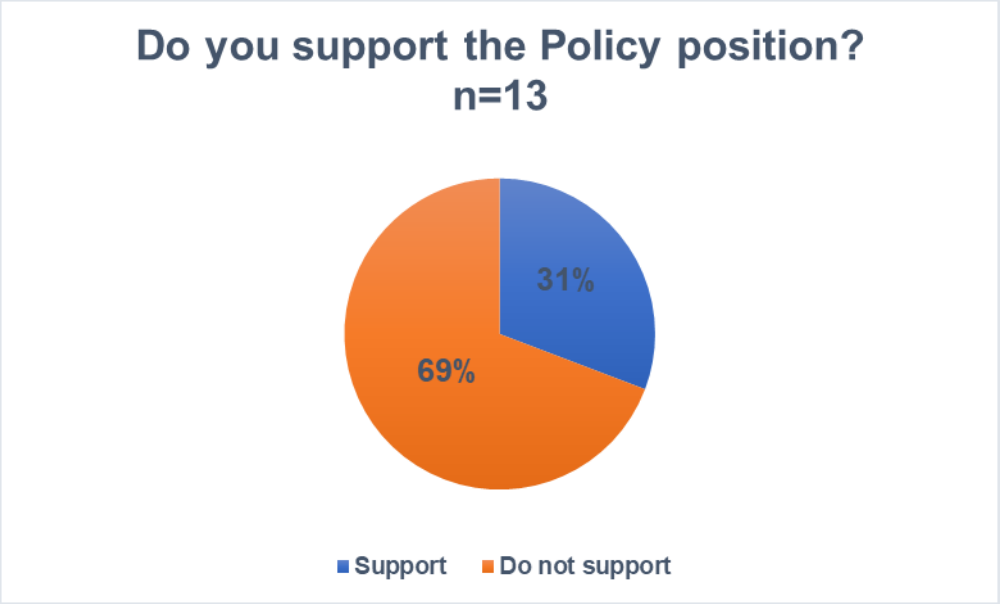
As this is a Policy Statement, a 13Q assessment was not completed following stakeholder testing and the statement was not subject to public consultation. This is in accordance with NHS England and NHS Improvement Policy Methods.

4. Engagement Results

There were 13 respondents in total: eight individuals, five organisations, which included three NHS Trusts, British Society of Rheumatology and Rare Autoinflammatory Conditions Community – UK. One organisation had misinterpreted the commissioning position and were contacted to provide an opportunity to alter their response.



Four respondents supported the commissioning position and nine respondents did not. Of the organisations who responded one supported the commissioning position and four did not. Of the individuals who responded three supported the commissioning position and five did not. The five individuals who responded who did not support the commissioning position were all clinicians. For the three individuals who responded who did support the commissioning position it was not possible to tell whether they were patients, carers or clinicians.



5. How has feedback been considered?

Responses to engagement have been reviewed by the Policy Working Group and the Internal Medicine PoC. The following themes were raised during engagement:

Keys themes in feedback	NHS England Response
Relevant Evidence	
It was highlighted that randomised controlled trials are not feasible in rare conditions such as CNO/ Chronic recurrent multifocal osteomyelitis and that stronger trial evidence will not be possible to obtain. Stakeholders also mentioned that randomised controlled trial proposals have not been successful in securing funding and this is frustrating for clinicians and patients.	The level of evidence in the context of a rare condition was taken into account in determining the commissioning position. The evidence review conclusion states that randomised controlled trials RCTs are challenging in this area and further research is recommended with clear and robust outcome measures. NHS England recognises that for rare conditions, randomised controlled trials are unlikely to be feasible and indeed, RCTs may not have been conducted to compare treatments. The selection of the most clinically impactful study publications to inform the policy statement proposition is based on the Preliminary Policy Proposal (PPP) document submitted by the Clinical Lead. Admissible publication types should be publications of original research that are peer reviewed and should not be letters, abstracts, or narrative review papers. RCTs and systematic

	reviews are considered to be the most robust study designs. In the absence of these being available, other study designs comparing treatment effects (e.g. controlled clinical trials or cohort studies) are preferred to the inclusion of non comparative study designs (case series), but all are admissible. In addition, NHS England and NHS Improvement has an Evaluative Commissioning Programme than can be applied for where a policy is not routinely commissioned (https://www.england.nhs.uk/publication/methods-commissioning-through-evaluation/).
NHS England does not support research initiatives	NHS England and NHS Improvement do not directly commission research, but works closely with the The National Institute for Health Research (NIHR) to identify research priorities. NIHR is a United Kingdom government agency which funds research into health and care. In addition, NHS England and NHS Improvement has an Evaluative Commissioning Programme than can be applied for policies that are not routinely commissioned (https://www.england.nhs.uk/publication/methods-commissioning-through-evaluation/).
Impact Assessment	
The alternative to trialling adalimumab (or other biologic) would be ongoing steroid treatment which has significant adverse event profile	This was noted and considered by the PWG; The original PPP submitted did take into account adverse effects of alternative medications, including corticosteroids.
Impact of long term chronic pain not considered	The three papers submitted by the Clinical Lead for this proposition and, used to inform the review did not consider long-term chronic pain as an outcome measure. Further evidence was provided by stakeholders and was reviewed by a Public Health Consultant. Long term chronic pain is a significant issue in this group of patients and this outcome measure should be used in future research. The evidence put forward by stakeholders during the response phase was judged not to materially change the outcome of the commissioning decision. The original PPP submitted included note of patient factors including impact of chronic pain on lifestyle, education function, sleep and effect on family.
Access to adalimumab if a patient has overlap with Juvenile Idiopathic Arthritis (enthesitis related arthritis)	A number of respondents highlighted that patients that have CNO with arthritis have access to adalimumab. NHS England and NHS Improvement has a Policy on this specific topic

	(E03/P/d Biologics for Juvenile Idiopathic Arthritis in Children and Adults). This does not affect this Policy Statement.
Potential impact on equality and health inequalities	
Inequity of current access, depends on response of different organisations	NHS England and NHS Improvement does not currently commission adalimumab for CNO. Patients who have access to adalimumab currently are being funded via other routes. This Policy Statement should not affect those funding routes. A national commissioning position will ensure there is equity within NHS England and NHS Improvement's commissioning remit.
Changes/addition to policy	
A national registry would be useful to better understand the condition and treatment options	This is outside the scope of the policy process but see comments on further research.

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

No changes have been made to the Policy Statement.

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

None. However, the majority of stakeholders responses (69%) did not support a not for routine commissioning policy although they did not supply any evidence which materially changed the commissioning position. They also highlighted the difficulties in obtaining quality research in rare conditions.

In line with the current NHS England Methods: National Clinical Policies document Clinical Commissioning Policy Statements do not require public consultation. This has been confirmed by the Patient and Public Voice Advisory Group and the Head of Engagement in the Communications & Engagement Team, Specialised Commissioning that consultation is not required.