Engagement Report

Topic details

Title of policy or policy statement:	Obinutuzumab elective therapy to prevent immune Thrombotic Thrombocytopenic Purpura (TTP) relapse in patients who are refractory or intolerant to rituximab
Programme of Care:	Blood and Infection
Clinical Reference Group:	Specialised Blood Disorders
URN:	2255

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.

2. Background

Immune thrombotic thrombocytopenic purpura (TTP) is a rare, potentially life-threatening condition that involves formation of blood clots in the small blood vessels in the body. This leads to organ damage, particularly the brain, digestive tract, heart and kidneys. Many require ICU admission and without treatment, the mortality in acute immune TTP is >90%.

Immune TTP happens when platelets stick together too readily. Platelets use a highly adhesive glue called von Willebrand Factor (vWF) to form a clot. The size of the vWF determines how easily platelets stick together and if the vWF becomes too long, platelets stick together even when they are not supposed to. A protein called ADAMTS13 regulated the size of the vWF. Less ADAMTS13 leads to vWF not being broken down causing unwanted clotting in small blood vessels. The shortage of ADAMTS13 can either be caused by a genetic problem that prevents enough enzyme being produced or an overactive immune system that destroys the enzyme.

Treatment of acute immune TTP is with urgent plasma exchange (PEX) to replace ADAMTS13 and immunosuppression to switch off the autoimmune response. Removal of causative antibodies requires high dose steroids initially and rituximab (anti-CD20). Rituximab can also be used in the outpatient setting to prevent an acute relapse of immune TTP. However, a small proportion of patients will become resistant or develop an allergy to rituximab.

The proposed intervention is obinutuzumab, a humanised type II monoclonal antibody. Like rituximab, obinutuzumab targets the CD20 molecule, improving circulating levels of ADAMTS13. However, unlike rituximab obinutuzumab is humanised, giving potential advantages in terms of response, tolerance, and development of reactions.

For those patients who are intolerant or refractory to rituximab, obinutuzumab would be a treatment option in those with immune TTP who have not achieved immunological remission or who achieved immunological remission, but their ADAMTS13 levels start to fall.

3. 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 underwent a two-week period of stakeholder testing between 27th April and 11th May 2023 with registered stakeholders for the Specialised Blood Disorders Clinical Reference Group. 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 consultation questions:

- Do you believe that there is any additional information that we should have considered in the evidence review?
- Do you support the inclusion criteria set out in the policy proposition?
- Do you support the exclusion criteria set out in the policy proposition?
- Do you have any further comments on the proposal?
- 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.

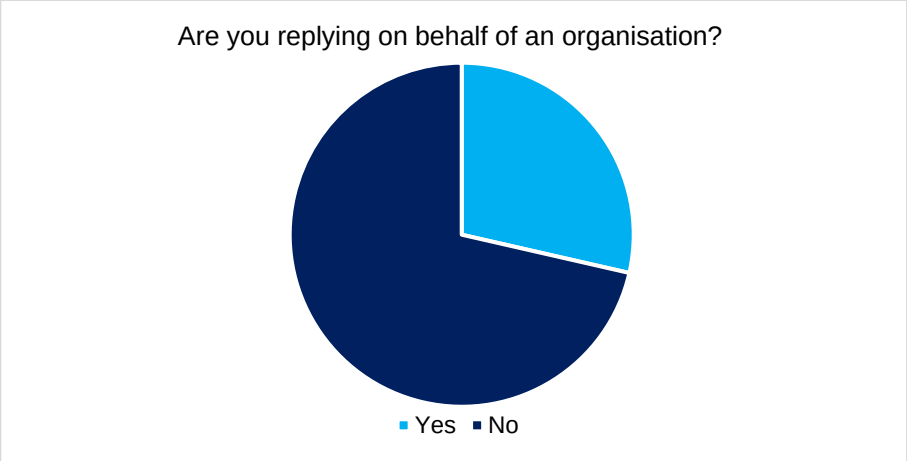
A 13Q assessment has been completed following stakeholder testing.

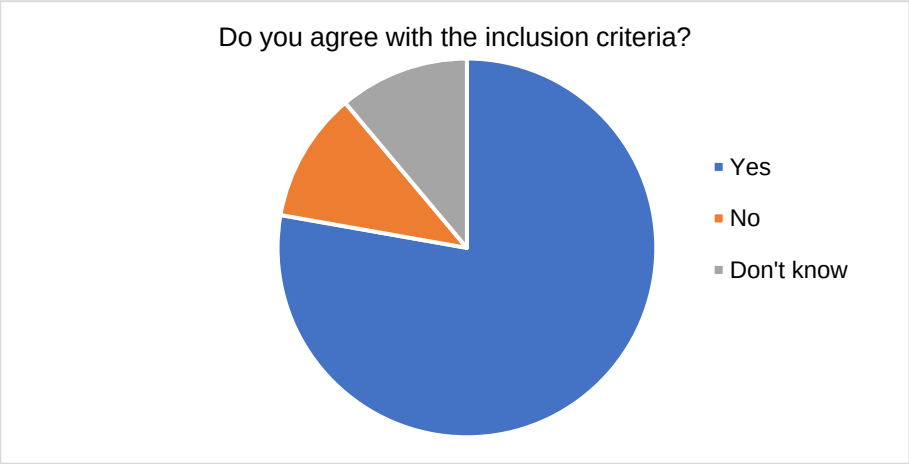
The Programme of Care has decided that the proposition offers a clear and positive impact on patient treatment, by potentially making a new treatment available which widens the range of treatment options without disrupting current care or limiting patient choice, and therefore further public consultation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

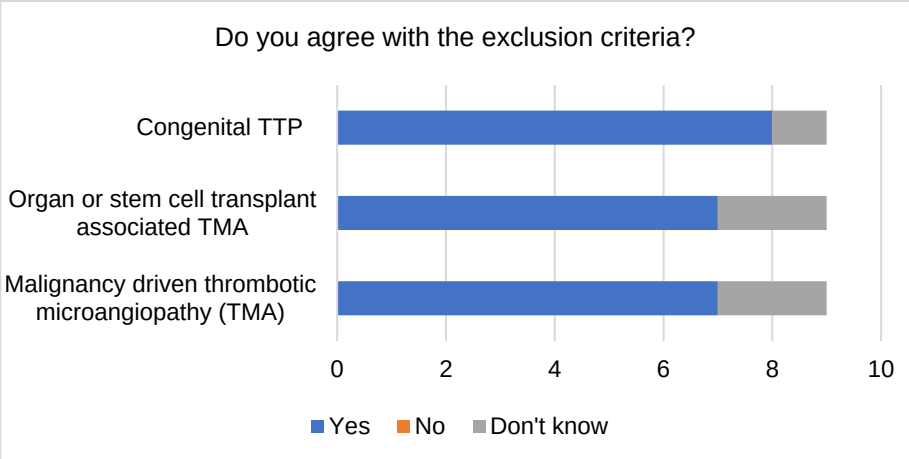
4. Engagement Results

9 stakeholders responded:

- 5 clinicians
- 1 NHS Trust
- 2 Patient Charities
- 1 other







In line with the 13Q assessment it was deemed that further public consultation was not required.

5. How has feedback been considered?

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

Keys themes in feedback	NHS England Response
Relevant Evidence	
All stakeholders agreed with the evidence for prevention of acute immune TTP. One stakeholder provided the reference for an additional article for treatment of acute immune TTP: https://pubmed.ncbi.nlm.nih.gov/31321811/	Noted. This paper was identified in the evidence review but excluded on the basis of being incorrect publication type.
Equalities and health inequalities impact assessment	
Most stakeholders supported the equalities and health inequalities impact assessment. One stakeholder did not support the EHIA.	Noted. No further justification given, so unclear what the stakeholder does not support.
Policy inclusion criteria	
Most stakeholders agreed with the inclusion criteria. One stakeholder disagreed with the inclusion criteria: a reduced ADAMTS13 activity level from baseline with clinical symptoms. Baseline ADAMTS13 activity level is > 50 iu/dl They felt that if a patient's ADAMTS13 levels were normal than symptoms would unlikely be a result of immune TTP and an alternative cause would need to be sought.	Noted. The wording has been amended for clarity.
Policy exclusion criteria	
All stakeholders agreed with the exclusion criteria.	Noted.
Patient impact assessment	
Most stakeholders felt the patient impact assessment represented the experience of patients. One stakeholder felt the impacts of the condition have been underestimated.	Noted. The patient impact assessment has been developed with clinicians and patient representatives to give as honest a depiction of the disease as possible.
Further comments	

All stakeholders felt this policy proposition was a welcomed addition to the clinical pathway and offered patients an alternative treatment option.	Noted.
One stakeholder felt it would be helpful if the policy proposition recommended how often obinutuzumab doses should be given.	Clinical consensus from the PWG was that this was not required.

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

The following changes based on the engagement responses have been made to the policy proposition:

- Inclusion criteria wording amended to: a reduced ADAMTS13 activity. The threshold for treatment will take clinical symptoms into account.

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

No.