NHS ENGLAND SPECIALISED SERVICES

CLINICAL PANEL REPORT

Date: 17 April 2024

Intervention: sirolimus

Indication: extracranial slow-flow vascular malformations refractory to standard therapies (all ages)

URN: 2316

Gateway: 2, Round 2

Programme: Internal Medicine

CRG: Vascular

Information provided to the Panel

Policy Proposition

Evidence Review completed by Solutions for Public Health

Clinical Priorities Advisory Group (CPAG) Summary Report

Evidence to Decision (EtD) Summary

Equalities and Health Inequalities (EHIA) Assessment

Patient Impact Assessment

Blueteq™ Forms – initiation and continuation

Policy Working Group (PWG) Appendix

This Policy Proposition recommends the off-label use of sirolimus in extracranial slow-flow vascular malformations refractory to standard therapies (all ages). Slow-flow vascular malformations are inborn errors of formation of blood vessels. They can affect any organ system, and patients may suffer with debilitating symptoms and complications including pain, swelling, ulceration, bleeding, blood clots, organ failure, limb loss and death. The current standard of care is limited to supportive and medical measures, such as compression hosiery, and invasive procedures that can be life and limb threatening, such as debulking surgery or cryotherapy. Approximately 70 people per annum would be eligible.

The proposition and the supporting documentation were considered by Clinical Panel members in January, who requested several amendments to be made. The Policy Working Group (PWG) considered the Panel's requests and responded by revising the documentation and explaining the actions taken. The Panel agreed that most of the amendments required had been fulfilled but some outstanding issues remained that needed addressing. Concern was raised particularly regarding the length of treatment – was this for a defined period or lifelong? This was not stated. Patients will accumulate health risks the longer they take the treatment, such as kidney function issues and immunosuppression. The risk-benefit issue is not clear in the proposition currently.

EHIA – revision made as previously requested to include reference to the national Healthcare Travel Cost Scheme.
PIA – no amendments requested.

Recommendation

Clinical Panel recommends that this proposition progresses as a routine commissioning policy proposition.

Why the panel made these recommendations

Panel members agreed that the evidence base supported the proposition. The further amendments requested could be considered via Chair's action, with support from the regional medical director who presented the proposition at the Panel meeting.

Documentation amendments required

Policy Proposition:

- Licensing clarification is required regarding the interchangeability of the formulations.
- Clarification required as to how long the treatment is prescribed for i.e. would it be stopped on improvement? The risk-benefit issue needs to be clear within the proposition and the Blueteq forms.
- Frequency of review of access needs to be clear.
- Monitoring section – the statement relating to 3 months and reduction of blood tests based on clinical judgement. The wording needs to be reviewed and tightened/strengthened.

Blueteq™ Form:

- A named lead consultant field needs to be added.
- Frequency of review of access via prior approval needs to be clear.
- The risk-benefit issue needs to be clear within the proposition and the Blueteq forms – in the criteria for stopping.

Declarations of Interest of Panel Members: Two received, one received due to clinical practice, one relating to a relative's interests.

Panel Chair: Anthony Kessel, Deputy Medical Director, Specialised Services

Post Panel Amendments

Policy proposition		
Panel Comment	**Amendment**	**Page number (if applicable)**
Licensing clarification is required regarding the interchangeability of the formulations.	Clarification has been sought. The formulations are not interchangeable due to a difference in bioavailability between oral tablets and oral liquid. The sentence has been revised, and now states: Caution is advised when switching between tablets and liquid due to varying bioavailability.	P6
Clarification required as to how long the treatment is prescribed for i.e. would it be stopped on improvement? The risk-benefit issue needs to be clear within the proposition and the Blueteq forms.	The following sentences have been added into the stopping criteria: • No clinical or radiological response after 6 months of treatment as determined by an appropriate MDT **OR** • After 2 years of treatment, a trial of sirolimus cessation must take place for at least 3-6 months to determine resurgence (symptomatically or radiologically). If there is symptomatic or radiological resurgence with objective measures of severe disease as described in the inclusion criteria of this policy, sirolimus may be restarted after specialist MDT discussion. In 'monitoring criteria', an additional sentence has been added: 'there is an acknowledgment that the risk and benefit of continuing sirolimus must be reviewed and discussed between the prescribing clinician and the patient. Issues include immunosuppression, future risks of malignancy, and risks around pregnancy and conception. This	P5 P6

	treatment is off-label with a lack of evidence for safety and clinical effectiveness in long-term use for this indication'.	
Frequency of review of access needs to be clear.	The monitoring criteria now states that clinical reviews need to take place at a minimum of every 3-months.	P6
Monitoring section – the statement relating to 3 months and reduction of blood tests based on clinical judgement. The wording needs to be reviewed and tightened/strengthened.	The wording has been tightened and now states: At 3 months, providing the patient is felt to be stable, frequency of blood tests and medical reviews can be reduced to a minimum of every 3 months based on clinical judgement.	P6
Blueteq™ Form:		
A named lead consultant field needs to be added.	This field has been added to both the Blueteq and the continuation form.	N/A
Frequency of review of access via prior approval needs to be clear.	The continuation form now has the additional statement: I confirm that the patient is being clinically reviewed at a minimum of 3-monthly. This is in line with the updated monitoring requirements described in the policy proposition.	N/A
The risk-benefit issue needs to be clear within the proposition and the Blueteq forms – in the criteria for stopping.	A statement has been added in the in the monitoring criteria of the policy proposition: There is an acknowledgment that the risk and benefit of continuing sirolimus must be reviewed and discussed between the prescribing clinician and the patient. Issues include immunosuppression, future risks of malignancy, and risks around pregnancy and conception. This treatment is off-label with a lack of evidence for safety and clinical effectiveness in long-term use for this indication. This supports the statement in the Blueteq form which states 'I confirm that the patient has received adequate pre-treatment counselling, in the form of both written and verbal information prior to starting, and that this is clearly documented in the patient records' and the continuation	Policy proposition, P6.

	form which states ‘I confirm that the risk and benefits of treatments have been discussed with the patient and they agree to continue’.	