NHS ENGLAND SPECIALISED SERVICES

CLINICAL PANEL REPORT

Date: March 2020

Intervention: Sapropterin

Indication: Phenylketonuria (all ages)

ID: 1840

Gateway: 2 Round 2

Programme: Women & Children

CRG: Metabolic Disorders

Information provided to the Panel

Clinical Panel Report – September 2018

Clinical Priorities Advisory Group (CPAG) Summary Report

Policy Proposition

Evidence Review undertaken by NICE Medicines and Technologies Programme on behalf of NHS England Specialised Commissioning

Blueteq form - initial and continuation

Policy Working Group Appendix

Key elements discussed

This policy proposition is for a routine commissioning proposition for sapropterin for phenylketonuria (PKU). Following consideration at the May 2019 prioritisation a new Population, Indication, Comparator and Outcome template (PICO), evidence review and policy proposition have been prepared with the aim of being considered at the CPAG prioritisation meeting in May 2020.

The Panel were informed that PKU is a genetic disorder which inhibits the patient's ability to break down this protein. Sapropterin can be given orally to reduce phenylalanine (Phe) levels in patients with PKU. Alternatively, the condition can be managed through a reduction in protein in the diet which can be challenging to manage and provides poor results. Without active management or treatment, the condition is considered to have a major impact on IQ due to variability in Phe levels. This has the most marked effect in the neonatal age group and those in the early childhood. There is also some impact on adults. The use of Sapropterin has been shown to restore some function for those patients with residual phenylalanine hydroxylase enzyme activity. It is considered that 500 patients would be eligible for treatment although 300-320 patients are expected to benefit from the treatment.

The evidence review presented findings from Qu et al (2019) systematic review which demonstrated sapropterin supported tolerance of high levels of Phe in diet. Levy et al (2007) double-blind control study also demonstrates better control of Phe with sapropterin use. Most evidence came from short term trials however Longo et al (2015) 7-year study demonstrated good bio-chemical control with this intervention. All studies demonstrated bio-chemical impact rather than clinical impact. Where dietary management was the comparator better control was demonstrated. There were no studies on cost effectiveness.

Panel considered whether the flowchart should include a route back to treatment for patients who had sapropterin usage discontinued previously or those who may get positive results to a responsive test later in life. Clinical Panel advise checking this with the Policy Working Group (PWG).

The Panel queried what the definition of no improvement would be. No biochemical improvement should be written to make it clear..

Panel discussed the dosage and the requirement for clinicians to titrate between the recommended range. It was noted that dosage was determined by ideal body weight.

Panel discussed the importance of recording patient outcomes and recommended the PWG consider what data should be included in reporting and monitoring. A specific Quality of Life (QoL) measure should be included.

Recommendation

Clinical Panel recommends that this proposition progresses as an interim routine commissioning policy proposition. They noted that a NICE Technology Appraisal (TA) is underway and this guidance will determine the final commissioning position. Required amendments agreed to be signed off by Chair's action.

Why the panel made these recommendations

The Panel considered that the proposition reflected the evidence base presented.

Documentation amendments required

Policy proposition:

- Title – state this is an interim policy proposition.
- Correct typographical error on page 9 bullet point 2 to 'or'.
- Amend typographical error on page 11 first paragraph after bullets
- Starting criteria - add exclusions first.
- Stopping criteria – amend text to 'no biochemical improvement' for clarity.
- Dosage to be amended for clarity. Adding child/adult dose and max dose. *Amended*
- Dosage: amend typographical error page 9. Include the word 'be' and specify need to titrate dose.
- Flowchart: amended to include 'nutritional status deteriorates' stopping criteria. All stopping criteria added for clarity
- Flowchart: amend monitoring to '6 monthly review' rather than 'month' *Amended*
- 'Null trans' to be added to definitions section of the proposition so it is clear what this means.
- PWG to check if there is a route back to testing should usage have been discontinued previously or if positive to the initial test later in adulthood
- Policy review date section to be amended to reflect that any published interim policy position would be superseded by NICE TA decision. *Amended*
- Data: A QoL measure to be added as a data collection requirement

Blueteq form:

- Remove reference to parenteral nutrition.

Declarations of Interest of Panel Members: N/A

Panel Chair: James Palmer, Medical Director Specialised Commissioning

Post-Panel Note

The above comments were relayed to the Policy Working Group. All typographical and clarity amendments and additions have been made to the policy proposition and blueteq form as recommended by Clinical Panel. To remain succinct, the flowchart states ‘Has the stopping criteria been met?’ rather than specify in full the biochemical criteria/ nutritional status deterioration.

On the point ‘PWG to check if there is a route back to testing should usage have been discontinued previously or if positive to the initial test later in adulthood’, advice was sought from the clinical lead. They advised that there is very unlikely to be a different outcome on re-testing or re-trialling treatment, unless the patient or carer had identified a specific issue during the testing or first 12 months of treatment. Response is mostly based on a patient’s genetics/ residual enzyme activity, and this will not change over time. They advised there would be no benefit of specifically referring to re-testing patients as this is unlikely to occur. Therefore, this section has remained unchanged.

The amendments have received chair’s sign off.