NHS ENGLAND SPECIALISED SERVICES

CLINICAL PANEL REPORT

Date: 21 June 2023

Intervention: Dabrafenib

Indication: BRAFV600E mutation positive histiocytic neoplasms where standard care has failed (all ages)

URN: 2268

Gateway: 2, Round 1

Programme: Cancer

CRG: Chemotherapy

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 Making (EtD) Report

Equalities and Health Inequalities (EHIA) Assessment

Patient Impact Assessment (PIA) Report

Blueteq™ Forms – adult and paediatric

Policy Working Group Appendix

This Policy Proposition recommends dabrafenib to be available as a routine commissioning treatment option for patients with histiocytic neoplasms caused by a $BRAF^{V600E}$ mutation where standard care treatment has failed within the specific implementation criteria set out in the document. Histiocytic neoplasms are haematological cancers caused by single mutations or fusions of mitochondrion activated protein kinase (MAPK) pathway genes. Dabrafenib is an oral BRAF inhibitor and its use in histiocytic neoplasms is off label. This policy proposition recommends that dabrafenib should be offered to all ages in line with the findings from the evidence review.

The proposition and the supporting evidence were presented to Panel members. The very rare, complex nature of the condition and high variability of histiocytic neoplasms was outlined, with four main clinical syndromes identified. The incidence is approximately 2 per million people per year with a prevalence of approximately 10 per million in the UK. 68 people in the last five years would have been considered eligible for this treatment.

The evidence review included four studies – one cohort study and three case series. The cohort study included 22 children who had previously received 1st line chemotherapy, 12 of which were then treated with dabrafenib compared to 10 with second line chemotherapy. A prospective case series followed 22 children. A retrospective case series examined the notes of 20 children.

One retrospective case series included 11 adult patients. No randomised controlled trial was identified. Duration of follow up in the studies varied.

Critical outcomes were identified as disease response, overall survival, and progression free survival (PFS). The cohort study provided very low certainty evidence of a statistically significant improvement in disease state following one month of daily dabrafenib compared with two cycles of chemotherapy. The other studies provided very low certainty evidence of partial or complete metabolic response, but these were not statically analysed. One case series reported non-comparative data of lower mortality rates when treated with dabrafenib. In PFS, the cohort study provided very low certainty evidence of statistically significant improvement. A case series reported very low certainty non-comparative evidence of a PFS of almost 50% at two years in those treated with Dabrafenib.

Very low certainty statistically significant evidence of improvement was found in the reporting of important outcomes within the cohort study – relapse rate and organ specific disease response.

Limitations of the studies were highlighted in the evidence review summary.

No quality of life evidence was reported.

No cost effectiveness studies were identified.

The proposition and supporting documents were considered and some amendments requested.

Conditional circumstances of treatment use are stated in the EtD and this has informed the criteria in the proposition.

EHIA – a further review requested.

PIA – a further review requested.

Recommendation

Clinical Panel agreed with the proposition and recommends this proceeds as a routine commissioning proposition.

Why the panel made these recommendations

Clinical Panel members noted that the intended population was very small (c.15 patients/yr) and highly clinically complex. Panel considered that the clinical benefit in terms of disease response and progression free survival outweighed the harms of treatment and would be highly valuable to these patients with limited alternative treatment options. It accepted that a routine commissioning position had been formed despite only very low certainty evidence being available from one retrospective cohort study and three case series. Due to the rarity of the condition, Panel members did not expect there to be any better available evidence of any higher certainty.

Documentation amendments required

Policy Proposition:

- Inclusion criteria –

    - final bullet point states no SOC but a paper suggests otherwise. This needs reviewing. Perhaps have a separate bullet point as some patients may receive have SoC and others may not, due to the nature of the condition.
- Monitoring and stopping criteria -
    - it needs to be is clearer that there is a review at 12 weeks and then continuation of monitoring and treatment until disease progression.

Patient Impact Assessment:

- This needs reviewing to include more detail of the impact of the condition

EHIA:

- Low economic section – this should be reviewed. It is good that this has been recognised but may need more evidence against it.

Blueteq™ Form:

- criterion two could be split into three questions and be reordered.
- The criteria need to be consistent with the wording in the proposition – such as the list of conditions and coding this needs to be the same in both.

Declarations of Interest of Panel Members: None received.

Panel Chair: James Palmer, Medical Director Specialised Services

Actioned amendments

Policy Proposition:

- Inclusion criteria –
    - final bullet point states no SOC but a paper suggests otherwise. This needs reviewing. Perhaps have a separate bullet point as some patients may receive have SoC and others may not, due to the nature of the condition.

      Actioned. Additional sentence added to epidemiology section on page 4 and inclusion criteria bullets separated out for clarity with additional footnote.
- Monitoring and stopping criteria -
    - it needs to be is clearer that there is a review at 12 weeks and then continuation of monitoring and treatment until disease progression.

      Actioned. Requirement for an annual review added to the monitoring criteria.

Patient Impact Assessment:

- This needs reviewing to include more detail of the impact of the condition

  Amended

EHIA:

- Low economic section – this should be reviewed. It is good that this has been recognised but may need more evidence against it.

  The PWG have noted this amendment but do not feel there is any additional evidence that can be added. The Liu et al paper is the largest epidemiological

study of histiocytic neoplasms (specifically Langerhans Cell Histiocytosis) and higher rates of LCH in lower deprived areas was noted in the study.

Blueteq™ Form:

- criterion two could be split into three questions and be reordered.

  Actioned

- The criteria need to be consistent with the wording in the proposition – such as the list of conditions and coding this needs to be the same in both.

  Actioned