NHS ENGLAND SPECIALISED SERVICES

CLINICAL PANEL REPORT

Date: 17th January 2024

Intervention: neoadjuvant vismodegib

Indication: locally advanced basal cell carcinoma (BCC) prior to curative treatment for lesions likely to result in functional sequelae or significant aesthetic sequelae (adults)

URN: 2269

Gateway: 2, Round 1

Programme: Cancer

CRG: Chemotherapy

Information provided to the Panel

Policy Proposition

Evidence Review completed by NICE

Clinical Priorities Advisory Group (CPAG) Summary Report

Evidence to Decision Summary

Equalities and Health Inequalities (EHIA) Assessment

Patient Impact Assessment

Blueteq™ Report

Policy Working Group (PWG) Appendix

This Policy Proposition recommends the use of neoadjuvant vismodegib as a treatment option for locally advanced basal cell carcinoma (BCC) prior to curative treatment for lesions likely to result functional sequelae or significant aesthetic sequelae. Patients must be suitable or potentially suitable for curative treatment at baseline. Vismodegib is an oral tablet which blocks one of the key cell (Hedgehog) signalling pathways that causes BCCs to grow and become locally advanced. It is proposed as an off-label neoadjuvant treatment for a defined period of up to 10 months, prior to treatment with potentially curative surgery and/or radiotherapy. The aim of the treatment is to downstage locally advanced BCC in order to de-escalate the extent of curative treatment required.

The proposition and the supporting evidence review were presented to Panel members. Three studies were included in the evidence review - single-arm non comparative, including 11, 34 and 55 people. No cost effectiveness studies were identified.

The critical outcomes for clinical effectiveness were tumour response downstaging of the surgical procedure and/or reduction in radiotherapy field size, organ-specific preservation and function. Identified important outcomes were reported also, which included relapse rates and quality of life (QoL). The presentation to Panel members covered all elements of the evidence.

There was evidence across all the studies of tumour size reduction compared to baseline in most people. Downstaging of surgical /radiotherapy treatment was reported. One study showed that, of 19 people predicted at baseline to need exenteration, none need exenteration after 12 months treatment of vismodegib, and all 34 people in the study had successful visual function on study completion. All studies reported a reduction in tumour recurrence. Two studies reported some evidence of histological remission after up to 12 months of treatment.
One study provided evidence of statistically significant improvement up to 10 months relating to QoL, using a Skindex-16 score. All studies reported adverse events as a result of the treatment, with some at grade 3.

Limitations of the studies presented were discussed. The evidence presented across all critical and important outcomes was reported as very low certainty using modified GRADE. Panel members discussed the low strength of the evidence but agreed that a clinical benefit can be seen particularly in relation to reduction in tumour size and downstaging of further treatment.

The proposition and supporting documents were considered and some amendments requested. There was quite a bit of debate regarding the table in Annex A of the proposition. Members were informed this is not a validated tool. It was considered to need strengthening as was considered to be open to interpretation as it is currently written, and it was not clear how this added to multidisciplinary team (MDT) decision making.

EHIA – no amendments recommended.
PIA – no amendments recommended.

Recommendation

Clinical Panel agreed with the proposition and recommended this proceeds as a routine commissioning proposition. It was agreed that requested amendments could be reviewed and approved via Chair's action.

Why the panel made these recommendations

The evidence and reported outcomes were considered carefully. Panel members discussed the low strength of the evidence but agreed that a clinical benefit can be seen particularly in relation to reduction in tumour size and downstaging of further treatment.

Documentation amendments required

Policy Proposition:

- Inclusion criteria –
    - Criteria need strengthening, with more detail regarding assessment required.
    - Multidisciplinary team membership – consider including a dermatologist as they see a lot of these patients.
    - Footnote regarding criteria needs to be strengthened as considered to be too loosely worded.
- Dosing – treatment break description needs to align with the wording used within the Blueteq form.
- Page 7 – Patient pathway diagram – Policy Working Group to review as doesn't currently flow well and requires more detail.
- Page 10 Annex A – it is open to interpretation as currently written and should be strengthened/tightened up, particularly in relation to the patient population.

Blueteq™ Form:

- The form will need to be updated in line with any revisions made to the eligibility criteria.

Declarations of Interest of Panel Members: None received.

Panel Chair: James Palmer, Medical Director, Specialised Services

Post Panel Amendments

Policy Proposition		
Panel Comment	**Action Taken**	**Page Number (if applicable)**
Inclusion criteria – ○ Criteria need strengthening, with more detail regarding assessment required. ○ Multidisciplinary team membership – consider including a dermatologist as they see a lot of these patients. ○ Footnote regarding criteria needs to be strengthened as considered to be too loosely worded.	Inclusion criteria strengthened to be more prescriptive and to more accurately describe the basis for what constitutes a functional or significant aesthetic sequalae. The Annex from Bertrand et al. 2021 which was previously suggested as a 'guide' has been removed. This has been strengthened to include the addition of a Consultant Dermatologist as suggested by Panel. In addition, all local MDT referrals will be further ratified by the appropriate subnetwork Specialist Skin Cancer MDT (SSMDT). As previous, Annex A (Bertrand et al. 2021) removed and replaced with strengthened eligibility criteria.	pp.8 (all)
Dosing – treatment break description needs to align with the wording used within the Blueteq form.	Amended to align with Blueteq form. Treatment breaks of up to 6 weeks permitted (standard).	pp. 6
Patient pathway diagram – Policy Working Group to review as doesn't currently flow well and requires more detail.	Amended with further detail.	pp. 7

Annex A – it is open to interpretation as currently written and should be strengthened/tightened up, particularly in relation to the patient population.	As above, Annex A has been removed and replaced with strengthened eligibility criteria that more accurately describe the constituents of functional or significant aesthetic sequalae. This was felt by the PWG to be less subjective than the inclusion of Annex A (Bertrand et al. 2021) and easier to standardise.	N/A
Blueteq Form		
The form will need to be updated in line with any revisions made to the eligibility criteria.	Form updated to align with above amends to eligibility criteria.	N/A