NHS ENGLAND SPECIALISED SERVICES

CLINICAL PANEL REPORT

Date: October 2019

Intervention: Vismodegib

Indication: Multiple basal cell carcinoma (adults)

ID: 1905

Gateway: 2 Round 1

Programme: Cancer

CRG: Chemotherapy

Information provided to the panel

Clinical Panel Report from Gateway 1

Evidence Review undertaken by Solutions for Public Health

Clinical Priorities Advisory Group Summary Report

Policy Proposition

Blueteq® Form

Key elements discussed

This proposition is proposed as for routine commissioning as an off-label use for this intervention.

There is a published Technology Appraisal Guidance for patients with metastatic BCC unsuitable for surgery and excludes patients with Gorlin Syndrome. The policy proposition covers patients with Gorlin Syndrome who have both operable and non-operable BCC.

Clinical Panel discussed the eligible population for this treatment as the focus of this proposition is largely for those patients with Gorlin syndrome, for non-metastatic localised multiple basal cell carcinomas (BCCs). However, the criteria also stated patients without Gorlin syndrome with no more than six BCCs. This needs to be made clearer in the proposition. The Panel considered that it was not clear why this population group was focused on mainly.

Epidemiology – 1:31000 with Gorlin syndrome of whom 90% develop BCCs with increasing age, yet the Policy Working Group (PWG) estimated 30 patients per year in England would be eligible for treatment under this proposition. The Panel could not understand how this figure was derived.

Members discussed the evidence base presented. They noted the definition of inclusion criteria (lesion size) in the Tang et al 2012 randomised controlled trial (RCT). This was not defined in the Dréno et al 2017 study. The Dréno study is referred to in the policy proposition criteria rather than Tang study. Clinical Panel considered that the criteria needed to be evidence based so they need to refer to Tang and not Dréno.

The evidence base did show a reduction in the size and number of and surgery required for BCCs. There was no comparison in the studies with radiotherapy or surgery.

Adverse Events were largely reported as low and medium grade.

The dosing regimen stated within the proposition (intermittent schedule) was questioned. The licensed dose referred to in the Tang et al study was shown to be also effective. The Panel asked that the Policy Working Group (PWG) justify why the dosing regimen used in the Dréno study was chosen over the Tang et al regimen. It was suggested that the dosing regimen stated in the Summary of Product Characteristics (SPC) could be used, even though this is an off-label use.

Some of the wording in the proposition was found to be confusing by Panel and didn't necessarily fit with the evidence base or the criteria.

The Panel reviewed the treatment flow diagram and ask the PWG if radiotherapy should be included?

There was general support for the proposition amongst Panel members however they considered that further work and revisions were required to clarify the eligible population. The evidence base presented was largely focused on those patients within Gorlin syndrome, yet patients without the syndrome and had no more than six BCCs was included. There are two different natural histories for these patient groups. The case is not currently well enough made to cover both populations.

The location of tumours was discussed by the Panel and the number of lesions selected in the proposition. The Panel considered whether the criteria should include whether location of the tumour (eye, face) should be considered a priority.

Recommendation

Clinical Panel recommended that this proposition needs to return to a future Panel meeting for further consideration.

Why the panel made these recommendations

The Clinical Panel considered that the proposition required further revisions.

Documentation amendments required

Policy Proposition:

- Introduction needs to be revised to be clearer why using this in the patient group stated.
- Typo to be corrected in 2nd bullet point, top of page 3 – scraped not scrapped.
- Page 3 'About Vismodegib' section, last sentence in paragraph. Need clearer wording as doesn't match the criteria stated. Doesn't mention metastatic and refers to unsuitable to surgery. Doesn't fit the criteria below. Need to add on this is not supported by NICE guidance and not available the NHS.
- Include prevalence of Gorlin's versus prevalence of BCC.
- Review the stats currently stated for eligible population, clarify the correct numbers.
- Tang criteria stated on Page 12 within the evidence review needs to be used for surgery eligibility.
- Inclusion criteria: combine bullet points 2 and 3 – '…BCCs and appropriate for surgery…'.
- Criterion needed for those with BCCs and not appropriate for surgery.
- PWG to consider tumour location understanding facial lesions involving eye or nose might need higher priority.
- Stopping criteria: Page 9 refers to 'the patient becomes intolerable' – rephrase.

- Page 10 – remove the word placebo from points 1 and 2 and refer to 'treatment break' instead.
- Provide justification for those patients with 6 BCCs (without Gorlin's). PWG to provide advice on the population size over and above the size of the population with Gorlin syndrome. The case needs to be strengthened or split out the populations.
- Intermittent dosing regimen – PWG to justify why the regimen stated is the preferred one to use as this is not reflected in the studies in the evidence base necessarily.
- Review and advise if radiotherapy required to be included in the flow diagram.

Declarations of Interest of Panel Members: None.

Panel Chair: James Palmer, Medical Director

Post Panel Notes and actions undertaken

Policy Proposition:

- Introduction needs to be revised to be clearer why using this in the patient group stated. **Complete, page 2.**
- Typo to be corrected in 2nd bullet point, top of page 3 – scraped not scrapped. **Complete.**
- Page 3 'About Vismodegib' section, last sentence in paragraph. Need clearer wording as doesn't match the criteria stated. Doesn't mention metastatic and refers to unsuitable to surgery. Doesn't fit the criteria below. Need to add on this is not supported by NICE guidance and not available the NHS. **Complete, page 3.**
- Include prevalence of Gorlin's versus prevalence of BCC. **Complete, page 5.**
- Review the stats currently stated for eligible population, clarify the correct numbers. **The number 45 is taken from actual usage; whilst vismodegib was available on the CDF the actual use was approximately 150 patients per year. In an East of England service review, 74 patients were treated with vismodegib, 10 had Gorlins (14%) and 12 had multiple BCCs (16%). So 30% of 150 is 45 patients (approximately half Gorlins and half non Gorlins multiple BCCs). Note vismodegib was available for more indications than within the proposed policy.**
- Tang criteria stated on Page 12 within the evidence review needs to be used for surgery eligibility. **The criteria used in Tang was over a 2 year period and concentrated on prevention rather than treatment. The PWG believe that the Dreno criteria is more appropriate as that study was about treatment rather than prevention and the BCCs needed to be present at baseline**.
- Inclusion criteria: combine bullet points 2 and 3 – '…BCCs and appropriate for surgery…'. **Complete, page 9.**
- Criterion needed for those with BCCs and not appropriate for surgery. **Complete, page 9.**
- PWG to consider tumour location understanding facial lesions involving eye or nose might need higher priority. **This was considered but deemed to bring inequality into the proposal as the evidence does not state that lesions in a certain part of the body respond better than other areas nor is the proposal aimed at reducing disfiguration. The minimum of 6 at presentation with 3 of them being over 5mm, which is based on the evidence, should be sufficient.**
- Stopping criteria: Page 9 refers to 'the patient becomes intolerable' – rephrase. **Complete, page 10.**
- Page 10 – remove the word placebo from points 1 and 2 and refer to 'treatment break' instead. **Complete, page 10.**

- Provide justification for those patients with 6 BCCs (without Gorlin's). PWG to provide advice on the population size over and above the size of the population with Gorlin syndrome. The case needs to be strengthened or split out the populations. **Complete, page 5.**
- Intermittent dosing regimen – PWG to justify why the regimen stated is the preferred one to use as this is not reflected in the studies in the evidence base necessarily. **The intermittent dose regimen had a lower discontinuation level due to adverse events of 23% compared to 54% hence why it has been chosen.**
- Review and advise if radiotherapy required to be included in the flow diagram. **Radiotherapy is contraindicated in Gorlins and relatively contraindicated in multiple BCCs because of potential problems with overlapping treatment fields.**