NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Vismodegib for treating basal cell carcinoma
Draft scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of vismodegib within its marketing authorisation for treating basal cell carcinoma.

Background

Basal cell carcinoma (BCC) is a non-melanoma form of skin cancer that develops in the deep basal cell layer of the epidermis around the hair follicle. It can occur anywhere on the body, but is most common in areas that are exposed to the sun, such as the face, head, neck and ears as well as areas where burns, scars or ulcers have damaged the skin[1, 2]. It can also develop on the back or lower legs and at multiple sites simultaneously. BCC can be cured in most cases and seldom spreads to other parts of the body, although if left untreated for prolonged periods, it can become locally advanced or metastasise, that is, the tumours can grow into deeper layers and affect other tissues such as cartilage and bone.

BCC is the most common type of skin cancer in the UK with around 75% of non-melanoma skin cancers being BCC[1]. It is a slow-growing, locally invasive, malignant epidermal skin tumour predominantly affecting fair skinned adults and is more common in men than women[4, 5] People with Gorlin syndrome also have an increased risk of developing BCCs with around 90% developing cancers at multiple sites. Although it is the most common malignancy worldwide, it is very difficult to estimate the incidence and prevalence of BCC because cases typically have been designated as non-melanoma skin cancers, which include both basal cell and squamous cell skin cancers, and these cases, unlike melanoma, are not required to be reported to cancer registries. Furthermore, there is no standardized staging system for BCC. As a result, the epidemiology and natural history of advanced BCC have been poorly described. Around 98,400 cases of non-melanoma skin cancer were registered in 2011 in the UK; registration however is incomplete with an estimated 30-50% of BCC going unreported[2]. Based on published data the incidence of metastatic BCC is believed to be significantly lower than 0.1% of cases of BCC[3]. Deaths from BCC are very rare.

The main treatment for basal cell carcinoma is surgery and treatment is successful in over 90% of cases[1]. However, in rare cases surgery is not an option or the cancer has metastasised, radiotherapy is commonly used. NICE interventional procedure guidance 155 recommends photodynamic therapy for non-melanoma skin tumours whereas NICE medical technology guidance 6 recommends ambulight photodynamic therapy for the treatment of non-melanoma skin cancer. Vismodegib has been available on the Cancer Drugs

Fund for locally advanced or metastatic BCC where surgery is not an option, and patients must have had radiotherapy unless it was not possible.

The technology

Vismodegib (Erivedge, Roche) is an oral antagonist of the Smo protein involved in activating the Hedgehog signalling pathway that plays a critical role in the development and homeostasis of many organs and tissues. It is administered orally.

Vismodegib has a conditional marketing authorisation in the UK for treatment of adult patients with symptomatic metastatic basal cell carcinoma and locally advanced basal cell carcinoma inappropriate for surgery or radiotherapy.It has been studied in clinical trials in people with locally advanced or metastatic basal cell carcinoma and has mainly been investigated in dose ranging studies without an active comparator.

Intervention(s)	Vismodegib
Population(s)	People with: • symptomatic metastatic basal cell carcinoma or • locally advanced basal cell carcinoma for whom surgery or radiotherapy is not appropriate
Comparators	• Best supportive care
Outcomes	The outcome measures to be considered include: • progression-free survival • overall survival • response rate • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective.

Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	Related Technology Appraisals: None Related Interventional Procedures: Interventional Procedures Guidance No. 478, 2014, 'Electrochemotherapy for primary basal cell carcinoma and primary squamous cell carcinoma'. Interventional Procedures Guidance No. 446, 2013, 'Electrochemotherapy for metastases in the skin from tumours of non-skin origin and melanoma'. Interventional Procedures Guidance No.155, 2006, 'Photodynamic therapy for non-melanoma skin tumours (including premalignant and primary non-metastatic skin lesions).' Related Medical Technology Guidance: Medical Technology Guidance No. 6, 2011, 'Ambulight photodynamic therapy for the treatment of non-melanoma skin cancer'. Related Guidelines: NICE cancer service guidance CSG8,2010,'Improving outcomes for people with skin tumours including melanoma' Related Quality Standards: Skin cancer (including melanoma) - in development. Publication expected: September 2016 http://www.nice.org.uk/guidance/qualitystandards/qualitystandards.jsp Related NICE Pathways: NICE Pathway: Skin cancer, Pathway created: 2015 https://pathways.nice.org.uk/pathways/skin-cancer#content=view-node%3Anodes-basal-cell-carcinoma
Related National Policy	Department of Health (2016) NHS outcomes framework 2016 to 2017 Independent Cancer Taskforce (2015) Achieving world-

	class cancer outcomes: a strategy for England 2015-2020 NHS England (2016) Manual for prescribed specialised services 16/17. Specialist cancer services (adults) 105 (page 228) https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2016/06/pss-manual-may16.pdf NHS England (2013) National cancer drug fund prioritisation scores: vismodegib for patients with advanced basal cell carcinoma (aBCC) who are no longer appropriate for any other treatment options National service framework: Cancer research and treatment, 2016 https://www.gov.uk/government/policies/cancer-research-and-treatment

Questions for consultation

Have all relevant comparators for vismodegib been included in the scope?

- Which treatments are considered to be established clinical practice in the NHS for locally advanced or metastatic basal cell carcinoma?
- Would treatment options vary for locally advanced or metastatic basal cell carcinoma?
- How should best supportive care be defined?
- Would it be suitable to consider topical treatments under best supportive care?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom vismodegib is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider vismodegib will fit into the existing NICE pathway, Skin cancer?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which vismodegib is licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider vismodegib to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of vismodegib can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

References

1. NHS Choices (2014) Skin cancer (non-melanoma). Accessed July 2016.

2. Cancer Research UK, Skin cancer incidence statistics. Accessed July 2016.

3. European Medicines Agency (2013) European Public Assessment Report. Section 2, p. 6.

4. American Cancer Society. Cancer facts and figures. Atlanta (GA): American Cancer Society, Inc. 2007.

5. Pfeiffer P, Hansen O, Rose C. Systemic cytotoxic therapy of basal cell carcinoma. A review of the literature. Eur J Cancer 1990;26: 73−7.