NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Highly Specialised Technology Evaluation

Afamelanotide for treating erythropoietic protoporphyria

Final scope

Remit

To evaluate the benefits and costs of afamelanotide within its licensed indication for treating erythropoietic protoporphyria for national commissioning by NHS England.

Background

The porphyrias are a group of 8 disorders in which chemical substances called porphyrins accumulate. Erythropoietic protoporphyria (EPP) is a genetic storage disorder which is usually caused by the impaired activity of the enzyme, ferrochelatase. EPP results in excessive amounts of protoporphyrin IX in the skin, bone marrow, blood plasma, and red blood cells.[1]

EPP is a cutaneous porphyria, and therefore the major symptom is hypersensitivity of the skin to sunlight and some types of artificial light, such as fluorescent lights, resulting in phototoxicity (a painful chemical reaction under the skin). After a person with EPP is exposed to sunlight, the skin may become swollen, itchy and red and the person may experience an intense burning sensation. The symptoms in response to sunlight typically last for between 2 and 3 days, but can last up to 10 days or longer, leading to severe pain and loss of sleep. The pain is unresponsive to non-opiate analgesics. These symptoms, along with anxiety and social isolation because of sunlight avoidance, can have a profound impact on quality of life. Over time, light exposure can cause thickening of skin on the knuckles and scarring on the face. Some people with EPP may have complications related to liver and gallbladder function.[2]

A study in 2006 suggests there are around 390 patients with EPP in England.[3] Experts suggest that accounting for underdiagnoses may increase the estimates to between 500 to 600 patients in England.

There are no specific pharmacological treatments for EPP. Non-pharmacological options include sunlight avoidance strategies, for example staying indoors, seeking shade during sunny periods, or wearing sunlight blocking clothing. The photosensitivity results from light in the visible spectrum, meaning that most sunscreens (with the exception of light-reflecting substances such as zinc oxide) are of little use. Other treatments for EPP include beta-carotene, activated charcoal and cholestyramine; these treatments are taken orally and are used to stop the porphyrins from being reabsorbed in the body but they are thought to be of limited benefit. Narrow

band UVB therapy is sometimes given in order to build up the skin's resistance to the effects of the sun but again is thought to be of limited use.

The technology

Afamelanotide (Scenesse, Clinuvel UK) activates the synthesis of eumelanin mediated by the MC1R receptor. Eumelanin contributes to photoprotection through strong broad band absorption of UV and visible light, where eumelanin acts as a filter; antioxidant activity; and inactivation of the superoxide anion and increased availability of superoxide dismutase to reduce oxidative stress..

Afamelanotide has a UK marketing authorisation under exceptional circumstances for 'prevention of phototoxicity in adult patients with erythropoietic protoporphyria (EPP)'. It is administered through a subcutaneous dissolving implant.

Intervention(s)	Afamelanotide
Population(s)	Adults with erythropoietic protoporphyria
Comparators	Best supportive care
Outcomes	The outcome measures to be considered include: • duration of tolerance to sunlight and other forms of visible light • phototoxic reactions • change in melanin density • adverse effects of treatment • health-related quality of life (for patients and carers) • mortality
Nature of the condition	• disease morbidity and patient clinical disability with current standard of care • impact of the disease on carer's quality of life • extent and nature of current treatment options

Impact of the new technology	• overall magnitude of health benefits to patients and, when relevant, carers • heterogeneity of health benefits within the population • robustness of the current evidence and the contribution the guidance might make to strengthen it • treatment continuation rules (if relevant)
Value for Money	• cost effectiveness using incremental cost per quality-adjusted life year • patient access schemes and other commercial agreements • the nature and extent of the resources needed to enable the new technology to be used
Impact of the technology beyond direct health benefits	• whether there are significant benefits other than health • whether a substantial proportion of the costs (savings) or benefits are incurred outside of the NHS and personal and social services • the potential for long-term benefits to the NHS of research and innovation • the impact of the technology on the overall delivery of the specialised service • staffing and infrastructure requirements, including training and planning for expertise.
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. Guidance will take into account any Managed Access Arrangements.
Related NICE recommendations and NICE Pathways	None
Related National Policy	**NHS England** NHS England (2013) 2013/14 NHS STANDARD

	CONTRACT FOR METABOLIC DISORDERS (ADULT): PARTICULARS, SCHEDULE 2 – THE SERVICES A. SERVICE SPECIFICATIONS/E06/S/a NHS England (2013) 2013/14 NHS STANDARD CONTRACT FOR SPECIALISED DERMATOLOGY SERVICES (ALL AGES) PARTICULARS, SCHEDULE 2- THE SERVICES, A- SERVICE SPECIFICATIONS A12/S/a **Other policies** Department of Health (2014) NHS outcomes framework 2015-2016 Department of Health (2013) The UK strategy for rare diseases

References

1. Erythropoietic Protoporphyria (EPP) (2008) European Porphyria Network
2. Porphyrias (2015) PatientUK
3. Holme SA, Anstey AV, Finlay AY et al. Erythropoietic protoporphyria in the UK: Clinical features and effect on quality of life. British Journal of Dermatology 2006; 155: 574-581.