NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Difelikefalin for treating pruritus in people having haemodialysis

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of difelikefalin within its marketing authorisation for treating pruritus associated with chronic kidney disease in adults having haemodialysis.

Background

Uraemic pruritus is also known as chronic kidney disease associated pruritus. Uraemia means high levels of urea in the blood, and occurs when the kidneys stop working properly. Pruritus, or itch, commonly affects people with chronic kidney disease. It can be caused by different factors including: dry skin, reduced sweating, abnormal metabolism of calcium and phosphorus, accumulation of toxins, growth of new nerves, systemic inflammation, and co-existing medical problems, particularly diabetes and liver disease.

Pruritus is a chronic, unpleasant symptom that can have a strong negative impact on people's quality of life, often leading to sleeplessness and mood disorders, including depression. The itching can be localised or generalised. When localised, it often occurs in the back, face, and shunt arm. The urge to scratch can result in skin abrasions. It is also associated with a 17% increase in mortality in people having haemodialysis.[1] The prevalence of moderate to severe pruritus in people having haemodialysis in the UK has been estimated to be 50%.[2] Data from the most recent UK Renal Registry report suggests that there are approximately 10,000 people having haemodialysis and with moderate to severe pruritus in the UK.[3]

There are currently no approved treatments for uraemic pruritus. Treatment instead focuses on symptom management and can include topical emollients and antihistamines. Treatments for neuropathic pain may be used off-label.

The technology

Difelikefalin (brand name unknown, Vifor Pharma UK) is a kappa opioid receptor agonist that suppresses itch and inflammation. Activation of kappa opioid receptors on immune cells results in reduced release of nerve-sensitising pro-inflammatory molecules. Difelikefalin does not cross the blood/brain barrier and does not activate central opioid receptors, thereby avoiding risks such as hallucination or opioid addiction.

Difelikefalin does not currently have a marketing authorisation for treating pruritus associated with chronic kidney disease in adults having haemodialysis. It has been studied in clinical trials in people having haemodialysis and with moderate to severe pruritus compared with placebo.

Intervention(s)	Difelikefalin
Population(s)	Adults having haemodialysis with moderate to severe pruritus
Comparators	Established clinical management without difelikefalin
Outcomes	The outcome measures to be considered include: • itching intensity • 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	Chronic kidney disease in adults: assessment and management (2014) NICE guideline 182 Chronic kidney disease in adults (2017) NICE quality standard 5
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Chapter 15 Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1, 2 and 4. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Which treatments are considered to be established clinical practice in the NHS for uraemic pruritus?

Are any treatments for other conditions used off-label to treat pruritus? If so, please specify the treatments and when these might be used.

Are the outcomes listed appropriate? Are there any other outcomes that should be included?

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

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 difelikefalin will be 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 difelikefalin 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 difelikefalin 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.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

References

1) DermNet NZ. Uraemic Pruritus. 2010. Available from: https://dermnetnz.org/topics/uraemic-pruritus/. Accessed February 2021.

2) Pisoni RL, Wikström B, Elder SJ, Akizawa T, Asano Y, Keen ML, et al. Pruritus in haemodialysis patients: International results from the Dialysis Outcomes and Practice Patterns Study (DOPPS). Nephrology Dialysis Transplantation. 2006;21(12):3495-505. Available from: https://doi.org/10.1093/ndt/gfl461. Accessed February 2021.

3) UK Renal Registry. UK Renal Registry 21st Annual Report – data to 31/12/2017, Bristol, UK. . 2019. Available from: https://www.renalreg.org/publications-reports/ Accessed February 2021.

