NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Belzutifan for treating tumours associated with von Hippel-Lindau disease [ID3932]

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of belzutifan within its marketing authorisation for tumours caused by von Hippel-Lindau disease.

Background

VHL is a rare disorder caused by a faulty gene. It affects about 1 in 35,000 people.[1] Tumours develop in one or more parts of the body and may be benign or malignant.[2] Many of these tumours involve the abnormal growth of blood vessels in parts of the body which are particularly rich in blood vessels. Areas most frequently affected are the eyes, the back of the brain (cerebellum), the spinal cord, the kidneys, the adrenal glands and the pancreas.[1] Disease management involves regular and lifelong screening to identify new or changed tumours.[2]

Kidney cancer (renal cell carcinoma [RCC]) affects around 24% to 45% of people with VHL.[3] People with VHL are offered a scan of the kidneys every year to check for tumours. If any are found, they are monitored carefully so people may have treatment at an appropriate time. Minimally invasive localised treatments may be offered to treat smaller tumours while surgery is used for tumours that are larger than 3 cm in diameter. If tumours are detected early and treated before they grow to a size of approximately 3 cm, in nearly every case the tumour will not come back or spread anywhere else in the body.[1]

Central nervous system (CNS) haemangioblastomas are found in the brain and spinal cord. These are the most common tumour type in VHL affecting around 70% of people.[2] These tumours are benign but can cause significant morbidity and mortality. Most tumours can be removed with surgery; however, this may be deferred depending on symptoms.[2]

Pancreatic neuroendocrine tumours (PNETs) affect around 15% people with VHL.[2] Treatment depends upon the size of the tumour. Small tumours are often monitored by regular scans. Larger tumours can usually be removed successfully by surgery.[1]

With regular screening, most tumours associated with VHL are detected at an early stage. For people with advanced or metastatic tumours, systemic treatments are similar to those for patients with cancers unrelated to VHL. Systemic treatments for RCC recommended by NICE include immunotherapies such as nivolumab, ipilimumab and avelumab; kinase inhibitors such as cabozantinib, tivozanib, axitinib, pazopanib, lenvatinib and sunitinib; and the immunosuppressant, everolimus. Combinations of drugs from different classes may be used. For unresectable or metastatic neuroendocrine tumours, NICE TA449 recommends everolimus and sunitinib and NICE TA539 recommmends lutetium (177Lu) oxodotreotide.

The technology

Belzutifan has a marketing authorisation in the UK for the treatment of RCC, CNS haemangioblastomas, or pNETs associated with VHL, where localised procedures are unsuitable or undesirable, in adults.[4]

Intervention	Belzutifan
Population	Adults with untreated renal cell carcinoma, central nervous system haemangioblastomas, or pancreatic neuroendocrine tumours caused by von Hippel-Lindau disease
Comparators	Renal cell carcinoma: • Active surveillance followed by minimally invasive treatments or surgery if required • For advanced or metastatic disease, monotherapy or combination therapy with immunotherapies or kinase inhibitors Central nervous system haemangioblastomas: • Active surveillance followed by surgery or radiotherapy if required Pancreatic neuroendocrine tumours: • Active surveillance followed by surgery if required • For unresectable or metastatic disease, monotherapy with lutetium (177Lu) oxodotreotide or combination therapy with everolimus and sunitinib
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • tumour size reduction • reduction in number of surgical interventions • 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. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability of any managed access arrangement for the intervention will be taken into account.
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	Suspected cancer: recognition and referral (2015, updated 2021) NICE guideline 12 Lutetium (177Lu) oxodotreotide for treating unresectable or metastatic neuroendocrine tumours (2018) NICE technology appraisal guidance 539 Everolimus and sunitinib for treating unresectable or metastatic neuroendocrine tumours in people with progressive disease (2017) NICE technology appraisal guidance 449
Related National Policy	**NHS England** NHS England (2022) National genomic test directory: testing criteria for rare and inherited disease v3 NHS England (2019) The NHS long term plan NHS England (2019) Specialised kidney, bladder and prostate cancer services (adults); Service specification NHS England (2018) Manual for prescribed specialised services 2018/19 Chapter 9 - Adult specialist endocrinology services Chapter 105 – Specialist cancer services (adults) Chapter 131 – Specialist services for complex liver, biliary and pancreatic diseases in adults NHS England (2013) A03/S/a 2013/14 NHS standard contract for specialised endocrinology services (adult) NHS England (2013) E01/S/a 2013/14 NHS standard contract for medical genetics (all ages) NHS England (2013) B13/S/a 2013/14 NHS standard contract for cancer: brain/central nervous system (adult) **Other policy documents**

	Department of Health and Social Care (2016) NHS outcomes framework 2016 to 2017 NHS Digital (2022) NHS Outcomes Framework England, March 2022 Annual Publication

Questions for consultation

Where do you consider belzutifan will fit into the existing care pathway for VHL?

Would belzutifan be a candidate for managed access?

Do you consider that the use of belzutifan can result in any potential 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 committee to take account of these benefits.

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 belzutifan 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.

NICE intends to evaluate this technology through its Single Technology Appraisal process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

References

1. University Hospital Southampton (2019). Available at: https://www.uhs.nhs.uk/Media/UHS-website-2019/Patientinformation/Genetics/Von-Hippel-Lindau-disease-VHL-1438-PIL.pdf. Accessed: 02 August 2022.

2. Patient UK (2022). Available at: https://patient.info/doctor/von-hippel-lindau-disease#:~:text=Von%20Hippel%2DLindau%20(VHL),)%2C%20renal%20cysts%20and%20phaeochromocytoma. Accessed: 02 August 2022.

3. Cancer Therapy Advisor (2022). Available at: https://www.cancertherapyadvisor.com/home/cancer-topics/renal-cell-carcinoma/vhl-and-the-risk-for-renal-cell-carcinoma-in-the-clinic/. Accessed: 2 August 2022

4. MHRA (2022). Available at: https://products.mhra.gov.uk/search/?search=belzutifan&page=1. Accessed 02 August 2022.