NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Belzutifan for previously treated advanced renal cell carcinoma [ID6154]

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of belzutifan within its marketing authorisation for previously treated advanced renal cell carcinoma.

Background

Renal cell carcinoma (RCC) is a cancer that usually originates in the lining of the tubules of the kidney (the smallest tubes inside the nephrons) that help filter the blood and make urine. RCC is the most common type of kidney cancer, accounting for more than 80% of cases.[1] There are several types of RCC. The main ones are clear cell (accounting for around 75% of cases), papillary and chromophobe.[1] RCC is categorised into stages I to IV. Stage I and II includes tumours which are localised to the kidney. Stage III denotes disease that is locally advanced and/or has spread to regional lymph nodes. Metastatic RCC, in which the tumour has spread beyond the regional lymph nodes to other parts of the body, is defined as stage IV.

In 2021, 10,193 new kidney cancer cases were diagnosed in England.[2] Around 39% to 45% were stage III or IV at diagnosis.[3] The 5-year survival is around 75% and 15% for stage III and stage IV disease, respectively.[4]

Current treatment options for untreated advanced RCC include tyrosine kinase inhibitors (TKIs) and PD-1 or PD-L1 immune checkpoint inhibitors. TKIs offered for untreated RCC include sunitinib, pazopanib or tivozanib as recommended by NICE technology appraisal guidance (TA169, TA215 and TA512). In addition, TA645 recommends avelumab with axitinib (a PD-1/PD-L1 inhibitor with a TKI) for use within the Cancer Drugs Fund for untreated advanced RCC. For people with intermediate or poor-risk cancer as defined by the International Metastatic RCC Database Consortium (IMDC), TA542 recommends cabozantinib (a TKI), TA780 recommends nivolumab plus ipilimumab (a PD-1 inhibitor with a CTLA-4 inhibitor) and TA858 recommends lenvatinib with pembrolizumab (a PD-1/PD-L1 inhibitor with a TKI). Cabozantinib with nivolumab is also being appraised by NICE for untreated advanced RCC (ID6186/ID6184).

If the disease progresses and people are fit enough to have further treatment, NICE recommends axitinib (TA333), nivolumab (TA417), cabozantinib (TA463), or lenvatinib plus everolimus (a mammalian target of rapamycin [mTOR] inhibitor) (TA498). If the disease progresses again, people may have, as third-line treatment, whichever of axitinib, nivolumab, cabozantinib or lenvatinib plus everolimus was not used as second-line treatment. Everolimus is also recommended by NICE (TA432) for disease that has progressed after VEGF therapy. Sunitinib, pazopanib (off-label) or tivozanib (off-label) may also be used for previously treated advanced RCC, if not used in the first-line setting.

The technology

Belzutifan (Welireg, Merck Sharp & Dohme) is indicated for treating RCC, central nervous system haemangioblastomas and pancreatic neuroendocrine tumours associated with von Hippel-Lindau disease and for whom localised procedures are unsuitable or undesirable, in adults.

It does not currently have a marketing authorisation in the UK for previously treated advanced RCC. It has been studied in a phase 3 clinical trial as monotherapy compared with everolimus in people with advanced RCC. People in the trial had unresectable, locally advanced or metastatic clear cell renal cell carcinoma, with disease that had progressed after a PD-1/PD-L1 inhibitor and a VEGF-TKI, in sequence or in combination.

Intervention(s)	Belzutifan
Population(s)	People with advanced renal cell carcinoma after a PD-1/PD-L1 inhibitor and a VEGF-TKI
Subgroups	If the evidence allows the following subgroups will be considered. These include: • People with advanced RCC that is intermediate- or poor-risk as defined in IMDC criteria • Prior treatment
Comparators	Established clinical management for advanced RCC without belzutifan, including: • Axitinib • Cabozantinib • Lenvatinib plus everolimus • Everolimus • Sunitinib • Pazopanib (off-label) • Tivozanib (off-label) • Best supportive care
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • 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.
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	**Related Technology Appraisals:** Lenvatinib with everolimus for previously treated advanced renal cell carcinoma (2018) NICE technology appraisal guidance 498 Cabozantinib for previously treated advanced renal cell carcinoma (2017) NICE technology appraisal guidance 463 Nivolumab for previously treated advanced renal cell carcinoma (2016) NICE technology appraisal guidance 417 Axitinib for treating advanced renal cell carcinoma after failure of prior systemic treatment. (2015) NICE technology appraisal guidance 333 Everolimus for advanced renal cell carcinoma after previous treatment. (2017) NICE technology appraisal guidance 432 **Related appraisals in development:** Belzutifan for treating clear-cell renal carcinoma caused by von Hippel-Lindau disease [ID3932] NICE technology appraisal guidance. Publication TBC **Related Guidelines:** Improving outcomes in urological cancers (2002) Cancer service guideline CSG2 **Related Quality Standards:**

	Suspected cancer (2016 updated 2017) NICE quality standard 124
Related National Policy	**NHS England:** NHS England (2019) The NHS long term plan NHS England (2018) Manual for prescribed specialised services 2018/19 Chapter 105 - Specialist cancer services (adults). NHS England (2019) Specialised kidney, bladder and prostate cancer services (Adults). Service specification. Reference: 170114S NHS England (2013) 2013/14 NHS Standard Contract for Cancer: Chemotherapy (Adult). Service specification. Ref: B15/S/a. NHS England (2013) 2013/14 NHS Standard Contract for Cancer: Radiotherapy (All Ages). Service specification. Ref: B01/S/a. **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

Is the population in the scope defined appropriately?

Where do you consider belzutifan will fit into the existing care pathway for advanced RCC? At what line(s) of treatment would belzutifan be used?If belzutifan can be used at different treatment lines, what are the relevant comparators for each?

Have all relevant comparators been included?

Would belzutifan be used after all available PD-1/PD-L1 inhibitors and VEGF therapies have failed or, after treatment with both a PD-1/PD-L1 inhibitor and a VEGF-TKI either in sequence or in combination?

If a VEGF-TKI alone or in combination with an immunotherapy has been used in earlier lines of treatment for advanced renal cell carcinoma, would another TKI be used in later lines in NHS practice?

Is it likely that a patient would not be fit enough for the proposed comparators but fit enough to have belzutifan?

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 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.

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. Cancer Research UK. Kidney cancer types and grades. Accessed 05 February 2024..

2. NHS England Digital. Cancer Registrations Statistics England, 2021 – first release counts only, counts of cancer diagnoses tables. Accessed 05 February 2024.

3. NHS England Digital. Cancer Registrations Statistics England 2021 – first release counts only, cancer incidence by stage. Accessed 05 February 2024.

4. Cancer Research UK. Survival for kidney cancer. Accessed 05 February 2024.