AWTTC
All Wales Therapeutics & Toxicology Centre
Canolfan Therapiwteg a Thocsicoleg Cymru Gyfan

Axitinib (Inlyta®) for the treatment of advanced renal cell carcinoma after failure of prior treatment with pazopanib

January 2019

ONE WALES INTERIM COMMISSIONING DECISION

Axitinib (Inlyta®) for the treatment of adult patients with advanced renal cell carcinoma (RCC) after failure of prior treatment with pazopanib

Date of original advice: August 2016
Date of review: January 2019

The following Interim Pathways Commissioning Group (IPCG) recommendation has been endorsed by health board Chief Executives.

It is the view of the Interim Pathways Commissioning Group (IPCG) that axitinib (Inlyta®) for the treatment of adult patients with advanced renal cell carcinoma after failure of prior treatment with pazopanib should no longer be made available through One Wales Interim Commissioning.

IPCG considered that based on the availability of suitability licensed and health technology-appraisal approved medicines for this indication, axitinib, when used after pazopanib, no longer meets the criteria for One Wales Interim Commissioning.

Patients who are currently receiving axitinib (Inlyta®) for the indication stated above should have the option to continue their therapy until they and their clinicians consider it appropriate to stop.

Individual Patient Funding Request (IPFR) consideration remains appropriate for those patients who are likely to obtain significantly more clinical benefit from the intervention than would normally be expected at a reasonable value for money.

One Wales advice assists consistency of access across NHS Wales.

This is a summary of new evidence available and patient outcome data collected, to inform the review.

Background

Axitinib (Inlyta®) has marketing authorisation for treatment of adult patients with advanced renal cell carcinoma after failure of prior treatment with sunitinib or a cytokine[1]. The National Institute for Health and Care Excellence (NICE) recommends pazopanib as an option for first-line treatment of advanced renal cell carcinoma[2]. The NICE appraisal committee acknowledges that it is not reasonable to limit axitinib use to patients who had received sunitinib as their prior-tyrosine kinase inhibitor as pazopanib is increasingly used in clinical practice[3]. Use of axitinib post-pazopanib is off-label and therefore is not subject to statutory funding.

Current One Wales Interim Commissioning Decision

Axitinib (Inlyta®) can be made available within NHS Wales to treat adult patients with advanced renal cell carcinoma (RCC) after failure of prior treatment with pazopanib where other licensed and health technology appraisal-approved regimens are unsuitable. Reviewed November 2017[4].

Licence status

Axitinib (Inlyta®) for adult patients with advanced RCC after failure of prior treatment with pazopanib is off-label.

Guidelines

There are no changes to the current guidelines.

Licensed alternative medicines/Health Technology Appraisal (HTA) advice for alternative medicines

NICE TA498: Lenvatinib plus everolimus is recommended as an option for treating advanced renal cell carcinoma in adults who have had 1 previous vascular endothelial growth factor (VEGF)-targeted therapy, only if their Eastern Cooperative Oncology Group (ECOG) performance status score is 0 or 1, January 2018[5].

Efficacy/Effectiveness

A literature search by AWTTC (5 October 2018) identified two systematic reviews which have been published, one included a mixed treatment comparison and economic evaluation, and the other a network meta analysis[6,7]. Both reviews include the AXIS study to inform the axitinib arm of the network where first-line VEGF-targeted therapy was sunitinib[6,7]. The AXIS study compared the effectiveness of axitinib versus sorafenib in advanced renal cell carcinoma[8]. Sorafenib is not recommended by NICE for this indication[9]. Clinical expert views have indicated that the tyrosine kinase inhibitors, sunitinib and pazopanib, have similar biochemical activity and are used interchangeably in clinical practice[10], this view is supported by two small prospective studies[11,12].

The first study, a British Medical Journal (BMJ) Technology group systematic review, compared progression-free survival and overall survival in second line treatment of renal cell carcinoma[6]. The systematic review focused on patients who had been previously treated with VEGF-targeted therapies, second-line treatments included for evaluation were: axitinib; cabozantinib; everolimus; nivolumab; sunitinib and best supportive care. A total of 12 studies met the inclusion criteria for the mixed treatment comparison[6].

The primary progression-free analysis was based on two randomised control trials (RCTs) which did not include axitinib. Sensitivity analysis for progression-free survival connected axitinib and sunitinib by including five non-RCTs and a third RCT. This analysis showed statistically significant benefits in progression-free survival for all active treatments compared with best supportive care. Cabozantinib showed statistically significantly better progression-free survival compared to all other treatments including axitinib (hazard ratio [HR] 0.54, 95% credible interval [CrI] 0.40 to 0.76). None of the differences in progression-free survival between sunitinib, everolimus and axitinib were statistically significant[6].

Primary overall survival analysis based on RCT data did not include axitinib[6]. The sensitivity analysis for overall survival included data for treatments with axitinib. Everolimus, cabozantinib, and nivolumab showed longer overall survival compared with axitinib (HR 0.74, 95% CrI 0.56 to 0.99; HR 0.48, 95% CrI 0.34 to 0.71; and HR 0.54, 95% CrI 0.38 to 0.77, respectively). Health-related

quality of life and adverse effects could not be compared using mixed treatment comparison due to heterogeneity of studies[6].

The second systematic review compared progression-free survival and overall survival following VEGF-targeted therapy[7]. Second-line treatment with cabozantinib was compared with everolimus, nivolumab, axitinib, sorafenib and best supportive care. Cabozantinib was found to significantly improve progression-free survival compared to all of the comparators. For overall survival cabozantinib did not show a significant difference with other therapies with the exception of everolimus[7].

A published abstract compared the effectiveness of axitinib and everolimus in 285 patients with metastatic renal cell carcinoma receiving second line therapy after first line pazopanib[13]. There was no statistically significant difference in progression-free survival and overall survival between the two groups[13].

Safety
No new significant safety issues were identified.

Cost effectiveness
Three cost-effectiveness studies have been published since the last review[6,14,15]. Two reflect use in the NHS in England and one in Scotland. All three studies used the AXIS study to inform the axitinib arm, where sunitinib was the VEGF-targeted therapy. A 30-year time horizon was used in all three studies[6,14,15]. The BMJ Technology Assessment Group report described in the efficacy section above also provides an economic evaluation reflective of the NHS in England[6]. In this report the base-case analysis showed that cabozantinib was the most effective treatment with 1.87 quality-adjusted life-years (QALYs). Nivolumab accrued 1.60 QALYs which was better than everolimus and axitinib (both accrued 1.31 QALYs). Best supportive care accrued 0.75 QALYs over the same time horizon. The differences in results were largely driven by differences in overall survival. When calculating the incremental cost effectiveness ratio (ICER) it was found that everolimus dominated axitinib as it was cheaper (based on list price) but had similar efficacy (same number of QALYs). Nivolumab was dominated by cabozantinib due to cost and efficacy. This left everolimus which had an ICER of £45,000 per QALY when compared with best supportive care and cabozantinib which had an ICER of £126,000 per QALY when compared with everolimus. The key drivers in the deterministic one-way sensitivity analyses were overall survival and relative dose intensity (RDI), the proportion of patients receiving the planned dose of the medicine as per protocol. If the lower range of the RDI for axitinib or the upper range of the RDI for everolimus was used then axitinib became more preferable than everolimus. As with the base case, in scenario analyses axitinib was dominated by everolimus in all scenarios including varying the distributions applied for overall survival[6].

In a comparison of the cost-effectiveness of cabozantinib versus everolimus, axitinib and nivolumab in NHS England the base-case analysis reported health gains of 1.78 QALYs for cabozantinib, 1.64 QALYs for nivolumab, and 1.4 QALYs for both axitinib and everolimus[15]. The base-case ICER for cabozantinib versus axitinib was £98,967 per QALY and for cabozantinib versus everolimus was £137,450 per QALY. Cabozantinib was dominant (less costly and more effective) compared with nivolumab[15].

A conference abstract reports on the comparative cost-effectiveness of cabozantinib, everolimus and axitinib from a Scottish perspective[14]. The base-case analysis reported health gain results for cabozantinib only at 2.21 QALYs. The ICERs for cabozantinib compared to axitinib and everolimus were £97,224 per QALY and £115,473 per QALY, respectively[14].

There are confidential patient access schemes in place for these medicines which provide them on the NHS at a reduced price. In all three cost-effectiveness analyses list prices were used in the models and therefore may not reflect the current situation in the UK and should be considered in that context[6,14,15].

Budget impact
No information on patient numbers has been received. Cost data from the Medusa database for the 12 month period after the original One Wales decision (August 2016) was 26% lower than that estimated in the One Wales evidence status report[10]. For the same period in 2017/18 the total spend on axitinib was 31% lower than the previous year. This decrease in prescribing follows NICE

positive recommendations for: nivolumab in November 2016; everolimus in February 2017; cabozantinib in August 2017; and lenvatinib with everolimus in January 2018[5,16-18].

Impact on health and social care services
No new information has been provided.

Patient outcome data
No patient outcome data have been received.

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