

Committee to Evaluate Drugs (CED)

Recommendations and Reasons

Document Posted: May 2015

Pazopanib as first-line therapy in metastatic renal cell carcinoma

Product: Pazopanib (Votrient®)

Class of Drugs: tyrosine kinase inhibitor (TKI)

Reason for Use: first-line therapy in metastatic renal cell carcinoma (mRCC)

Manufacturer: GlaxoSmithKline Inc.

Date of Review: September 11, 2013

CED Recommendation

The CED recommended that pazopanib (Votrient®) be funded as a first-line therapy in metastatic renal cell carcinoma according to specific criteria. The CED noted that pazopanib has similar efficacy as the existing standard first-line treatment and it represents an added therapeutic option for patients.

Executive Officer Decision*

Based on the CED's recommendation and an agreement with manufacturer, the Executive Officer decided to fund pazopanib (Votrient®) through the Ontario Drug Benefit's (ODB) Exceptional Access Program for first-line therapy in metastatic renal cell carcinoma according to specific criteria.

Funding Status*

Funded through the ODB's Exceptional Access Program (EAP) according to specific criteria.

(EAP criteria can be found at: http://www.health.gov.on.ca/en/pro/programs/drugs/eap_criteria.aspx)

** This information is current as of the posting date of the document. For the most up-to-date information on Executive Officer decision and funding status, see: www.health.gov.on.ca/en/pro/programs/drugs/status_single_source_subm.aspx.*

Highlights of Recommendation:

- Pazopanib is an oral anti-cancer drug and is already funded through the ODB's Exceptional Access Program for the treatment of metastatic renal cell carcinoma (mRCC) for patients who are unable to take sunitinib, which is considered the usual standard of care for mRCC. This CED review considered the use of pazopanib as an initial treatment option for mRCC.
- The COMPARZ study showed that pazopanib was non-inferior to (i.e., not worse than) sunitinib, with respect to progression-free survival (PFS). Furthermore, the COMPARZ and PISCES studies suggested that patients preferred taking pazopanib since certain side effects experienced with sunitinib were less frequent with pazopanib.
- At the recommended dose of 800 mg per day, the average cost per 28-day course of pazopanib is approximately \$4,000. At the list price, pazopanib is less expensive than sunitinib.
- Overall, based on the results of the COMPARZ study, pazopanib was found to be non-inferior to (i.e., not worse than) sunitinib with respect to PFS. Sunitinib can cause significant side effects in some patients, and since the side effect profile of pazopanib differs from that of sunitinib, pazopanib would offer an alternative treatment choice for patients.

Background:

In Canada, kidney cancers account for approximately 3% of all cancers. About 90% of kidney cancers consist of renal cell carcinomas (RCC), of which approximately 80% of them are of clear-cell histology. Approximately 75% of newly diagnosed patients with RCC have localized disease. About 25% of RCCs are metastatic at the time of diagnosis and approximately 30-50% of patients, who are initially diagnosed with localized disease, will eventually relapse and metastasize.

Conventional chemotherapy and radiation are typically not effective for metastatic RCC (mRCC). Historically, immunotherapy with cytokines was the treatment of choice for mRCC, although clinical benefit was seen in only a small group of patients. Tyrosine kinase inhibitors (TKIs) have replaced immunotherapy as the standard treatment for patients with mRCC. The use of TKIs is limited by their side effects. For mRCC, the first choice of treatment has been a TKI called sunitinib.

Detailed Discussions:

- For this evaluation, the CED took into consideration:
 - Findings from the pan-Canadian Oncology Drug Review (pCODR) and the recommendation of the pCODR Expert Review Committee.
 - Information in the manufacturer's submission.
 - A patient group submission to pCODR.
 - Feedback from Cancer Care Ontario's Genitourinary Disease Site Group.
- The CED evaluated two randomized controlled trials, COMPARZ and PISCES. COMPARZ was a non-inferiority study designed to compare pazopanib to sunitinib, whereas PISCES was a patient preference study.

- The primary outcome of the COMPARZ study was progression free survival (PFS). Based on the results of the COMPARZ study, pazopanib was demonstrated to be non-inferior to sunitinib with respect to PFS (HR 1.05; 95% CI 0.90 – 1.22) in the intention-to-treat analysis. *(An intention-to-treat analysis is an assessment of the people taking part in a clinical trial, based on the group they were initially, and randomly, allocated to. This is regardless of whether or not they dropped out, fully adhered to the treatment or switched to an alternative treatment. Intention-to-treat analyses are often used to assess clinical effectiveness because they mirror actual practice: not everyone adheres to the treatment, and the treatment people receive may be changed according to how their condition responds to it.)*
- Health-related quality of life (QOL) was evaluated in both COMPARZ and PISCES. Although pazopanib appeared to be preferred by patients, there were difficulties relating to the interpretation and timing of the QOL data collection which may have affected the results.
- While both pazopanib and sunitinib have side effects, the adverse event profile differs for each product. Pazopanib appeared to be tolerable, and certain side effects experienced with sunitinib were less frequent with pazopanib.
- The CED also discussed the use of pazopanib in patients whose disease has progressed after using sunitinib. It was noted that there are no studies evaluating pazopanib in these patients, and the usual second-line treatment of advanced or metastatic renal cell carcinoma is everolimus.
- At the recommended dose of 800 mg per day, the average cost per 28-day course of pazopanib is approximately \$4,000. At the list price, pazopanib is less expensive than sunitinib.
- The CED considered a patient group submission received by pCODR. The patient submission highlighted the impact of the disease and patients' wishes for a treatment that offers a different side effect profile than sunitinib.
- Overall, based on the results of the COMPARZ study, pazopanib was found to be non-inferior to sunitinib with respect to PFS. Sunitinib can cause significant side effects in some patients, and since the side effect profile of pazopanib differs from that of sunitinib, pazopanib would offer an alternative treatment choice for patients.

Committee to Evaluate Drugs (CED)

The Committee to Evaluate Drugs (CED) is comprised of practicing physicians, pharmacists, health economists, and patient representatives. In conducting its review, the CED considers data contained in the drug manufacturer's submission, input provided by patient groups, findings from the national Common Drug Review and the pan-Canadian Oncology Drug Review, and other scientific information as necessary.

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