Committee to Evaluate Drugs (CED)

Recommendations and Reasons

Document Posted: May 2015

Abiraterone

Product: abiraterone (Zytiga®)

Class of Drugs: androgen biosynthesis inhibitor

Reason for Use: metastatic castration-resistant prostate cancer (mCRPC)

Manufacturer: Janssen Inc.

Date of Review: November 13, 2013

CED Recommendation

The CED recommended abiraterone (Zytiga®) not be funded for the treatment of metastatic castration-resistant prostate cancer (mCRPC) in patients with none or mild symptoms after failure of androgen deprivation therapy (ADT). The CED noted that while studies suggest abiraterone does not improve overall survival, the drug may provide some clinical benefits considered important to patients. This treatment is not cost-effective at the submitted price.

Executive Officer Decision*

Based on the CED's recommendation and an agreement with the manufacturer to help address concerns raised by the CED, the Executive Officer decided to fund abiraterone (Zytiga®) for the treatment of mCRPC in patients with none or mild symptoms after failure of ADT through the Ontario Drug Benefit's (ODB) Exceptional Access Program 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.*

Ontario

Highlights of Recommendation:

- Abiraterone is an androgen biosynthesis inhibitor that is used in combination with prednisone for the treatment of metastatic castration-resistant prostate cancer (mCRPC). Abiraterone is already funded for use in the later stages of mCRPC following chemotherapy. This review examined the funding of abiraterone in mCRPC patients with none or mild symptoms after failure of androgen deprivation therapy (ADT).
- The CED reviewed one study, COU-AA-302. The study showed that abiraterone plus prednisone, compared to prednisone alone, improved progression-free survival (as shown on x-ray), but not overall survival, in mCRPC patients with none or mild symptoms who had failed ADT but had not received prior chemotherapy.
- The study also showed that abiraterone plus prednisone improved other outcomes such quality of life, median time to decline in functional status, median time to opiate use, prostate specific antigen (PSA) response, and median time to PSA progression.
- The overall safety of abiraterone in the study was acceptable.
- At the recommended dose, the average cost per 28-day course of abiraterone is $3,173. Based on economic analyses conducted by the manufacturer and by the pan-Canadian Oncology Drug Review, abiraterone was not considered cost-effective.

Background:

Prostate cancer is the most commonly diagnosed cancer in Canadian men. Treatment options for localized prostate cancer include removal of the prostate, radiation therapy, or active surveillance for patients with lower risk disease. There is no clear evidence that one treatment modality is superior in efficacy.

Despite treatment, some patients develop recurrent disease as evidenced by an increase in prostate specific antigen with or without metastases. Standard first-line therapy for recurrence remains androgen deprivation therapy (ADT). The majority of patients initially respond to ADT but almost all eventually go on to develop castration resistant prostate cancer (CRPC).

For those with metastatic CRPC (mCRPC) who are asymptomatic or minimally symptomatic, secondary treatment (i.e., chemotherapy) is often used, although no survival benefit has been demonstrated. Such treatment is palliative, and eventually all patients develop progressive disease.

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;
    - Submission from one patient group.
- The CED evaluated one double-blind, placebo-controlled, phase III randomized trial, the COU-AA-302 study, that evaluated the efficacy and safety of abiraterone (1000 mg orally

once daily) plus prednisone (5mg twice daily) compared to placebo plus prednisone (5mg twice daily), in patients with asymptomatic or mildly symptomatic mCRPC who had failed ADT and had not received prior chemotherapy.

- Radiographic progression-free survival (rPFS) was a co-primary endpoint of the study. A statistically significant improvement in median rPFS was observed at the second interim analysis for the abiraterone group compared to the placebo group (16.5 months versus 8.3 months, HR = 0.53, 95% CI 0.45 to 0.62, $p<0.0001$).
- Overall survival (OS) was also a co-primary endpoint. Statistical significance was not reached at either the second or third interim analysis of OS. Unblinding and crossover of patients from placebo to abiraterone was permitted after the second interim analysis and this may have impacted overall survival estimates.
- There was a consistent and statistically significant benefit observed in several secondary outcomes, such as quality of life (except in one category of measurement), median time to decline in functional status, median time to opiate use, prostate specific antigen (PSA) response and median time to PSA progression.
- The most frequent adverse events seen with abiraterone included arthralgia, nausea and constipation.
- At the recommended dose of 1000 mg per day, the average cost per 28-day course of abiraterone is $3,173. Based on economic analyses conducted by the manufacturer and by pCODR, abiraterone was found to be not cost-effective.
- The Committee considered one patient group submission. The patient submission highlighted the impact of the disease and patients' wishes for treatments that maintained quality of life while delaying the onset of symptoms and the need for chemotherapy.
- Overall, the results of the COU-AA-302 study demonstrated that abiraterone plus prednisone improves rPFS when compared to prednisone alone. Although there was no OS advantage seen with abiraterone at either the second or the third interim analysis, it was noted that there were improvements in a number of other secondary endpoints that are considered important to patients. However, abiraterone was not considered to be cost-effective in this treatment setting.

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.

For more information, please contact:

Ministry of Health and Long-Term Care

Ontario Public Drug Programs

Hepburn Block, 9th Floor

80 Grosvenor Street, Queen's Park

Toronto, Ontario M7A 1R3

www.health.gov.on.ca/en/pro/programs/drugs/