

Committee to Evaluate Drugs (CED)

Recommendations and Reasons

Document Posted: January 2016

Vismodegib

Product: vismodegib (Erivedge®)

Class of Drugs: hedgehog inhibitor

Reason for Use: metastatic or locally advanced basal cell carcinoma

Manufacturer: Hoffmann-La Roche Ltd.

Date of Review: January 15, 2014

CED Recommendation

The CED recommended vismodegib (Erivedge®) be funded for the treatment of metastatic or locally advanced basal cell carcinoma in patients who are inappropriate for surgery or radiotherapy. Although there are some limitations with the clinical trial evidence and the drug is not cost-effective, the Committee acknowledged that vismodegib has been shown to provide a positive clinical response in reducing tumour size and few other treatment options exist.

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 vismodegib 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.*

Highlights of Recommendation:

- The ERIVANCE study showed that the use of vismodegib was associated with tumour response (reduction in tumour size) in patients with metastatic basal cell carcinoma (mBCC) or locally advanced basal cell carcinoma (laBCC) who were inappropriate for surgery or radiotherapy.
- Because ERIVANCE was a non-randomized, non-comparative phase II study, there was considerable uncertainty around the magnitude of the observed treatment benefit.
- It was not possible to interpret the study results on patients' quality of life due to missing data and the absence of a control group in the trial.
- In the study, 25% of patients experienced serious adverse events.
- At the recommended dose, the average cost per 28-day course of vismodegib is \$8238. Based on economic analyses conducted by the pan-Canadian Oncology Drug Review, the treatment was not considered cost-effective.
- The Committee recognized that mBCC or laBCC is a devastating disease and patients who are not eligible for surgery or radiotherapy have limited treatment options.

Background:

Basal cell carcinoma (BCC) is a type of skin cancer. It usually develops on sun-exposed parts of the body, especially the head and neck. In the vast majority of cases, BCC is localized and can be successfully managed with surgery or radiotherapy. Although rare, the condition has the potential to progress to locally advanced or metastatic disease (laBCC or mBCC). For patients with laBCC or mBCC in whom surgery and radiation have been deemed inappropriate, there are no established standard treatments.

Detailed Discussions:

- For this evaluation, the CED considered:
 - Findings from the pan-Canadian Oncology Drug Review (pCODR) and the recommendation of the pCODR Expert Review Committee;
 - Information in the manufacturer's submission;
 - Patient input received by pCODR;
 - Input from a clinical expert who treat BCC.
- There are no randomized controlled trials evaluating vismodegib in the treatment of metastatic basal cell carcinoma (mBCC) or locally advanced BCC (laBCC).
- The CED evaluated one non-randomized, non-comparative phase II trial, ERIVANCE, in patients with mBCC or laBCC who were inappropriate for surgery or radiotherapy. In the study, 22% of patients had Gorlin syndrome, a genetic condition that often causes BCC.
- The primary outcome of ERIVANCE was objective response assessed by an independent review committee, defined as a $\geq 30\%$ reduction in the externally visible or radiographic dimension.

- Objective response rates (ORR) were 43% (95% CI: 16-48%) and 30% (95% CI: 30-56%) in patients with laBCC and mBCC, respectively. In both cases, the ORR exceeded the pre-defined criteria for a minimally acceptable response (20% and 10%, respectively). The ORR results were considered to be meaningful. No patients with mBCC had a complete response, while 21% of patients with laBCC had a complete response.
- In a post-hoc analysis of the subgroup of patients with Gorlin syndrome, ORR was 67% (95% CI: 45%-85%) compared to 30% (95% CI: 19%-46%) in the other patients with laBCC. The observed benefit in patients with Gorlin syndrome was considered substantial.
- Because ERIVANCE was a non-randomized, non-comparative phase II study, there was considerable uncertainty around the magnitude of the observed treatment benefit.
- Although some quality of life data were collected in ERIVANCE, the large amount of missing data and the lack of a control group made the quality of life results impossible to interpret.
- It was noted that 25% of patients in the study experienced serious adverse events. Dose reduction was not an option since vismodegib is available only in one format (i.e., 150 mg capsules) and the appropriateness of alternative dosing schedules is unknown. Vismodegib is teratogenic and there are prescribing restrictions in place to limit the exposure to this risk.
- The STEVIE study is an ongoing, single-arm, non-randomized, safety study evaluating the use of vismodegib in patients with laBCC and mBCC. The data from STEVIE have not been published.
- At the list price, vismodegib costs \$294 per 150 mg capsule. At the recommended dose of 150 mg daily, the cost per 28-day course is \$8,238. Based on economic analyses conducted by the pan-Canadian Oncology Drug Review, the treatment was not considered cost-effective.
- The CED reviewed a patient group submission received by pCODR. The patient submission highlighted the impact of the disease and patients' wishes to avoid recurring surgeries. Patients prefer non-invasive treatments.
- Overall, vismodegib has been shown to provide tumour response in patients with laBCC or mBCC who are inappropriate for surgery or radiotherapy. Because ERIVANCE was a non-randomized, non-comparative phase II study, there was considerable uncertainty around the magnitude of the observed treatment benefit. Vismodegib was not considered to be cost-effective. The Committee acknowledged that mBCC or laBCC is a devastating disease and patients who are not eligible for surgery or radiotherapy could benefit from vismodegib.

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/