

Committee to Evaluate Drugs (CED)

Recommendations and Reasons

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Dimethyl fumarate

Product: Dimethyl fumarate (Tecfidera®)

Class of Drugs: central nervous system agent

Reason for Use: relapsing-remitting multiple sclerosis (RRMS)

Manufacturer: Biogen Idec Canada Inc.

Date of Review: October 9, 2013

CED Recommendation

The Committee recommended that dimethyl fumarate (Tecfidera®) be funded for the treatment of relapsing-remitting multiple sclerosis (RRMS) according to specific criteria. The Committee noted that dimethyl fumarate has been shown to reduce relapse rates in RRMS but the drug is not cost-effective as an initial treatment option.

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 dimethyl fumarate (Tecfidera®) through the Ontario Drug Benefit's (ODB) Exceptional Access Program for the treatment of relapsing-remitting multiple sclerosis (RRMS) 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:

- Two placebo-controlled randomized trials, DEFINE and CONFIRM, showed that dimethyl fumarate reduced relapses in patients with RRMS.
- There are no head-to-head comparison studies evaluating the efficacy and safety of dimethyl fumarate relative to other drug therapies for RRMS.
- The manufacturer submitted a confidential price for dimethyl fumarate. At the publicly listed price, dimethyl fumarate costs \$23,000 per year. An economic assessment showed that dimethyl fumarate is not a cost-effective first-line treatment option for RRMS.
- Overall, dimethyl fumarate has been shown to reduce relapse rates in RRMS but the drug is not cost-effective as an initial treatment option.

Background:

Multiple sclerosis (MS) is a progressively disabling disease that destroys the protective myelin sheath that surrounds nerves in the central nervous system (CNS). This gradual loss of myelin impairs nerve conduction and leads to disorders in movement, sensation, cognition, resulting in substantial disability.

Four different types (or patterns of progression) of MS are generally recognized: relapsing-remitting (RRMS); primary progressive MS; secondary progressive MS; and progressive relapsing MS.

A number of different drug treatments are currently available for RRMS. Dimethyl fumarate (Tecfidera®) is a new oral treatment.

Detailed Discussions:

- For this evaluation, the CED took into consideration:
 - Findings from the Common Drug Review (CDR) and the recommendation of the Canadian Drug Expert Committee;
 - Information in the manufacturer's submission;
 - A patient group submission.
- The CED reviewed two randomized controlled trials, DEFINE and CONFIRM. The results of the trials demonstrated that the proportion of patients who were relapse-free after two years of treatment with dimethyl fumarate was statistically greater versus placebo. Moreover, the annualized relapse rate was also statistically lower with dimethyl fumarate compared with placebo.
- Statistically fewer dimethyl fumarate patients experienced disability progression compared to placebo in DEFINE but not in CONFIRM. The reason for this difference is unclear.
- The Committee noted that because dimethyl fumarate is a chronic treatment, longer term safety data beyond the two years examined in DEFINE and CONFIRM would be valuable.
- There are no head-to-head comparison studies between dimethyl fumarate and alternative treatments for RRMS; therefore, the efficacy and safety of dimethyl fumarate relative to other treatment options are unknown.

- The CED considered a patient submission received by CDR. The patient submission highlighted the impact of the disease and patients' preference for oral medication.
- The manufacturer submitted a confidential price for dimethyl fumarate. At the public list price, the annual cost of dimethyl fumarate is \$23,000, which is more expensive than some of the other treatments for RRMS. Economic analyses showed that dimethyl fumarate is not a cost-effective first-line treatment for RRMS.
- Overall, two placebo-controlled randomized studies demonstrated statistically significant decreases in relapses in RRMS with dimethyl fumarate. A significantly lower rate of disability progression with dimethyl fumarate compared to placebo was also demonstrated in one of the trials. However, dimethyl fumarate is not as cost-effective as some of the existing treatment options for RRMS.

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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