Mesalamine (5-aminosalicylic acid, 5-ASA)

Product:
MESALAMINE (Mezavant®)
1.2g delayed and extended release tablet

Class of drugs:
Gastrointestinal anti-inflammatory agent

Indication:
Treatment of mild to moderate ulcerative colitis

Manufacturer:
Shire Canada Inc.

CED Recommendation-

The CED recommended that mesalamine (Mezavant®) 1.2g delayed- and extended-release tablet not be listed on the Ontario Drug Benefit Formulary nor be reimbursed through the Exceptional Access Program, on the basis of insufficient evidence to show improved efficacy or better safety compared to currently available alternatives, and the price premium is not justified.

Executive Officer Decision

Taking into consideration the CED's recommendation and a subsequent lisiting agreement with the manufacturer that addresses price, the Executive Officer decided to list mesalamine (Mezavant®) on the Ontario Drug Benefit Formulary as General Benefit.

Status

Funding available through the Ontario Public Drug Programs.

Highlights of Recommendation:

- Mezavant 1.2g is a higher-strength, delayed and extended-release tablet formulation of mesalamine, a drug also known as 5-aminosalicylic acid (5-ASA).
- The drug is indicated for the treatment of active, mild to moderate ulcerative colitis (UC), and when effective can lead to a remission the disease.
- This formulation allows patients to take it once a day, reducing the number of pills that patients currently have to take.
- Other formulations of 5-ASA products are already listed on the Ontario Drug Benefit Formulary, including Asacol®, Mesasal®, Pentasa® and Salofalk®.
- The CED examined several studies which demonstrated this delayed and extended-release formulation of 5-ASA once a day is effective for inducing a remission in patients with mild to moderate ulcerative colitis.
- The results of two published studies indicate there was no difference in once-daily dosing compared to twice-daily dosing, and that a total dose of 2.4g per day is as effective as a total dose of 4.8g per day.
- **Overall, the CED noted that Mezavant is an effective and safe 5-ASA product. However, there is no evidence to suggest a therapeutic or safety advantage over other 5-ASA products that can justify the added price premium. The CED recommended Mezavant not be funded.**

Background:

Ulcerative colitis (UC) is a form of inflammatory bowel disease, along with Crohn's disease. It is a chronic, relapsing-remitting inflammatory disease of the colon and rectum. Patients may experience abdominal pain, bloating, diarrhea and bloody stools. Ulcerative colitis is designated as mild, moderate, severe or in remission, depending on the severity and number of symptoms present.

Mesalamine, a form of 5-aminosalicylic acid (5-ASA), is a gastrointestinal agent commonly used to induce and maintain remission for patients with mild to moderate ulcerative colitis. Other classes of drugs such as corticosteroids, immunosuppressants and anti-TNF agents are typically used for patients with more severe ulcerative colitis or for patients who do not continue to be in remission on 5-ASA.

Mezavant delayed and extended-release tablets use new technology to delay and extend the release of 5-ASA in the colon. The active part of the drug is slowly released in the colon, where the disease is more active, instead of the less acidic areas of the stomach and small bowel.

continued...

Detailed Discussion:

- Mezavant is a delayed and extended release tablet containing high-dose 5-ASA indicated for once daily dosing in mild to moderate ulcerative colitis.
- The manufacturer submitted several published and unpublished trials to support the efficacy. The CED considered two published multicentre randomized trials:
    - Lichtenstein et al. *Clin Gastroenterol Hepatol*. 2007;5:95-102.
    - Kamm et al. *Gastroenterol* 2007;132:66-75.
- The manufacturer does not permit the Ministry to share the details of the unpublished, proprietary information.
- The Lichtenstein trial is a randomized, double-blind, placebo-controlled trial of 8 weeks treatment with Mezavant, comparing one tablet (1.2g) twice daily to four tablets (4.8g) once daily and to placebo. This trial demonstrated that Mezavant was more effective than placebo in achieving clinical and endoscopic remission of ulcerative colitis.
- The Kamm trial is a randomized, double blind, placebo- and active-controlled study of 8 weeks duration comparing Mezavant two tablets (2.4g) once daily and Mezavant four tablets (4.8g) once daily to placebo and two Asacol 400mg tablets three times daily (total of 2.4g/ day). The results showed that patients in both dosage groups of Mezavant achieved clinical and endoscopic remission versus placebo, but patients in the standard dose Asacol treatment group did not. Patients tolerated Mezavant as well as placebo and Asacol.
- The results of these trials indicate no difference in once-daily dosing compared to twice-daily dosing and the total dose of 2.4g per day is as effective as the total dose of 4.8g per day for the induction of remission in patients with mild to moderate UC. According to the Kamm trial, it appears that once-daily dosing of Mezavant is more efficacious than the standard dosing of Asacol.
- The CED noted the problem with compliance and high pill burden associated with current 5-ASA products, where patients may need to take 6 to 16 tablets of other 5-ASA products to achieve the same results. Non-compliance with therapy may be associated with relapses, which require additional health care resources and/or treatment with corticosteroids, immunosuppressants or potentially, anti-TNF agents.
- Mezavant costs more than many of the available 5-ASA alternatives on the ODB Formulary/CDI. The convenience of once-daily dosing may substantially increase the use of Mezavant over other 5-ASA products; therefore, listing this product at the submitted price may have an excessive budgetary impact.
- **Overall, the CED noted there was insufficient evidence to demonstrate that Mezavant has any efficacy or safety advantage over other 5-ASA products on the ODB Formulary to warrant its price premium. The CED recommended that Mezavant not be listed in the ODB Formulary nor be reimbursed through the Exceptional Access Program (EAP).**

CEDAC Recommendation:

(http://www.cadth.ca/index.php/en/cdr/recommendations)

The Canadian Expert Drug Advisory Committee (CEDAC) did not review this product.

Ontario
Ministry of
Health and Long-Term Care
Ontario Public Drug Programs

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
or click: http://www.health.gov.on.ca/english/providers/program/drugs/ced_rec_table.html