

Committee to Evaluate Drugs (CED)

Recommendations and Reasons

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Ocriplasmin

Product: ocriplasmin (Jetrea®)

Class of Drugs: recombinant proteolytic plasmin

Reason for Use: symptomatic vitreomacular adhesion (VMA)

Manufacturer: Alcon Canada Inc.

Date of Review: January 15, 2014

CED Recommendation

The CED recommended ocriplasmin (Jetrea®) not be funded for the treatment of symptomatic vitreomacular adhesion (VMA). Ocriplasmin was shown to improve VMA resolution rates compared with placebo. The long-term effectiveness of ocriplasmin is unknown and the drug is not cost-effective. The CED noted that the current surgical treatment alternative, vitrectomy, is an invasive procedure with significant post-operative care burden.

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 ocriplasmin (Jetrea®) on the Ontario Drug Benefit Formulary as a Limited Use Benefit.

Funding Status*

Funded on the Ontario Drug Benefit Formulary as a Limited Use Benefit.

** 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 clinical trials, TG-MV-006 and TG-MV-007, showed that vitreomacular adhesion (VMA) resolved in a greater proportion of patients treated with ocriplasmin compared with patients given placebo. The resolution rates were 27.9% in one study and 25.3% in the other.
- The two studies failed to show meaningful improvements in patients' quality of life.
- There are no head-to-head trials comparing ocriplasmin to the standard of care for VMA (watchful waiting and surgery). Long-term data on the effectiveness and safety of ocriplasmin are lacking.
- At the submitted price, ocriplasmin costs \$3,950 per single-use vial. Ocriplasmin was not considered to be cost-effective.

Background:

Vitreomacular adhesion (VMA) is a rare eye condition caused by an incomplete detachment of the posterior vitreous from the macula. Stretching and distortion of the macula may occur, resulting in irreversible visual deterioration and blindness.

The current standard of care is “watchful waiting” and vitrectomy (surgical removal of the vitreous from the eye). Vitrectomy has a high success rate, but it is an invasive procedure and is typically only recommended for patients who have clinically significant visual loss.

Detailed Discussions:

- For this evaluation, the CED considered:
 - Findings of the Common Drug Review (CDR) and the recommendation of the Canadian Drug Expert Committee (CDEC);
 - Information in the manufacturer's submission;
 - Submissions from two patient groups received by CDR;
 - Input from a clinical expert in vitreomacular adhesion (VMA).
- The CED evaluated two double-masked randomized controlled trials, TG-MV-006 and TG-MV-007. In both studies, a higher proportion of patients achieved the primary outcome of resolution of VMA at day 28 with ocriplasmin compared with placebo. The resolution rates were low (27.9% and 25.3% in TG-MV-006 and -007, respectively). The proportion of patients who achieved resolution of VMA was similar at all follow-up periods (i.e., 3 months and 6 months) for the ocriplasmin groups.
- The main secondary outcome was the percentage of eyes with total posterior vitreous detachment (PVD) at day 28. In both studies, patients in the ocriplasmin groups revealed greater achievement of total PVD compared to placebo.
- Other secondary outcomes included non-surgical closure of a baseline full-thickness macular hole (FTMH) at day 28 and 6 months; vitrectomy at day 28 and 6 months, and change in baseline best corrected visual acuity (BCVA) at day 28 and 6 months:

- At day 28, the ocriplasmin groups were statistically superior to placebo for the achievement of nonsurgical closure of FTMH. Similar results were seen at 6 months. Statistical significance was reached only in the TG-MV-006 study.
- Low rates of vitrectomy were observed in both studies. There were no statistically significant differences in the proportion of patients receiving vitrectomy between the ocriplasmin and placebo groups at day 28 and 6 months.
- The proportion of patients who had an improvement in BCVA was statistically significantly greater in the ocriplasmin group compared to placebo at 6 months only in the TG-MV-007 study.
- The ocriplasmin group had a statistically significantly better health-related quality of life (QOL) score than the placebo group in TG-MV-007, but the difference was small and not considered to be clinically meaningful.
- The incidence of serious adverse events in the two studies was similar between ocriplasmin and placebo.
- There are no clinical studies comparing ocriplasmin with watchful waiting or vitrectomy. There is also a lack of data on the long-term efficacy and safety of ocriplasmin.
- At the submitted price, ocriplasmin costs \$3,950 per single-use vial. Based on an economic analysis conducted by the CDR, ocriplasmin was not considered to be cost-effective.
- The CED reviewed two patient group submissions received by the CDR. The patient submissions outlined the impact of VMA on patients' quality of life and the burden associated with vitrectomy. Ocriplasmin is the only drug treatment indicated for symptomatic VMA and patients preferred this treatment over surgery.
- Overall, two studies found that VMA resolved in a greater proportion of patients treated with ocriplasmin compared with patients given placebo. The resolution rates from the two studies were low and longer-term effectiveness is unknown. There is no evidence that ocriplasmin reduces the need for vitrectomy, improves visual acuity, or reduces blindness. Furthermore, ocriplasmin is not cost-effective.

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/