Drug Coverage Decision for B.C. PharmaCare

About PharmaCare B.C. PharmaCare is a government-funded drug plan. It helps British Columbians with the cost of eligible prescription drugs and specific medical supplies.

Details of Drug Reviewed

Drug	**trientine hydrochloride**
Brand Name	**MAR-Trientine**
Dosage Form	250 mg capsule
Manufacturer	Marcan Pharmaceuticals Inc.
Submission Type	**New Submission**
Use Reviewed	Wilson's disease
Common Drug Review (CDR)	Yes, CDR recommended: **to Reimburse with clinical criteria and/or conditions**. Visit the CDR website for more details: www.cadth.ca/sites/default/files/DRR/2021/SR0680%20MAR-Trientine%20-%20CADTH%20Final%20Rec-meta.pdf
Drug Benefit Council (DBC)	DBC met on December 6, 2021. DBC considered various inputs including: the final reviews completed by the CDR on November 11, 2021, which included clinical and pharmacoeconomic evidence review material and the recommendations from the Canadian Drug Expert Committee (CDEC). The DBC also considered a Patient Input Questionnaire from one patient, as well as input provided by one patient group to the CDR, a Clinical Practice Review from a specialist, and a Budget Impact Assessment.
Drug Coverage Decision	Limited Coverage Benefit Access the trientine criteria. Access the trientine criteria from:**www.gov.bc.ca/pharmacarespecialauthority**
Date	May 17, 2022
Reasons	**Drug coverage decision is consistent with CDR recommendation and inconsistent with the DBC recommendation.** • Trientine was similar to d-penicillamine in patients with Wilson's disease in respect to efficacy. • Treatment discontinuations due to adverse events were more common with d-penicillamine compared with trientine. • Based on the Limited Coverage criteria, trientine will be available to patients with intolerance to d-penicillamine, addressing some of the concerns raised by the DBC.

	• The Ministry participated in the pan-Canadian Pharmaceutical Alliance negotiations with the manufacturer which were able to address the cost concerns identified by the DBC and CDEC.
Other Information	None

The Drug Review Process in B.C.

A manufacturer submits a request to the Ministry of Health (Ministry).

An independent group called the Drug Benefit Council (DBC) gives advice to the Ministry. The DBC looks at:

- whether the drug is safe and effective
- advice from a national group called the Common Drug Review (CDR)
- what the drug costs and whether it is a good value for the people of B.C.
- ethical considerations involved with covering or not covering the drug
- input from physicians, patients, caregivers, patient groups and drug submission sponsors

The Ministry makes PharmaCare coverage decisions by taking into account:

- the existing PharmaCare policies, programs, and resources
- the evidence-informed advice of the DBC
- the drugs already covered by PharmaCare that are used to treat similar medical conditions
- the overall cost of covering the drug

Visit The Drug Review Process in B.C. - Overview and Ministry of Health - PharmaCare for more information.

This document is intended for information only.
It does not take the place of advice from a physician or other qualified health care provider.

Appendix

Drug Benefit Council (DBC) Recommendation and Reasons for Recommendation

FINAL

trientine hydrochloride (MAR-Trientine)

Marcan Pharmaceuticals Inc.

Description:

Drug review of **trientine hydrochloride (MAR-Trientine)** for the following Health Canada approved indications:

For the treatment of Wilson's Disease in patients who are intolerant to penicillamine.

In their review, the DBC considered the following: the final reviews completed by the Common Drug Review (CDR) on November 11, 2021, which included clinical and pharmacoeconomic evidence review material and the recommendations from the Canadian Drug Expert Committee (CDEC). The DBC also considered a Patient Input Questionnaire from one patient, as well as input provided by one patient group to the CDR, a Clinical Practice Review from a specialist, and a Budget Impact Assessment.

Dosage Forms:

MAR-Trientine is available as trientine hydrochloride 250 mg capsule.

Recommendations:

1. The Drug Benefit Council (DBC) recommends not to list MAR-Trientine for the treatment of Wilson's disease in patients who are intolerant to penicillamine.

Of Note:

- There is a need for an effective and tolerable copper chelating drug for patients who cannot tolerate d-penicillamine or for patients in whom d-penicillamine should not be used.

Reasons for the Recommendation:

1. Summary

- Results from one retrospective cohort analysis that evaluated the efficacy and safety of trientine compared to d-penicillamine in patients with Wilson's disease suggested that treatment with trientine had comparable efficacy to d-penicillamine.
- Treatment discontinuations due to adverse events were statistically significantly more common with d-penicillamine compared with trientine treatments.
- Clinical evidence regarding the efficacy and tolerability of trientine is limited due to the lack of randomized trials.
- The cost-effectiveness of trientine is highly uncertain due to limitations with the economic model and clinical evidence.

2. Clinical Efficacy

- The DBC considered the CADTH systematic review, which included two pivotal trials submitted by the sponsor: Study 16-VIN-0315 and Weiss et al., 2013.
- As the purpose of Study 16-VIN-0315 was to assess bioequivalence in healthy volunteers and not the efficacy and safety of trientine in patients with Wilson's disease, this study was not reviewed in detail by CADTH.
- Weiss et al., 2013 was a retrospective cohort analysis that evaluated the efficacy and safety of trientine compared to d-penicillamine in 405 patients with Wilson's disease based on hepatic and neurologic outcomes and treatment discontinuations due to adverse events.
- Weiss et al., 2013 suggested that treatment with trientine had comparable efficacy to d-penicillamine. Specifically, hepatic improvement scores for all patients were comparable in the first line treatments group, as well as the second-line treatments group. Similarly, neurologic improvement scores for all patients were comparable in the first-line treatments group as well as the second-line treatments group.
- For detailed information on the systematic review of trientine please see the CDEC Final Recommendation at: https://www.cadth.ca/trientine-hydrochloride.

3. Safety

- In Weiss et al., 2013, treatment discontinuations due to adverse events were more common with d-penicillamine compared with trientine treatments. The difference between d-penicillamine and trientine treatments was statistically significant.
- For detailed information on the safety and tolerability of trientine, please see the CDEC Final Recommendations at the links above.

4. Economic Considerations

- The cost-effectiveness of trientine is highly uncertain due to limitations with the economic model and clinical evidence.
- CADTH determined that MAR-Trientine would likely not be considered cost-effective at a $50,000 per quality-adjusted life-year (QALY) willingness to pay (WTP) threshold. Based on exploratory analyses, a significant price reduction would be required for MAR-Trientine to achieve an ICER of $50,000 per QALY.

5. Of Note

- One patient who had tried trientine responded to the request for patient input. This patient reported that Wilson's Disease had given them cirrhosis, and made it impossible to work, participate in activities of daily living, including activities with family. This patient felt that being unable to tolerate d-penicillamine, without the option of trientine they would not still be alive.
- The CDEC recommendation considered the evidence for trientine in light of the lack of another option for copper chelating agents for patients who cannot tolerate d-penicillamine, and the high morbidity and mortality associated with the lack of treatment.