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	**romosozumab**
Brand Name	Evenity®
Dosage Form(s)	105 mg/1.17 mL solution in a prefilled syringe (PFS)
Manufacturer	Amgen Canada Inc.
Submission Type	**New Submission**
Use Reviewed	The treatment of osteoporosis in postmenopausal women at high risk for fractures
Canada's Agency for Drugs and Technologies in Health (CADTH) Reimbursement Reviews (CRR)	Yes, CRR recommended: **to Reimburse with clinical criteria and/or conditions**. Visit the CRR website for more details: www.cadth.ca/node/88649
Drug Benefit Council (DBC)	The DBC met on February 7, 2022, and considered the following: the final reviews completed by the CRR on November 25, 2021, which included clinical and pharmacoeconomic evidence review material and the recommendations from the CADTH. The DBC also considered Patient Input Questionnaire responses from one caregiver, patient input provided to the CRR, Clinical Practice Reviews from one specialist and one general physician, and a Budget Impact Assessment.
Drug Coverage Decision	Limited Coverage Benefit. Access the criteria from **www.gov.bc.ca/pharmacarespecialauthority**
Date	**December 12, 2023**
Reasons	**Drug coverage decision is consistent with the CDEC and DBC recommendations**. • Results from ARCH, a double-blind randomized controlled trial (RCT) indicated that romosozumab 210 mg subcutaneous monthly for 12 months followed by alendronate reduced the risk of fractures (new vertebral fractures and clinical fractures) compared with alendronate alone.

	• At the manufacturer's submitted price, romosozumab was not considered cost-effective compared to treatments that are already reimbursed by public drug plans for the treatment of osteoporosis in postmenopausal women at high risk for fractures. • The Ministry participated in the pan-Canadian Pharmaceutical Alliance negotiations with the manufacturer which were able to address the concerns identified by the CADTH with respect to the cost-effectiveness and value for money.
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 Canadian Agency for Drugs and Technologies in Health (CADTH) Reimbursement Reviews(CRR)
- 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

Romosozumab (Evenity™)

Amgen Canada Inc.

Description:

Drug review of **romosozumab (Evenity™)** for the following Health Canada approved indications:

> For the treatment of osteoporosis in postmenopausal women at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture.

In their review, the DBC considered the following: the final reviews completed by the Common Drug Review (CDR) on November 25, 2021, which included clinical and pharmacoeconomic evidence review material and the recommendations from the Canadian Agency for Drugs and Technologies in Health (CADTH). The DBC also considered Patient Input Questionnaire responses from one caregiver, patient input provided to the CDR, Clinical Practice Reviews from one specialist and one general physician, and a Budget Impact Assessment.

Dosage Forms:

Evenity™ is available as 105 mg/1.17 mL solution for subcutaneous injection in single-use prefilled syringe.

Recommendations:

1. The Drug Benefit Council (DBC) recommends not to list romosozumab (Evenity™) at the submitted price.

Of Note:

- If the Ministry is able to negotiate a significant price reduction, the reimbursement criteria and conditions recommended by CADTH are an appropriate basis for coverage.

Reasons for the Recommendation:

1. Summary

- Results from ARCH, a double-blind randomized controlled trial (RCT) indicated that romosozumab 210 mg subcutaneous monthly for 12 months followed by alendronate reduced the risk of fractures (new vertebral fractures and clinical fractures) compared with alendronate alone.
- More than 90% of patients enrolled in the ARCH trial were treatment naive to osteoporosis medications. ARCH was not designed to inform the effects of romosozumab in those who were intolerant or not responsive to other osteoporosis medications such as bisphosphonates.
- At the manufacture-submitted price, romosozumab is not considered cost-effective relative to treatments that are already reimbursed by public drug plans for the indicated patient population. CADTH recommended a price reduction of at least 53% for romosozumab to be considered cost-effective.

2. Clinical Efficacy

- The DBC considered the CDR systematic review, which included two phase III studies (ARCH and FRAME) in postmenopausal women (aged 55 years to 90 years) with osteoporosis.
- ARCH was a double-blind RCT that assessed the efficacy and safety of romosozumab 210 mg subcutaneous monthly followed by alendronate 70 mg weekly versus alendronate 70 mg weekly alone for the treatment of osteoporosis in postmenopausal women at high risk of fracture.
- The primary efficacy end points in ARCH were incidence of new vertebral fracture at month 24 and incidence of clinical fracture (nonvertebral fracture and clinical vertebral fracture) during the primary analysis period. Secondary efficacy end points included the incidence of various types of fracture and change from baseline in bone mineral density (BMD) T-score.
- Given the key limitations of FRAME (i.e., it did not include the target patient population and it used a placebo comparator), the CDR and DBC only considered the results as supportive of the efficacy of romosozumab and not sufficient evidence to inform the comparative clinical effects of romosozumab.
- In ARCH, romosozumab 210 mg subcutaneous monthly for 12 months followed by an oral bisphosphonate reduced the risk of fractures compared with an oral bisphosphonate alone.
- Fewer patients treated with romosozumab for 12 months followed by alendronate for 12 months had a new vertebral fracture compared with alendronate alone at 24 months.
- Treatment with romosozumab followed by alendronate was also associated with a lower incidence of clinical fracture (nonvertebral fracture and clinical vertebral fracture) compared with alendronate alone.
- More than 90% of patients enrolled in the ARCH and FRAME trials were treatment naive to osteoporosis medications. ARCH was not designed to inform the effects of romosozumab in those who were intolerant or not responsive to other osteoporosis medications, such as bisphosphonates.
- The currently available evidence, in addition to the bone-forming mechanism of action of romosozumab, supports its use before an antiresorptive medication in patients who have had a fracture, are at high risk for future fracture, and have not previously received medications for osteoporosis.

- For detailed information on the systematic review of romosozumab please see the CADTH Final Recommendation at: https://www.cadth.ca/romosozumab.

3. Safety

- CDEC noted a potentially increased risk of cardiovascular events with romosozumab treatment, including an increase in myocardial infarction and stroke in the ARCH trial. Health Canada and other regulatory agencies considered that serious cardiac and cerebrovascular events were the primary events of concern.
- The product monograph for romosozumab has a boxed warning regarding the potentially increased risk of myocardial infarction, stroke, and cardiovascular death and that romosozumab is not recommended in patients with a history of myocardial infarction or stroke and treatment should be discontinued in patients who experience a myocardial infarction or stroke.
- For detailed information on the safety and tolerability of romosozumab, please see the CDEC Final Recommendations at the links above.

4. Economic Considerations

- At the manufacture-submitted price, romosozumab is not considered cost-effective relative to treatments that are already reimbursed by public drug plans at a willingness-to-pay threshold of $50,000 per quality-adjusted life-year (QALY) in postmenopausal women with a history of osteoporotic fracture and who are at very high risk for future fracture.
- CADTH recommended a price reduction of at least 53% for romosozumab to be considered cost-effective in this patient population. However, these price reductions are based on an indirect treatment comparison (ITC) which was deemed to have substantial uncertainty associated with it. Therefore, a higher price reduction may be required to ensure cost-effectiveness, given that romosozumab is substantially more expensive than alternatives for which there is no direct evidence. In addition, the economic model did not take the conservative approach of incorporating the potentially increased risk of myocardial infarction, stroke and cardiovascular death described in the product monograph.

5. Of Note

- The one patient group responding to CADTH reported that outcomes that were of most importance to them were the following: preserving health-related quality of life, preventing fracture-related deaths, preventing admission to long-term care homes, preserving their ability to perform daily physical and social activities, preventing osteoporotic fractures, and avoiding serious side effects.
- The DBC received Patient Input Questionnaire responses from one caregiver, who reported that their patient had not tried romosozumab but had tried other treatments for osteoporosis that did not increase bone density.