

Zoledronic acid (for osteoporosis)

Product:
ZOLEDRONIC ACID (Aclasta®)
5mg/100 mL intravenous solution

Class of drugs:
Bisphosphonate

Indication:
Treatment of osteoporosis

Manufacturer:
Novartis Pharmaceuticals Canada Inc.

CED Recommendation

The CED recommended that zoledronic acid (Aclasta) be funded through the Exceptional Access Program for the treatment of osteoporosis according to specific criteria. The CED's recommendation was made on the basis that zoledronic acid (Aclasta) has been shown to provide clinical efficacy but not value for money

Executive Officer Decision

Based on the CED's recommendation, the Executive Officer decided to fund zoledronic acid (Aclasta) through the Exceptional Access Program for the treatment of osteoporosis according to specific criteria

Status

Funding available through the Ontario Public Drug Programs via the Exceptional Access Program.

Highlights of Recommendation:

- ◆ Zoledronic acid (Aclasta) is an injectable drug indicated for the treatment of osteoporosis in post-menopausal women. It belongs to a class of drugs called bisphosphonates. Zoledronic acid (Aclasta) is given as a once-yearly injection.
- ◆ The Ministry currently funds other bisphosphonate treatments that are taken orally as once-daily or once-weekly tablets.
- ◆ A study in post-menopausal women with osteoporosis has shown that zoledronic acid (Aclasta) is effective in reducing the risk of hip, spine and other fractures.
- ◆ There is no evidence that zoledronic acid (Aclasta) is clinically superior to oral bisphosphonates, in terms of ability to reduce bone fractures or safety.
- ◆ Zoledronic acid (Aclasta) costs \$645 for a once-yearly injection. This is approximately three times the annual cost of alendronate, an oral bisphosphonate agent listed as a General Benefit on the Ontario Drug Benefit Formulary. The Committee indicated that the large price premium for zoledronic acid (Aclasta) is not justified given the lack of a therapeutic advantage. As such, the Committee recommended that zoledronic acid (Aclasta) be reserved for exceptional cases where patients are unable to take oral medications.
- ◆ **Overall, the Committee noted that zoledronic acid (Aclasta) has been shown to provide clinical efficacy in the treatment of osteoporosis. However, given the high cost of treatment, the Committee recommended that zoledronic acid (Aclasta) be funded through the Exceptional Access Program according to specific criteria.**

Background:

Osteoporosis is a condition in which bones in the body lose mass and density. The bones become brittle and are vulnerable to fractures, most commonly in the hips, wrists and spine. Osteoporosis affects both men and women, usually as they grow older.

Treatment and prevention of osteoporosis always includes making sure patients consume enough calcium and vitamin D. Weight-bearing exercise will also strengthen bones. Patients should stop smoking, reduce alcohol use, and try to prevent falls.

Bisphosphonates are a class of drugs used to maintain bone density and strength. This class includes etidronate/calcium, alendronate and risedronate. These are oral tablets that are taken once-daily or once-weekly. All of these oral agents are currently listed on the Ontario Drug Benefit (ODB) Formulary. Other treatments include raloxifene and hormone replacement therapy, which have only been studied in post-menopausal women. Raloxifene and hormone replacement therapy are also listed on the ODB Formulary.

Zoledronic acid (Aclasta) is an injectable bisphosphonate drug. It is indicated for the treatment of osteoporosis in post-menopausal women. It is also indicated for the treatment of Paget's disease of the bone. This particular review only considered the use of zoledronic acid (Aclasta) in the treatment of osteoporosis.

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Detailed Discussion:

- ◆ The Committee considered four randomized controlled studies evaluating the efficacy and safety of zoledronic acid (Aclasta).
- ◆ The focus of the review was a randomized controlled study that compared zoledronic acid (Aclasta) to placebo in over 7,000 post-menopausal women with osteoporosis. The study reported that after receiving three years of treatment, patients who received zoledronic acid (Aclasta) experienced significantly fewer hip fractures, vertebral (spine) fractures and other (non-vertebral) fractures.
- ◆ A second study was conducted in over 2,000 patients (women and men) aged 50 years or more who had undergone surgical repair of a hip fracture. Zoledronic acid (Aclasta) was compared with placebo. Patients who received zoledronic acid (Aclasta) experienced reductions in new vertebral and non-vertebral fractures.
- ◆ Two of the four studies compared the effects of zoledronic acid (Aclasta) with alendronate in postmenopausal women with a low bone mineral density. The Committee did not find these two studies helpful because the trials were small and short, and did not assess the effect of zoledronic acid (Aclasta) on fracture rate.
- ◆ There are no direct comparison studies to assess the efficacy of zoledronic acid (Aclasta) versus oral bisphosphonates in terms of fracture reduction. Therefore, it is unknown whether zoledronic acid (Aclasta) provides any improvements in clinical outcomes over oral bisphosphonates.
- ◆ There is also no evidence that zoledronic acid (Aclasta) provides any safety advantage over oral bisphosphonate treatments.
- ◆ The manufacturer requested that funding be provided for the treatment of osteoporosis in post-menopausal women who have failed or are intolerant to oral bisphosphonate treatment. However, the Committee noted that there are no studies that evaluated zoledronic acid (Aclasta) in this specific patient population. It is not known whether patients who have failed or are intolerant to oral bisphosphonates (i.e. those patients who have either experienced a fracture or had intolerable side effects while on oral bisphosphonates) would benefit from zoledronic acid (Aclasta), another agent (albeit an injectable) from the same drug class.

- ◆ Common side effects with zoledronic acid (Aclasta) include flu-like symptoms, fever, stomach disturbance, nausea, headache, dizziness, bone pain, muscle or joint pain, and fatigue. Uncommon, but significant, side effects include decreased kidney function and irregular heartbeat.
- ◆ Zoledronic acid (Aclasta) costs \$645 for a once-yearly injection. This is approximately three times the annual cost of alendronate. The Committee indicated that the large price premium for zoledronic acid (Aclasta) is not justified given the lack of a therapeutic advantage.
- ◆ Overall, the Committee noted that zoledronic acid (Aclasta) has been shown to provide clinical efficacy but not value for money in the treatment of osteoporosis.

EAP Criteria:

- ◆ The CED recommended that zoledronic acid (Aclasta) be funded through the Exceptional Access Program (EAP) according to the following criteria:
 - *For the treatment of osteoporosis in post-menopausal women who are unable to absorb or take oral products (e.g., short gut syndrome, inability to swallow).*
 - *Requests for children and peri/pre-menopausal women will not be considered, as there is no evidence of benefit in these patient populations.*

CEDAC Recommendation:

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

The Canadian Expert Drug Advisory Committee (CEDAC) recommended that zoledronic acid (Aclasta) not be listed.



Ministry of
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