Physician's Guide

A Physician's Guide to Aclasta® for the Treatment of Osteoporosis

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This reminder card is designed to help you prescribe Aclasta® (zoledronic acid 5 mg) appropriately for patients with osteoporosis.

It is meant to be used as a guide only.

Please consult the Summary of Product Characteristics before prescribing Aclasta®.

- Aclasta® is approved for treating osteoporosis in postmenopausal women and men at increased risk of fracture, including those with a recent low-trauma hip fracture and for the treatment of osteoporosis associated with long-term systemic glucocorticoid therapy in postmenopausal women and in men at increased risk of fracture.
- The use of Aclasta® in patients with severe renal impairment (CrCl < 35mL/min) is contraindicated due to an increased risk of renal failure in this population.
- The following precautions are recommended to minimize the risk of renal adverse reactions:
  - Creatinine Clearance (CrCl) should be calculated based on actual body weight using the Cockcroft-Gault formula before each Aclasta® dose.
  - Transient increase in serum creatinine may be greater in patients with underlying impaired renal function.
  - Monitoring of serum creatinine should be considered in at-risk patients.
  - Aclasta® should be used with caution when concomitantly used with other drugs that could impact renal function.
  - Patients, especially elderly patients and those receiving diuretic therapy, should be **appropriately hydrated** prior to administration of Aclasta®.
  - A single dose of Aclasta® should not exceed 5 mg and the duration of infusion should be **at least 15 minutes.**
- Aclasta® is given **once a year** as a single intravenous infusion.
- The optimal duration of bisphosphonate treatment for osteoporosis has not been established. The need for continued treatment should be re-evaluated periodically based on the benefits and potential risks of Aclasta® on an individual patient basis, particularly after 5 or more years of use.
- Pre-existing hypocalcaemia and other mineral metabolism disturbances must be treated with adequate intake of calcium and vitamin D before initiating therapy with Aclasta®. Physicians should consider clinical monitoring for these patients.
- It is recommended that patients should receive **adequate calcium and vitamin D** supplementation. For patients with a recent low-trauma hip fracture, a loading dose of 50.000 to 125.000 IU of vitamin D given orally or via intramuscular route is recommended prior to the first Aclasta® infusion.
- Aclasta® is **contraindicated during pregnancy and breast-feeding**, due to potential teratogenicity. Aclasta® is not recommended in women of childbearing potential.
- A healthy lifestyle plays an important part in maintaining strong bones. Patients should be reminded that there are things which they can do to help in keeping their bones as strong as possible.
  - **A healthy diet** is very important in maintaining strong bones. Patients should be advised on the benefits of a good diet. Calcium and vitamin D supplementation are recommended in conjunction with Aclasta®.
  - Vitamin D is important in the absorption of calcium from the diet. Sunlight helps the body to make vitamin D. As little as 15 minutes of natural light can have a beneficial effect.
  - **Physical activity**, especially weight bearing exercise such as walking, is important in keeping the bones and surrounding muscles strong and healthy.
  - Smoking and alcohol intake can impact on bone status. **Stopping smoking** and moderating alcohol intake can have a beneficial effect on bone health.
- The majority of side effects with Aclasta® are mild to moderate and occur within the first three days of administration. Patients should be advised about the post-dose symptoms which are commonly seen following administration of an intravenous bisphosphonate. These include flu-like symptoms such as fever, myalgia, flu-like illness, headache, and arthralgia. These can be managed with mild pain relievers such as paracetamol and ibuprofen.
- Atypical subtrochanteric and diaphyseal femur fractures have been reported with bisphosphonate therapy, primarily in patients receiving long-term treatment for osteoporosis. These fractures occur after minimal or no trauma and some patients experience thigh or groin pain, often associated with imaging features of stress fractures, weeks to months before presenting with a completed femur fracture. Discontinuation of bisphosphonate therapy in patients suspected to have an atypical femur fracture should be considered pending evaluation of the patient, based on an individual benefit risk assessment.

ACLASTA® 5mg Solution for Infusion

PRESENTATION: 100 mL solution bottle containing: 5 mg zoledronic acid corresponding to 5.330 mg zoledronic acid monohydrate. **INDICATIONS**: Treatment of osteoporosis in post-menopausal women and men at increased risk of fracture, including those with a recent low-trauma hip fracture. Treatment of osteoporosis associated with long-term systemic glucocorticoid therapy in post-menopausal women and in men at increased risk of fracture. Treatment of Paget's disease of the bone. **DOSAGE AND ADMINISTRATION**: **Osteoporosis**: Patients must be appropriately hydrated prior to administration of Aclasta. This is especially important for the elderly (≥65 years) and for patients receiving diuretic therapy. Adequate calcium and vitamin D intake are recommended in association with Aclasta administration. A single intravenous infusion of 5 mg Aclasta administered once a year. The optimal duration of bisphosphonate treatment for osteoporosis has not been established. The need for continued treatment should be re-evaluated periodically based on the benefits and potential risks of Aclasta on an individual patient basis, particularly after 5 or more years of use. In patients with a recent low-trauma hip fracture, it is recommended to give the Aclasta infusion two weeks after hip fracture repair. In patients with a recent low-trauma hip fracture, a loading dose of 50 000 to 125 000 IU of vitamin D given orally or via the intramuscular route is recommended prior to the first Aclasta infusion. **Paget's Disease**: A single intravenous infusion of 5 mg Aclasta. Specific re-treatment data are not available for Paget's disease. Aclasta is administered via a vented infusion line and given at a constant infusion rate. The infusion time must not be less than 15 minutes. No dose adjustment in patients with creatinine clearance ≥35 mL/min, or in patients with hepatic impairment, or in elderly patients (≥65 years). The safety and efficacy of Aclasta in children and adolescents below 18 years of age has not been established. In patients with Paget's disease, it is strongly advised that adequate supplemental calcium corresponding to at least 500 mg elemental calcium twice daily is ensured for at least 10 days following Aclasta administration. Re-treatment of Paget's disease: After initial treatment with Aclasta in Paget's disease, an extended remission period is observed in responding patients. Re-treatment consists of an additional intravenous infusion of 5mg Aclasta after an interval of one year or longer from initial treatment in patients who have relapsed. Limited data on re-treatment of Paget's disease are available. Aclasta is essentially sodium-free. **CONTRAINDICATIONS**: ♦ Hypersensitivity to zoledronic acid or to any of the excipients or to any bisphosphonate ♦ hypocalcaemia ♦ pregnancy ♦ lactation ♦ childbearing potential. **WARNINGS/PRECAUTIONS**: ♦ Serum creatinine should be measured before each Aclasta dose. Aclasta should not be used in patients with creatinine clearance <35 ml/min. Transient increase in serum creatinine may be greater in patients with underlying impaired renal function. Monitoring of serum creatinine should be considered in at-risk patients. ♦ Patients must be appropriately hydrated prior to administration of Aclasta, especially important for the elderly and for patients receiving diuretic therapy. Use with caution in conjunction with medicinal products that can impact renal function. A single dose of Aclasta should not exceed 5mg and the duration of infusion should be at least 15 minutes. ♦ Pre-existing hypocalcaemia and other disturbances of mineral metabolism must be treated by adequate intake of calcium and vitamin D before initiating therapy with Aclasta. It is strongly advised that patients with Paget's disease receive supplemental calcium and vitamin D. Measurement of serum calcium before infusion is recommended for patients with Paget's disease. Severe and occasionally incapacitating bone, joint and/or muscle pain have been infrequently reported with bisphosphonate therapy. ♦ The start of treatment or of a new course of treatment should be delayed in patients with unhealed open soft tissue lesions in the mouth. A dental examination with preventive dentistry and an individual benefit-risk assessment is recommended prior to treatment with Aclasta in patients with concomitant risk factors.All patients should be encouraged to maintain good oral hygiene, undergo routine dental check-ups, and immediately report any oral symptoms such as dental mobility, pain or swelling, non-healing of sores or discharge during treatment with zoledronic The management plan for patients who develop ONJ should be set up in close collaboration between the treating physician and a dentist or oral surgeon with expertise in ONJ. Temporary interruption of zoledronic acid treatment should be considered until the condition resolves and contributing risk factors are mitigated where possible. ♦ Atypical subtrochanteric and diaphyseal femoral fractures have been reported with bisphosphonate therapy, primarily in patients receiving long-term treatment for osteoporosis. These fractures occur after minimal or no trauma and some patients experience thigh or groin pain, often associated with imaging features of stress fractures, weeks to months before presenting with a completed femoral fracture. Fractures are often bilateral; therefore the contralateral femur should be examined in bisphosphonate-treated patients who have sustained a femoral shaft fracture. Poor healing of these fractures has also been reported. Discontinuation of bisphosphonate therapy in patients suspected to have an atypical femur fracture should be considered pending evaluation of the patient, based on an individual benefit risk assessment. During bisphosphonate treatment patients should be advised to report any thigh, hip or groin pain and any patient presenting with such symptoms should be evaluated for an incomplete femur fracture. ♦ Aclasta is not recommended in women of childbearing potential. ♦ Other products containing zoledronic acid as an active substance are available for oncology indications. Patients being treated with Aclasta should not be treated with such products or any other bisphosphonate concomitantly, since the combined effects of these agents are unknown. This medicinal product contains less than 1 mmol sodium (23 mg) per 100 ml vial of Aclasta, i.e. essentially "sodium free". **INTERACTIONS**: ♦ Specific drug-drug interaction studies have not been conducted with zoledronic acid. ♦ Caution is recommended when Aclasta is used concomitantly with drugs that can significantly impact renal function, such as aminoglycosides and diuretics that can cause dehydration. ♦ In patients with renal impairment, the systemic exposure to concomitant medicinal products that are primarily excreted via the kidney may increase. **ADVERSE REACTIONS**: ♦ The incidence of adverse reactions (e.g. fever, myalgia, flu-like symptoms, arthralgia and headache) are greatest with the first infusion and decrease markedly with subsequent infusions. The majority of these reactions occur within the first three days and were mild to moderate and resolved within three days of the event onset. The incidence of these adverse reactions can be reduced with the administration of paracetamol or ibuprofen shortly following Aclasta administration. ♦ Very common: Pyrexia. ♦ Common: Influenza-like illness, chills, fatigue, pain, asthenia, malaise, arthralgia, myalgia, bone pain, back pain, pain in extremity, vomiting, nausea, headache, dizziness, atrial fibrillation, hypocalcaemia†, ocular hyperaemia, diarrhoea, increased C-reactive protein, infusion site reactions. ♦ Uncommon: Hypertension, flushing, palpitations and others. ♦ Not known: Scleritis, pareophtalmia, hypotension, renal impairment, osteonecrosis of the jaw, osteonecrosis of the external auditory canal, dehydration secondary to post dose symptoms, hypersensitivity reactions. ♦ Rare: Atypical subtrochanteric and diaphyseal femoral fractures† (bisphosphonate class adverse reaction) *† Common in Paget's disease only.* Please refer to SmPC for a full list of adverse events. **LEGAL CATEGORY**: POM. **PACK SIZE**: Aclasta is supplied in packs containing one 100ml bottle **MARKETING AUTHORISATION HOLDER**: Novartis Europharm Limited, Frimley Business Park, Camberley GU16 7SR, United Kingdom. **MARKETING AUTHORISATION NUMBER**: EU/1/05/308/001. **Please refer to Summary of Product Characteristics (SmPC) before prescribing.** Full prescribing information is available on request from Novartis Pharma Services Inc., Representative Office Malta, P.O. Box 4, Marsa, MRS 1000, Malta. Tel: +356 21222872. 2015-MT-ACL-7-DEC-2015.

Any suspected adverse reactions and medication errors can be reported via the national Adverse Drug Reactions (ADRs) reporting system. Report forms can be downloaded from http://www.medicinesauthority.gov.mt/adrportal and posted to Malta Medicines Authority Post-licensing Directorate, Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000, Malta, or sent by email to postlicensing.medicinesauthority@gov.mt

Healthcare professionals may also report any adverse events suspected to be associated with the use of Aclasta to Novartis Pharma Services Inc. Representative Office Malta by phone on 21222872, by fax on 22487219 or e-mail at drug_safety.malta@novartis.com.