Aclasta BSS [1]

ACLASTA® Important note: Before proceeding with the prescription of this medication, consult all the information about it. Presentation: Zoledronic acid. A bottle with 100 ml of solution contains 5 mg of zoledronic acid (anhydrous), which corresponds to 5.330 mg of zoledronic acid monohydrate. ¨**Indications:** Treatment and prevention of osteoporosis in postmenopausal women, to reduce the incidence of hip fractures, vertebral fractures and other non-vertebral fractures, and to increase bone mineral density. ¨Prevention of clinical fractures after a hip fracture in males and women. ¨Treatment of male osteoporosis. ¨Treatment and prevention of osteoporosis induced by glucocorticoids. ¨Treatment of Paget's disease (osteitis deformans). **Dosage:** ¨**In all indications:** The infusion time should not be less than 15 minutes. ¨**Osteoporosis and prevention of clinical fractures after a hip fracture:** A unique intravenous infusion of 5 mg of Aclasta® administered once a year. Aclasta (5 mg/100 ml solution, ready for infusion) is administered by an infusion guide with separate air intake and at a constant speed. Aclasta should not be mixed or administered intravenously with other drugs, and should not come in contact with other solutions containing calcium or other divalent cations. In osteoporosis it is important to take adequate calcium and vitamin D supplements if the amounts coming from the food are insufficient. For the prevention of clinical fractures after a hip fracture due to low-intensity trauma, it is recommended to administer a loading dose of 50,000 to 125,000 IU of vitamin D orally or intramuscularly before the first infusion of Aclasta. ¨**Prevention of osteoporosis:** An intravenous infusion of 5 mg of zoledronic acid (anhydrous) dissolved in 100 ml of aqueous solution. In osteoporosis it is important to take adequate calcium and vitamin D supplements if the amounts coming from the food are insufficient. ¨**An intravenous infusion of 5 mg of zoledronic acid (anhydrous) dissolved in 100 ml of aqueous solution. In osteoporosis it is important to take adequate calcium and vitamin D supplements if the amounts coming from the food are insufficient.):** The recommended dose is a single intravenous infusion of 5 mg of Aclasta. The repetition of the treatment for osteitis deformans consists in an additional intravenous infusion of 5 mg of Aclasta, allowing an interval of at least one year to elapse. In the absence of an aggravation of the clinical symptoms or of a bone scintigraphy indicative of a recurrence of the disease, a second intravenous infusion of Aclasta should not be administered before at least 12 months have elapsed after the initial treatment. The consumption of vitamin D and calcium is recommended for at least during 10 days after the administration of Aclasta. ¨It is not necessary to adjust the dose in patients with a creatinine clearance <35 ml/min nor in patients with hepatic dysfunction. ¨Aclasta should not be used in children or adolescents. **Contraindications:** ¨Hypocalcemia. ¨¨Severe renal dysfunction with a creatinine clearance <35 ml/min. ¨Pregnancy. ¨Lactation. ¨Hypersensitivity to zoledronic acid, to any of the excipients or to any bisphosphonate. **Warnings and precautions:** ¨Aclasta is contraindicated in patients with severe renal dysfunction (creatinine clearance <35 ml/min). ¨Before administering Aclasta, the patient's creatinine clearance should be calculated (e.g., using the Cockcroft Gault formula). ¨Patients should be adequately hydrated before and after the administration of Aclasta; this is particularly important in the elderly and patients treated

with diuretics. ¨Caution is advised in associating Aclasta with drugs that may have an important effect on renal function (e.g., aminoglycosides or diuretics, which can lead to dehydration). ¨Transient increases in serum creatinine may be greater in patients with underlying renal dysfunction; in patients who present a risk, to carry out intermediate controls of serum creatinine should be considered. ¨Before starting treatment with Aclasta, pre-existing hypocalcemia should be treated with adequate calcium and vitamin D supplements. ¨Any other preexisting mineral metabolism disorder (e.g., decreased parathyroid reserve, intestinal calcium hypoabsorption) should also be treated). ¨Clinicians should consider clinical supervision of these patients. ¨It is important that patients take calcium and vitamin D supplements. ¨It is strongly recommended that people with Paget's disease receive adequate calcium supplements (at least 500 mg elemental calcium twice a day) and vitamin D for ten days after the infusion of Aclasta. ¨Patients should receive information about the symptoms of hypocalcemia and be subject to an adequate clinical supervision during the period of risk. ¨Infrequent cases of severe bone, joint or muscle pain have been reported, sometimes incapacitating, in patients treated with bisphosphonates, included Aclasta. ¨Aclasta contains the same active substance (zoledronic acid) as Zometa, a medicine used in oncological indications; patients treated with Zometa should not receive Aclasta. ¨Cases of osteonecrosis of the jaw have been reported, especially in cancer patients treated with bisphosphonates, including Aclasta. The majority of these cases have been associated with dental interventions; consequently, patients must communicate this information to their dentist during any dental

treatment or if a dental surgery is planned. ¨ During treatment with zoledronic acid, it is prudent to maintain good oral hygiene, to undergo regular dental examinations and to immediately report any oral symptom. ¨ Other types of osteonecrosis (for example, femur, hip, knee and humerus) have also been reported. ¨Atypical subtrochanteric and diaphyseal fractures of the femur have been reported with the administration of bisphosphonates, especially in patients with long-term treatment of osteoporosis. The possibility of interrupting bisphosphonate treatment should be considered until the patient's evaluation is carried out. Patients should be advised to report any pain in the thigh, hip or groin during treatment with bisphosphonates (including Aclasta). **Other types of osteonecrosis (for example, femur, hip, knee and humerus) have also been reported.** ¨ Atypical subtrochanteric and diaphyseal fractures of the femur have been reported with the administration of bisphosphonates, especially in patients with long-term treatment of osteoporosis**.** The possibility of interrupting bisphosphonate treatment should be considered until the patient's evaluation is carried out. Patients should be advised to report any pain in the thigh, hip or groin during treatment with bisphosphonates (including Aclasta)**:** ¨Caution is advised when using Aclasta in association with drugs that may significantly affect renal function, e.g. aminoglycosides or diuretics, which can lead to dehydration. **Adverse reactions:** ¨Adverse reactions presumably related to the medication (as evaluated by the investigators): ¨ **Treatment of postmenopausal osteoporosis and male osteoporosis; prevention of clinical fractures after a hip fracture caused by low-intensity trauma; treatment and prevention of osteoporosis induced by glucocorticoids and Paget's disease (osteitis deformans):** ¨*Very common*: pyrexia. ¨*Common*: headache, dizziness, nausea, vomiting, diarrhea, myalgia, arthralgia, bone pain, low back pain, limb pain, flu-like illness, chills, fatigue, asthenia, pain, malaise. ¨*Infrequent*: flu, rhinopharyngitis, anemia, decreased appetite, insomnia, lethargy, paresthesia, drowsiness, tremor, syncope, conjunctivitis, eye pain, vertigo, high blood pressure, hot flushes, cough, dyspnea, dyspepsia, pain in the upper abdomen, abdominal pain, constipation, xerostomia, esophagitis, gastroesophageal reflux, rash, hyperdrosis, pruritus, erythema, cervical pain, osteomuscular rigidity, joint swelling, myospasms, shoulder pain, thoracic osteomuscular pain, joint stiffness, arthritis, adynamia,

musculoskeletal pain, elevation of creatininemia, urinary frequency, proteinuria, peripheral edema, thirst, acute phase reaction and non-cardiac chest pain. ¨*Rare*: uveitis, episcleritis and iritis. ¨ *Other side effects observed*: ocular hyperemia, increased C-reactive protein, dysgeusia, dental pain, gastritis, palpitations, hypocalcemia, reactions at the site of the infusion. ¨**Prevention of postmenopausal osteoporosis:** (reactions that have not been reported in other indications or that have been reported more frequently in this indication): ¨ *Very frequent*: headache, nausea, myalgia, pain, chills. ¨*Common*: decreased appetite, tremor, lethargy, conjunctivitis, eye pain, iritis, abdominal pain, pain in the upper abdomen, constipation, night sweats, musculoskeletal pain, myospasms, osteomuscular thoracic pain, jaw pain, cervical pain, peripheral edema, reaction related to infusion, non-cardiac chest pain. ¨ *Infrequent*: anxiety, hypoaesthesia, dysgeusia, blurred vision, back pain (kidney pain). ¨Cases of osteonecrosis of the jaw (ONJ) have been reported mainly in cancer patients receiving bisphosphonate therapy, including Aclasta. ¨**Atrial fibrillation** has been reported in a clinical study on osteoporosis in postmenopausal women. ¨**Use of Aclasta since the marketing authorization:** the following adverse reactions have been reported: hypersensitivity reactions, including anaphylactic reaction, anaphylactic shock, bronchospasm, nettle rash and angioneurotic edema, renal dysfunction, including renal failure that required dialysis or had a fatal outcome, especially in patients with underlying renal dysfunction or other risk factors, such as advanced age, coadministration of nephrotoxic drugs or diuretics or dehydration after infusion, arterial hypotension in patients with underlying risk factors, dehydration due to the symptoms after the administration, such as fever, vomiting and diarrhea, osteonecrosis of the jaw, scleritis and parophthalmia **CDS August 2015**

Links
[1] https://www.sandozca.com/en/aclasta-bss