Pamifos® / Disodium Pamidronate 3 mg/ml

Qualitative and quantitative composition: Each ml sterile concentrate contains 3 mg pamidronate disodium as pamidronic acid 2,527 mg. 1 vial with 5 (10; 20; 30) ml concentrate contains 15 (30; 60; 90) mg pamidronate disodium. *Excipients:* sodium hydroxide, hydrochloric acid, water for injections. **Therapeutic indications:** Treatment of conditions associated with increased osteoclast activity: Tumour-induced hypercalcaemia; osteolytic lesions in patients with bone metastases associated with breast cancer; Multiple myeloma stage III. **Contraindications:** Hypersensitivity to pamidronate, other bisphosphonates or to any of the excipients; breast-feeding. **Posology and method of administration:** Medac Disodium Pamidronate 3 mg/ml is a sterile concentrate and must therefore always be diluted in a calcium-free infusion solution (0.9 % sodium chloride or 5 % glucose) before use. The resulting solution must be infused slowly. The infusion rate should never exceed 60 mg/hour (1 mg/min), and the concentration of pamidronate disodium in the infusion solution should not exceed 90 mg/250 ml. A dose of 90 mg must usually be administered as a 2 hour infusion in a 250 ml solution for infusion. In patients with multiple myeloma and patients with tumour induced hypercalcaemia, the infusion rate must not exceed 90 mg in 500 ml over 4 hours. To minimise local reactions at the infusion site, the cannula should be inserted carefully into a relatively large vein. Pamidronate disodium should be given under the supervision of a physician with the facilities to monitor the clinical and biochemical effects. Use only freshly prepared and clear dilutions! The safety and efficacy in children and adolescents (<18 years) have not been established. Tumour-induced hypercalcaemia: Patients must be rehydrated with 0.9% w/v sodium chloride solution before or/and during administration. The total dose of pamidronate disodium to be used for a treatment course depends on the patient's initial serum calcium levels. Initial plasma calcium level <3.0 (3.0–3.5; 3.5–4.0; >4.0) mmol/l => recommended dose: 15–30 (30–60; 60–90; 90) mg pamidronate disodium. The total dose of pamidronate disodium may be administered either in a single infusion or in multiple infusions over 2-4 consecutive days. The maximum dose per treatment course is 90 mg for both initial and repeat courses. Osteolytic lesions in multiple myeloma: 90 mg/4h every 4 weeks. Osteolytic lesions in bone metastases associated with breast cancer: 90mg/2h every 4 weeks (90mg/250ml; 45mg/h). Renal impairment: Pamidronate should not be administered to patients with severe renal impairment (creatinine clearance < 30 mL/min) unless in case of life-threatening tumour induced hypercalcaemia where the benefit outweighs the potential risk. Dose adjustment is not necessary in mild (creatinine clearance 61-90 mL/min) to moderate renal impairment (creatinine clearance 30-60 mL/min). In such patients, the infusion rate should not exceed 90 mg/4h (approximately 20-22 mg/h). Pregnancy: Pamidronate should not be administered to pregnant women except in cases of life-threatening hypercalcaemia. Patients treated with Pamifos 3 mg/ml should be given the package leaflet and the patient reminder card. **Undesirable effects:** Adverse reactions to pamidronate disodium are usually mild and transient. The most common adverse reactions are asymptomatic hypocalcaemia and fever (an increase in body temperature of 1-2°C), typically occurring within the first 48 hours of infusion. Fever usually resolves spontaneously. ***Infections:*** *Very rare:* reactivation of herpes simplex, herpes zoster. ***Blood, lymphatic system:*** *Common:* anaemia, thrombocytopenia, lymphocytopenia; *very rare:* leukopenia. ***Immune system:*** *Uncommon:* allergic reactions including anaphylactoid reactions, bronchospasm/dyspnoea, Quincke's (angioneurotic) oedema; *very rare*: anaphylactic shock. ***Metabolism, nutrition:*** *Very common:* hypocalcaemia, hypophosphataemia; *common:* hypokalaemia, hypomagnesaemia; *very rare:* hyperkalaemia, hypernatraemia. ***Nervous system:*** *Common:* symptomatic hypocalcaemia (paraesthesia, tetany), headache, insomnia, somnolence; *uncommon:* seizures, agitation, dizziness, lethargy; *very rare:* confusion, visual hallucinations. ***Eyes:*** *Common:* conjunctivitis*; uncommon:* uveitis (iritis, iridocyclitis); *very rare:* scleritis, episcleritis, xanthopsia; *frequency not known:* orbital inflammation. ***Cardiac*** *Very rare:* left ventricular failure (dyspnoea, pulmonary oedema), congestive heart failure (oedema) due to fluid overload; *frequency not known:* atrial fibrillation. ***Vascular:*** *Common:* hypertension; *uncommon:* hypotension. ***Respiratory:*** *Very rare:* acute respiratory distress syndrome, interstitial lung disease. ***Gastrointestinal:*** *Common:* nausea, vomiting*,* anorexia, abdominal pain, diarrhoea, constipation, gastritis; *uncommon:* dyspepsia. ***Skin, subcutaneous tissue****: Common:* rash; *uncommon:* pruritus. ***Musculoskeletal, connective tissue:*** *Common:* transient bone pain, arthralgia, myalgia; *uncommon:* muscle cramp, osteonecrosis; *rare:* atypical subtrochanteric and diaphyseal femoral fractures; *very rare:* osteonecrosis of the external auditory canal (bisphosphonate class adverse reaction); *frequency not known:* osteonecrosis of the jaw. ***Renal, urinary:*** *Uncommon:* acute renal failure; *rare:* focal segmental glomerulosclerosis including the collapsing variant, nephrotic syndrome; *very rare:* deterioration of pre-existing renal disease, haematuria, renal tubular disorder, tubulointerstitial nephritis, glomerulonephropathy. ***General disorders, administration site conditions:*** *Very common:* fever and influenza like symptoms sometimes accompanied by malaise, rigors, fatigue and flushes*; common:* reactions at the infusion site (pain, redness, swelling, induration, phlebitis, thrombophlebitis), general body pain. ***Investigations:*** *Common:* increase in serum creatinine; *uncommon:* abnormal liver function tests, increase in serum urea. **Legal classification**: POM (prescription only medicine). **Marketing authorisation holder:** medac GmbH, Theaterstraße 6; 22880 Wedel, Germany. **Date of revision of text**: 12/2021

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