Osteonorm; Osteostab; ***Malaysia:*** Bonefos; ***Mex.:*** Bonefos; ***Neth.:*** Bonefos; Ostac; ***Norw.:*** Bonefos; ***Philipp.:*** Bonefos; ***Pol.:*** Bonefos; Sindronat; ***Port.:*** Bonefos; Ostac; ***Rus.:*** Bonefos (Бонефос); ***S.Afr.:*** Bonephos; Ostac†; ***Singapore:*** Bonefos; ***Spain:*** Bonefos; Hemocalcin†; Mebonat†; ***Swed.:*** Bonefos; Ostac; ***Switz.:*** Bonefos; Ostac; ***Thai.:*** Bonefos; ***Turk.:*** Bonefos; ***UK:*** Bonefos; Clasteon; Loron.

### Denosumab *(USAN, rINN)*

AMG-162; Dénosumab; Denosumabum.

Денозумаб

*CAS — 615258-40-7.*

#### Profile

Denosumab is a human monoclonal antibody that specifically targets the receptor activator of nuclear factor-kappa B ligand (RANKL), a mediator of the resorptive phase of bone remodelling. Denosumab is under investigation for various conditions, including osteoporosis, treatment-induced bone loss, rheumatoid arthritis, bone metastases, and multiple myeloma.

◊ References.


1. Lewiecki EM. RANK ligand inhibition with denosumab for the management of osteoporosis. *Expert Opin Biol Ther* 2006; **6:** 1041–50.
2. Body J-J, *et al.* A study of the biological receptor activator of nuclear factor-kappaB ligand inhibitor, denosumab, in patients with multiple myeloma or bone metastases from breast cancer. *Clin Cancer Res* 2006; **12:** 1221–8.
3. McClung MR, *et al.* Denosumab in postmenopausal women with low bone mineral density. *N Engl J Med* 2006; **354:** 821–31.
4. Hamdy NA. Targeting the RANK/RANKL/OPG signaling pathway: a novel approach in the management of osteoporosis. *Curr Opin Investig Drugs* 2007; **8:** 299–303.
5. Lewiecki EM, *et al.* AMG 162 Bone Loss Study Group. Two-year treatment with denosumab (AMG 162) in a randomized phase 2 study of postmenopausal women with low BMD. *J Bone Miner Res* 2007; **22:** 1832–41.
6. Lipton A, *et al.* Randomized active-controlled phase II study of denosumab efficacy and safety in patients with breast cancer-related bone metastases. *J Clin Oncol* 2007; **25:** 4431–7.
7. Bone HG, *et al.* Effects of denosumab on bone mineral density and bone turnover in postmenopausal women. *J Clin Endocrinol Metab* 2008; **93:** 2149–57.
8. Cohen SB, *et al.* Denosumab Rheumatoid Arthritis Study Group. Denosumab treatment effects on structural damage, bone mineral density, and bone turnover in rheumatoid arthritis: a twelve-month, multicenter, randomized, double-blind, placebo-controlled, phase II clinical trial. *Arthritis Rheum* 2008; **58:** 1299–1309.
9. Miller PD, *et al.* Effect of denosumab on bone density and turnover in postmenopausal women with low bone mass after long-term continued, discontinued, and restarting of therapy: a randomized blinded phase 2 clinical trial. *Bone* 2008; **43:** 222–9.


## Etidronate

*ATC — M05BA01.*

*ATC Vet — QM05BA01.*

### Etidronic Acid *(BAN, USAN, rINN)*

Acide Étidronique; Ácido etidrónico; Acidum Etidronicum; Etidronihappo; Etidronsyra. 1-Hydroxyethylidenedi(phosphonic acid).

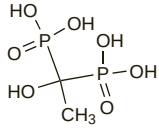
Этидроновая Кислота

$C_2H_8O_7P_2$ = 206.0.

*CAS — 2809-21-4.*

*ATC — M05BA01.*

*ATC Vet — QM05BA01.*



### Etidronate Disodium *(USAN, rINNM)*

Dinatrii etidronas; Dinatriumetidronaatti; Dinatriumetidronat; Dinatrium-etidronát; Disodium Etidronate *(BANM)*; Disodu etydronian; Disodyum Etidronat; EHDP; Etidronas Dinatricum; Étidronate disodique; Etidronate Disodique; Etidronato disódico. Disodium dihydrogen (1-hydroxyethylidene)diphosphonate.

Динатрий Этидронат

$C_2H_6Na_2O_7P_2$ = 250.0.

*CAS — 7414-83-7.*

*ATC — M05BA01.*

*ATC Vet — QM05BA01.*

NOTE. Other etidronic acid sodium salts are designated as etidronate monosodium, etidronate trisodium, and etidronate tetrasodium. The name etidronate sodium is used only in *Martindale* where the salt cannot be identified more precisely.

**Pharmacopoeias.** In *Eur.* (see p.vii), *Jpn*, and *US.*

**Ph. Eur. 6.2** (Etidronate Disodium). A white or yellowish, hygroscopic powder. Freely soluble in water; practically insoluble in alcohol and in acetone. A 1% solution in water has a pH of 4.2 to 5.2. Store in airtight containers.

**USP 31** (Etidronate Disodium). A white powder that may contain lumps. Freely soluble in water; practically insoluble in alcohol. Store in airtight containers. pH of a 1% solution in water is between 4.2 and 5.2.

### Adverse Effects, Treatment, and Precautions

As for the bisphosphonates in general, p.1089. Unlike the newer bisphosphonates etidronate produces marked impairment of bone mineralisation at high therapeutic doses. An increase in bone pain may occur in patients with Paget's disease. Impairment of bone mineralisation may result in osteomalacia, and fractures have been reported. If a fracture occurs etidronate should be stopped until healing is complete. Hyperphosphataemia may occur, usually at high doses, but generally resolves 2 to 4 weeks after the end of therapy. There have been reports of paraesthesias, peripheral neuropathy, and confusion. Burning of the tongue, alopecia, erythema multiforme, and exacerbation of asthma have occurred rarely. Transient loss or alteration of taste has been reported mainly during and after intravenous infusion.

**Effects on the blood.** For a report of pancytopenia caused by etidronate therapy, see Effects on the Skin, below.

**Effects on the ears.** Ototoxicity, manifest as tinnitus and hearing loss, has been reported[1] in 2 patients given etidronate for osteoporosis; both patients had pre-existing otosclerosis and the authors recommended that those with ear pathology be monitored audiometrically when given bisphosphonates.

1. Yeşil S, *et al.* Further hearing loss during osteoporosis treatment with etidronate. *Postgrad Med J* 1998; **74:** 363–4.

**Effects on the eyes.** For reports of ocular effects associated with the bisphosphonates, including etidronate, see under Bisphosphonates, p.1090.

**Effects on the gastrointestinal tract.** Oral etidronate was not associated with an increased incidence of upper gastrointestinal problems in a retrospective cohort study.[1] There was also no evidence of an increased incidence of gastrointestinal effects when given with NSAIDs or corticosteroids. Similarly, another large cohort study found no increased risk of peptic ulcer disease associated with the use of cyclical etidronate.[2] However, oesophageal ulceration has been reported with daily etidronate;[3,4] in one case possibly associated with incorrect use,[3] and in another, complicated by prior use of diclofenac, and a history of gastro-oesophageal reflux disease.[4]

1. van Staa T, *et al.* Upper gastrointestinal adverse events and cyclical etidronate. *Am J Med* 1997; **103:** 462–7.
2. Burger H, *et al.* Cyclical etidronate use is not associated with symptoms of peptic ulcer disease. *Eur J Clin Pharmacol* 2000; **56:** 319–22.
3. Macedo G, *et al.* Ulcerative esophagitis caused by etidronate. *Gastrointest Endosc* 2001; **53:** 250–1.
4. Maroy B. Ulcère géant de l'œsophage probablement dû à la prise d'étidronate. *Gastroenterol Clin Biol* 2001; **25:** 917–18.

**Effects on the kidneys.** Bisphosphonates are excreted by the kidneys, thus caution is advised in patients with renal impairment. When given by intravenous infusion for the treatment of hypercalcaemia of malignancy they have been reported to affect renal function adversely; hypercalcaemia or malignancy may also have contributed. For reports of renal failure associated with etidronate see under Bisphosphonates, p.1091.

**Effects on mental state.** Sensory hallucinations and confusion were reported in an elderly woman given daily etidronate for a week. Symptoms resolved on stopping the drug and recurred on rechallenge.[1] Mood disturbances, lack of concentration, and memory impairment were also reported in 3 patients receiving longer-term cyclical treatment; symptoms again diminished on stopping etidronate and reappeared after rechallenge.[2]

1. Burnet SP, Petrie JP. 'Wake up and smell the roses'—a drug reaction to etidronate. *Aust N Z J Med* 1999; **29:** 93.
2. Wolffenbuttel BHR, van der Klauw MM. Psychische bijwerkingen van behandeling met bisfosfonaten. *Ned Tijdschr Geneeskd* 2003; **147:** 35–7.

**Effects on the respiratory system.** For a report of bronchospasm induced by etidronate in an aspirin-sensitive asthmatic, see p.1091. For a report of fatal cardiorespiratory failure secondary to acute respiratory distress syndrome caused by etidronate, see Effects on the Skin, below.

**Effects on the skin.** A 47-year old woman with a history of auto-immune rheumatic disease developed toxic epidermal necrolysis, pancytopenia, and acute respiratory distress syndrome 7 days after starting etidronate for osteoporosis; she died of cardiorespiratory failure, secondary to the acute respiratory distress syndrome, despite aggressive supportive measures.[1]

1. Coakley G, Isenberg DA. Toxic epidermal necrolysis, pancytopenia and adult respiratory syndrome. *Br J Rheumatol* 1995; **34:** 798.

**Hypersensitivity.** Allergic reactions to bisphosphonates do occur but appear to be rare (see p.1091).

### Interactions

As for the bisphosphonates in general, p.1091.

**Anti-inflammatory drugs.** For a lack of apparent interaction between cyclical etidronate and corticosteroids or NSAIDs see under Effects on the Gastrointestinal Tract, above.

### Pharmacokinetics

After oral doses of etidronate, absorption is variable and appears to be dose dependent. At usual doses about 1 to 6% of a dose is absorbed. Absorption is reduced by food, especially by products containing calcium or other polyvalent cations. Etidronate is rapidly cleared from the blood and has been reported to have a plasma half-life of 1 to 6 hours. It is not metabolised. About 50% is excreted in the urine within 24 hours, the remainder being sequestered to bone and slowly eliminated. The half-life of etidronate in bone exceeds 90 days. Unabsorbed etidronate appears in the faeces.

### Uses and Administration

Etidronate is a bisphosphonate with general properties similar to those of the other bisphosphonates (p.1091). It inhibits the growth and dissolution of hydroxyapatite crystals in bone and may also directly impair osteoclast activity. It diminishes bone resorption and thus reduces bone turnover.

Etidronate is used as an adjunct in the treatment of severe hypercalcaemia, especially when associated with malignancy. It is also given in bone disorders in which excessive bone resorption is a problem, such as Paget's disease of bone and osteoporosis. In addition, it may be used for the prevention and treatment of ectopic (heterotopic) ossification. A chelate of etidronate with radioactive technetium-99m (p.2055) is used diagnostically as a bone scanning agent and a similar compound with rhenium-186 for the palliation of bone metastases in prostate cancer (see below).

Etidronate is given as the disodium salt, by intravenous infusion over at least 2 hours, or orally, usually as a single daily dose. Food should be avoided for 2 hours before and after oral doses.

In the treatment of **Paget's disease**, etidronate disodium is given orally in a usual initial dose of 5 mg/kg daily for not more than 6 months. Doses above 10 mg/kg daily should be reserved for severe disease and should not be given for more than 3 months at a time. The maximum dose is 20 mg/kg daily. The response to etidronate may be slow in onset and may continue for several months after stopping therapy. Therefore, further treatment should only be given after a drug-free interval of at least 3 months and after evidence of relapse; it should not be given for longer than the initial treatment.

In the treatment of **hypercalcaemia of malignancy** the recommended dose of etidronate disodium by slow intravenous infusion is 7.5 mg/kg daily for 3 successive days, although infusions may be continued for up to 7 days if necessary. This daily dose should be diluted in at least 250 mL of sodium chloride 0.9% and infused over at least 2 hours. There should be at least a 7-day interval between courses of treatment. Once serum-calcium concentrations have been reduced to an acceptable level, maintenance therapy with oral etidronate disodium 20 mg/kg daily for 30 days may be started on the day after the last intravenous dose; treatment may be extended to a maximum of 90 days.

For the prevention and treatment of **ectopic ossification** complicating hip replacement etidronate disodium has been given orally in a dose of 20 mg/kg daily for 1 month before and 3 months after the operation. For ectopic ossification due to spinal cord injury it has been

given in a dose of 20 mg/kg daily for 2 weeks followed by 10 mg/kg daily for 10 weeks.

For the treatment of **osteoporosis**, the prevention of bone loss in postmenopausal women, and the prevention and treatment of corticosteroid-induced osteoporosis, etidronate is given in an intermittent or cyclical regimen with a calcium salt; oral etidronate disodium 400 mg is given daily for 14 days followed by the equivalent of 500 mg of elemental calcium orally for 76 days. Treatment has continued for 3 years in most patients; a small number of patients have been successfully treated for up to 7 years. The optimum duration of treatment has not been established.

**Administration in renal impairment.** Some manufacturers have recommended that etidronate disodium should not be given *intravenously* to patients with serum-creatinine concentrations greater than 50 mg/litre, and that doses may need to be reduced in those with concentrations between 25 and 49 mg/litre. Reduced *oral* doses are similarly recommended in mild renal impairment, and avoidance in moderate to severe impairment.

**Ectopic ossification.** Bisphosphonates that inhibit bone mineralisation such as etidronate have been used to prevent ectopic ossification (p.100). Some studies, using higher and more prolonged dosage (20 mg/kg daily by mouth for 6 months) than is generally recommended for treatment after spinal cord injury, have suggested that this may improve effectiveness.[1,2] Etidronate has also been used to treat calciphylaxis and vascular and soft-tissue calcification associated with haemodialysis.[3-5]

1. Banovac K, *et al.* Treatment of heterotopic ossification after spinal cord injury. *J Spinal Cord Med* 1997; **20:** 60–65.
2. Banovac K. The effect of etidronate on late development of heterotopic ossification after spinal cord injury. *J Spinal Cord Med* 2000; **23:** 40–4.
3. Hashiba H, *et al.* Inhibition of the progression of aortic calcification by etidronate treatment in hemodialysis patients: long-term effects. *Ther Apher Dial* 2006; **10:** 59–64.
4. Shiraishi N, *et al.* Successful treatment of a patient with severe calcific uremic arteriolopathy (calciphylaxis) by etidronate disodium. *Am J Kidney Dis* 2006; **48:** 151–4.
5. Mori H, *et al.* Etidronate for the treatment of progressive tumoral calcinosis in hemodialysis patients. *Intern Med* 2007; **46:** 1485–6.

**Hypercalcaemia.** Bisphosphonates (including etidronate although other bisphosphonates may be more suitable) are the preferred drugs for treating hypercalcaemia of malignancy (p.1083) once the patient has been adequately rehydrated.

There are reports of response[1-3] to etidronate 5 mg/kg twice daily by mouth in the treatment of hypercalcaemia associated with subcutaneous fat necrosis of the newborn refractory to standard treatment.

1. Rice AM, Rivkees SA. Etidronate therapy for hypercalcemia in subcutaneous fat necrosis of the newborn. *J Pediatr* 1999; **134:** 349–51.
2. Wiadrowski TP, Marshman G. Subcutaneous fat necrosis of the newborn following hypothermia and complicated by pain and hypercalcaemia. *Australas J Dermatol* 2001; **42:** 207–10.
3. Trullemans B, *et al.* Etidronate per os dans le cadre d'une hypercalcémie secondaire à une cytostéatonécrose compliquée de néphrocalcinose. *Arch Pediatr* 2007; **14:** 170–2.

**Malignant neoplasms of the bone.** Bisphosphonates are of benefit in some patients with metastatic bone disease (p.660). Etidronate, labelled with rhenium-186 or its isotope rhenium-188, is used for the palliation of painful bone metastases of prostate,[1,2] breast,[3,4] lung,[4,5] and various other cancers.[4]

1. Han SH, *et al.* The Placorhen study: a double-blind, placebo-controlled, randomized radionuclide study with Re-etidronate in hormone-resistant prostate cancer patients with painful bone metastases. *J Nucl Med* 2002; **43:** 1150–6.
2. Liepe K, *et al.* Therapeutic efficiency of rhenium-188-HEDP in human prostate cancer skeletal metastases. *Br J Cancer* 2003; **89:** 625–9.
3. Sciuto R, *et al.* Metastatic bone pain palliation with 89-Sr and 186-Re-HEDP in breast cancer patients. *Breast Cancer Res Treat* 2001; **66:** 101–9.
4. Li S, *et al.* Rhenium-188 HEDP to treat painful bone metastases. *Clin Nucl Med* 2001; **26:** 919–22.
5. Zhang H, *et al.* Rhenium-188-HEDP therapy for the palliation of pain due to osseous metastases in lung cancer patients. *Cancer Biother Radiopharm* 2003; **18:** 719–26.

**Osteoporosis.** Bisphosphonates are used in the prevention and treatment of osteoporosis (p.1084). Etidronate is used in a cyclical regimen for both the treatment and prevention of **postmenopausal** osteoporosis. It increases bone mineral density (BMD), largely in the lumbar spine and femoral neck, and reduces the risk of vertebral fractures,[1,2] but not non-vertebral fractures.[2] Additive effects on BMD have been found when etidronate was used with oestrogen.[1] Etidronate also prevents bone loss and maintains or increases BMD in **corticosteroid-induced** osteoporosis,[1,3] and has shown some benefit in reducing bone loss after organ transplantation.[1] In an uncontrolled study[4] in **men** with idiopathic vertebral osteoporosis, cyclical etidronate increased BMD at the lumbar spine.

1. Hanley DA, *et al.* Etidronate therapy in the treatment and prevention of osteoporosis. *J Clin Densitom* 2000; **3:** 79–95.
2. Wells GA, *et al.* Etidronate for the primary and secondary prevention of osteoporotic fractures in postmenopausal women. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2008 (accessed 15/04/08).
3. Adachi JD, *et al.* A pooled data analysis on the use of intermittent cyclical etidronate therapy for the prevention and treatment of corticosteroid induced bone loss. *J Rheumatol* 2000; **27:** 2424–31.
4. Anderson FH, *et al.* Effect of intermittent cyclical disodium etidronate therapy on bone mineral density in men with vertebral fractures. *Age Ageing* 1997; **26:** 359–65.

**Paget's disease of bone.** Bisphosphonates may be indicated for patients with Paget's disease of bone (p.1086) if bone pain is persistent, or to prevent further progression of the disease. Initial experience was with etidronate, but bisphosphonates that have less effect on bone mineralisation may be preferred. In studies, alendronate[1] and risedronate[2] were found to be more effective than etidronate.

1. Siris E, *et al.* Comparative study of alendronate versus etidronate for the treatment of Paget's disease of bone. *J Clin Endocrinol Metab* 1996; **81:** 961–7.
2. Miller PD, *et al.* A randomized, double-blind comparison of risedronate and etidronate in the treatment of Paget's disease of bone. *Am J Med* 1999; **106:** 513–20.

### Preparations

***USP 31:*** Etidronate Disodium Tablets.

**Proprietary Preparations** (details are given in Part 3)
***Arg.:*** Difosfen; ***Austral.:*** Didronel; ***Austria:*** Detidron; Didronel; ***Belg.:*** Didronel†; Osteodidronel; ***Canad.:*** Didronel; ***Chile:*** Osteotop†; ***Denm.:*** Didronate; ***Fin.:*** Didronate; ***Fr.:*** Didronel; ***Ger.:*** Didronel; Diphos; Etidron; ***Gr.:*** Anfozan; Biotredine†; Dralen†; Etidron; Etiplus; Feminoflex; Maxibral; Oflocin; Osfo; Ostedron; Osteodrug; Osteoton; Ostogene; Ostopor; Somaflex†; Sterodome†; Sviroxit; Tilferan†; ***Hong Kong:*** Didronel†; ***India:*** Dronate-OS; ***Irl.:*** Didronel; ***Israel:*** Didronel; ***Ital.:*** Didronel†; Etidron; ***Jpn:*** Didronel; ***Neth.:*** Didronel; ***NZ:*** Didronel; Etidrate; ***Pol.:*** Ostedron; ***Port.:*** Didronel†; ***Singapore:*** Difosfen; ***Spain:*** Difosfen; Osteum; ***Swed.:*** Didronate; Etidrel; ***Switz.:*** Didronel; ***Thai.:*** Difosfen; ***Turk.:*** Didronat; ***UK:*** Didronel; ***USA:*** Didronel.

**Multi-ingredient:** ***Arg.:*** Emoform Total; Squam; ***Austral.:*** Didrocal; ***Canad.:*** Didrocal; ***Denm.:*** Didronate Calcium; ***Fin.:*** Didronate + Calcium; ***Ger.:*** Didronel Kit; Etidron Kombi; ***Irl.:*** Didronel PMO; ***Neth.:*** Didrokit; ***Norw.:*** Didronate + Calsium; ***Swed.:*** Didronate + Calcium; Etidrel Kit; ***UK:*** Didronel PMO; Tiloetca Combi.

## Gallium Nitrate *(USAN)*

Galio, nitrato de; NSC-15200; WR-135675.
$Ga(NO_3)_3,9H_2O$ = 417.9.
*CAS — 13494-90-1 (anhydrous gallium nitrate); 135886-70-3 (gallium nitrate nonahydrate).*

### Adverse Effects, Treatment, and Precautions

Gallium nitrate may produce serious nephrotoxicity, especially when given as a brief intravenous infusion; continuous infusion, with adequate hydration, may reduce the incidence of renal damage. Serum creatinine should be monitored during therapy and treatment stopped if it exceeds 25 mg/litre. Gallium nitrate should be given with great care and in reduced doses, if at all, to patients with existing renal impairment.

Gastrointestinal disturbances, rashes, metallic taste, visual and auditory disturbances, anaemia, hypophosphataemia, and hypocalcaemia have also been reported.

**Effects on the nervous system.** Although it has been suggested, given the chemical similarity of gallium to aluminium, that repeated doses, particularly in the presence of renal impairment, might lead to severe neurotoxicity,[1] studies in *rats* do not provide any evidence of central neurological abnormalities.[2]

1. Altmann P, Cunningham J. Hazards of gallium for the treatment of Paget's disease of bone. *Lancet* 1990; **335:** 477.
2. Matkovic V, *et al.* Hazards of gallium for Paget's disease of bone. *Lancet* 1990; **335:** 1099. Correction. *ibid.*; 1352.

### Uses and Administration

Gallium nitrate is an inorganic metallic salt with hypocalcaemic properties. It acts to decrease bone resorption by osteoclasts, with a lesser and probably indirect increase in bone formation, and a consequent decline in serum calcium.

Gallium nitrate is used in the treatment of hypercalcaemia associated with malignant neoplasms. It has been investigated in other disorders associated with abnormally enhanced bone turnover, such as Paget's disease of bone, and is under investigation in refractory non-Hodgkin's lymphoma. For the treatment of hypercalcaemia of malignancy doses of 100 to 200 mg/m$^2$ may be given daily for up to 5 days, diluted in 1 litre of sodium chloride 0.9% or glucose 5% and infused intravenously over 24 hours. Treatment may be repeated after 2 to 4 weeks, if necessary. Adequate hydration before and during treatment is essential: a urinary output of at least 2 litres daily should be maintained, and renal function should be regularly monitored.

**Hypercalcaemia.** Gallium nitrate is used in the treatment of hypercalcaemia of malignancy (p.1083). It appears to be effective in patients with solid tumours and increased levels of parathyroid-related protein.[1,2]

1. Chitambar CR. Gallium nitrate revisited. *Semin Oncol* 2003; **30** (suppl): 1–4.
2. Leyland-Jones B. Treatment of cancer-related hypercalcemia: the role of gallium nitrate. *Semin Oncol* 2003; **30** (suppl); 13–19.

**Paget's disease of bone.** Beneficial results[1] were reported when gallium nitrate was given subcutaneously in doses of 250 or 500 micrograms/kg daily for 14 days to patients with advanced Paget's disease of bone (p.1086). In this pilot multicentre study 14 days of gallium nitrate injections were followed by 4 weeks off medication and the cycle repeated once.

1. Bockman RS, *et al.* A multicenter trial of low dose gallium nitrate in patients with advanced Paget's disease of bone. *J Clin Endocrinol Metab* 1995; **80:** 595–602.

### Preparations

**Proprietary Preparations** (details are given in Part 3)
***USA:*** Ganite.

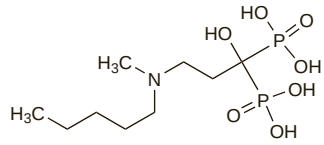
# Ibandronate

*ATC — M05BA06.*
*ATC Vet — QM05BA06.*

## Ibandronic Acid *(BAN, rINN)*

Acide Ibandronique; Ácido ibandrónico; Acidum Ibandronicum; BM-21.0955; Ibandronik Asit. [1-Hydroxy-3-(methylpentylamino)propylidene]diphosphonic acid.

Ибандроновая Кислота
$C_9H_{23}NO_7P_2$ = 319.2.
*CAS — 114084-78-5.*
*ATC — M05BA06.*
*ATC Vet — QM05BA06.*



## Ibandronate Sodium *(USAN)*

Sodium Ibandronate *(BANM, rINNM)*; Ibandronate de Sodium; Ibandronato sódico; Natrii Ibandronas; Natriumibandronaatti; Natriumibandronat.

Натрий Ибандронат
$C_9H_{22}NNaO_7P_2,H_2O$ = 359.2.
*CAS — 138926-19-9.*
*ATC — M05BA06.*
*ATC Vet — QM05BA06.*

### Adverse Effects, Treatment, and Precautions

As for the bisphosphonates in general, p.1089. Gastrointestinal symptoms such as abdominal pain, dyspepsia, and nausea are the most frequent adverse effects with oral ibandronate. Severe oesophageal reactions such as oesophagitis, and ulceration have occurred; patients should be advised to stop taking the tablets and seek medical attention if they develop symptoms such as new or worsening dysphagia, pain on swallowing, retrosternal pain, or heartburn. Gastric ulceration has been reported. To minimise the risk of oesophageal reactions, precautions similar to those for alendronate (see p.1088) should be observed. Anaemia and bronchospasm have occurred rarely, as has taste disturbance, paraesthesia, and uraemia. Serum calcium, magnesium, and phosphate should be monitored. Hypocalcaemia should be corrected before starting ibandronate therapy; adequate intake of calcium and vitamin D is important. Transient fever after parenteral use is common. Flu-like symptoms have been reported after both parenteral and intermittent oral use, typically after the first dose.

**Effects on the musculoskeletal system.** Osteonecrosis of the jaw has been reported after the use of bisphosphonates, including ibandronate (see Effects on the Musculoskeletal System, under Adverse Effects of Bisphosphonates, p.1091).

### Interactions

As for the bisphosphonates in general, p.1091.

### Pharmacokinetics

Like other bisphosphonates, ibandronate is poorly absorbed after oral doses; absolute bioavailability is less than 1%. Absorption is decreased by food, especially by products containing calcium or other polyvalent cations. Bioavailability is reduced by about 90% when given with food, by about 30% when given half an hour before food, and by about 75% when given