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.

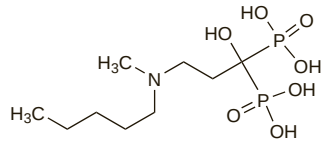
Ibandronate

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

2 hours after food. About half of the absorbed portion is sequestered to bone; the remainder is excreted in urine. Plasma protein binding is about 87%. Bisphosphonates do not appear to be metabolised, and the unabsorbed fraction of ibandronate is excreted unchanged in the faeces.

◊ References.

1. Bergner R, *et al.* Renal safety and pharmacokinetics of ibandronate in multiple myeloma patients with or without impaired renal function. *J Clin Pharmacol* 2007; **47:** 942–50.

Uses and Administration

Ibandronate is an aminobisphosphonate (p.1089) that is a potent inhibitor of bone resorption. It is used as the sodium salt in hypercalcaemia of malignancy, for the prevention of fracture and bone complications in patients with breast cancer and bone metastases, and for the treatment and prevention of postmenopausal osteoporosis.

Ibandronate sodium is given by intravenous infusion or orally, the dose being expressed in terms of ibandronic acid; ibandronate sodium 1.13 mg is equivalent to about 1 mg of ibandronic acid. Specific instructions for oral use (see Precautions in Alendronate, p.1088) should be followed to minimise adverse effects and permit adequate absorption.

For **hypercalcaemia of malignancy**, a single intravenous dose of the equivalent of 2 to 4 mg ibandronic acid is given, up to a maximum of 6 mg; it is diluted in 500 mL of sodium chloride 0.9% or glucose 5%, and infused over 2 hours.

For the prevention of skeletal events in patients with breast cancer and **bone metastases**, the equivalent of 6 mg ibandronic acid is given intravenously, diluted in 100 mL of sodium chloride 0.9% or glucose 5%, and infused over at least 15 minutes. The dose is repeated every 3 to 4 weeks. Alternatively, ibandronic acid 50 mg daily may be given orally.

For the prevention and treatment of postmenopausal **osteoporosis**, ibandronate is given orally in a usual dose equivalent to 150 mg of ibandronic acid once monthly on the same date each month; alternatively, 2.5 mg daily by mouth may be given. If the once-monthly dose is missed, and the next scheduled dose is more than 7 days away, the dose should be taken the next morning, and the patient should then return to the original schedule. However, if the next dose is less than 7 days away, then the patient should wait until that next scheduled dose; 2 tablets must not be taken within the same week. Alternatively, treatment may be given intravenously, in a dose equivalent to 3 mg of ibandronic acid once every 3 months; the injection is given over 15 to 30 seconds. If the dose is missed, the injection should be given as soon as possible; the next injection should then be rescheduled 3 months from this injection, as it should not be given more frequently than once every 3 months.

◊ General references.

1. Dooley M, Balfour JA. Ibandronate. *Drugs* 1999; **57:** 101–108.
2. Barrett J, *et al.* Ibandronate: a clinical pharmacological and pharmacokinetic update. *J Clin Pharmacol* 2004; **44:** 951–65.
3. Anonymous. Ibandronate (Boniva): a new oral bisphosphonate. *Med Lett Drugs Ther* 2005; **47:** 35.
4. Guay DR. Ibandronate, an experimental intravenous bisphosphonate for osteoporosis, bone metastases, and hypercalcemia of malignancy. *Pharmacotherapy* 2006; **26:** 655–73.
5. Zaidi M, *et al.* Progression of efficacy with ibandronate: a paradigm for the development of new bisphosphonates. *Ann N Y Acad Sci* 2007; **1117:** 273–82.
6. Reginster JY, *et al.* Ibandronate in profile: drug characteristics and clinical efficacy. *Expert Opin Drug Metab Toxicol* 2008; **4:** 941–51.

Administration in renal impairment. UK and US licensed product information for ibandronate states that the dose should be adjusted on the basis of creatinine clearance (CC).

When used for the prevention of skeletal events in patients with breast cancer and **bone metastases**, the following *oral* doses are recommended:

- mild or moderate renal impairment (CC equal to or greater than 30 mL/minute): no adjustment necessary
- CC below 30 mL/minute: 50 mg once weekly

Since a 15-minute infusion time has not been studied in cancer patients with a CC less than 50 mL/minute, the following *intravenous* doses are recommended, to be given every 3 to 4 weeks in a solution of sodium chloride 0.9% or glucose 5%:

- CC equal to or greater than 50 mL/minute: no adjustment necessary
- CC less than 50 mL/minute, but equal to or greater than 30 mL/minute: 6 mg in 500 mL of infusion solution, infused over 1 hour
- CC less than 30 mL/minute: 2 mg in 500 mL of infusion solution, infused over 1 hour

In patients with **osteoporosis**, the following recommendations are given, for *oral* or *intravenous* use:

- mild or moderate renal impairment (CC equal to or greater than 30 mL/minute): no adjustment necessary
- CC below 30 mL/minute: not recommended

Hypercalcaemia. Bisphosphonates are the preferred drugs for treating hypercalcaemia of malignancy (p.1083) once the patient has been adequately rehydrated. In a dose-response study,[1] 2 mg of ibandronate was found to be significantly less effective than 4 or 6 mg in correcting hypercalcaemia, and response was better in those patients with breast cancer or haematological tumours. In comparison to pamidronate,[2] ibandronate was reported to be more effective in those patients with higher initial baseline serum calcium; duration of response was also longer with ibandronate. In a series of case reports, intravenous ibandronate rapidly corrected hypercalcaemia and restored renal function in multiple myeloma patients. The authors suggested that, although unlicensed for this use, ibandronate should be considered in this patient population.[3]

1. Ralston SH, *et al.* Dose-response study of ibandronate in the treatment of cancer-associated hypercalcaemia. *Br J Cancer* 1997; **75:** 295–300.
2. Pecherstorfer M, *et al.* Efficacy and safety of ibandronate in the treatment of hypercalcemia of malignancy: a randomized multicentric comparison to pamidronate. *Support Care Cancer* 2003; **11:** 539–47.
3. Henrich D, *et al.* Ibandronate for the treatment of hypercalcemia or nephrocalcinosis in patients with multiple myeloma and acute renal failure: case reports. *Acta Haematol (Basel)* 2006; **116:** 165–72.

Malignant neoplasms of the bone. Bisphosphonates are of benefit in some patients with metastatic bone disease (p.660) not only to manage bone pain and hypercalcaemia, but to reduce skeletal complications such as fractures. Ibandronate is licensed for such use in many countries. In patients with bone metastases from breast cancer, both oral[1] and intravenous[2] ibandronate reduced the skeletal morbidity period rate (the number of 12-week periods with new bone complications). A pilot study[3] in 18 patients with skeletal metastases from various tumours, and with bone pain insufficiently controlled with opioid analgesics, found short-term intensive intravenous ibandronate (4 mg for 4 consecutive days) to significantly reduce bone pain scores; this analgesic effect was obtained within 7 days, and sustained for a further 5 weeks. A review[4] concluded that once-monthly intravenous dosing could aid compliance, since it can be given simultaneously with cancer therapy; the absence of any apparent renal toxicity associated with ibandronate was a further advantage in its use in cancer patients.

Whether bisphosphonates can prevent the development of new skeletal metastases is unclear.

1. Tripathy D, *et al.* Oral ibandronate for the treatment of metastatic bone disease in breast cancer: efficacy and safety results from a randomized, double-blind, placebo-controlled trial. *Ann Oncol* 2004; **15:** 743–50.
2. Body J-J, *et al.* Intravenous ibandronate reduces the incidence of skeletal complications in patients with breast cancer and bone metastases. *Ann Oncol* 2003; **14:** 1399–1405.
3. Mancini I, *et al.* Efficacy and safety of ibandronate in the treatment of opioid-resistant bone pain associated with metastatic bone disease: a pilot study. *J Clin Oncol* 2004; **22:** 3587–92.
4. McCormack PL, Plosker GL. Ibandronic acid: a review of its use in the treatment of bone metastases of breast cancer. *Drugs* 2006; **66:** 711–28.

Osteoporosis. Bisphosphonates are used for the prevention and treatment of osteoporosis (p.1084). In the treatment of **postmenopausal** osteoporosis, *oral* ibandronate in intermittent regimens of 20 mg every alternate day,[1] or 20 mg weekly[2] has been found to have equivalent effects on bone mineral density (BMD) to 2.5 mg daily. Intermittent oral ibandronate (20 mg every alternate day for 12 doses every 3 months) was also as effective as the lower daily dose in reducing the incidence of osteoporotic fractures in postmenopausal women.[3] In the prevention of postmenopausal osteoporosis, both 2.5 mg daily[4] and 20 mg weekly[5] prevented bone loss at the spine and hip. A large study comparing three different monthly regimens with the 2.5 mg daily regimen found them to be of similar efficacy in terms of improvement in lumbar BMD after 1 year; 150 mg given once monthly was considered to be superior to the low-dose daily regimen.[6] A review[7] concluded that this unique once-monthly regime could benefit patients by improving compliance.

Intravenous ibandronate 2 mg given every 3 months has also proven effective in increasing BMD in the treatment[8] and prevention[9] of postmenopausal osteoporosis. A large, randomised, double-blind study compared 2 intravenous regimens (2 mg every 2 months and 3 mg every 3 months) with oral ibandronate 2.5 mg daily in postmenopausal women with osteoporosis. After 1 year, both intravenous regimens increased lumbar BMD scores significantly more than the oral regimen. Similar results were obtained for proximal femoral BMD scores, except that for femoral neck BMD, the 2-monthly regimen and daily oral regimen were not significantly different.[10] After 2 years, these results were reported to have been maintained.[11] In **corticosteroid-induced** osteoporosis, intravenous ibandronate 2 mg every 3 months was better than daily oral alfacalcidol at reducing vertebral fractures.[12,13] Intravenous ibandronate has also shown to be of benefit in reducing bone loss after kidney **transplantation**.[14] A pilot study[15] of intermittent ibandronate given intravenously to **men** with severe osteoporosis significantly increased BMD at the lumbar spine, trochanter, and femoral neck.

1. Riis BJ, *et al.* Ibandronate: a comparison of oral daily dosing versus intermittent dosing in postmenopausal osteoporosis. *J Bone Miner Res* 2001; **16:** 1871–8.
2. Cooper C, *et al.* Efficacy and safety of oral weekly ibandronate in the treatment of postmenopausal osteoporosis. *J Clin Endocrinol Metab* 2003; **88:** 4609–15.
3. Chesnut CH, *et al.* Effects of oral ibandronate administered daily or intermittently on fracture risk in postmenopausal osteoporosis. *J Bone Miner Res* 2004; **19:** 1241–9.
4. McClung MR, *et al.* Oral daily ibandronate prevents bone loss in early postmenopausal women without osteoporosis. *J Bone Miner Res* 2004; **19:** 11–18.
5. Tankó LB, *et al.* Oral weekly ibandronate prevents bone loss in postmenopausal women. *J Intern Med* 2003; **254:** 159–67.
6. Miller PD, *et al.* Monthly oral ibandronate therapy in postmenopausal osteoporosis: 1-year results from the MOBILE study. *J Bone Miner Res* 2005; **20:** 1315–22.
7. Chesnut CH. Treating osteoporosis with bisphosphonates and addressing adherence: a review of oral ibandronate. *Drugs* 2006; **66:** 1351–9.
8. Adami S, *et al.* Efficacy and safety of ibandronate given by intravenous injection once every 3 months. *Bone* 2004; **34:** 881–9.
9. Stakkestad JA, *et al.* Intravenous ibandronate injections given every three months: a new treatment option to prevent bone loss in postmenopausal women. *Ann Rheum Dis* 2003; **62:** 969–75.
10. Delmas PD, *et al.* Intravenous ibandronate injections in postmenopausal women with osteoporosis: one-year results from the dosing intravenous administration study. *Arthritis Rheum* 2006; **54:** 1838–46.
11. Croom KF, Scott LJ. Intravenous ibandronate: in the treatment of osteoporosis. *Drugs* 2006; **66:** 1593–1601.
12. Ringe JD, *et al.* Intermittent intravenous ibandronate injections reduce vertebral fracture risk in corticosteroid-induced osteoporosis: results from a long-term comparative study. *Osteoporosis Int* 2003; **14:** 801–7.
13. Ringe JD, *et al.* Three-month ibandronate bolus injection offers favourable tolerability and sustained efficacy advantage over two years in established corticosteroid-induced osteoporosis. *Rheumatology (Oxford)* 2003; **42:** 743–9.
14. Grotz W, *et al.* Effect of ibandronate on bone loss and renal function after kidney transplantation. *J Am Soc Nephrol* 2001; **12:** 1530–7.
15. Lamy O, *et al.* Intravenous ibandronate in men with osteoporosis: an open pilot study over 2 years. *J Endocrinol Invest* 2003; **26:** 728–32.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Bandrobon; Bonviva; Elasterin; Femorel; Idena; Modifical; ***Austria:*** Bondronat; ***Belg.:*** Bondronat; ***Chile:*** Bondronat; Bonviva; ***Cz.:*** Bondenza; Bondronat; Bonviva; ***Denm.:*** Bondronat; ***Fin.:*** Bondronat; Bonviva; ***Fr.:*** Bondronat; Bonviva; ***Ger.:*** Bondronat; Bonviva; ***Gr.:*** Bondronat; Bonviva; ***Hong Kong:*** Bondronat; ***Hung.:*** Bondronat; Bonviva; ***Indon.:*** Bonviva; ***Irl.:*** Bondronat; Bonviva; ***Israel:*** Bonat; ***Ital.:*** Bondronat; Bonviva; ***Malaysia:*** Bonviva; ***Mex.:*** Bondronat; ***Neth.:*** Bondenza; Bondronat; Bonviva; Destara; ***Norw.:*** Bondronat; ***Philipp.:*** Bondronat; Bonviva; ***Pol.:*** Bondronat; Bonviva†; ***Port.:*** Bondenza; Bondronat; Bonviva; ***Rus.:*** Bondronat (Бондронат); ***S.Afr.:*** Bondronat; ***Singapore:*** Bondronat; Bonviva; ***Spain:*** Bondronat; ***Swed.:*** Bondronat; Bonviva; ***Switz.:*** Bondronat; ***Thai.:*** Bondronat; ***UK:*** Bondronat; Bonviva; ***USA:*** Boniva.

Multi-ingredient: ***Arg.:*** Femorel Max.

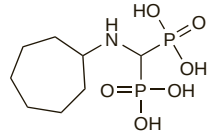
Incadronate

Incadronic Acid *(rINN)*

Acide Incadronique; Ácido incadrónico; Acidum Incadronicum; Cimadronic Acid; YM-175. [(Cycloheptylamino)methylene]diphosphonic acid.

Инкадроновая Кислота

$C_8H_{19}NO_6P_2$ = 287.2.
CAS — 124351-85-5.



Incadronate Disodium

Disodium Incadronate *(rINNM)*; Incadronas Dinatricum; Incadronate Disodique; Incadronato disódico. Disodium [(cycloheptylamino)methylene]diphosphonate.

Динатрий Инкадронат

$C_8H_{17}NNa_2O_6P_2$ = 331.2.
CAS — 138330-18-4.

Profile

Incadronate is an aminobisphosphonate (p.1089) that is a potent inhibitor of bone resorption. It is given by intravenous infusion