4. Winer KK, *et al.* Synthetic human parathyroid hormone 1-34 vs calcitriol and calcium in the treatment of hypoparathyroidism: results of a short-term randomized crossover trial. *JAMA* 1996; **276:** 631–6.
5. Winer KK, *et al.* Long-term treatment of hypoparathyroidism: a randomized controlled study comparing parathyroid hormone-(1-34) versus calcitriol and calcium. *J Clin Endocrinol Metab* 2003; **88:** 4214–20.
6. Decker GAG, *et al.* Allotransplantation of parathyroid cells. *Lancet* 1995; **345:** 124. Correction. *ibid.*; 464.
7. Hasse C, *et al.* Parathyroid allotransplantation without immunosuppression. *Lancet* 1997; **350:** 1296–7.

Alendronate

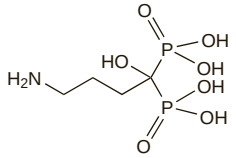
ATC — M05BA04.
ATC Vet — QM05BA04.

Alendronic Acid *(BAN, rINN)*

Acide Alendronique; Ácido alendrónico; Acidum Alendronicum; AHButBP; Alendronihappo; Alendronik Asit; Alendronsyra; Aminohydroxybutylidene Diphosphonic Acid. 4-Amino-1-hydroxybutane-1,1-diylbis(phosphonic acid).

Алендроновая Кислота

$C_4H_{13}NO_7P_2$ = 249.1.
CAS — 66376-36-1.
ATC — M05BA04.
ATC Vet — QM05BA04.



Alendronate Sodium *(USAN, rINNM)*

Alendronat Sodyum; Alendronate de Sodium; Alendronato sódico; G-704650; L-670452; MK-0217; MK-217; Monosodium alendronate; Natrii alendronas; Natrii Alendronas Trihydricus; Natrio alendronatas; Natriumalendronaatti; Natriumalendronat; Nátrium-alendronát; Natrium-alendronát trihydrát; Sodium Alendronate *(BANM)*; Sodium, alendronate de. Sodium trihydrogen (4-amino-1-hydroxybutylidene)diphosphonate trihydrate.

Натрий Алендронат

$C_4H_{12}NNaO_7P_2,3H_2O$ = 325.1.
CAS — 121268-17-5.
ATC — M05BA04.
ATC Vet — QM05BA04.

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

Ph. Eur. 6.2 (Sodium Alendronate). A white or almost white crystalline powder. Soluble in water; practically insoluble in dichloromethane; very slightly soluble in methyl alcohol. A 1% solution in water has a pH of 4.0 to 5.0.

USP 31 (Alendronate Sodium). A white, free-flowing powder. Soluble in water; practically insoluble in alcohol, in acetone, in acetonitrile, in chloroform, and in isopropyl alcohol; very slightly soluble in dimethyl sulfoxide, in methyl alcohol, and in propylene glycol.

Adverse Effects, Treatment, and Precautions

As for the bisphosphonates in general, p.1089. Gastrointestinal symptoms such as abdominal pain, dyspepsia, diarrhoea or constipation are the most frequent adverse effects with alendronate. Severe oesophageal reactions such as oesophagitis, erosions, ulceration, and stricture have occurred (see below); patients should be advised to stop taking the tablets and seek medical attention if they develop symptoms such as dysphagia, new or worsening heartburn, pain on swallowing, or retrosternal pain. Peptic ulceration has also been reported.

Alendronate should not be given to patients with abnormalities of the oesophagus or other factors that might delay oesophageal emptying, or those unable to stand or sit upright for at least 30 minutes. It should be used with caution in patients with upper gastrointestinal abnormalities. To minimise the risk of oesophageal reactions:

- patients should be instructed to swallow alendronate tablets whole with plenty of water (not less than 200 mL), in an upright position (standing or sitting). Mineral water with a high concentration of calcium should be avoided
- tablets should be taken on rising for the day, on an empty stomach, at least 30 minutes before breakfast and any other oral medication
- patients should remain upright after taking the tablets (the *BNF* recommends standing or sitting upright for at least 30 minutes), and should not lie down before eating the first meal of the day
- alendronate should not be taken at bedtime, or before getting up for the day

Hypocalcaemia should be corrected before starting alendronate therapy, and other disorders affecting mineral metabolism such as vitamin D deficiency or hypoparathyroidism should also be treated; serum calcium in these patients should be monitored during therapy.

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

Effects on the heart. For a report of a possible association between alendronate and atrial fibrillation, see Effects on the Heart, under Bisphosphonates, p.1090.

Effects on the kidneys. Renal failure has been associated with the aminobisphosphonates, including alendronate, see under Bisphosphonates, p.1091.

Effects on the liver. Hepatitis[1,2] and hepatocellular damage with raised liver enzyme concentrations[3,4] have been reported after therapy with alendronate.

1. Lieverse RJ. Hepatitis after alendronate. *Neth J Med* 1998; **53:** 271–2.
2. Carrère C, *et al.* Hépatite aiguë sévère imputable á l'alendronate. *Gastroenterol Clin Biol* 2002; **26:** 179–80.
3. Halabe A, *et al.* Liver damage due to alendronate. *N Engl J Med* 2000; **343:** 365.
4. de la Serna Higuera C, *et al.* Lesión hepatocelular inducida por alendronato. *Gastroenterol Hepatol* 2001; **24:** 244–6.

Effects on mental state. Auditory hallucinations and red-coloured visual disturbances were reported[1] in a patient taking alendronate for osteoporosis.

1. Coleman CI, *et al.* Alendronate-induced auditory hallucinations and visual disturbances. *Pharmacotherapy* 2004; **24:** 799–802.

Effects on the musculoskeletal system. A 63-year old woman given alendronate 70 mg once weekly for osteoporosis developed diffuse severe myalgia and transient acute symmetrical polyarthritis 12 hours after ingestion. Symptoms did not recur after stopping the drug.[1] From the initial marketing of alendronate up until November 2002, the FDA had received reports of severe bone, joint, and/or muscle pain in 118 patients, including a child given the drug in error. Of 83 patients for whom information was available, 55 improved after stopping alendronate; in most of these improvement was gradual, although some experienced immediate relief. Nine of these 83 patients had recurrence of pain when given alendronate again. It was suggested that pain might tend to be under-reported since it is subjective, and might be attributed to underlying osteoporosis.[2] As of May 2006, 7 cases of synovitis linked to alendronate use had been reported in New Zealand; in one case, severe synovitis caused carpal tunnel syndrome that required urgent decompression.[3]

Concerns have been raised about potential oversuppression of bone turnover during long-term therapy with alendronate. In a report on 9 patients who developed spontaneous non-spinal fractures while taking alendronate, fracture healing was absent or incomplete in 6 patients who continued therapy for between 3 months and 2 years after fracture onset. When alendronate was stopped, fracture healing was still incomplete in 4 patients after 8 to 12 months. Use of estrogen (in 3 cases) or the presence of glucocorticoid-induced osteoporosis (in 2) may have contributed to the development of bone turnover suppression in some, but 4 patients had received alendronate as monotherapy; duration of therapy was also considered to be a factor as bone suppression might be cumulative.[4]

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

1. Gerster JC, Nicole F. Acute polyarthritis related to once-weekly alendronate in a woman with osteoporosis. *J Rheumatol* 2004; **31:** 829–30.
2. Wysowski DK, Chang JT. Alendronate and risedronate: reports of severe bone, joint, and muscle pain. *Arch Intern Med* 2005; **165:** 346–7.
3. Savage R. Alendronate and inflammatory adverse reactions (issued May 2006). Available at: http://www.medsafe.govt.nz/profs/puarticles/alendinflam.htm#Myalgia (accessed 15/04/08)
4. Odvina CV, *et al.* Severely suppressed bone turnover: a potential complication of alendronate therapy. *J Clin Endocrinol Metab* 2005; **90:** 1294–1301.

Effects on the oesophagus. Between September 1995 and March 1996 the UK CSM had received 10 reports of adverse effects on the oesophagus in patients receiving alendronate sodium.[1] Of these, 4 were of oesophageal reflux, 4 of oesophagitis, and 2 of oesophageal ulceration. As of March 1996, worldwide an estimated 475 000 patients had received alendronate and 199 patients had oesophageal reactions reported to the manufacturer, of which 51 were serious or severe.[2] Endoscopic findings included erosions, ulcerations, exudative inflammation, and thickening of the oesophagus. Bleeding was rare, and oesophageal perforation was not reported. Most oesophageal reactions occurred within 1 week to 2 months of starting alendronate therapy. Recovery occurred when alendronate was stopped; however, it was considered important that patients be followed up for the possible development of strictures.[2] In about 60% of the cases where the information was available, alendronate had not been taken in accordance with the precautions for use (see above).

The CSM subsequently noted[3] that it had continued to receive reports of reactions; by July 1998 there had been 97 reports in the UK, in 1 case associated with a fatality. It was estimated that 1 to 2% of patients might experience oesophageal reactions even when following the precautions for use. Some have reported a much higher incidence of unacceptable upper gastrointestinal symptoms in clinical practice.[4] However, a large placebo-controlled trial of alendronate did not find any increase in upper gastrointestinal events in patients taking alendronate.[5]

1. Committee on Safety of Medicines/Medicines Control Agency. Oesophageal reactions with alendronate sodium (Fosamax). *Current Problems* 1996; **22:** 5. Available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2015620&RevisionSelectionMethod=LatestReleased (accessed 23/07/08)
2. de Groen PC, *et al.* Esophagitis associated with the use of alendronate. *N Engl J Med* 1996; **335:** 1016–21.
3. Committee on Safety of Medicines/Medicines Control Agency. Reminder: severe oesophageal reactions with alendronate sodium (Fosamax). *Current Problems* 1998; **24:** 13. Also available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2023231&RevisionSelectionMethod=LatestReleased (accessed 25/05/06)
4. Kelly R, Taggart H. Incidence of gastrointestinal side effects due to alendronate is high in clinical practice. *BMJ* 1997; **315:** 1235.
5. Bauer DC, *et al.* Upper gastrointestinal tract safety profile of alendronate: the fracture intervention trial. *Arch Intern Med* 2000; **160:** 517–25.

Hypersensitivity. Allergic reactions to bisphosphonates do occur but appear to be rare, see p.1091.

Interactions

As for the bisphosphonates in general, p.1091.

Pharmacokinetics

Like other bisphosphonates, alendronate is poorly absorbed after oral doses. Absorption is decreased by food, especially by products containing calcium or other polyvalent cations. Bioavailability is about 0.4% when taken half an hour before food, reduced from 0.7% in the fasting state; absorption is negligible when taken up to 2 hours after a meal. Plasma protein binding is about 78%. Bisphosphonates do not appear to be metabolised. About half of the absorbed portion is excreted in the urine; the remainder is sequestered to bone for a prolonged period.

◊ References.

1. Gertz BJ, *et al.* Studies of the oral bioavailability of alendronate. *Clin Pharmacol Ther* 1995; **58:** 288–98.
2. Cocquyt V, *et al.* Pharmacokinetics of intravenous alendronate. *J Clin Pharmacol* 1999; **39:** 385–93.
3. Porras AG, *et al.* Pharmacokinetics of alendronate. *Clin Pharmacokinet* 1999; **36:** 315–28.

Uses and Administration

Alendronate is an aminobisphosphonate with general properties similar to those of the other bisphosphonates (p.1091). It is a potent inhibitor of bone resorption and is given in the management of osteoporosis either alone or with vitamin D. Alendronate is used for the treatment of Paget's disease of bone. It has also been given in the treatment of bone metastases and hypercalcaemia of malignancy.

Alendronate is given orally as the sodium salt, but doses are expressed in terms of alendronic acid; alendronate sodium 1.3 mg is equivalent to about 1 mg of alendronic acid. The specific instructions given in Adverse Effects and Precautions, above should be followed to minimise adverse effects and permit adequate absorption.

The usual dosage for the treatment of **osteoporosis** in men and women is 10 mg daily. Postmenopausal women may be given 5 mg daily for prophylaxis. It may also be given once weekly to postmenopausal women in a dose of 70 mg for treatment of osteoporosis, or 35 mg for prophylaxis. Men with osteoporosis may be treated with 70 mg once weekly.

For the treatment and prevention of corticosteroid-induced osteoporosis a dose of 5 mg daily is given; postmenopausal women who do not take HRT should be given 10 mg daily.

In adults with **Paget's disease** of bone the usual dose is 40 mg daily for 6 months; treatment may be repeated if necessary after an interval of a further 6 months.

Alendronate has also been given by intravenous infusion.

Administration. Alendronate once-weekly was considered to be therapeutically equivalent to once-daily dosing in both the treatment[1,2] and prevention[3] of osteoporosis, although the treatment study[1] was considered[4,5] to lack information about other drugs being taken and reasons for withdrawal, and studied bone mineral density, not fracture. Tolerability of a once-weekly regimen was comparable to placebo in one study[6] and to once-daily dosing in another;[7] a review[5] concluded that weekly dosage carried a lower risk of upper gastrointestinal symptoms.

1. Schnitzer T, *et al.* Therapeutic equivalence of alendronate 70 mg once-weekly and alendronate 10 mg daily in the treatment of osteoporosis. *Aging (Milano)* 2000; **12:** 1–12.
2. The Alendronate Once-Weekly Study Group. Two-year results of once-weekly administration of alendronate 70 mg for the treatment of postmenopausal osteoporosis. *J Bone Miner Res* 2002; **17:** 1988–96.
3. Luckey MM, *et al.* Therapeutic equivalence of alendronate 35 milligrams once weekly and 5 milligrams daily in the prevention of postmenopausal osteoporosis. *Obstet Gynecol* 2003; **101:** 711–21.
4. Tsun EC, Heck AM. Intermittent dosing of alendronate. *Ann Pharmacother* 2001; **35:** 1471–5.
5. Sambrook P. Once weekly alendronate. *Drugs Today* 2003; **39:** 339–46.
6. Greenspan S, *et al.* Tolerability of once-weekly alendronate in patients with osteoporosis: a randomized, double-blind, placebo-controlled study. *Mayo Clin Proc* 2002; **77:** 1044–52.
7. Simon JA, *et al.* Patient preference for once-weekly alendronate 70 mg versus once-daily alendronate 10 mg: a multicenter, randomized, open-label, crossover study. *Clin Ther* 2002; **24:** 1871–86.

Administration in renal impairment. Elimination of alendronate is reduced in *rats* with kidney failure and is likely to be reduced in patients with renal impairment. Licensed product information makes the following recommendations for oral dosage based on creatinine clearance (CC):

- mild to moderate renal impairment (CC greater than 35 mL/minute): no dose adjustment needed
- severe renal impairment (CC less than 35 mL/minute): use is not recommended due to lack of experience with alendronate in this population

Charcot neuroarthropathy. Six months of treatment with once-weekly alendronate has been reported[1] to improve signs and symptoms of Charcot neuroarthropathy (a sometimes painful deformity in limbs that have lost sensory innervation).

1. Pitocco D, *et al.* Six-month treatment with alendronate in acute Charcot neuroarthropathy: a randomized controlled trial. *Diabetes Care* 2005; **28:** 1214–15.

Complex regional pain syndrome. Osteoporosis is one of the features of complex regional pain syndrome (p.6). Bisphosphonates may be of benefit in controlling associated pain in some patients. In a small study,[1] intravenous alendronate 7.5 mg daily for 3 days significantly improved pain, tenderness, swelling, and motion compared with placebo.

1. Adami S, *et al.* Bisphosphonate therapy of reflex sympathetic dystrophy syndrome. *Ann Rheum Dis* 1997; **56:** 201–4.

Gaucher disease. In a placebo-controlled study of patients with Gaucher disease (p.2249), the addition of oral alendronate 40 mg daily to enzyme therapy increased lumbar bone mineral density, but had no effect on focal lesions;[1] the authors concluded that alendronate may be useful adjunctive therapy especially in those patients at risk of osteopenic fracture.

1. Wenstrup RJ, *et al.* Gaucher disease: alendronate disodium improves bone mineral density in adults receiving enzyme therapy. *Blood* 2004; **104:** 1253–7.

Hypercalcaemia. Bisphosphonates are the preferred drugs for treating hypercalcaemia of malignancy (p.1083) once the patient has been adequately rehydrated. A randomised dose-response study[1] found that single intravenous doses of alendronate 5 mg or more effectively lowered serum-calcium concentrations in patients with tumour-induced hypercalcaemia. Alendronate has also been used to treat hypercalcaemia associated with vitamin D intoxication in children.[2,3]

1. Nussbaum SR, *et al.* Dose-response study of alendronate sodium for the treatment of cancer-associated hypercalcemia. *J Clin Oncol* 1993; **11:** 1618–23.
2. Orbak Z, *et al.* Vitamin D intoxication and therapy with alendronate (case report and review of literature). *Eur J Pediatr* 2006; **165:** 583–4.
3. Doneray H, *et al.* Intragastric alendronate therapy in two infants with vitamin D intoxication: a new method. *Clin Toxicol* 2008; **46:** 300–2.

Hyperparathyroidism. Bisphosphonates have been used to inhibit bone resorption in the treatment of hypercalcaemia associated with hyperparathyroidism (p.1087), but seem to be of little benefit for long-term treatment. In patients with primary hyperparathyroidism, oral alendronate significantly increased bone mineral density, especially at the lumbar spine; virtually all of this gain appeared to occur within the first year of treatment. Alendronate is considered to be useful in those patients for whom parathyroidectomy is not possible.[1-4]

1. Rossini M, *et al.* Effects of oral alendronate in elderly patients with osteoporosis and mild primary hyperparathyroidism. *J Bone Miner Res* 2001; **16:** 113–19.
2. Parker CR, *et al.* Alendronate in the treatment of primary hyperparathyroid-related osteoporosis: a 2-year study. *J Clin Endocrinol Metab* 2002; **87:** 4482–9.
3. Chow CC, *et al.* Oral alendronate increases bone mineral density in postmenopausal women with primary hyperparathyroidism. *J Clin Endocrinol Metab* 2003; **88:** 581–7.
4. Khan AA, *et al.* Alendronate in primary hyperparathyroidism: a double-blind, randomized, placebo-controlled trial. *J Clin Endocrinol Metab* 2004; **89:** 3319–25.

Osteoporosis. Bisphosphonates are used for the prevention and treatment of osteoporosis (p.1084). Alendronate significantly increases bone mineral density (BMD) of the lumbar spine and femoral neck in **postmenopausal women** with osteoporosis;[1,2] it increases vertebral BMD in postmenopausal women without osteoporosis, but not quite to the same extent as HRT.[1]

Continuous long-term therapy appears to be more effective than short-term treatment in terms of skeletal benefits,[1-4] but a residual effect on BMD remains for several years after stopping treatment,[3-5] despite resumption of bone loss after withdrawal of alendronate.[4-6] Studies[7,8] in early postmenopausal women suggested that a *higher initial dosage* might be more effective in terms of BMD gain and residual effect.

The effect of alendronate on fracture risk may depend on *baseline bone mineral density*.[2] Treatment reduced the incidence of new vertebral and nonvertebral fractures in women with prior fractures; in women without prior fractures, alendronate reduced the incidence of clinical fractures in those with osteoporosis,[9] but not in those with higher BMD.[10] A systematic review[11] found that alendronate showed a clinically important benefit in the secondary prevention of all osteoporotic fractures; statistically significant reductions in vertebral, non-vertebral, hip, and wrist fractures were seen. No significant reductions were found for primary prevention of osteoporotic fractures, but the reduction in vertebral fractures with alendronate was deemed to be clinically important.

Alendronate is also used in **men** with osteoporosis; in a 2-year randomised study, 10 mg daily by mouth was found to increase vertebral and nonvertebral BMD and help prevent vertebral fractures.[12] Alendronate at 70 mg weekly by mouth also increased BMD significantly in osteoporotic men after 1 year when compared to placebo; fracture incidence, not a primary end-point, was similar in both groups.[13]

Alendronate also increases bone mass density in men and women receiving oral **corticosteroids** at doses equivalent to at least 7.5 mg prednisone daily,[14,15] and may be of some benefit in reducing bone loss after heart[16] and liver[17] **transplantation**.

In men with prostate cancer given androgen deprivation therapy, BMD of the spine and hip significantly improved in those given once-weekly alendronate compared with those given calcium and vitamin D supplementation alone.[18]

Limited available data suggest that alendronate may be safe and effective for patients with HIV who have decreased BMD.[19]

1. Sharpe M, *et al.* Alendronate: an update of its use in osteoporosis. *Drugs* 2001; **61:** 999–1039.
2. Pérez-López FR. Postmenopausal osteoporosis and alendronate. *Maturitas* 2004; **48:** 179–92.
3. Tonino RP, *et al.* Skeletal benefits of alendronate: 7-year treatment of postmenopausal osteoporotic women. *J Clin Endocrinol Metab* 2000; **85:** 3109–15.
4. Bone HG, *et al.* Ten years' experience with alendronate for osteoporosis in postmenopausal women. *N Engl J Med* 2004; **350:** 1189–99.
5. Black DM, *et al.* FLEX Research Group. Effects of continuing or stopping alendronate after 5 years of treatment: the Fracture Intervention Trial Long-term Extension (FLEX): a randomized trial. *JAMA* 2006; **296:** 2927–38.
6. Ravn P, *et al.* Alendronate in early postmenopausal women: effects on bone mass during long-term treatment and after withdrawal. *J Clin Endocrinol Metab* 2000; **85:** 1492–7.
7. Sambrook PN, *et al.* Alendronate in the prevention of osteoporosis: 7-year follow-up. *Osteoporosis Int* 2004; **15:** 483–8.
8. McClung MR, *et al.* Early Postmenopausal Intervention Cohort (EPIC) Group Study. Prevention of postmenopausal bone loss: six-year results from the Early Postmenopausal Intervention Cohort Study. *J Clin Endocrinol Metab* 2004; **89:** 4879–85.
9. Black DM, *et al.* Fracture risk reduction with alendronate in women with osteoporosis: the fracture intervention trial. *J Clin Endocrinol Metab* 2000; **85:** 4118–24.
10. Cummings SR, *et al.* Effect of alendronate on risk of fracture in women with low bone density but without vertebral fractures: results from the Fracture Intervention Trial. *JAMA* 1998; **280:** 2077–82.
11. Wells GA, *et al.* Alendronate 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).
12. Orwoll E, *et al.* Alendronate for the treatment of osteoporosis in men. *N Engl J Med* 2000; **343:** 604–10.
13. Miller PD, *et al.* Weekly oral alendronic acid in male osteoporosis. *Clin Drug Invest* 2004; **24:** 333–41.
14. Saag KG, *et al.* Alendronate for the prevention and treatment of glucocorticoid-induced osteoporosis. *N Engl J Med* 1998; **339:** 292–9.
15. de Nijs RNJ, *et al.* STOP Investigators. Alendronate or alfacalcidol in glucocorticoid-induced osteoporosis. *N Engl J Med* 2006; **355:** 675–84.
16. Shane E, *et al.* Alendronate versus calcitriol for the prevention of bone loss after cardiac transplantation. *N Engl J Med* 2004; **350:** 767–76.
17. Atamaz F, *et al.* The prevention of bone fractures after liver transplantation: experience with alendronate treatment. *Transplant Proc* 2006; **38:** 1448–52.
18. Greenspan SL, *et al.* Effect of once-weekly oral alendronate on bone loss in men receiving androgen deprivation therapy for prostate cancer: a randomized trial. *Ann Intern Med* 2007; **146:** 416–24.
19. Lin D, Rieder MJ. Interventions for the treatment of decreased bone mineral density associated with HIV infection. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2007 (accessed 15/04/08).

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. Alendronate, at oral doses of 40 mg daily for 6 months, has been shown to be more effective than both etidronate and placebo in the treatment of Paget's disease,[1] although an earlier study[2] found a more sustained reduction in biochemical markers with an oral dose of 80 mg daily.

1. Reid IR, Siris E. Alendronate in the treatment of Paget's disease of bone. *Int J Clin Pract* 1999; **101** (suppl): 62–6.
2. Khan SA, *et al.* Alendronate in the treatment of Paget's disease of bone. *Bone* 1997; **20:** 263–71.

Polymyositis and dermatomyositis. Alendronate has been reported to be effective in the treatment of calcinosis[1] associated with juvenile dermatomyositis (p.1510).

1. Mukamel M, *et al.* New insight into calcinosis of juvenile dermatomyositis: a study of composition and treatment. *J Pediatr* 2001; **138:** 763–6.

Preparations

USP 31: Alendronate Sodium Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Actimax; Alenato; Arendal; Berlex; Brek; Dronat; Elandur†; Filxine; Findeclin; Findeclin Combi; Fosamax; Lafedam†; Lendronal; Marvil; Maxtral†; Oseotenk; Osteobon; Osteofene; Osteonate; Phostarac†; Regenesis; Silidral; Tilios; ***Austral.:*** Adronat; Alendro; Fosamax; Ossmax; ***Austria:*** AlendronHexal; Fosamax; ***Belg.:*** Fosamax; ***Braz.:*** Alendil; Bonalen; Cleveron; Endronax; Fosamax; Minusorb†; Ossomax†; Ostenan; Osteofar; Osteoform; Osteoral; Osteotrat†; Recalfe†; Terost; ***Canad.:*** Fosamax; ***Chile:*** Aldrox; Arendal; Fosamax; Fosval; Holadren; Leodrin; Osdren; Oseotal; Osteofem†; Osteosan; Pasodron; ***Cz.:*** Alendrogen; Alenwin; Bonalen; Fosamax; Fosteofos; Gendron; Lindron; Ralenost; Siranin; ***Denm.:*** Fosamax; ***Fin.:*** Fosamax; ***Fr.:*** Fosamax; ***Ger.:*** Alendro-Q; Fosamax; Tevanate; ***Gr.:*** Aldromax; Alefos; Alendo; Alendral; Ampine; Aurodren; Bestalen; Bonedron; Caltera; Dargol; Debenal; Deparex; Difonate; Discozal; Dronalent; Fosalen; Fosamax; Fosazom; Jamax-S; Osaston; Ostalert; Ostomax; Promax; Ridon; Riledron; Tevanate; Tivarun; ***Hong Kong:*** Fosamax; Osteofos; ***Hung.:*** Alendromax; Alendron; Epolar; Fortimax; Fosamax; Massidron; Sedron; Trabecan; ***India:*** Bifosa; Osteofos; ***Indon.:*** Alexonal; Alovell; Fosamax; Nichospor; Osteofar; Voroste; ***Irl.:*** Fosamax; Osteomel; ***Israel:*** Fosalan; Maxibone; ***Ital.:*** Adronat; Alendros; Dronal; Fosamax; Genalen; ***Jpn:*** Bonalon; Onclast†; ***Malaysia:*** Fosamax; ***Mex.:*** Apodrolen; Blindafe; Dronadil; Drovitan; Fosamax; Fosfacid; Landrolen; Sinfract; Synostep; Zondra; ***Neth.:*** Fosamax; ***Norw.:*** Fosamax; ***NZ:*** Fosamax; ***Philipp.:*** Fosamax; ***Pol.:*** Alenato; Fosamax; Lindron; Osalen; Ostemax; Ostenil; Ostolek; Rekostin; ***Port.:*** Adronat; Fosamax; ***Rus.:*** Fosamax (Фосамакс); Tevanate (Теванат); ***S.Afr.:*** Fosagen; Fosamax; Osteobon; ***Singapore:*** Fosamax; ***Spain:*** Fosamax; ***Swed.:*** Alenat; Fosamax; ***Switz.:*** Fosamax; ***Thai.:*** Fosamax; ***Turk.:*** Andante; Bonemax; Fosamax; Osteomax; ***UK:*** Fosamax; ***USA:*** Fosamax; ***Venez.:*** Aldronac; Aliot; Defixal; Denfos†; Fixopan; Fosamax; Genalmen†; Osteodur; Osteomax; Porosal.

Multi-ingredient: ***Arg.:*** Fosamax Plus; Regenesis Max; Silidral Plus; ***Austral.:*** Fosamax Plus; ***Belg.:*** Fosavance; ***Braz.:*** Alendil Calcio D; ***Cz.:*** Adrovance; Fosavance; ***Fin.:*** Fosavance; ***Fr.:*** Adrovance; Fosavance; ***Ger.:*** Fosavance; ***Gr.:*** Adrovance; Fosavance; ***Hong Kong:*** Fosamax Plus; ***Hung.:*** Calcisedron-D; Fosavance; ***Indon.:*** Fosamax Plus; ***Irl.:*** Fosavance; ***Ital.:*** Fosavance; ***Malaysia:*** Fosamax Plus; ***Mex.:*** Fosamax Plus; ***NZ:*** Fosamax Plus; ***Philipp.:*** Fosavance; ***Port.:*** Fosavance; ***Singapore:*** Fosamax Plus; ***Spain:*** Fosavance; ***UK:*** Fosavance; ***USA:*** Fosamax Plus.

Bisphosphonates

Bifosfonatos; Biphosphonates; Diphosphonates.

Bisphosphonates are analogues of pyrophosphate, in which the central oxygen atom is replaced by a carbon atom with two further substituents—see Figure 1, p.1090. Like pyrophosphate they have a strong affinity for bone. The bisphosphonates are used chiefly for their antiresorptive and hypocalcaemic properties (see Uses and Administration, below).

Adverse Effects, Treatment, and Precautions

Bisphosphonates may cause gastrointestinal disturbances including abdominal pain, nausea and vomiting, and diarrhoea or constipation. Peptic ulceration has been reported. Existing gastrointestinal problems may be exacerbated, and oral bisphosphonates should generally be given with care or avoided if acute upper gastrointestinal inflammation is present. Gastrointestinal disturbances may be more frequent with aminobisphosphonates such as alendronate, ibandronate, and risedronate; oesophagitis has also occurred. General