Effects on the musculoskeletal system. From the initial marketing of risedronate until June 2003, the FDA had received 6 reports of severe bone, joint, or muscle pain. It was suggested that pain might tend to be under-reported since it is subjective, and might be attributed to underlying osteoporosis.[1]

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

1. Wysowski DK, Chang JT. Alendronate and risedronate: reports of severe bone, joint, and muscle pain. *Arch Intern Med* 2005; **165:** 346–7.

Effects on the respiratory system. For a report of bronchiolitis obliterans organising pneumonia induced by risedronate, see p.1091.

Hypersensitivity. Allergic reactions to bisphosphonates are rare, see p.1091. Angioedema, generalised rashes, and bullous skin reactions, some severe, have been reported with risedronate.

Interactions

As for the bisphosphonates in general, p.1091.

Pharmacokinetics

Like other bisphosphonates, risedronate is poorly absorbed orally. Absorption is reduced by food, especially by products containing calcium or other polyvalent cations. The mean bioavailability is 0.63% in the fasting state, and is reduced by 30% when given 1 hour before breakfast, and by 55% when given half an hour before breakfast. Plasma protein binding is about 24%. Risedronate is not metabolised. About half of the absorbed portion is excreted in the urine within 24 hours; the remainder is sequestered to bone for a prolonged period. Unabsorbed drug is eliminated unchanged in the faeces.

Absorption. Absorption of a single dose of risedronate was comparable when given 0.5 to 1 hour before breakfast or 2 hours after an evening meal in a study in healthy subjects.[1] The pharmacokinetics of risedronate are dose-proportional after a single oral dose.[2]

1. Mitchell DY, *et al.* The effect of dosing regimen on the pharmacokinetics of risedronate. *Br J Clin Pharmacol* 1999; **48:** 536–42.
2. Mitchell DY, *et al.* Dose-proportional pharmacokinetics of risedronate on single-dose oral administration to healthy volunteers. *J Clin Pharmacol* 2000; **40:** 258–65.

Uses and Administration

Risedronate is an aminobisphosphonate with similar properties to those of the bisphosphonates in general (p.1091). It inhibits bone resorption and is used either alone or with calcium, or with calcium and vitamin D for the prevention and treatment of postmenopausal osteoporosis. It is also used for the treatment of osteoporosis in men. Risedronate is also used for prevention and treatment of corticosteroid-induced osteoporosis, and for the treatment of Paget's disease of bone.

Risedronate is given orally as the sodium salt. The specific instructions given in Adverse Effects and Precautions, above should be followed to minimise gastrointestinal adverse effects and permit adequate absorption. The recommended dosage for **Paget's disease** of bone is 30 mg of risedronate sodium once daily for 2 months. Treatment may be repeated once if necessary after an interval of a further 2 months. The recommended dosage for the treatment or prevention of postmenopausal or corticosteroid-induced **osteoporosis** is 5 mg daily. Alternatively, for postmenopausal osteoporosis, 35 mg may be taken once weekly, 75 mg may be taken on 2 consecutive days of each month, or 150 mg may be taken once a month. For men with osteoporosis, the recommended dose is 35 mg once weekly.

◊ General references.

1. Crandall C. Risedronate: a clinical review. *Arch Intern Med* 2001; **161:** 353–60.
2. Dunn CJ, Goa KL. Risedronate: a review of its pharmacological properties and clinical use in resorptive bone disease. *Drugs* 2001; **61:** 685–712.
3. Umland EM, Boyce EG. Risedronate: a new oral bisphosphonate. *Clin Ther* 2001; **23:** 1409–21.
4. White NJ, Perry CM. Risedronate once a week. *Treat Endocrinol* 2003; **2:** 415–20.

Administration. A procedure for the extemporaneous preparation of an oral solution from risedronate tablets has been proposed,[1] for use in patients who cannot swallow whole tablets or require feeding tubes.

1. Dansereau RJ, Crail DJ. Extemporaneous procedures for dissolving risedronate tablets for oral administration and for feeding tubes. *Ann Pharmacother* 2005; **39:** 63–7.

Administration in renal impairment. Renal clearance of risedronate significantly correlated to renal function in a pharmacokinetic study,[1] although the authors concluded that generally no dosage adjustment appears necessary for patients with mild to moderate renal impairment (creatinine clearance (CC) greater than 20 mL/minute). Licensed product information states that no dosage adjustment is necessary when CC is greater than 30 mL/minute; however, use of risedronate is contra-indicated in patients with severe renal impairment (CC less than 30 mL/minute), due to a lack of clinical data.

1. Mitchell DY, *et al.* Effect of renal function on risedronate pharmacokinetics after a single oral dose. *Br J Clin Pharmacol* 2000; **49:** 215–22.

Osteoporosis. Bisphosphonates are used for the prevention and treatment of osteoporosis (p.1084). Risedronate improves bone mineral density (BMD) and reduces the risk of both vertebral and non-vertebral fractures in **postmenopausal** osteoporosis;[1-4] effects are maintained for at least 5 years.[5] In **corticosteroid-induced** osteoporosis, risedronate increases BMD at the lumbar spine, femoral neck, and trochanter.[3,6] Risedronate is also used to treat **men** with osteoporosis. In a controlled study in elderly men after a stroke, those given risedronate had increased BMD and a decreased risk of hip fracture.[7] In a prospective controlled study, 12 months of daily risedronate significantly increased BMD at the lumbar spine, femoral neck, and hip, and significantly reduced the incidence of new vertebral fractures in men with primary or secondary osteoporosis.[8]

A once-monthly regimen of risedronate was found to be similar in efficacy and safety to the once-daily regimen.[9]

1. Sickels JM, Nip C-S. Risedronate for the prevention of fractures in postmenopausal osteoporosis. *Ann Pharmacother* 2002; **36:** 664–70.
2. Crandall C. Risedronate: a clinical review. *Arch Intern Med* 2001; **161:** 353–60.
3. Umland EM, Boyce EG. Risedronate: a new oral bisphosphonate. *Clin Ther* 2001; **23:** 1409–21.
4. Wells G, *et al.* Risedronate 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 16/04/08).
5. Sorensen OH, *et al.* Long-term efficacy of risedronate: a 5-year placebo-controlled clinical experience. *Bone* 2003; **32:** 120–6.
6. Dougherty JA. Risedronate for the prevention and treatment of corticosteroid-induced osteoporosis. *Ann Pharmacother* 2002; **36:** 512–16.
7. Sato Y, *et al.* Risedronate sodium therapy for prevention of hip fracture in men 65 years or older after stroke. *Arch Intern Med* 2005; **165:** 1743–8.
8. Ringe JD, *et al.* Efficacy of risedronate in men with primary and secondary osteoporosis: results of a 1-year study. *Rheumatol Int* 2006; **26:** 427–31.
9. Delmas PD, *et al.* Efficacy and safety of risedronate 150 mg once a month in the treatment of postmenopausal osteoporosis. *Bone* 2008; **42:** 36–42.

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. Risedronate has been found to improve pagetic bone lesions,[1] and to be more effective than etidronate.[2]

1. Brown JP, *et al.* Improvement of pagetic bone lesions with risedronate treatment: a radiologic study. *Bone* 2000; **26:** 263–7.
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

Proprietary Preparations (details are given in Part 3)

Arg.: Actonel; Ductonar; Rentop; Ribastamin; Ridron; Risedon; ***Austral.:*** Actonel; ***Austria:*** Actonel; ***Belg.:*** Actonel; ***Braz.:*** Actonel; Risedross; ***Canad.:*** Actonel; ***Chile:*** Actonel; ***Cz.:*** Actonel; Norsed; Risendros; ***Fin.:*** Optinate; ***Fr.:*** Actonel; ***Ger.:*** Actonel; ***Gr.:*** Actonel; ***Hong Kong:*** Actonel; ***Hung.:*** Actonel; ***India:*** Actonel; Risofos; ***Indon.:*** Actonel; Osteonate; ***Irl.:*** Actonel; ***Israel:*** Actonel; ***Ital.:*** Actonel; Optinate; ***Jpn:*** Benet; ***Malaysia:*** Actonel; ***Mex.:*** Actonel; Seralis; ***Neth.:*** Actonel; ***Norw.:*** Optinate; ***Philipp.:*** Actonel; ***Pol.:*** Actonel; ***Port.:*** Actonel; Norsed; ***S.Afr.:*** Actonel; ***Singapore:*** Actonel; ***Spain:*** Acrel; Actonel; ***Swed.:*** Optinate; Optinate Septimum; ***Switz.:*** Actonel; ***Thai.:*** Actonel; ***Turk.:*** Actonel; ***UK:*** Actonel; ***USA:*** Actonel; ***Venez.:*** Actonel.

Multi-ingredient: ***Arg.:*** Ribastamin Duo; Ridron Pack; ***Austral.:*** Actonel Combi; ***Fr.:*** Actonelcombi; ***Hung.:*** Actonel Trio; ***Irl.:*** Actonel Combi; ***Neth.:*** Actokit; ***Swed.:*** Optinate Combi; ***UK:*** Actonel Combi; ***USA:*** Actonel with Calcium.

Strontium Ranelate *(rINNM)*

FK-481; Ranelate de Strontium; Ranelato de estroncio; S-12911; Strontii Ranelas. 2-(2-Carboxy-4-cyano-5-[*N,N*-di(carboxymethyl)amino]thiophen-3-yl) acetic acid distrontium salt.

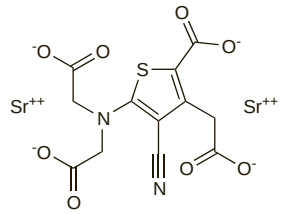
Стронций Ранелат

$C_{12}H_6N_2O_8SSr_2$ = 513.5.

CAS — 135459-87-9.

ATC — M05BX03.

ATC Vet — QM05BX03.



Adverse Effects and Precautions

Common adverse effects of strontium ranelate include gastrointestinal disturbances, headache, dermatitis, and eczema. Disturbances in consciousness, memory loss, and seizures may occur. Treatment with strontium ranelate has been associated with an increased incidence in venous thromboembolism including pulmonary embolism, and should be given with caution to those patients considered at risk or with a history of thromboembolic disorders. Transient reversible increases in creatine kinase activity have been reported. Hypersensitivity reactions, including rash, pruritus, urticaria, angioedema, and Stevens-Johnson syndrome have occurred. Drug rash with eosinophilia and systemic symptoms (DRESS), sometimes fatal, has also been reported. Strontium may interfere with certain methods used for the determination of serum and urinary calcium.

Strontium ranelate should not be given with food or antacids—see Interactions, below.

Hypersensitivity. As of November 2007, the EMEA had received reports of 16 cases of drug rash with eosinophilia and systemic symptoms (DRESS), a serious and life-threatening condition, in patients treated with strontium ranelate. Two fatalities were reported. Reactions appeared within 3 to 6 weeks of starting therapy, with skin rash, accompanied by fever, swollen glands, eosinophilia, and effects on the liver, kidneys, and lungs. Patients are advised to stop treatment with strontium ranelate if a rash occurs and to seek medical advice; treatment should not be restarted.[1] Similar advice, and a reminder that the drug should also be used with caution in patients with risk factors for venous thromboembolism, was issued in June 2008 by the Australian regulatory authorities; although there had been no fatalities, they had seen 16 reports of rash, one accompanied by fever and one by eosinophilia.[2]

1. EMEA. EMEA recommends changes in the product information for Protelos/Osseor due to the risk of severe hypersensitivity reactions (issued 16th November 2007). Available at: http://www.emea.europa.eu/humandocs/PDFs/EPAR/protelos/PressRelease_Protelos_41745807en.pdf (accessed 21/01/08)
2. Adverse Drug Reactions Advisory Committee (ADRAC). Severe skin reactions and venous thromboembolism with strontium ranelate (Protos). *Aust Adverse Drug React Bull* 2008; **27:** 10. Also available at: http://www.tga.gov.au/adr/aadrb/aadr0806.pdf (accessed 17/07/08)

Interactions

Food, milk, and calcium-containing compounds may reduce the bioavailability of strontium ranelate; antacids containing aluminium or magnesium may reduce its absorption. Such products should be given at least 2 hours apart from, and, in the case of antacids, preferably after, strontium ranelate. Because of possible complex formation, strontium ranelate should not be given with oral tetracyclines or quinolones.

Pharmacokinetics

Strontium ranelate has an absolute bioavailability of about 25% after an oral dose; calcium or food reduces the bioavailability by about 60 to 70%. Peak plasma concentrations are achieved 3 to 5 hours after an oral dose. Plasma protein binding is low. Strontium ranelate has a high affinity for bone tissue. It is not metabolised, and has a half-life of about 60 hours. Excretion occurs via the kidneys and gastrointestinal tract.

Uses and Administration

Strontium ranelate is claimed to stimulate bone formation as well as reduce bone resorption. It is given orally in the treatment of postmenopausal osteoporosis to reduce the risk of vertebral and hip fractures. The recommended dose is 2 g daily by mouth, given preferably at night and at least 2 hours after food.

◊ References.

1. Marie PJ. Strontium ranelate: new insights into its dual mode of action. *Bone* 2007; **40** (suppl 1): S5–S8.
2. Fonseca JE. Rebalancing bone turnover in favour of formation with strontium ranelate: implications for bone strength. *Rheumatology (Oxford)* 2008; **47** (suppl 4): iv17–iv19.

Administration in renal impairment. Strontium excretion occurs via the kidneys and clearance decreases as creatinine clearance (CC) decreases. UK licensed product information states that no dosage adjustment of strontium ranelate is required in patients with mild to moderate renal impairment (CC 30 to 70 mL/minute). However, it is not recommended for those with severe renal impairment (CC below 30 mL/minute) because of a lack of pharmacokinetic data in these patients; continuation of treatment in patients developing severe renal impairment should be considered on an individual basis.

Osteoporosis. Strontium ranelate, given orally with calcium and vitamin D supplements, has been found to reduce the risk of vertebral[1] and non-vertebral[2] fractures in postmenopausal women with osteoporosis. A pooled analysis of data from these 2 studies concluded that strontium ranelate reduced both vertebral and non-vertebral fractures in patients aged 80 years or older.[3] Protection against fractures was detected within 12 months, and sustained throughout 3 years of treatment. Hip fractures were also reduced over 3 years, but this did not reach statistical significance; the authors concluded that the analysis may not have been sufficiently powered in this respect. A systematic review[4] concluded that while strontium ranelate reduces vertebral fractures, there is less of a reduction with non-vertebral fractures, and the effect on hip fracture remains unclear. Some have cautioned about the interpretation of bone mineral density (BMD) changes with strontium ranelate, since stronger X-ray attenuation by strontium compared with calcium must be corrected for to avoid overestimating the effect. However, increases in BMD could be useful clinically in gauging long-term compliance.[5]

A review[6] of the place of strontium ranelate in therapy considered that although it might be an alternative in patients who could not tolerate a bisphosphonate there was no convincing published evidence to support claims that it stimulated bone formation as well as reducing resorption. Further reviews[4,7] concluded that additional research to confirm its mechanism of action is required and that long-term fracture data are needed, along with comparative trials evaluating the efficacy of strontium ranelate relative to other therapies such as bisphosphonates.

1. Meunier PJ, *et al.* The effects of strontium ranelate on the risk of vertebral fracture in women with postmenopausal osteoporosis. *N Engl J Med* 2004; **350:** 459–68.
2. Reginster JY, *et al.* Strontium ranelate reduces the risk of nonvertebral fractures in postmenopausal women with osteoporosis: treatment of peripheral osteoporosis (TROPOS) study. *J Clin Endocrinol Metab* 2005; **90:** 2816–22.
3. Seeman E, *et al.* Strontium ranelate reduces the risk of vertebral and nonvertebral fractures in women eighty years of age and older. *J Bone Miner Res* 2006; **21:** 1113–20.
4. O'Donnell S, *et al.* Strontium ranelate for preventing and treating postmenopausal osteoporosis. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2006 (accessed 01/06/07).
5. Fogelman I, Blake GM. Strontium ranelate for the treatment of osteoporosis: is useful, but changes in bone mineral density need careful interpretation. *BMJ* 2005; **330:** 1400–1.
6. Anonymous. Strontium ranelate for osteoporosis? *Drug Ther Bull* 2006; **44:** 29–32.
7. Stevenson M, *et al.* The clinical effectiveness and cost-effectiveness of strontium ranelate for the prevention of osteoporotic fragility fractures in postmenopausal women. *Health Technol Assess* 2007; **11:** 1–134.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Osteovital; Protos; ***Austral.:*** Protos; ***Belg.:*** Protelos; ***Braz.:*** Protos; ***Cz.:*** Osseor; Protelos; ***Denm.:*** Protelos; ***Fr.:*** Protelos; ***Ger.:*** Protelos; ***Gr.:*** Protelos; ***Hong Kong:*** Protos; ***Hung.:*** Protelos; ***Indon.:*** Protos; ***Irl.:*** Protelos; ***Ital.:*** Osseor; Protelos; ***Malaysia:*** Protaxos; ***Neth.:*** Osseor; Protelos; ***NZ:*** Protos; ***Philipp.:*** Protos; ***Pol.:*** Protelos; ***Port.:*** Osseor; Protelos; ***Rus.:*** Bivalos (Бивалос); ***S.Afr.:*** Protos; ***Singapore:*** Protos; ***Spain:*** Osseor; Protelos; ***Swed.:*** Protelos; ***UK:*** Protelos.

Teriparatide *(USAN, rINN)*

(1-34) Human parathormone; (1-34) Human parathyroid hormone; 1-34 Parathormone (human); hPTH 1-34; Human parathormone (1-34); Human parathyroid hormone (1-34); Human PTH (1-34); LY-333334; Parathyroid hormone peptide (1-34); Teriparatid; Teriparatida; Tériparatide; Teriparatidum.

Терипаратид

$C_{181}H_{291}N_{55}O_{51}S_2$.
CAS — 52232-67-4.
ATC — H05AA02.
ATC Vet — QH05AA02.

Teriparatide Acetate *(USAN, rINNM)*

Acetato de teriparatida; Tériparatide, Acétate de; Teriparatidi Acetas.

Терипаратида Ацетат

$C_{181}H_{291}N_{55}O_{51}S_2.xH_2O.yC_2H_4O_2$.
CAS — 99294-94-7 (teriparatide acetate).
ATC — H05AA02.
ATC Vet — QH05AA02.

Adverse Effects and Precautions

Gastrointestinal disturbances, pain in the limb of injection, headache, and dizziness are the most common adverse effects in patients treated with subcutaneous teriparatide. Dizziness, vertigo, and syncope may be associated with transient orthostatic hypotension in some patients, particularly when beginning treatment. Those so affected should not drive or operate potentially hazardous machinery. Asthenia, arthralgia, and rhinitis may occur. Angina pectoris, depression, dyspnoea, leg cramps, pneumonia, urinary disorders, and sciatica have also been reported. A metallic taste, tingling of the extremities, and pain at the site of injection have occasionally been associated with the intravenous infusion of teriparatide acetate. It is a peptide and the possibility of systemic hypersensitivity reactions should be borne in mind. Hypercalcaemia may develop with teriparatide or the acetate and it is therefore contra-indicated in patients with pre-existing hypercalcaemia.

Teriparatide is contra-indicated in patients with severe renal impairment and should be used with caution with those with moderate impairment.

There have been reports of osteosarcoma in *rats* given teriparatide and patients who may be at increased risk, including those with a history of skeletal metastases or previous radiotherapy to the skeleton, should not receive it. It is also contra-indicated in those with metabolic bone disease including Paget's disease and hyperparathyroidism, or unexplained elevations of serum alkaline phosphatase. Use in children or those with open epiphyses is also contra-indicated. In the UK treatment is also limited to a maximum of 18 months.

Pharmacokinetics

Teriparatide is extensively absorbed after subcutaneous injection; peak plasma concentrations are reached after about 30 minutes. Absolute bioavailability is reported to be about 95%. The serum half-life is 5 minutes after intravenous use, and approximately 1 hour after subcutaneous injection (reflecting time needed for absorption from the injection site). No studies have been done on the metabolism or excretion of teriparatide; parathyroid hormone is believed to be enzymatically metabolised in the liver and excreted by the kidneys.

Uses and Administration

Teriparatide is a synthetic polypeptide that consists of the 1-34 amino-acid biologically active N-terminal region of human parathyroid hormone (p.1103). It is used in the treatment of established postmenopausal osteoporosis, especially in those with a high fracture risk, and in men with primary or hypogonadal osteoporosis who are at increased risk of fracture. The usual dose is 20 micrograms subcutaneously daily into the thigh or abdominal wall. Treatment is limited to a maximum of 18 months in the UK, although it has been used for up to 2 years in the USA. Teriparatide acetate has been given by intravenous infusion in the differential diagnosis of hypoparathyroidism and pseudohypoparathyroidism.

Hypoparathyroidism. Hypoparathyroidism is characterised by a deficiency in endogenous parathyroid hormone, whereas pseudohypoparathyroidism is characterised by resistance to the effects of parathyroid hormone (see p.1087). Teriparatide acetate is used *diagnostically* to distinguish between these 2 conditions.[1] A synthetic 1-38 fragment of human parathyroid hormone (hPTH 1-38) has been used similarly.[2] Teriparatide has also been used to *treat* hypoparathyroidism.[3-5]

1. Mallette LE. Synthetic human parathyroid hormone 1-34 fragment for diagnostic testing. *Ann Intern Med* 1988; **109:** 800–4.
2. Kruse K, Kracht U. A simplified diagnostic test in hypoparathyroidism and pseudohypoparathyroidism type I with synthetic 1-38 fragment of human parathyroid hormone. *Eur J Pediatr* 1987; **146:** 373–7.
3. Winer KK, *et al.* Synthetic human parathyroid hormone 1-34 vs calcitriol and calcium in the treatment of hypoparathyroidism. *JAMA* 1996; **276:** 631–6.
4. Winer KK, *et al.* A randomized, cross-over trial of once-daily versus twice-daily parathyroid hormone 1-34 in treatment of hypoparathyroidism. *J Clin Endocrinol Metab* 1998; **83:** 3480–6.
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.

Osteoporosis. Parathyroid hormone is capable of stimulating both formation and resorption of bone. Continuous infusion of teriparatide leads to a persistent elevation of parathyroid hormone and greater bone resorption by stimulating osteoclasts, with a net decrease in bone volume, and resultant hypercalcaemia; in contrast, daily (intermittent) injections increase bone volume by increasing osteoblastic proliferation.[1-3] Teriparatide appears to have less effect on cortical than trabecular bone,[3] suggesting that, although it may be helpful in preventing vertebral fractures, its impact on fractures of the proximal femur may be more limited. However, while treatment with teriparatide substantially increases lumbar spine bone mineral density (BMD), beneficial increases are also seen at the hip,[1] and in a pivotal study (the Fracture Prevention Trial)[4] in **postmenopausal** women with osteoporosis (p.1084), it decreased the risk of both vertebral and non-vertebral fracture. In a follow-up study, the reduction in vertebral fracture risk in patients treated with teriparatide for a mean of 19 months persisted for at least an additional 18 months after daily treatment was stopped.[5] Teriparatide appears to improve bone geometry, with no detrimental effect on cortical bone.[6] In the UK, NICE recommends teriparatide as an option for the secondary prevention of osteoporotic fragility fractures in women aged 65 years and older who have had an unsatisfactory response to bisphosphonates or who are intolerant to bisphosphonates, and who have an extremely low BMD (4 standard deviations or more below the mean) or a very low BMD (3 standard deviations or more) plus one or more additional risk factors.[7] It has been pointed out that evidence of reduction in teriparatide's effect with current or recent alendronate therapy (see below) might make its use as a second-line agent problematic.[8]

Data on combination therapy are limited, but some studies suggest that teriparatide with HRT is more effective than HRT alone.[9] The effect of teriparatide with the antiresorptive bisphosphonates has yet to be determined.[2,6,9,10] Although there is some suggestion that teriparatide still increases bone formation after treatment with alendronate,[9] a study in men found that, when given together, alendronate impaired the anabolic effects of teriparatide.[11] For this reason, some consider that teriparatide be started immediately after stopping bisphosphonates.[10] It has been suggested that the degree of suppression of bone turnover before treatment may dictate the response to teriparatide.[6] A study of daily or cyclical teriparatide in women with osteoporosis found that although the teriparatide-induced increase in BMD may be slightly lower in women who had previously taken alendronate than in those who had never received it, the increase in spinal BMD was still impressive. Intermittent cyclical treatment with teriparatide was found to have similar effects on BMD to those induced by daily dosage.[12]

In postmenopausal women with osteoporosis taking HRT and **corticosteroids**,[13] the addition of teriparatide significantly increased BMD of the lumbar spine; modest changes in hip bone mass were not significant.

In **men** with osteoporosis, teriparatide increased BMD in the lumbar spine and at the femoral neck;[9] risk of fracture was also reduced.[1]

1. Cappuzzo KA, Delafuente JC. Teriparatide for severe osteoporosis. *Ann Pharmacother* 2004; **38:** 294–302.
2. Madore GR, *et al.* Parathyroid hormone. *J Am Acad Orthop Surg* 2004; **12:** 67–71.
3. Brixen KT, *et al.* Teriparatide (biosynthetic human parathyroid hormone 1–34): a new paradigm in the treatment of osteoporosis. *Basic Clin Pharmacol Toxicol* 2004; **94:** 260–70.
4. Neer RM, *et al.* Effect of parathyroid hormone (1-34) on fractures and bone mineral density in postmenopausal women with osteoporosis. *N Engl J Med* 2001; **344:** 1434–41.
5. Lindsay R,*et al.* Sustained vertebral fracture risk reduction after withdrawal of teriparatide in postmenopausal women with osteoporosis. *Arch Intern Med* 2004; **164:** 2024–30.
6. Rubin MR, Bilezikian JP. Parathyroid hormone as an anabolic skeletal therapy. *Drugs* 2005; **65:** 2481–98.
7. NICE. Bisphosphonates (alendronate, etidronate, risedronate), selective oestrogen receptor modulators (raloxifene) and parathyroid hormone (teriparatide) for the secondary prevention of osteoporotic fragility fractures in postmenopausal women: Technology Appraisal 87 (issued January 2005). Available at: http://www.nice.org.uk/nicemedia/pdf/TA087guidance.pdf (accessed 23/07/08)
8. Anonymous. Teriparatide for postmenopausal osteoporosis. *Drug Ther Bull* 2004; **42:** 93–5.
9. Quattrocchi E, Kourlas H. Teriparatide: a review. *Clin Ther* 2004; **26:** 841–54.
10. Deal C. The use of intermittent human parathyroid hormone as a treatment for osteoporosis. *Curr Rheumatol Rep* 2004; **6:** 49–58.
11. Finkelstein JS, *et al.* The effects of parathyroid hormone, alendronate, or both in men with osteoporosis. *N Engl J Med* 2003; **349:** 1216–26.
12. Cosman F, *et al.* Daily and cyclic parathyroid hormone in women receiving alendronate. *N Engl J Med* 2005; **353:** 566–75.
13. Lane NE, *et al.* Parathyroid hormone treatment can reverse corticosteroid-induced osteoporosis. *J Clin Invest* 1998; **102:** 1627–33.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Forteo; ***Austral.:*** Forteo; ***Belg.:*** Forsteo; ***Braz.:*** Forteo; ***Canad.:*** Forteo; ***Chile:*** Forteo; ***Cz.:*** Forsteo; ***Denm.:*** Forsteo; ***Fin.:*** Forsteo; ***Fr.:*** Forsteo; ***Ger.:*** Forsteo; ***Gr.:*** Forsteo; ***Hong Kong:*** Forteo; ***Hung.:*** Forsteo; ***Irl.:*** Forsteo; ***Israel:*** Forteo; ***Ital.:*** Forsteo; ***Malaysia:*** Forteo; ***Mex.:*** Forteo; ***Norw.:*** Forsteo; ***NZ:*** Forteo; ***Philipp.:*** Forteo; ***Port.:*** Forsteo; ***S.Afr.:*** Forteo; ***Singapore:*** Forteo; ***Spain:*** Forsteo; ***Swed.:*** Forsteo; ***Switz.:*** Forsteo; ***Thai.:*** Forteo; ***UK:*** Forsteo; ***USA:*** Forteo; ***Venez.:*** Forteo.

Tiludronate

ATC — M05BA05.
ATC Vet — QM05BA05.

Tiludronic Acid *(BAN, rINN)*

Acide Tiludronique; Ácido tildrónico; Acidum Tiludronicum; ME-3737; SR-41319; Tiludronihappo; Tiludronik Asit; Tiludronsyra. {[(*p*-Chlorophenyl)thio]methylene}diphosphonic acid.

Тилудроновая Кислота

$C_7H_9ClO_6P_2S$ = 318.6.
CAS — 89987-06-4.
ATC — M05BA05.
ATC Vet — QM05BA05.