

## UPDATE ON OSTEOPOROSIS

-  **Osteoporosis is a significant cause of morbidity and mortality, especially in the elderly population**
-  **Individuals  $\geq 50$  years with risk factors for osteoporosis should be considered for evaluation**
-  **Bisphosphonates are the usual first-line option for patients with osteoporosis**
-  **Adherence to osteoporosis medications has been reported to be  $< 50\%$**

### INTRODUCTION

Osteoporosis is a skeletal disorder characterised by **loss of bone mass** and deterioration of micro-architecture, leading to bone fragility with a consequent increase in risk of fracture.<sup>1,2</sup> It is the most common global bone disease, and is a risk factor for fracture of a magnitude similar to the way that hypertension is a risk factor for stroke.<sup>1</sup> It is estimated that approximately 50% of women and 20% of men  $>50$  years experience an osteoporosis-related fracture at some point in their lifetime.<sup>1,3</sup> The most common fractures are those of the vertebrae, proximal femur and distal forearm. **Vertebral fractures are experienced by 1 in 8 patients  $>50$  years**, of which two thirds are clinically silent.<sup>1,3,4</sup> They are associated with a high risk of future fracture, morbidity and mortality. **Hip fractures, which affect 1 in 3 women and 1 in 9 men  $>80$  years**, are among the most devastating results of osteoporosis.<sup>4</sup> They are associated with a 36% increase in mortality within one year (higher in men than women). Complications include emboli, pneumonia and a 2.5 fold risk of future fractures.<sup>1,3</sup> Up to 20% of patients who experience a hip fracture require long-term nursing care and only 40% of patients fully regain their pre-fracture level of independence.

Osteoporosis represents a major public health problem. Current Irish figures indicate that approximately 300,000 people  $\geq 50$  years have osteoporosis and that these figures may double in the next 20 years.<sup>3</sup> Osteoporosis-related fractures carry a heavy economic burden; it is estimated that in Ireland, osteoporotic fractures cost up to €551 million to treat in 2010 and will cost more than €1 billion by 2020.<sup>3</sup> **Osteoporosis is preventable and treatable but because there are no warning signs, many people are not diagnosed in time to receive effective therapy during the early phases of the disease.**<sup>1</sup> This bulletin will provide an update on the management of osteoporosis.

### PATHOPHYSIOLOGY

Bone mass increases throughout childhood, peaks in adolescence, remains relatively constant in early/late adulthood and declines in old age.<sup>1,2,5</sup> Peak bone mass is determined largely by genetic factors, in association with other factors including nutrition, endocrine status, physical activity and health during growth.<sup>1,2</sup> In adult life, the skeleton is continually re-modelled, in an orderly sequence of bone resorption followed by bone formation. The rate of re-modelling is affected by many factors including sex hormones, vitamin D and parathyroid hormone.<sup>3</sup> Bone loss occurs when the balance is altered, such as with advancing age and menopause. This results in greater bone removal than replacement, leading to a disordered skeletal architecture, the development of osteoporosis and a consequent increase in osteoporosis-related fracture risk.<sup>1,2</sup> Fractures occur when weakened bone is overloaded, often by falls or certain activities of daily living.

### ASSESSMENT AND DIAGNOSIS

A comprehensive approach to the diagnosis and management of osteoporosis is recommended.<sup>1,3,6,7</sup> The aims of the risk assessment are to exclude diseases that mimic osteoporosis (e.g. osteomalacia), identify the cause of osteoporosis, assess the risk of fractures and select the most appropriate form of treatment.<sup>8</sup>

**Risk assessment:** There is no universal screening policy for osteoporosis. However, **postmenopausal women and men  $>50$  years should be considered for evaluation of osteoporosis risk factors** to determine if there is a need for bone mineral density (BMD) testing and/or vertebral imaging.<sup>1,8,9</sup> There are many clinical risk factors associated with an increased risk of osteoporosis-related fracture; the more risk factors that are present, the greater the risk of fracture (Table 1).

**Table 1: Clinical risk factors used for the assessment of fracture probability<sup>8</sup>**

Risk Factors include:	Secondary causes of osteoporosis include:
Age	Rheumatoid arthritis
Gender	Untreated hypogonadism in men and women
Low body mass index	Prolonged immobility
Previous fragility fracture	Organ transplantation
Parental history of fractured hip	Type I diabetes
Current glucocorticoid treatment (any dose, by mouth for $\geq 3$ months)	Hyperthyroidism
Current smoking	Gastrointestinal disease
Alcohol intake of $\geq 3$ units daily	Chronic liver disease
	Chronic obstructive pulmonary disease

The 10-year probability of a major osteoporotic fracture may be determined using a computer generated algorithm FRAX®, which is used to incorporate risk factors (Table 1) with or without information on BMD (available on [www.sheffield.ac.uk/FRAX](http://www.sheffield.ac.uk/FRAX)).<sup>10</sup> Patients may be classified on FRAX® as low, intermediate or high risk of fracture. Those with **low risk** can be reassured and reassessed when risk factors change, those with **intermediate risk** should be considered for BMD assessment (and their fracture risk probability reassessed) and those with **high risk** should be considered for treatment.<sup>8</sup> FRAX® can be used to aid management decisions but should not replace clinical judgement.<sup>8</sup> Limitations of FRAX® include the omission of other important risk factors such as falls, patients living in care homes and those on drugs that impair bone metabolism and BMD (e.g. anticonvulsants, selective serotonin reuptake inhibitors).<sup>6,7</sup>

**Investigations** depend on the severity of symptoms, age at presentation and the presence or absence of individual risk factors.<sup>8</sup> Routine investigations include: full blood count, ESR or C-reactive protein, serum calcium, albumin, creatinine, phosphate, alkaline phosphatase, liver transaminases, thyroid stimulating hormone and bone densitometry.<sup>8</sup> Other procedures may also be required for individual patients.

**Diagnosis:** The diagnosis of osteoporosis is established by measurement of BMD or by the occurrence of adult hip or vertebral fracture in the absence of major trauma.<sup>1</sup> BMD correlates with bone strength and is a predictor of future fracture risk; fracture risk increases exponentially as BMD decreases.<sup>1,3</sup> Dual Energy X-ray Absorptiometry (DXA) of the hip and spine is currently the most widely used method of assessing BMD.<sup>1,3</sup> BMD testing should be considered in women  $\geq 65$  years and men  $\geq 70$  years, younger postmenopausal women and men aged 50–69 years with risk factors for osteoporosis, adults  $>50$  years with fragility fractures and adults with a condition or taking a medication associated with low bone mass.<sup>1,3</sup> **The WHO defines osteoporosis as a T-score  $\leq -2.5$ , where the T score is a comparison of the patient's BMD with the BMD of a healthy young adult.**<sup>1</sup> (Table 2). Vertebral imaging should also be considered in patients aged 50–69 years with a height loss of  $\geq 4$  cm and women  $\geq 65$  years and men  $\geq 70$  years, with a T-score of  $\leq -1.5$ .<sup>1</sup>

**Table 2: WHO definition of osteoporosis by BMD<sup>1</sup>**

Classification	BMD	T-score
Normal	Within 1 SD* of a young-adult reference population	T-score $\geq -1.0$
Osteopenia (Low bone mass)	Between 1.0 SD* and 2.5 SD below that of a young-adult reference population	T-score between -1.0 and -2.5
Osteoporosis	2.5 SD* or more below that of a young-adult reference population	T-score at or below -2.5
Severe or established osteoporosis	2.5 SD* or more below that of a young-adult reference population	T-score at or below -2.5 with one or more fractures

\* standard deviation

## MANAGEMENT

It is essential to rule out secondary causes of osteoporosis before initiation of treatment.<sup>11</sup> The main objective of treatment is to prevent fractures; the decision to initiate treatment rests on the estimated risk of having a fracture in the next 10 years.<sup>11</sup> The National Osteoporosis Guideline Group in the UK recommend that **all women with fragility fractures should be considered for treatment with no need for further risk assessment (although BMD should be obtained if possible) and those with a 10-year fracture probability above the intervention threshold on FRAX® should be considered for treatment.**<sup>8</sup> The potential risks and benefits of all osteoporotic interventions should be discussed with the patient and a decision made on the most appropriate treatment at an individual level.<sup>1</sup>

### NON-PHARMACOLOGICAL MANAGEMENT

Several interventions should be recommended to patients to reduce fracture risk including an adequate dietary intake of calcium and vitamin D (Vit D), participation in regular weight-bearing (e.g. walking, jogging) and muscle-strengthening exercise (e.g. weight training and other resistive exercises), cessation of smoking and reduction in alcohol intake.<sup>1,3,9</sup> The importance of preventing falls cannot be over-emphasised; **over 80% of non-vertebral fractures are related to falls.**<sup>11</sup> Fall prevention relies on multiple factors such as home environment modification, physical exercise, visual defect correction and adjustment and rationalisation of antihypertensive, hypnotic and other medications.<sup>11</sup> Hip protectors may protect an individual from injuring the hip on falling, however the evidence regarding their anti-fracture benefits is inconclusive.<sup>1,9</sup> Adequate calcium is necessary for maintaining bone health. Vit D enhances the absorption of calcium. Low levels of calcium and Vit D are associated with an increased risk of hip fractures in the elderly.<sup>3</sup> **Recent guidelines recommend that the total calcium intake for men  $\geq 50$ –70 years should be 1,000 mg calcium daily and for women  $\geq 50$  years and men  $\geq 70$  years 1,200 mg daily.**<sup>1,12</sup> Important dietary sources of calcium include dairy products, bread, tinned fish and green vegetables.<sup>3</sup> Patients should be educated on the importance of adequate dietary calcium intake and to consider the use of 'calcium calculators' (e.g. <http://www.rheum.med.ed.ac.uk/calcium-calculator.php>).<sup>13</sup> It has been estimated that adults  $\geq 50$  years only consume  $\leq 700$ mg calcium daily, therefore supplements, including fortified food products, may be required.<sup>1,5</sup> Vit D is obtained from exposure to UVB light and from dietary sources such as oily fish, liver, cereals and fortified milk.<sup>1,14</sup> The US Institute of Medicine recommends a daily intake of 600–800 International Units (IU) Vit D for adults  $\geq 50$  years.<sup>12,15</sup> It is estimated that in Ireland 74% of adults have  $<50\%$  of the recommended daily intake of Vit D.<sup>3</sup> Patients at risk of Vit D deficiency include dark-skinned people living in northern latitudes (including Ireland), elderly and institutionalised individuals, individuals with malabsorption, short bowel or renal or liver disease, vegetarians and obese people.<sup>3,14,16</sup>

### PHARMACOLOGICAL MANAGEMENT

Drugs used in osteoporosis act mainly on bone resorption (inhibiting osteoclasts) or on bone formation (stimulating osteoblast activity). Most of the evidence on osteoporosis therapy is from studies in postmenopausal osteoporosis; there is limited information on glucocorticoid-induced osteoporosis and osteoporosis in men.<sup>1</sup>

**Calcium and Vit D supplements** are recommended for those unable to get the recommended daily amounts through food.<sup>3</sup> There is some evidence to support the use of calcium and Vit D supplements in reducing fracture risk in the elderly;<sup>17–22</sup> the use of calcium supplements alone is controversial.<sup>9,11,22</sup> A number of calcium and Vit D supplements are available. There is debate in the literature as to whether daily calcium intakes in excess of 1,200 mg may increase the risk of developing kidney stones, cardiovascular disease and stroke.<sup>1,23–32</sup> A calcium calculator (see above) can be a helpful tool to determine how much calcium supplementation is required. Supplements should be started contemporaneously with anti-resorptive agents as appropriate.<sup>33–40</sup> There is also controversy regarding the evaluation and management of Vit D deficiency.<sup>13,14,41</sup> The measurement of serum 25-hydroxyvitamin D [25(OH)D] is not necessary for patients with osteoporosis but is a good measure of risk and compliance.<sup>13,15</sup> A level  $<30$  nmol/L indicates an insufficient state; a level  $>50$  nmol/L indicates adequacy of Vit D.<sup>12,15,42</sup> The estimated average requirement of Vit D for people with minimal or no sun exposure is 400 IU daily.<sup>42</sup>

### ANTI-RESORPTIVE AGENTS

**Bisphosphonates** inhibit bone resorption by inducing apoptosis of osteoclasts.<sup>17,43</sup> Nitrogen-containing bisphosphonates (alendronate, risedronate, ibandronate and zoledronic acid) have the most potent anti-resorptive properties and are most commonly prescribed in osteoporosis.<sup>44</sup> Compared to placebo, all bisphosphonates significantly reduce vertebral fractures (relative risk reduction [RRR] of up to 70%), while alendronate, risedronate and zoledronic acid have been shown to reduce the risk of both non-vertebral and hip fractures (RRR up to 51%).<sup>6,11,17,43,44</sup> There are different formulations of bisphosphonates available; daily, weekly or monthly oral formulations and intravenous (IV) formulations (3 monthly or yearly). Oral formulations are poorly absorbed;  $<1\%$  of an orally administered dose is absorbed; therefore they must be taken after a prolonged fast, with water only, followed by avoidance of food for 30 minutes.<sup>17</sup> Bisphosphonates are contraindicated in patients with severe renal impairment (creatinine clearance  $<30$ –35 mL/min) or with hypocalcaemia.<sup>17,33–39</sup>

**Adverse effects:** The most common adverse effects of oral formulations are gastrointestinal effects (e.g. oesophagitis). These can be reduced by standing or sitting upright for 60 minutes after taking the dose. Bisphosphonates are contraindicated in patients with active upper gastrointestinal symptoms, delayed oesophageal emptying, strictures, achalasia or severe dysmotility.<sup>17</sup> Hypocalcaemia may occur with bisphosphonate use, but is usually mild except in patients with predisposing conditions such as hypoparathyroidism and metastatic bone disease.<sup>17</sup> **Osteonecrosis of the jaw (ONJ)** has been described with chronic bisphosphonate therapy but is extremely rare in the treatment of osteoporosis; a causal link with ONJ appears likely but has not been established.<sup>17,44</sup> More than 90% of reported cases have been in cancer patients receiving doses of bisphosphonates 10 times higher than those used to treat osteoporosis.<sup>17</sup> Other factors associated with an increased risk of ONJ include concomitant glucocorticoids, smoking and pre-existing dental disease. Risk minimisation measures include a dental assessment prior to initiating treatment, and advising patients of the importance of dental hygiene and dental examination if symptoms develop.<sup>45</sup> Evidence supports a strong association between bisphosphonate therapy and a **risk of atypical femoral fractures**, particularly for those on long-term therapy but the absolute risk appears to be low.<sup>46</sup> They are rare, accounting for approximately 1% of all hip and femoral fractures; the **estimated incidence being 5/10,000 per year of bisphosphonate use**.<sup>44</sup> Fractures are frequently bilateral, associated with minimal or no trauma and present with prodromal pain in the region of the fracture.<sup>17</sup> Patients on bisphosphonates should be advised to report any thigh, hip or groin pain. Those presenting with these symptoms should be evaluated for an incomplete fracture of the femur, and discontinuation of therapy should be considered while the patient is being evaluated.<sup>46</sup> Other adverse effects include influenza-like symptoms with monthly oral or IV therapy and inflammatory eye disorders.<sup>43</sup> There has been contradictory evidence as to whether bisphosphonates are associated with an increased risk of atrial fibrillation and oesophageal cancer, however overall evidence does not support a causal association in either case.<sup>17,43,44</sup>

**Duration of bisphosphonate use:** The optimal duration of bisphosphonate treatment has yet to be established. Evidence suggests that there is some continuing protection from bone loss following discontinuation of bisphosphonates.<sup>43,47,48</sup> This has been termed the “offset” effect by some clinicians.<sup>49</sup> Continuation of treatment up to 10 years with bisphosphonates (alendronate, risedronate and zoledronic acid) may reduce the risk of vertebral fractures.<sup>43,47-50</sup> **The need for continued treatment should be evaluated after 5 years of use.**<sup>46</sup> The anti-fracture effects of bisphosphonate treatment up to 5 years outweighs the risk of atypical fracture, however there is insufficient information to fully evaluate the effects of longer-term therapy.<sup>49</sup> Some experts advise that in patients at low risk of fracture (e.g. younger patients without a fracture history and with a BMD approaching normal) bisphosphonates may be discontinued after 3-5 years, while patients at increased risk of fracture (e.g. older patients with a history of fracture and a BMD in the osteoporotic range) may benefit from further therapy.<sup>1,43,47</sup> After 5 years of therapy a “drug holiday” is an option considered by some experts; patients can then be re-evaluated after this time.<sup>17,43,49</sup>

**Selective oestrogen-receptor modulators (SERMs)** are drugs that exhibit oestrogen receptor agonist activity on some tissues (e.g. bone and lipids) and antagonist activity on other tissues (e.g. breast and uterus).<sup>4,51</sup> Raloxifene and bazedoxifene increase BMD in postmenopausal women and have been shown to reduce the risk of vertebral fractures (RRR 30% with raloxifene and 42% with bazedoxifene), however their efficacy in reducing non-vertebral fractures has not been established.<sup>4,51-55</sup>

**Adverse effects** include an increased risk of venous thrombosis (VT) and exacerbation of hot flushes.<sup>4,51,52</sup> Fatal strokes have also been reported (<1%) with raloxifene.<sup>52,53</sup> SERMs are contraindicated in patients with a history of VT, unexplained uterine bleeding and patients with signs or symptoms of uterine cancer.<sup>53,54</sup>

**Denosumab** is a monoclonal antibody, which is given subcutaneously every 6 months. Denosumab binds to a receptor on the osteoclast surface, which results in reduced osteoclast formation, differentiation and survival.<sup>56</sup> Denosumab has been shown to reduce the risk of vertebral (RRR 68%), hip fractures (RRR 40%) and non-vertebral fractures (RRR 20%).<sup>11,56,57</sup> Denosumab may be useful for patients unable to adhere to, or who have contraindications to bisphosphonate treatment.<sup>58</sup>

**Adverse effects** most commonly include infections (e.g. skin, urinary tract and respiratory tract infections), rash and cataracts.<sup>40</sup> Rare cases of hypersensitivity, hypocalcaemia, ONJ and atypical femoral fractures have also been reported in patients on denosumab.<sup>40,59</sup> Hypocalcaemia is of particular concern in patients with severe renal impairment and on dialysis and in patients on high-dose denosumab for bone metastases.<sup>40,60</sup> Most cases of ONJ reported with denosumab have been in patients with advanced cancer. Prior to treatment, those with risk factors for ONJ should be considered for dental examination.<sup>40</sup> Patients should report new unusual hip, thigh or groin pain and treatment discontinuation should be considered pending evaluation of the patient for an atypical fracture.<sup>40,59</sup>

**Calcitriol** (1,25-dihydroxycholecalciferol) is the active form of vitamin D, which acts mainly by bone resorption.<sup>61</sup> It has been shown to reduce vertebral fractures in postmenopausal women, but not to prevent non-vertebral and hip fractures. It is contraindicated in patients with hypercalcaemia; calcium and creatinine levels need to be monitored.

## OTHER AGENTS

**Strontium ranelate** has a dual mode of action, increasing bone formation and decreasing bone resorption, thereby rebalancing bone turnover in favour of bone formation.<sup>62</sup> It has been shown to prevent vertebral (RRR 41%), non-vertebral and hip (RRR 36%) fractures in menopausal women and men.<sup>11,52,62-64</sup>

**Adverse effects:** In April 2013, following a review of data by the European Medicines Agency, which showed an **increased risk of myocardial infarcts (1.7% versus 1.1% in placebo) with no observed increased risk in mortality, and other cardiovascular effects with use of strontium ranelate**, a decision was made to restrict its use.<sup>65</sup> **Strontium ranelate should only be used to treat severe osteoporosis in postmenopausal women at high risk of fracture and severe osteoporosis in men at increased risk of fracture.** It is contraindicated in patients with uncontrolled blood pressure and those with a current or past history of ischaemic heart disease, peripheral arterial disease and cerebrovascular disease.<sup>65</sup> In addition, its use has been associated with increased risk of venous thromboembolism, very rare severe allergic reactions and life-threatening cutaneous reactions.<sup>62,65</sup>

**Parathyroid hormone:** Recombinant human parathyroid hormone (PTH) 1-34 - (teriparatide) and PTH 1-84 are anabolic bone agents which stimulate osteoblastic activity.<sup>6</sup> They are administered subcutaneously daily.<sup>1</sup> They have been shown to reduce the risk of vertebral (RRR 65%), non-vertebral and hip fractures (RRR 53%).<sup>1,11,66,67</sup> They are recommended for patients with severe osteoporosis, especially those with incident vertebral fractures, and for those who cannot tolerate other therapy. Their use is restricted to two years.<sup>6</sup> Since bone mineral content is lost quickly on discontinuation, it is important to commence an anti-resorptive agent following discontinuation.<sup>1,6</sup>

**Adverse effects** include nausea, dizziness, muscle cramps and infrequent hypercalcaemia.<sup>6</sup>

**Hormone replacement therapy (HRT):** The Women’s Health Initiative study found that 5 years’ HRT in women (50-79 years) reduced the risk of vertebral and hip fractures by 34%. However HRT was also associated with an increased risk of cardiovascular disease and breast cancer.<sup>1</sup> In women with early natural or surgical menopause (before age 45 years), HRT may be considered until 50 years of age, since these patients are at high risk of osteoporosis. However, if osteoporosis is the main concern, alternative therapies should be considered.<sup>68</sup> Due to concerns regarding their risk/benefit, HRT (including tibolone) is

not recommended as first-line treatment in postmenopausal women and should only be used for prevention of osteoporosis in women at high risk of future fractures who are intolerant of other medicinal products, and where contraindications exist.<sup>1,68,69</sup>

## OSTEOPOROSIS IN MEN

Osteoporosis therapy in men has not been evaluated as extensively as in women. It is considered that osteoporosis in men is underestimated and more poorly treated than in women.<sup>70,71</sup> Secondary causes of osteoporosis occur in up to 65% of men due to metabolic causes, toxic substances or iatrogenic adverse effects.<sup>70</sup> Investigation is required to exclude secondary causes.<sup>61,70</sup> Risedronate, zoledronic acid, strontium ranelate and teriparatide are approved for the treatment of osteoporosis in men. **Testosterone undecanoate** is authorised for osteoporosis due to androgen deficiency in men.<sup>72</sup> **Adverse effects** associated with its use include prostate cancer, polycythaemia, gynecomastia and prostatic hypertrophy.<sup>72</sup>

## OVERVIEW OF MANAGEMENT OF OSTEOPOROSIS IN PRACTICE

The management of osteoporosis requires a comprehensive approach, which is summarised in Table 3. The Irish Osteoporosis Society (IOS) have also produced useful guidelines, updated in 2012. They can be accessed on ([www.irishosteoporosis.ie](http://www.irishosteoporosis.ie)).<sup>3</sup>

**Table 3: Overview of management of osteoporosis**<sup>8,9,17,43,44</sup>

<ul style="list-style-type: none"> <li>• Men and women ≥50 years should be considered for evaluation of osteoporosis</li> <li>• Secondary causes of osteoporosis should be excluded prior to commencing drug therapy</li> <li>• All patients should be provided with advice on lifestyle, nutrition, exercise and in particular, measures to reduce falls</li> <li>• Supplemental calcium and vitamin D should be considered, unless there is evidence of adequate dietary calcium intake and normal vitamin D status</li> <li>• Bisphosphonates should be considered the first-line treatment; the anti-fracture benefit of bisphosphonates outweighs the potential risks of therapy in most patients at high risk of fracture. Their use should be re-evaluated after 5 years</li> <li>• Other major pharmacological interventions are: SERMs, strontium ranelate, denosumab, and parathyroid hormone peptides             <ul style="list-style-type: none"> <li>• Strontium ranelate should only be used in postmenopausal women at high risk of fracture and in men with severe osteoporosis at increased risk of fracture; use is contraindicated in cardiovascular disease and uncontrolled hypertension</li> </ul> </li> <li>• Clinicians should be aware of the possible adverse reactions to pharmacological therapy:             <ul style="list-style-type: none"> <li>• Bisphosphonates have been associated with ONJ principally in patients receiving oncologic dose schedules, atypical femoral fractures with prolonged use, and hypocalcaemia in patients with renal disease. Denosumab is likely to have similar adverse reactions to bisphosphonates, but it has a much shorter residual effect</li> <li>• SERMs are associated with an increased risk of venous thromboembolism</li> <li>• Strontium ranelate is associated with increased risk of myocardial infarction and venous thromboembolism.</li> </ul> </li> <li>• Referral to a specialist in osteoporosis should be considered for patients who experience a fracture or significant BMD loss despite good adherence on first line therapy, intolerance of first and second line therapy, extremely low BMD and for secondary causes of osteoporosis</li> </ul>
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**Adherence to treatment** is an important aspect to consider in patients on therapy for osteoporosis. A recent Irish study found that patients' adherence to osteoporosis medication one year post-initiation of therapy was <50%.<sup>73</sup> Adherence has been shown to be better with weekly compared to daily doses of osteoporosis medications; the most common barriers to adherence are adverse effects.<sup>22</sup>

**Monitoring:** There is little evidence for repeat BMD testing on persistence with treatment or reduction of fractures. Some guidelines recommend repeat assessment after 2-3 years treatment and at the end of the treatment period.<sup>9,11</sup> If one or more fractures occur during treatment, check compliance, exclude secondary causes of osteoporosis and consider referral to a specialist.<sup>44</sup>

Table 4 summarises the authorised indications, dosages and costs for the main pharmacological interventions used in Ireland. (Full details of prescribing information for each product can be found in the Summary of Product Characteristics (SmPC), available at [www.imb.ie](http://www.imb.ie) and [www.medicines.ie](http://www.medicines.ie)).

## SUMMARY OF PHARMACOLOGICAL AGENTS

**Table 4: Authorised indications, frequency and costs of main agents used in osteoporosis**<sup>33-40,62,66,67,74-80</sup>

Drug	Postmenopausal Osteoporosis	Male Osteoporosis	Corticosteroid Induced Osteoporosis	Frequency	Monthly costs# €
Alendronate‡	Treatment			Weekly PO	13.19-22.17
Risedronate‡	Treatment	Treatment	Prevention in postmenopausal women	Daily PO Weekly PO	20.55 15.42-18.63
Ibandronic acid	Treatment			Monthly PO 3-monthly IV	13.86-20.80 103.89 (3 mth)
Zoledronic acid	Treatment	Treatment	Treatment	Yearly IV	424.86 (yearly)
Etidronate	Prevention and treatment		Prevention and treatment	14/90 days with calcium PO	Not available
Raloxifene	Prevention and treatment			Daily PO	21.73
Bazedoxifene	Treatment			Daily PO	20.86
Strontium ranelate *	Treatment	Treatment		Daily PO	32.49
Calcitriol	Treatment			Daily PO	22.73
Denosumab	Treatment	Only prostate cancer patients receiving HAT		6 monthly subcutaneous	215 (6 mths)
Teriparatide**	Treatment	Treatment	Treatment	Daily subcutaneous	389.98##
Parathyroid hormone **	Treatment			Daily subcutaneous	404.86##
Calcium and Vit D supplements	As adjunct therapy in patients with established, or at high risk, of combined Vit D and calcium deficiencies			Daily or twice daily	4.74—8.51

HAT=hormone ablation therapy

# monthly costs according to MIMS Ireland April 2013, unless otherwise stated, ## costs are ex-wholesale prices January 2013, ‡ combination products with Vit D +/- calcium are also available \*use restricted to those at high risk of future fractures who are intolerant of, or have contraindications to, other medicinal products; contraindicated in cardiovascular disease and uncontrolled hypertension, \*\* for patients with severe osteoporosis and for those who cannot tolerate other therapy

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List of references available on request. Date of preparation: June 2013

Every effort has been made to ensure that this information is correct and is prepared from the best available resources at our disposal at the time of issue. Prescribers are recommended to refer to the individual Summary of Product Characteristics (SmPC) for specific information on a drug.

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