1162

Final decision analytic protocol (DAP) to guide the assessment of bone mineral density analyses using dual energy X-ray absorptiometry (DXA) for women in their 50th year

July 2013

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MSAC and PASC

The Medical Services Advisory Committee (MSAC) is an independent expert committee appointed by the Australian Government Health Minister to strengthen the role of evidence in health financing decisions in Australia. MSAC advises the Commonwealth Minister for Health and Ageing on the evidence relating to the safety, effectiveness, and cost-effectiveness of new and existing medical technologies and procedures and under what circumstances public funding should be supported.

The Protocol Advisory Sub-Committee (PASC) is a standing sub-committee of MSAC. Its primary objective is the determination of protocols to guide clinical and economic assessments of medical interventions proposed for public funding.

Purpose of this document

This document is intended to provide a draft decision analytic protocol that will be used to guide the assessment of an intervention for a particular population of patients. The draft protocol will be finalised after inviting relevant stakeholders to provide input to the protocol. The final protocol will provide the basis for the assessment of the intervention.

The protocol guiding the assessment of the health intervention has been developed using the widely accepted "PICO" approach. The PICO approach involves a clear articulation of the following aspects of the research question that the assessment is intended to answer:

Patients – specification of the characteristics of the patients in whom the intervention is to be considered for use;
Intervention – specification of the proposed intervention
Comparator – specification of the therapy most likely to be replaced by the proposed intervention
Outcomes – specification of the health outcomes and the healthcare resources likely to be affected by the introduction of the proposed intervention

Purpose of application

A proposal for an application requesting MBS listing of dual energy X-ray absorptiometry (DXA) for women in their 50th year was received by the Department of Health and Ageing from Professor Christopher Nordin in June 2011.

The proposal is for the provision of an MBS item number for femoral neck and lumbar spine bone densitometry by dual energy X-ray absorptiometry (DXA) for all women in their 50th year with a view to, at an early stage, identifying individuals with a low or low-normal bone mineral density (BMD) (that is individuals with a negative T-score) who may be at future increased fracture risk and who would be given appropriate dietary and lifestyle healthy bone advice. The basis of this proposal is that patients with a diagnosed low or low-normal bone mineral density score may be more likely to persist with good bone health lifestyle and dietary advice than those who have not received the results of a bone mineral density test.

PASC note that the Applicant recently amended the proposal to consider testing of pre-menopausal women (at the age of 45 years). Following discussion, PASC agreed that the DAP should be based around the original submission of testing bone mineral density of women in their 50th year.

Intervention

Description

The World Health Organization (WHO) defines osteoporosis (OP) as a 'skeletal disorder characterised by compromised bone strength predisposing a person to an increased risk of fracture' (WHO 2003). It may also be defined as 'too little bone in the bone' (Albright and Reifenstein 1948), or of low bone mineral density.

The disease causes more than 8.9 million fractures annually worldwide, of which more than half occur in the Americas and Europe (WHO 2007). According to the Australian Institute of Health and Welfare (AIHW), in 2007-08, an estimated 692,000 Australians (3.4% of the total population) received a principal diagnosis of OP (AIHW 2011). Of these, 84 per cent of cases were in people aged 55 and over, and 82 per cent of cases were in women (AIHW 2011). However, it is likely this estimation of OP prevalence underestimates the number of people with the disease, as overt physical symptoms of OP are often not apparent, whereas a positive diagnosis is usually made following a symptomatic minimal trauma fracture (AIHW 2011). Based on an analysis conducted by the Geelong Osteoporosis Study it was estimated that there are 1.2 million Australians with osteoporosis and a further 5.4 million with osteopenia, in accordance with WHO definitions (Henry et al 2011). Low bone mineral density increases the risk of minimal trauma fracture.

Fractures are defined as minimal trauma fractures when the trauma is a result of a fall from standing height or less, and comprise a significant portion of the health burden caused by OP. Patients with minimal trauma fractures have increased morbidity, complications, and increased mortality compared

to age- and gender-matched peers. Predictors of minimal trauma fracture include age, muscle weakness, low bone mineral density, history of smoking, increased body sway and less physical activity (Center et al 2007). Common sites of minimal trauma fracture are the hip, pelvis, wrist, forearm and spine. Some fractures may not come to medical attention, for example it has been estimated that 50-75% of vertebral fractures are not diagnosed (Sanders et al 1999a). While the disease is not usually recorded as the primary cause of death, OP was listed as the underlying cause of 240 deaths in Australia in 2007 (AIHW 2011).

There are several factors which may increase a person's likelihood of developing OP (Table 1). The prevalence of OP is high in women, due to the decrease in oestrogen levels after menopause which result in higher levels of bone loss per year than in men. Low body mass index (BMI) (<18.5 kg/m^2) is also considered a risk factor for OP as it is often associated with lower levels of oestrogen.

Table 1 Risk factors for the development of osteoporosis

Type of risk factor	Examples
Fixed (non-modifiable) risk factors	Age (increases with the age after 40-50) Sex (osteoporosis affects women at an earlier age) Menopause Family history of osteoporosis (genetic predisposition) Previous low trauma fracture (fragility fracture) particularly of the hip spine or wrist.
Lifestyle (modifiable) risk factors	Physical inactivity Diet: low calcium intake Vitamin D deficiency Tobacco smoking Excessive alcohol consumption Low body mass index (BMI <18.5) Anorexia/exercise induced amenorrhoea Excessively high body mass index
Diseases implicated in OP	Rheumatoid arthritis Hyperthyroidism Hyperparathyroidism Hypogonadism, including early menopause Cushing's syndrome Chronic gut conditions including coeliac disease, and inflammatory bowel disease Chronic liver disease Chronic renal disease Some cancers (e.g. myeloma) Type 1 diabetes Gastrectomy Ankylosing spondylitis
Drug therapies implicated in OP	Chemotherapy Aromatase inhibitors for the treatment of breast cancer Long term corticosteroid use Anti-androgenic treatments for prostate cancer

Source; AIHW (2008 and 2010a,b), Osteoporosis Australia 2011, Smith 2006

Bone remodelling is a continual process which exists in adults to maintain bone mass and is mediated through osteoblasts, osteocytes and osteoclasts (Santen et al, 2011).

- Osteoblasts are bone forming cells which produce organic bone matrix and aid its mineralisation.
- Osteoclasts are bone resorptive cells which digest bone mineral and degrade extracellular matrix proteins and form bone resorptive "pits".
- Osteocytes are osteoblasts which do not undergo apoptosis and become incorporated into the bone matrix and are important in the coupling mechanism of bone formation and resorption.

The dynamics of bone remodelling require appropriate balance between bone formation and resorption. In a healthy individual, from birth until the age of approximately 20 years, bone formation exceeds resorption. At the end of this period, peak bone mass is achieved and between the ages of 20 and 40 is roughly maintained through the balance of bone formation and resorption (Marcus et al 2008). Following this period of equilibrium and with increasing age, bone resorption exceeds bone formation resulting in net bone loss. In women, bone density starts to fall at menopause and this is associated with increases in fracture rates, particularly at the forearm, spine and hip (Figure 1, Figure 2).

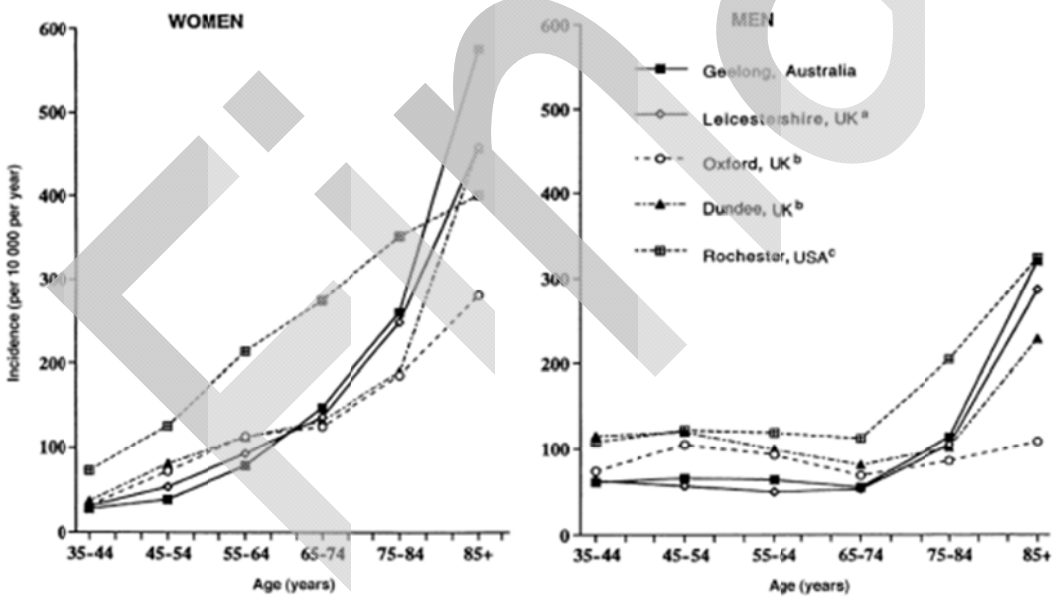


Figure 1 **The rise in fracture rates with age in men and women (Sanders et al 1999b)**

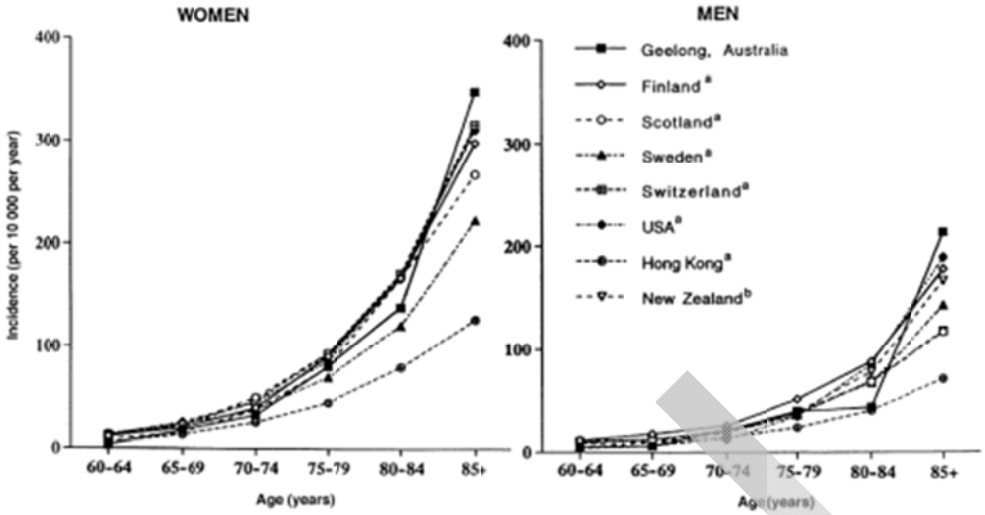


Figure 2 **The rise in hip fracture rates with age in men and women (Sanders et al 1999b)**

The processes underlying bone remodelling are complex and not completely understood; however, OP and low BMD are thought to occur as a result of an increase in the numbers and activity of osteoclasts. Oestrogen promotes the apoptosis of osteoclasts and as a result women who are oestrogen deficient, particularly post-menopausal women, experience a higher activity rate of osteoclasts resulting in net bone resorption (Santen 2011).The loss of oestrogen at menopause also increases the need for calcium. If this requirement is not met through the diet the resultant calcium deficiency is also involved in bringing about a reduction in bone density (Morris et al 1995). Calcium deficiency as a result of low levels of dietary calcium leading to reduced bone density may also occur in young adults.

Vitamin D_3 insufficiency can also contribute to bone loss. Vitamin D_3 (or cholecalciferol) is formed in the skin under the influence of sunlight and is converted by the liver and kidneys respectively to the pro-hormone calcidiol and the active form calcitriol (Jones et al 1998). With advancing age there is a progressive decline in serum calcidiol level in both sexes in western countries, partly because elderly people have less sun exposure and also because thinning of the skin with age reduces its capacity to make vitamin D_3 (Need et al 1993). Low vitamin D status raises blood parathyroid hormone levels (Carlsson & Lindquist 1955) which in turn accelerates bone resorption. Vitamin D insufficiency is common in Australia due to the avoidance of sun exposure.

As a result of these changes, bone strength is affected, increasing the risk of developing OP (Riggs 2000). Prior to menopause in women, approximately at the age of 40, net bone loss proceeds at an initial rate of approximately 0.3-0.5 per cent per annum. In the first five years post-menopause the rate of bone loss increases to 2-3 per cent per annum, and may exceed 5 per cent per annum (Elders et al 1988). Following this the bone loss rate slows to around one per cent per annum. A similar phenomenon occurs in men, but often does not occur until later in life or in association with other conditions.

Detecting low bone mineral density

Dual energy X-ray absorptiometry (DXA) and quantitative computed tomography (QCT) can be used in measuring BMD. DXA is more widely used, has better reproducibility, and is considered more appropriate in general use than QCT which delivers higher doses of radiation. QCT is often preferred when measuring BMD in the presence of fractures. Another tool for measuring BMD is quantitative ultrasound (QUS).

The DXA scan is used to generate T-scores which is a comparison of a patient's bone density to that of optimal peak bone density for the patient's gender and is reported as the number of standard deviations above or below the normal average (WHO 2007).

DXA is currently reimbursed through the MBS item to men and women aged 70+, for people who have previously experienced a minimal trauma fracture and for those with one of several risk factors including: prolonged corticosteroid use, hypogonadism, primary hyperparathyroidism, chronic liver disease, chronic renal disease, proven malabsorptive disorders, rheumatoid arthritis, or conditions associated with thyroxine excess (Table 3).

Bone mineral density in OP is characterised by the WHO as a T-score that is less than or equal to 2.5 standard deviations below the young normal mean (a T-score of -2.5 or less) (WHO 2007). Another threshold value of 2.0 standard deviations below the young normal mean has also been suggested to discriminate between fracture and non-fracture cases (Nordin 1987, Nordin 2008a, Wu et al 2010). Bone mineral density reflects the bone strength, the amount of bone (i.e. mass), its spatial distribution (i.e. shape and microarchitecture) and the intrinsic properties of the materials that comprise it, such as density, matrix mineralization, collagen traits and micro-damage (Marcus et al 2008). Osteopenia is a precursor to OP and according to WHO definitions is characterised when the T-score is between -1 to -2.5 (Table 2).

Table 2 Diagnosis of osteoporosis according to WHO definitions

T-score	Diagnosis
Equal or greater than -1	Normal bone density
<-1 to >-2.5	Low bone mass ("osteopenia": at risk for developing OP and increasing fracture risk)
Equal to or less than -2.5	Osteoporosis

Source: WHO 2007, RACGP 2010

Administration, dose, frequency of administration, duration of the intervention

Bone density scanning can be performed at any location which has both a DXA machine and qualified technician. A radiologist, nuclear medicine specialist or other accredited specialist is required to analyse the results, and communication of results to the patient is facilitated through the patient's general practitioner. One potential limitation to the availability of DXA scanning is the accessibility of

such devices, which was identified as a possible reason for low testing rates in Australian remote and rural settings (Ewald et al 2009). It is possible that this problem is being somewhat addressed through the growth of commercial mobile DXA scanning services travelling to remote areas.

Diagnosis of low bone mineral density is dependent on the measurement site and number of sites measured; accurate diagnosis can only be achieved by measuring BMD at two or more sites. A DXA scan of a patient's lower spine and hips is usually performed.

Absorbed radiation doses from DXA are negligible for first-generation pencil beam scanners (below the estimated dose from natural background radiation of 7 uSv per day). Newer fan beam scanners produce slightly more radiation, with absorbed dose ranging from approximately 10 to 20 uSv per examination (Damilakis and Guglielmi 2010), and generating a combined dose from anterior-posterior (AP) spine, lateral spine, and hip scans of <30 uSv (SIGN 2003). The estimated dose of radiation is lower for DXA measurements than most diagnostic X-ray examinations including mammography. However, the radiation dose can vary considerably between sites and DXA systems from different manufacturers based on scanning technique, x-ray tube filtration, efficiency of detection systems, exposure parameters, scan speed, scan size and patient body size (Damilakis and Guglielmi 2010).

Although the DXA device measures total density, the use of both high- and low-energy X-rays facilitates the separation of soft tissue and bone contributions to overall density (Dasher et al 2010). Scanning of the hip and spine usually takes up to a maximum of approximately 15-20 minutes (Dasher et al 2010). Several different MBS items provide services on a variety of indications with repeat scans dependent on the indication (Table 3). Current guidelines are based on the premise that for patients with low risk factors and T-scores above osteopoenic values (>-1.0), scans are rarely required and need only be considered with advancing age or a change in circumstance (minimal trauma fracture or increased risk conditions) (WHO 2007, RACGP 2010). In patients with confirmed OP and receiving anti-osteoporotic treatment, repeat DXA scans are recommended at 2 yearly intervals in order to effectively differentiate responders from non-responders and to assess compliance. For those patients who are at risk of developing OP, it is recommended that repeat BMD measurements are taken after 2 years. The BMD at the time of screening is the most important factor in determining treatment and the time to repeat scan. The rate of change between scans are not as important in overall management decisions.

Summary of the approach to assessment for the test

The **proposed test** is DXA.

In line with other DAPs, bone testing with QCT is excluded for the following reasons:

- QCT results are less reproducible than DXA
- There is less robust evidence currently available to support the use of QCT
- Although QCT radiation doses are reducing over time, currently the use of QCT involves a higher dose of radiation than DXA so exposes patients to a greater degree of potential harm.
- There are no standardised Australian normalised data for QCT.

- QCT assessment of the spine may overestimate osteoporosis compared to DXA using the WHO standard definitions.
- PASC recognise that QCT may be considered an alternative to DXA in the future.

Co-administered interventions

When individuals are aware of their bone mineral density status they may be more likely to take preventive measures to slow bone loss. There are several options for maintaining good bone health. The preventive modalities indicated for use in this proposal are:

- Exercise. Regular, progressive weight-bearing and resistance exercise aids in the preservation and increase of bone density.
- Calcium and vitamin D. It is recommended that to optimise clinical efficacy to maintain adequate bone mineralisation, adequate calcium and vitamin D are required. If sufficient calcium cannot be obtained from diet, and adequate vitamin D levels are not achieved by sun exposure, supplements may be needed.
- The 2011 Osteoporosis Australia Summit provides broad recommendations for all stages of life in terms of calcium, vitamin D, exercise and other modifiable health factors to promote healthy bones (Ebeling et al 2013).

According to the applicant, the most important features of the lifestyle advice would be adequate calcium intake, possibly including ingestion of dairy products, restriction of salt intake (sodium promotes urinary calcium loss) and exercise, which is known to maintain bone density. This advice would be provided by the doctor who ordered the test.

Pharmaceutical medications are available for the treatment of osteoporosis in certain patient groups (NHMRC 2010). Pharmaceutical intervention is not proposed as part of this submission. However, the Applicant acknowledges that cases of osteoporosis discovered fortuitously would be treated in accordance with current practice. Currently, no anti-osteoporotic drug listed on the PBS is available for otherwise healthy women aged 50-70 years, regardless of their T-score, unless this is associated with a minimal trauma fracture or other specific medical condition.

PASC agrees that prescription medicines used in the management of osteoporosis should not be included as part of the intervention. Supplemental information regarding pharmaceutical treatment for osteoporosis is provided in Appendix 1, 2, 3 and 4.

Calcium

In Australia the current recommended total calcium intake for postmenopausal women is 1,300 mg daily; this level has allowed for the menopausal rise in obligatory calcium loss (NHMRC 2006, NHMRC 2010). This level was based on FAO/WHO Recommendations (FAO/WHO 2002). However, when the fall in calcium absorption is also taken into account the allowance should probably be about 1,500 mg (Nordin 2008b) as originally suggested by a National Institutes of Health Consensus Development

Conference (NIHCDP 1994). Few postmenopausal women reach this intake (Pasco et al 2000) unless they use calcium-fortified milk or calcium tablets.

There have been at least 32 trials of the effect of calcium supplementation on bone density in postmenopausal women in the last forty years (Nordin 2009). In the 28 trials where diet histories were provided, the difference between the mean change in BMD at calcium intakes below and above 1,300 mg was significant (p=0.001).

Vitamin D status

The inhibitory effect of calcium on bone loss in elderly women is enhanced by the addition of vitamin D (Zhu et al 2008), which also has the advantage of decreasing fracture risk by strengthening muscle and reducing the risk of falls (Bischoff-Ferrari 2009a). The preventive effect of calcium with vitamin D on fracture risk is well documented with a relative fracture risk about 0.75 in high risk populations (Boonen et al 2007, Tang et al 2007, Bischoff-Ferrari et al 2009b, Abrahamsen et al 2010).

Where sun exposure is not adequate to generate sufficient vitamin D levels, supplementation of vitamin D in the order of 700-800 IU/day is recommended (Nowson et al 2012).

Combined calcium and vitamin D supplementation

Combined treatment with calcium and vitamin D reduces the risk of fractures in general and hip fractures in particular, not only in aged-care homes but also in the community. In one meta-analysis, the fracture risk reduction was greatest in the compliers (24%) and greater in those on the higher supplements of vitamin D and calcium than on the lower supplements (Tang et al 2007).

Attempts to separate the effects of vitamin D and calcium on fracture risk are largely futile because most trials have used both, but the largest meta-analysis, found no benefit from vitamin D alone but a relative fracture risk of 0.74 (0.60 to 0.91) (p=0.005) when vitamin D was combined with calcium (Abrahamsen 2010).

Threshold for therapy

The appropriate threshold for therapy (change in clinical management) is a test result with a negative T-score: this defines a group with either a low-normal (i.e. within 1 standard deviation of young adult mean) or a low bone mineral density. PASC notes that some of this population would still be within the normal range in terms of their bone mineral density as the T-score provides a measure of the variance of the individual's bone mineral density compared with the mean density of a healthy 30 year old sex-matched population. The assessment phase should address the issue of when to initiate therapy and provide evidence to determine the best threshold for intervention.

Clinical research questions for the assessment relating to the intervention:

- What is the compliance of the population to therapy with and without DXA? Evidence relating to this question will inform on the effect of the results of a DXA test on the adherence to appropriate diet and lifestyle changes.

- What is the effect of diet and lifestyle changes on the rate of minimal trauma fracture in the defined population?
- What is the most effective therapy for the prevention of minimal trauma fracture in the proposed population (e.g. dose of vitamin D, appropriate calcium supplement)?
- What is the rate of bone loss over time in the population who are not provided test and therapy? What is the rate of bone loss over time in the population who are provided test and therapy? Evidence provided in response to these questions will inform the number and frequency of DXA re-testing and monitoring (respectively). The frequency of re-testing and monitoring should be justified by the submission of available evidence.
- As detailed in the next section under 'Population', the population is defined as women in their 50th year. However, the assessment should also undertake sensitivity analyses around the initial testing of other age groups, specifically women in their 55th and 60th years. Accordingly, the assessment should provide evidence relating to the following clinical questions relating to the intervention:
    - What proportion of the population at each defined age (at their 50th, 55th and 60th year) will have a negative T-score? This population will be provided with the proposed therapy. Similar evidence should be provided for any other relevant age thresholds identified as part of the assessment.
    - What proportion of the population at each defined age (at their 50th, 55th and 60th year) will have a T-score of less than -2.5? This population will be eligible for repeat tests under existing items. Some of this population may choose to pay for their own prescription anti-resorptive medications available through the TGA.

Summary of the approach to assessment for the intervention

Test

The proposed test is DXA. PASC consider that testing for serum vitamin D adequacy would occur during standard clinical evaluation of a patient for low bone mineral density. Therefore the use of this resource would be the same in both the current and proposed scenario.

Therapy

The proposed therapy is dietary and lifestyle advice (calcium, vitamin D, salt restriction and exercise). This is in line with recommendations from recent evidence-informed Osteoporosis Australia guidance (Ebeling et al 2013).

The evaluation stage should provide evidence to determine the best **threshold for therapy**. PASC acknowledges that threshold for therapy does not need to align with other usual international thresholds (e.g. WHO cut-off for osteoporosis at a T-score of -2.5). The threshold for therapy will mean that the population will be provided dietary and lifestyle advice (not pharmaceutical or surgical intervention). The assessment should address threshold to therapy as:

- Negative T-score (i.e. defining a group with low-normal or low bone mineral density).

- The assessment should provide evidence to inform the appropriate threshold T-score(s) for therapy so that MSAC can determine the best threshold for intervention.
- The assessment should undertake sensitivity analyses around various relevant thresholds for therapy.

PASC considers that the **timing and frequency of monitoring and re-testing** should be informed by the evidence of the change in BMD and consequent change in the risk of minimal trauma fracture over time. The analysis of this evidence should identify the precision (reproducibility) of the BMD measurement (including whether bone loss over time can be distinguished over other sources of variation between measurements). For sensitivity analysis the following options should be evaluated regarding re-testing and monitoring of the population:

- No repeat test;
- Monitoring test after an initial negative test at 5 or 10 years up to the age of 70 years when they will become eligible for an existing MBS item;
- Monitoring or repeat test for all women at 5 or 10 years up to the age of 70 years when they will become eligible for an existing MBS item.
- Monitoring or repeat test at a time as informed by the evidence of change in bone mineral density and minimal trauma fracture over time for the population with or without intervention, respectively.

For the population identified with osteoporosis (taken to be a T-score of ≤ -2.5, see MBS Note D1.27, Appendix 5) monitoring would be available through current MBS items (12306, 12309).

Co-dependency

This DAP has no **co-dependency** with any pharmaceutical agent. However, for the purposes of modelling and resource use in Australia, it is acknowledged that some women, with a test result of osteoporosis, may choose to pay for TGA-listed prescription anti-resorptive pharmaceutical agents. The assessment phase should consider this possibility through sensitivity analysis.

This DAP has no **co-dependent PBS submission**.

Background

Current arrangements for public reimbursement

DXA scanning is not currently funded for women below the age of 70 unless they suffer from certain pre-defined conditions. There are currently MBS item numbers for a variety of indications. Unconditional access to DXA scanning under the schedule is currently available to persons aged 70 years and over (MBS item number 12323). A variety of other populations are covered for DXA under the MBS, including:

- Presumed low BMD following 1 or more fractures occurring after minimal trauma;
- Who have undergone prolonged glucocorticoid therapy and conditions associated with excess glucocorticoid secretion;
- Male (all) and female (lasting > 6 months before the age of 45) hypogonadism;
- Primary hyperparathyroidism;
- Chronic liver and/or renal disease;
- Proven malabsorptive disorders;
- Rheumatoid arthritis; or
- Conditions associated with thyroxine excess

Table 3 lists the currently available MBS item numbers for DXA and QCT. Relevant explanatory notes are provided in Appendix 5.

Table 3 Current MBS items for dual-energy X-ray absorptiometry and quantitative computed tomography

Category 2 – DIAGNOSTIC PROCEDURES AND INVESTIGATIONS, Bone Densitometry **MBS 12306** Bone densitometry (performed by a specialist or consultant physician where the patient is referred by another medical practitioner), **using dual energy X-ray absorptiometry**, for: • The confirmation of a presumptive diagnosis of low bone mineral density made on the basis of 1 or more fractures occurring after minimal trauma; or • For the monitoring of low bone mineral density proven by bone densitometry at least 12 months previously. Measurement of 2 or more sites – **1 service only in a period of 24 months** – including interpretation and report; not being a service associated with a service to which item 12309, 12312, 12315, 12318 or 12321 applies (Ministerial Determination). **Fee: $100.50 Benefit: 75% = $75.40 85% = $85.45**
Category 2 – DIAGNOSTIC PROCEDURES AND INVESTIGATIONS, Bone Densitometry **MBS 12309** Bone densitometry (performed by a specialist or consultant physician where the patient is referred by another medical practitioner), using quantitative computerised tomography, for: • the confirmation of a presumptive diagnosis of low bone mineral density made on the basis of 1 or more fractures occurring after minimal trauma; or • for the monitoring of low bone mineral density proven by bone densitometry at least 12 months previously. Measurement of 2 or more sites - 1 service only in a period of 24 months - including interpretation and report; not being a service associated with a service to which item 12306, 12312, 12315, 12318 or 12321 applies (Ministerial Determination) **Fee: $100.50 Benefit: 75% = $75.40 85% = $85.45**
Category 2 – DIAGNOSTIC PROCEDURES AND INVESTIGATIONS, Bone Densitometry **MBS 12312** Bone densitometry (performed by a specialist or consultant physician where the patient is referred by another medical practitioner), **using dual energy X-ray absorptiometry**, for the diagnosis and monitoring of bone loss associated with 1 or more of the following conditions: • Prolonged glucocorticoid therapy; • Conditions associated with excess glucocorticoid secretion; • Male hypogonadism; or • Female hypogonadism lasting more than 6 months before the age of 45

Where the bone density measurement will contribute to the management of a patient with any of the above conditions – measurement of 2 or more sites – **1 service only in a period of 12 consecutive months** – including interpretation and report; not being a service associated with a service to which item 12306, 12309, 12315, 12318 or 12321 applies (Ministerial Determination)

Fee: $100.50 Benefit: 75% = $75.40 85% = $85.45

Relevant explanatory notes

(a) 'Prolonged glucocorticoid therapy' is defined as the commencement of a dosage of inhaled clucocorticoid equivalent to or greater than 800 micrograms beclomethasone dipropionate or budesonide per day; or

(b) A supraphysiological glucocorticoid dosage equivalent to or greater than 7.5 mg prednisolone in an adult taken orally per day;

For a period anticipated to last for at least 4 months.

Glucocorticoid therapy must be contemporaneous with the current scan. Patients no longer on steroids would not qualify for benefits.

(a) Male hypogonadism is defined as serum testosterone levels below the age matched normal range

(b) Female hypogonadism is defined as serum oestrogen levels below the age matched normal range

Category 2 – DIAGNOSTIC PROCEDURES AND INVESTIGATIONS, Bone Densitometry

MBS 12315

Bone densitometry (performed by a specialist or consultant physician where the patient is referred by another medical practitioner), **using dual energy X-ray absorptiometry**, for the diagnosis and monitoring of bone loss associated with 1 or more of the following conditions:

- Primary hyperparathyroidism;
- Chronic liver disease;
- Chronic renal disease;
- Proven malabsorptive disorders;
- Rheumatoid arthritis; or
- Conditions associated with thyroxine excess

Where the bone density measurement will contribute to the management of a patient with any of the above conditions – measurement of 2 or more sites – **1 service only in a period of 24 consecutive months** – including interpretation and report; not being a service associated with a service to which items 12306, 12309, 12312, 12318 or 12321 applies (Ministerial Determination)

Fee: $100.50 Benefit: 75% = $75.40 85% = $85.45

Relevant explanatory notes

A malabsorptive disorder is defined as one or more of the following:

(a) Malabsorption of fat, defined as faecal fat estimated at greater than 18 gm per 72 hours on a normal fat diet; or

(b) Bowel disease with presumptive vitamin D malabsorption as indicated by a sub-normal circulating 25-hydroxyvitamin D level; or

(c) Histologically proven Coeliac disease

Category 2 – DIAGNOSTIC PROCEDURES AND INVESTIGATIONS, Bone Densitometry

MBS 12318

Bone densitometry (performed by a specialist or consultant physician where the patient is referred by another medical practitioner), using quantitative computerised tomography, for the diagnosis and monitoring of bone loss associated with 1 or more of the following conditions:

- prolonged glucocorticoid therapy;
- conditions associated with excess glucocorticoid secretion;
- male hypogonadism;

- female hypogonadism lasting more than 6 months before the age of 45;
- primary hyperparathyroidism;
- chronic liver disease;
- chronic renal disease;
- proven malabsorptive disorders;
- rheumatoid arthritis; or
- conditions associated with thyroxine excess.

Where the bone density measurement will contribute to the management of a patient with any of the above conditions - measurement of 2 or more sites - 1 service only in a period of 24 consecutive months - including interpretation and report; not being a service associated with a service to which item 12306, 12309, 12312, 12315 or 12321 applies (Ministerial Determination)

Fee: $100.50 Benefit: 75% = $75.40 85% = $85.45

Category 2 – DIAGNOSTIC PROCEDURES AND INVESTIGATIONS, Bone Densitometry

MBS 12321

Bone densitometry (performed by a specialist or consultant physician where the patient is referred by another medical practitioner), **using dual energy X-ray absorptiometry**, for the measurement of bone density 12 months following a significant change in therapy for:

- Established low bone mineral density; or
- The confirmation of a presumptive diagnosis of low bone mineral density made on the basis of 1 or more fractures occurring after minimal trauma.

Measurement of 2 or more sites – **1 service only in a period of 12 consecutive months** – including interpretation and report; not being a service associated with a service to which item 12306, 12309, 12312, 12315 or 12318 applies (Ministerial Determination)

Fee: $100.50 Benefit: 75% = $75.40 85% = $85.45

Relevant explanatory notes

Item 12321 is intended to allow for bone mineral density measurement following a significant change in therapy – e.g. a change in the class of drugs – rather than for a change in the dosage regimen.

Category 2 – DIAGNOSTIC PROCEDURES AND INVESTIGATIONS, Bone Densitometry

MBS 12323

Bone densitometry (performed by a specialist or consultant physician where the patient is referred by another medical practitioner), **using dual energy X-ray absorptiometry** or **quantitative computerised tomography**, for the measurement of bone mineral density, for a person aged 70 years or over.

Measurement of 2 or more sites – including interpretation and report; not being a service associated with a service to which item 12306, 12309, 12312, 12315, 12318 or 12321 applies (Ministerial Determination)

Fee: $100.50 Benefit: 75% = $75.40 85% = $85.45

Relevant explanatory notes

Item 12323 enables the payment of a Medicare benefit for a bone densitometry service performed on a patient aged 70 years or over. The Government has decided to expand access to Medicare subsided bone mineral density testing to coincide with the expanded eligibility for the osteoporosis medication 'alendronate' under the Pharmaceutical Benefits Scheme.

Taken from http://www9.health.gov.au/mbs/search.cfm, accessed 15 March 2012

Table 4 provides utilization of DXA services between July 2009 and June 2010.

Table 4 MBS items utilized between July 2009 and June 2010 for DXA scanning.

MBS item	45-54 years *(per 100,000)*	55-64 years *(per 100,000)*	65-74 years *(per 100,000)*	75-84 years *(per 100,000)*	≥85 years *(per 100,000)*	TOTAL – all ages *(per 100,000)*
12306	9,024 *(587)*	23,509 *(1,854)*	18,179 *(2,261)*	7,335 *(1,358)*	1,391 *(555)*	**59,438** *(571)*
12312	11,426 *(743)*	16,176 *(1,276)*	10,235 *(1,273)*	2,923 *(541)*	394 *(157)*	**41,154** *(436)*
12315	5,028 *(327)*	7,231 *(570)*	3,915 *(487)*	970 *(180)*	129 *(52)*	**17,273** *(183)*
12321	1,623 *(106)*	5,639 *(445)*	4,906 *(610)*	2,258 *(418)*	369 *(147)*	**14,795** *(140)*
12323	N/A	N/A	26,280 *(3,268)*	31,833 *(5,893)*	5,775 *(2,306)*	**63,888** *(580)*
TOTAL	27,101 *(441)*	52,555 *(1,036)*	63,515 *(1,580)*	45,319 *(1678)*	8,058 *(643)*	**196,548** *(382)*

Note: the low figures provided for 12306, 12312, 12315 and 12321 for patients ≥75 years of age may not reflect the true incidence of DXA scans clinically included under these item numbers, but instead may have been processed under the >70 years of age MBS item (12323). Source: https://www.medicareaustralia.gov.au/statistics/mbs_item.shtml, accessed 7 August 2012

A test for vitamin D is available through MBS item 66608 (Vitamin D or D fractions - 1 or more tests, Fee, $39.05). In financial year 2011-12, 3,481,966 services were provided under this item.

Regulatory status

Four DXA devices are used in Australia – Hologic, Lunar, Norland and Medilink. All devices are listed in the ARTG as category IIb devices (medium-high level of risk; Table 5) (Global Medical Device Nomenclature (GMDN) code 37661).

Table 5 Regulatory status of dual energy X-ray absorptiometry devices

ARTG number	Approval date	Manufacturer	Product name	Approved indication
97975	10/11/2003	GE Medical Systems Lunar	GE Medical Systems Australia Pty Ltd - X-ray system, diagnostic, bone absorptiometer, dual-energy	X-ray imaging for bone densitometry
117461	16/03/2005	Norland Corp	Inderlec Medical Systems Pty Ltd - X-ray system, diagnostic, bone absorptiometer, dual-energy	For the estimation of bone density and other structural parameters using x-ray absorptiometry for the purpose of aiding in the diagnoasis of osteoporosis including bone regeneration and loss.
119491	25/05/2005	Medilink	Inderlec Medical Systems Pty Ltd - X-ray system, diagnostic, bone absorptiometer, dual-energy	For the estimation of bone density and other structural parameters of bones using x-ray absorptiometry for the purpose of aiding in the diagnosis of osteoporosis including bone regeration and loss.
158772	23/01/2009	Hologic Inc	Cytyc Australia Pty Ltd - X-ray system, diagnostic, bone absorptiometer, dual-energy	Intended to be used to estimate bone density. The data can then be used to calculate bone mineral density.

Taken from https://www.ebs.tga.gov.au/, accessed 9 August 2012

Patient population

DXA scanning is proposed for the target population of women in their 50th year who are not eligible for a DXA scan through existing MBS items. The choice of the 50th year was proposed since this approximates to the average age of menopause in Australia.

PASC notes that the applicant proposed a target population of women at the age of 45 to assess peak bone mineral density. As this population is not linked with any specific risk factor PASC decided not to pursue this target population but to remain with the population initially proposed.

Not all women in the target population will choose to receive the test. The assessment should provide evidence regarding the proportion of women who would be expected to undertake DXA testing as proposed.

Risk factors

The specific risk factors associated with this population are gender (women) and age (approximately at or beyond menopause, which is an accepted risk factor for osteoporosis). No other risk factors are considered.

Baseline population

The target population is all women in their 50th year.

The baseline population is younger women (below the age of 50). Evidence should be provided showing any change in minimal trauma fracture between the target and baseline population.

The justification for this proposal is that bone mineral density loss increases with age and especially after menopause. Early identification of women at risk enables early intervention with dietary and lifestyle changes.

Benchmark population

Due to the broad nature of the proposed population, there are no other relevant populations which should be considered 'benchmark populations' for the purposes of this DAP. Access to current items or drugs is not similar to any other population; proposed thresholds for eligibility to current items or drugs are not similar to any other population; proposed thresholds for re-testing or monitoring are not similar to any other population.

The rationale for this submission is that early testing for low bone mineral density will identify otherwise normal women who may be at higher risk of future minimal trauma fracture.

Questions for the review relating to the population

- What proportion of women in the population would accept and receive a DXA scan as proposed?

Summary of the approach to assessment for the population

The **population** is women in their 50th year. The **baseline population** is younger women (below the age of 50). There are no **benchmark populations** for this DAP.

PASC advises that alternative ages for initial scanning for the purposes of sensitivity analysis should include:

- Women in their 55th year;
- Women in their 60th year.

The assessment should provide evidence regarding what age the test should be performed.

The assessment should provide evidence relating to testing women older than their 50th year (and who are <70 years) who have not previously been tested under this item. This should include consideration of 'rollout' in otherwise eligible women in cohorts older than their 50th year (and who are <70 years) at the time of the introduction of the proposed testing).

The assessment should provide evidence regarding the proportion of women who would be expected to undertake DXA testing as proposed.

Excluded populations

- All women at age 70 and over are excluded, as these are eligible for current MBS items for DXA scanning.
- Women presenting with a minimal trauma fracture are excluded, as these are eligible for current MBS items for DXA scanning (12306, 12309).
- Women eligible for any other current MBS item for DXA scanning are excluded.

Proposed MBS listing

At present, otherwise healthy individuals under the age of 70 are not covered for DXA analysis. Table 6 shows the proposed MSB item descriptor for bone densitometry in women in their 50th year. Women diagnosed with osteoporosis (T-score ≤-2.5) would be eligible for repeat testing as required under item number 12306. It is envisaged that the fees for the services would remain unchanged as any additional infrastructure costs incurred will be able to be offset by additional scans.

The proposed MBS item would provide BMD measured by DXA but not by QCT for several reasons; firstly the much higher cost of QCT, secondly the much higher radiation dose from QCT; and thirdly the much lower availability of QCT for bone densitometry because of other clinical needs. DXA also has improved reproducibility over QCT.

This proposed item number would be in addition to existing MBS items for DXA and QCT. At 70 all women will be eligible for an existing MBS item (12323).

Table 6 **Proposed MBS item descriptor**

Category 2 – DIAGNOSTIC PROCEDURES AND INVESTIGATIONS, Bone Densitometry
MBS XXXXX
Bone densitometry (performed by a specialist or consultant physician where the patient is referred by another medical practitioner), using **dual energy X-ray absorptiometry**, for the measurement of hip and spine bone mineral density in **women in their 50th (or 55th or 60th) year**.
Measurement of 2 or more sites –1 service only – including interpretation and report; not being a service associated with a service to which item 12306, 12309, 12312, 12315, 12318, 12321 or 12323 applies (Ministerial Determination).
Fee: $100.50 Benefit: 75% = $75.40 85% = $85.45
Other relevant notes from D1.27, Bone Densitometry – (Items 12306 to 12323)

Currently, no specific medication is proposed for use in the proposed population.

Clinical place for proposed intervention

The current diagnosis and management algorithm for suspected or proven low bone mineral density follows in Figure 2. The current and proposed algorithms follow in Figure 3 and Figure 4.

Figure 2 **Current clinical management algorithm for eligibility to MBS and PBS items for osteoporosis**

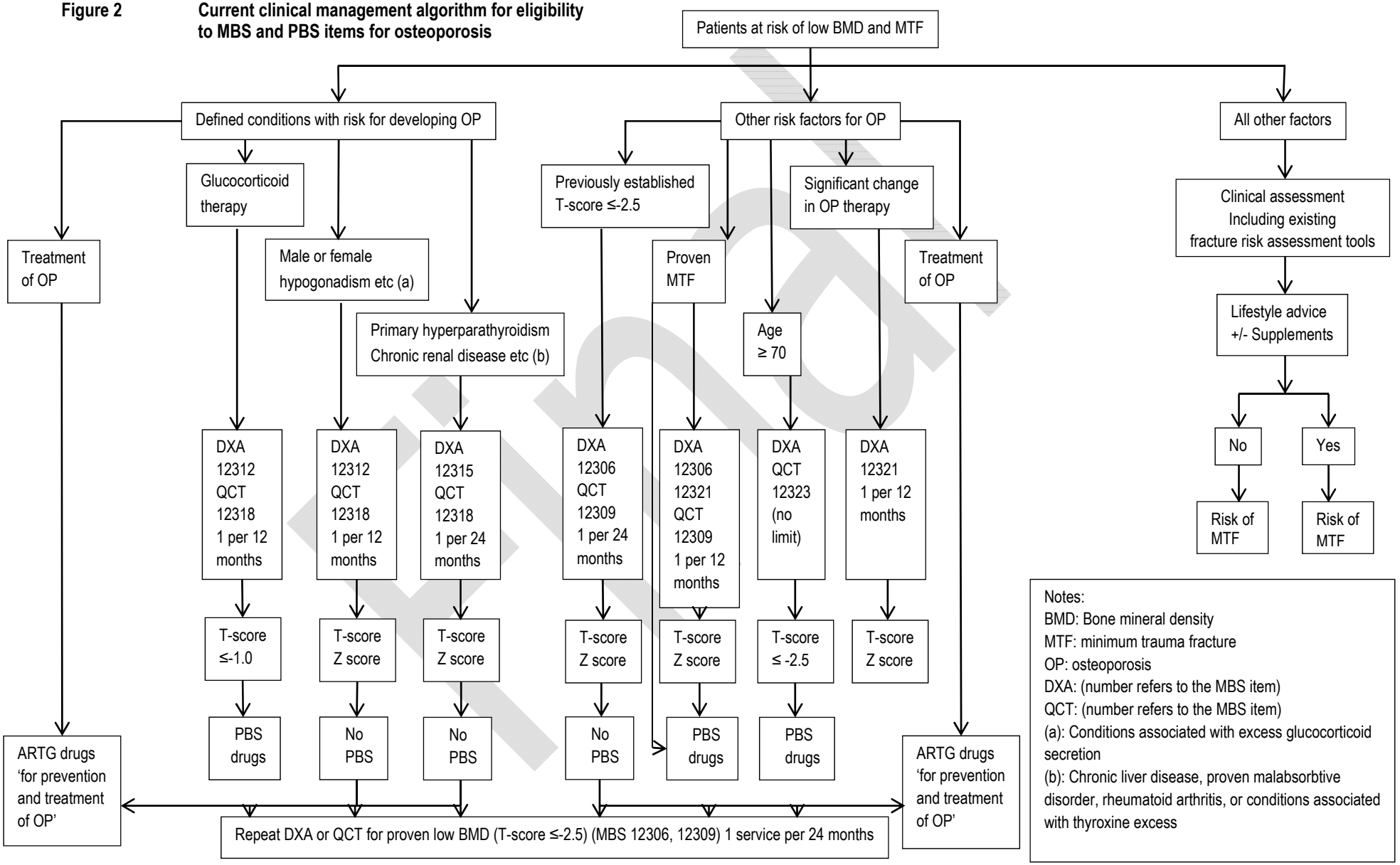


Figure 3 **Current clinical management algorithm for osteoporosis management of women in their 50th year**

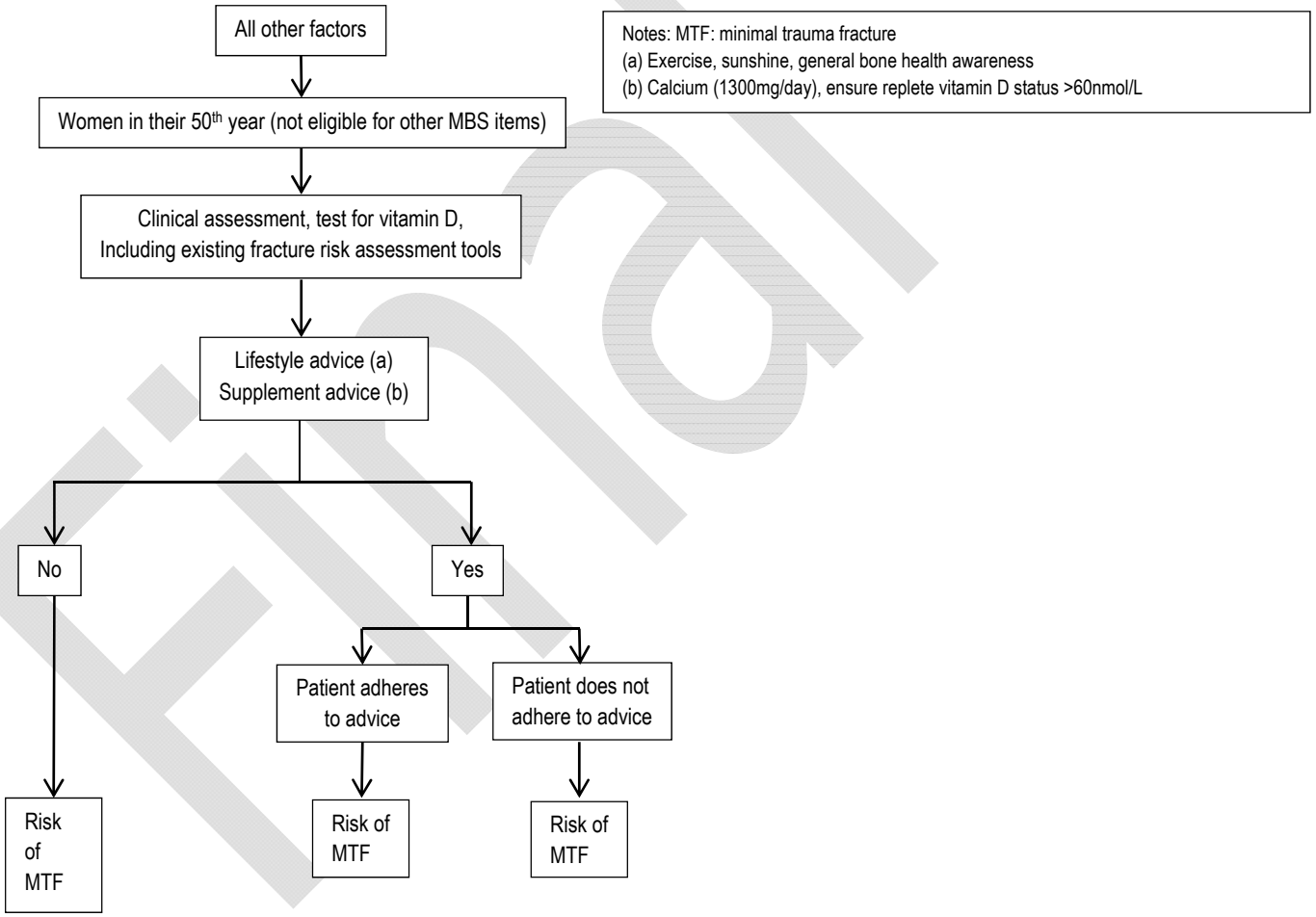
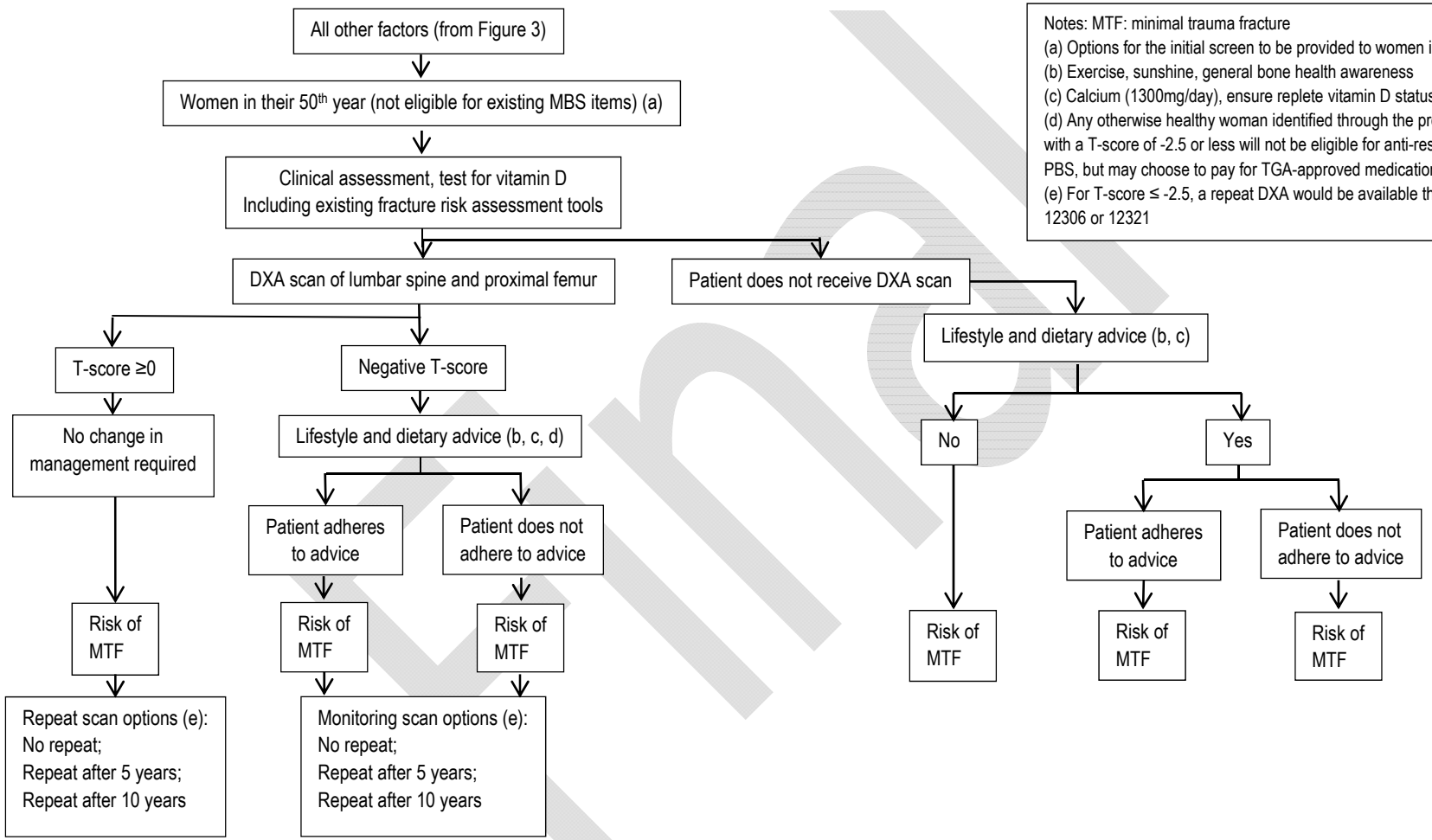


Figure 4 **Proposed clinical management algorithm for osteoporosis management of women in their 50th year**



Comparator

Currently most women in their 50th year will not receive DXA scanning for OP. Vulnerability to the condition may be predicted through a clinical assessment, including the use of existing fracture risk tools. Determining the probability of 10-year fracture risk can be assessed through use of the FRAX algorithm, developed by The University of Sheffield on behalf of the WHO (WHO 2007). This system can be used successfully in combination with DXA results, or without DXA as a predictor of risk of fracture. A variation of FRAX supported with Australian data is available at http://www.shef.ac.uk/FRAX/tool.jsp?country=31.

Part of the population may be readily able to adapt their diet and lifestyle to have an adequate calcium intake, exercise and/or sufficient sun exposure to ensure adequate vitamin D levels. Some women may take supplements (calcium and vitamin D) as a prophylactic measure for osteoporosis. These supplements are available without prescription. Even when supplements are recommended by GPs as a prophylactic measure for OP, persistence with such therapies may be an issue in the absence of a clear diagnosis or test result.

The comparator is:

- Lifestyle and dietary advice (calcium and vitamin D) based on a general clinical assessment by a general practitioner using existing fracture risk assessment tools (for example the FRAX algorithm) without the results of a bone mineral density test. This clinical assessment would include a test for vitamin D sufficiency (MBS item 66608).

Clinical claim

DXA scanning of women in their 50th year will facilitate the early identification of those with low-normal bone mineral density who may be at increased risk of future fractures. Secondarily, knowledge of low-normal bone mineral density, as established by the T-score, could improve compliance in this population with preventive measures of dietary and lifestyle changes (Winzenberg et al 2010, Marci et al 2000, Rimes et al 1999, Silverman et al 1997), which will reduce the rate of bone mineral density loss and maintain good bone health. Early identification and management of healthy women who may be at risk of osteopenia and osteoporosis may significantly impact on the clinical progression of the disease and prevent fractures.

DXA scanning of the spine and hip is reported as the number of standard deviations from the young normal mean (the T-score). Fracture risk is inversely related to BMD, and studies have shown that low BMD at menopause is predictive of future fracture risk. Women with negative T-scores at menopause have 2–3 times the long-term fracture risk of those with positive T-scores. The ten-year fracture predictive power of a negative T-score at menopause is 31.6 per cent and the negative predictive power of a positive T-score is 92.4 per cent (Abrahamsen et al 2006), and participants with T-scores below -1.4 at menopause (mean age 50.7 years range 45-58) had a 56% risk of fracture or low bone mineral density at 10 years (Abrahamsen et al 2006). Also a reduction in bone mass of one

standard deviation at a mean age of 56.5 years has a relative risk for hip fracture of 1.66 over a 23.5 year follow-up (Düppe et al 1997). Therefore women who have been identified with lower bone mineral density at a younger age will be at higher risk of fracture as they age.

The applicant proposes that all women should be entitled to bone densitometry in their 50th year to identify those with negative T-scores who would be given appropriate lifestyle and dietary advice. According to the applicant there are nearly 600 bone densitometers in Australia, many of them under-utilised, and it is believed that there is sufficient capacity to cope with the increased load if only a single age cohort of women is tested each year.

Table 7 Classification of an intervention for determination of economic evaluation to be presented

<table>
<tr><td colspan="2" rowspan="2"></td><td colspan="3">Comparative effectiveness (DXA scanning) versus comparator</td></tr>
<tr><td>Superior</td><td>Non-inferior</td><td>Inferior</td></tr>
<tr><td rowspan="5">Comparative safety versus comparator</td><td rowspan="3">Superior</td><td rowspan="3">CEA/CUA</td><td rowspan="3">CEA/CUA</td><td>Net clinical benefit</td><td>CEA/CUA</td></tr>
<tr><td>Neutral benefit</td><td>CEA/CUA*</td></tr>
<tr><td>Net harms</td><td>None^</td></tr>
<tr><td>Non-inferior</td><td>CEA/CUA</td><td>CEA/CUA*</td><td colspan="2">None^</td></tr>
<tr><td rowspan="3">Inferior</td><td>Net clinical benefit</td><td>CEA/CUA</td><td rowspan="3">None^</td><td colspan="2" rowspan="3">None^</td></tr>
<tr><td>Neutral benefit</td><td>CEA/CUA*</td></tr>
<tr><td>Net harms</td><td>None^</td></tr>
</table>

Abbreviations: CEA = cost-effectiveness analysis; CUA = cost-utility analysis

* May be reduced to cost-minimisation analysis. Cost-minimisation analysis should only be presented when the proposed service has been indisputably demonstrated to be no worse than its main comparator(s) in terms of both effectiveness and safety, so the difference between the service and the appropriate comparator can be reduced to a comparison of costs. In most cases, there will be some uncertainty around such a conclusion (i.e., the conclusion is often not indisputable). Therefore, when an assessment concludes that an intervention was no worse than a comparator, an assessment of the uncertainty around this conclusion should be provided by presentation of cost-effectiveness and/or cost-utility analyses.

^ No economic evaluation needs to be presented; MSAC is unlikely to recommend government subsidy of this intervention

The intention is to do a cost utility analysis considering both quality of life and treatment costs under both scenarios.

Questions for the review relating to the economic evaluation

Cost effectiveness models should be undertaken:

- To establish the baseline scenario: What are the downstream costs and outcomes without the proposed intervention?
- To assess the proposed scenario: What are the downstream costs and outcomes with the proposed intervention?
- As noted throughout the DAP, sensitivity analyses should be undertaken around:
    - The factors, ages and eligibility criteria as specified in the proposal;
    - The variables as advised by the available evidence;
    - The variables as advised by PASC as being informative for sensitivity analyses to inform the final decision making.
- The economic analysis should account for different thresholds for therapy as advised by the available evidence.

- The economic evaluation should account for all patients in the target population who become eligible for current MBS items (for example through age or minimal trauma fracture).
- The economic evaluation should account for a proportion of women who have a DXA result of low bone mineral density (taken as a T-score of less than or equal to -2.5) and choose to pay for TGA listed prescription anti-resorptive medications. These women will not be eligible for PBS reimbursement.

Outcomes and health care resources affected by introduction of proposed intervention

Outcomes

Several outcomes are highlighted in the clinical pathway algorithms. While the clinical pathway does not differ significantly between the two scenarios, the difference in outcomes will occur as a result of there being a greater number of women identified early and treated early, with improved compliance to therapy, thus delaying the progression of the disease and minimising bone loss.

Primary effectiveness outcomes:

- Proportion of women offered the scan who receive the scan
- Proportion of women who adhere to dietary and lifestyle change
- Incidence of MTF
- Incidence of all fractures
- Patient-related quality of life.

Secondary effectiveness outcomes:

- Change in morbidity/mortality

Safety outcomes and adverse events:

- Any adverse event or complication related to the DXA scanning or treatments for OP
- Any adverse event arising from exposure to ionising radiation

Please note:

- For this DAP, PASC considers that bone mineral density loss is not an appropriate surrogate for minimal trauma fracture.

- Where possible, the outcome of minimal trauma fracture should be disaggregated to type and location of fracture (eg hip vs non-hip) as this is important to translate to any possible effects

on life-years and quality-adjusted life-years.

- The site of the DXA exam (for example, proximal femur, lumbar spine, hip, distal radius) should be reported for all studies where possible. This is to account for any variability related to the site of the body where the testing is conducted.

- Where women are re-tested or monitored, it should be noted whether subsequent tests are undertaken on the same machine, or a different machine but the same model, or at the same or different practice. This is to account for any variability of test results between machines.

- PASC acknowledges that DXA is associated with low radiation doses, but that increasing the availability of DXA may significantly increase the exposure of the proposed population of otherwise healthy women to ionising radiation. This issue should be addressed in the assessment of evidence.

- Any evidence related to the relationship between the magnitude of the bone mineral density test result with the magnitude of lifestyle change should be reported.

Health care resources

Table 8 List of resources to be considered in the economic analysis

	Provider of resource	Setting in which resource is provided	Proportion of patients receiving resource	Number of units of resource per relevant time horizon per patient receiving resource	Disaggregated unit cost					
					MBS	Safety nets*	Other govt budget	Private health insurer	Patient	Total cost
Resources provided to identify eligible population										
- Confirmation of age and risk factor status	GP	public	TBA							
-										
Resources provided to deliver comparator 1										
- Education and healthy lifestyle promotion	Government Osteoporosis Australia	public	TBA	Unknown						
- Vitamin D test					85%= $33.20					
- Dietary supplements			TBA						Patient cost	
Resources provided in association with comparator 1 (e.g., pre-treatments, co-administered interventions, resources used to monitor or in follow-up, resources used in management of adverse events, resources used for treatment of down-stream conditions)										
- Costs associated with a fracture	Public or private hospital									
- Costs associated with recovery from a fracture									Patient cost	
Resources provided to deliver proposed intervention										
- Dual-energy X-ray absorptiometry device	Technician	Mainly private, but there may be some public	TBA	1 per patient	MBS					
- GP visit for referral to DXA	GP				MBS					
- GP visit to discuss results and to provide advice	GP				MBS					
Resources provided in association with proposed intervention										
- Dietary supplements									Patient cost	
- Vitamin D testing			TBA		85%= $33.20					
- Treatment	Pharmacy	Private	Unknown	Variable**	$37.38 to $589.17	$5.60 to $34.20				
- Costs associated with a fracture	Public or private hospital									
- Costs associated with recovery from a fracture									Patient cost	

*eligible patients will be referred to have a DXA scan performed through their GP or other health professional in each case

**although the duration of treatment per prescription varies, prescriptions usually contain sufficient medicine to treat the patient for 28 days.

Proposed structure of economic evaluation (decision-analytic)

This table will be finalised following the consultation, and may change depending on consultation responses and the final decision of PASC.

Table 9 Summary of extended PICO to define research question that assessment will investigate.

Patients	Intervention	Comparator	Outcomes to be assessed	Healthcare resources to be considered
Initial scan in otherwise healthy women in 50th year Additional groups for consideration: • Women in their 55th year • Women in their 60th year. Follow-up options to be evaluated: • No repeat test • Repeat test for initial negative test • Repeat test for all women (at 5 or 10 years) Exclude: • All women at age 70 and over, women with a previous minimal trauma fracture, all women currently eligible for MBS items for scanning for bone mineral density.	Dual energy X-ray absorptiometry (DXA) for bone mineral density, and treatment (lifestyle and dietary advice, including vitamin D test) for all women with negative T-scores. • Pharmaceutical intervention for low BMD is excluded. • QCT is excluded. • The evidence should also be used to determine the best threshold for intervention.	Clinical assessment including the use of existing fracture risk assessment tools (including vitamin D test) with lifestyle and dietary advice. • DXA and QCT are excluded.	**Primary effectiveness outcomes**: • Proportion of women offered the scan who receive the scan • Proportion of women who adhere to dietary and lifestyle advice • Incidence of MTF • Incidence of all fractures • Patient-related quality of life Safety outcomes and adverse events: • Any adverse event or complication related to the DXA scanning or treatments for OP • Any adverse event arising from exposure to ionising radiation See also 'Outcomes' section above.	• GP consultation (clinical examination and use of existing fracture risk tools). • Vitamin D tests. • Use of dietary supplements. • Costs associated with a fracture • Costs associated with recovery from a fracture • DXA test • Follow-up GP consultation for advice • Use of non-PBS reimbursable anti-resorptive drugs (sensitivity analysis).

PASC has specified a range of questions which will need to be addressed during the assessment phase. These questions will guide the evaluation and have been raised throughout the DAP. The assessment should address the questions raised throughout the DAP in relation to the population and intervention in order to provide MSAC with the necessary information to make an informed decision.

PASC also identified a need to appropriately structure the assessment phase so as to inform on broad issues of testing thresholds and monitoring protocols. Given the number and complexity of the questions for the assessment phase the key components and requests from PASC are summarised in Table 10 below.

Table 10 Summary of issues relating to the approach to assessment

Population	Women in their 50th year
Context	The population consists of women in their 50th year. PASC advises that alternative ages for initial scanning for the purposes of sensitivity analysis should include: • Women in their 55th year; • Women in their 60th year. All women at age 70 and over are excluded, as these are eligible for current MBS items for DXA scanning. Women presenting with a minimal trauma fracture are excluded, as these are eligible for current MBS items for DXA scanning (12306, 12309).
Baseline population	Younger women (below the age of 50)
Benchmark population	Not relevant
Approach to assessment	The assessment should provide evidence regarding at what age the test should be performed. Not all women in the target population will choose to receive the test. The assessment should provide evidence regarding the proportion of women who would be expected to undertake DXA testing as proposed.
Intervention	DXA test with dietary and lifestyle advice (for women with negative T-scores)
Context	The proposed test is DXA. QCT is excluded. The proposed therapy is dietary and lifestyle advice (calcium, vitamin D, salt restriction and exercise).
Co-dependency	There is no co-dependent pharmaceutical therapy.
Treatment threshold	The proposed threshold for therapy is any test result with a negative T-score (defining a low-normal or low bone mineral density).
Context	PASC identified a need to define the best threshold for intervention and to explore multiple thresholds.
Approach to assessment	The evaluation stage should provide evidence to determine the best threshold for intervention. PASC acknowledges that threshold to therapy does not need to align with other usual international thresholds (e.g. WHO cut-off for osteoporosis at a T-score of -2.5). The assessment should address threshold to therapy as: • Any negative T-score (i.e. low or low-normal bone mineral density). • The assessment should provide evidence to inform on the appropriate threshold T-score(s) for therapy so that MSAC can determine the best threshold for intervention. • The assessment should undertake sensitivity analyses around various relevant thresholds for therapy.
Re-testing and monitoring	Should repeat testing be conducted in women with a known T-score? The assessment should provide evidence regarding the rate of bone loss and minimal trauma fracture (with no test or intervention) in the population. This will inform the rate of re-testing. The assessment should provide evidence regarding the rate of bone loss and minimal trauma fracture (with test and intervention) in the population. This will inform the rate of monitoring.
Context	PASC considers that the timing and frequency of monitoring and re-testing should be informed by the evidence of the change of risk of minimal trauma fracture or bone mineral density over time.
Approach to assessment	For sensitivity analysis the following options should be evaluated regarding re-testing and monitoring of the population: • No repeat test; • Monitoring test after an initial negative test at 5 or 10 years up to the age of 70 years when they will become eligible for an existing MBS item; • Monitoring or repeat test for all women at 5 or 10 years up to the age of 70 years when they will become eligible for an existing MBS item. • Monitoring or repeat test at a time as informed by the evidence of change in bone mineral density and minimal trauma fracture over time for the population with or without intervention, respectively.
Comparator	Lifestyle and dietary advice (calcium and vitamin D) based on a general clinical assessment by a general practitioner using existing fracture risk assessment tools (for example the FRAX algorithm) without the

	results of a bone mineral density test. This clinical assessment would include a test for vitamin D sufficiency (MBS item 66608).
Outcomes	Outcomes include primary effectiveness, secondary effectiveness and safety outcomes. Adherence to the intervention is a primary effectiveness outcome.
Context	Primary effectiveness outcomes: • Proportion of women offered the scan who receive the scan • Proportion of women who adhere to dietary and lifestyle change • Incidence of MTF • Incidence of all fractures • Patient-related quality of life. Secondary effectiveness outcomes: • Change in morbidity/mortality Safety outcomes and adverse events: • Any adverse event or complication related to the DXA scanning or treatments for OP • Including any adverse event arising from exposure to ionising radiation
Approach to assessment	PASC considers that bone mineral density loss is not an appropriate surrogate for minimal trauma fracture. Where possible, the outcome of minimal trauma fracture should be disaggregated to type and location of fracture (eg hip vs non-hip) as this is important to translate to any possible effects on life-years and quality-adjusted life-years. The location of the DXA exam (for example, proximal femur, lumbar spine, hip, distal radius) should be reported for all studies where possible. Where women are re-tested, it should be noted whether subsequent tests are undertaken on the same machine, or a different machine but the same model, or at the same or different practice. PASC acknowledges that DXA is associated with low radiation doses, but that increasing the availability of DXA may significantly increase the exposure of the proposed population of otherwise healthy women to ionising radiation. This issue should be addressed in the assessment of evidence. Any evidence related to the relationship between the magnitude of the bone mineral density test result with the magnitude of lifestyle change should be reported. Any evidence relating to the proportion of women in the target population who will have a T-Score of ≤-2.5 should be presented.

Clinical research questions for public funding

The overall questions of the review will be:

- What is the safety of DXA and lifestyle and dietary advice compared with no DXA?
- What is the effectiveness of DXA and lifestyle and dietary advice compared with no DXA?
    - Does the result of a DXA scan improve compliance to therapy?
    - Does dietary and lifestyle advice reduce the incidence of minimal trauma fracture?
    - Does the intervention (test and therapy) reduce the rate of minimal trauma fracture?
- What is the cost-effectiveness of DXA and management of bone mineral density compared with no DXA?
    - Sensitivity analyses should be undertaken to provide information on the range of variables identified throughout the DAP.
- What is the role of DXA for monitoring and re-testing?

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Appendix 1 Examples of treatments currently listed on the ARTG for the treatment of osteoporosis

ARTG number	Product name	Approved indication
Selective oestrogen receptor modulators (SERMs)		
161797	Femarelle	Standard: For the symptomatic relief of menopause. Specific: Maintenance of bone health.
64709	Evista	Evista is indicated for the prevention and treatment of osteoporosis in post-menopausal women. Evista is indicated for the reduction in the risk of invasive breast cancer in postmenopausal women with osteoporosis. Evista is indicated for the reduction in the risk of invasive breast cancer in postmenopausal women at high risk of invasive breast cancer.
Bisphosphonates		
ARTG number	Product name	Approved indication
113482,120028,136846,157805, 161137, 53158, 54380, 67262, 68428, 73520, 73772, 76851, 93333, 98944	Fosamax	Specific: Treatment of osteoporosis in postmenopausal women to prevent fractures, including those of the hip and spine (vertebral compression fractures) and to help ensure vitamin D adequacy and/or to reduce the risk of Vitamin D insufficiency. Treatment of osteoporosis in men to prevent fractures and to help ensure vitamin D adequacy and/or to reduce the risk of Vitamin D insufficiency indicated for the treatment of Paget's disease of bone in men & women.
46852	Didrocal	Specific: Treatment of osteoporosis. Osteoporosis must be confirmed by the finding of low bone mass (at least two standard deviations below the gender-specific mean for young adults) or by the presence or history of osteoporotic fracture. Prevention of bone loss in patients for whom long-term treatment with high-dose corticosteroids is either about to be commenced or has been recently initiated
117667, 138211, 141530, 150618, 166838, 166853, 166942,74135, 74136, 82746	Actonel	Specific: Treatment of osteoporosis. Treatment of glucocorticoid-induced osteoporosis. Preservation of bone mineral density in patients on long-term corticosteroid therapy.
134664	Aclasta	Specific: Treatment of osteoporosis in postmenopausal women to reduce the incidence of hip, vertebral and non-vertebral fractures. - Treatment of osteoporosis in patients over 50 years of age with a history of at least one low trauma hip fracture, to reduce the incidence of further fractures. - To increase bone mineral density in men with osteoporosis. - To increase bone

		mineral density in patients with osteoporosis associated with long term glucocorticoid use. To prevent glucocorticoid-induced bone mineral density loss. - Treatment of Paget's disease of bone.

Monoclonal antibodies		
ARTG number	Product name	Approved indication
159322, 159323, 159324	Denosumab	The treatment of osteoporosis in postmenopausal women. Prolia significantly reduces the risk of vertebral, non-vertebral and hip fractures.
Parathyroid hormone		
ARTG number	Product name	Approved indication
80333	Teriparatide	indicated for the treatment of osteoporosis in postmenopausal women and the treatment of primary osteoporosis in men when other agents are considered unsuitable and when there is a high risk of fractures. Teriparatide is indicated for the treatment of osteoporosis associated with sustained systemic glucocorticoid therapy in women and men at high risk for fracture.

Strontium ranelate		
ARTG number	Product name	Approved indication
99978	Strontium ranelate (Protos)	Treatment of postmenopausal osteoporosis to reduce the risk of fracture. Treatment of osteoporosis in men at increased risk of fracture.

Source: Australian Register of Therapeutic Goods (ARTG) searched on 01/08/2012 < https://www.ebs.tga.gov.au/>

Appendix 2 Indications, contraindications and potential complications of the co-administered interventions

Co-administered interventions		
Bisphosphonates; Alendronate (Fosamax), Disodium etidronate (Didrocal), Risedronate（Actonel), Zoledronic Acid (Aclasta) ***[prevention (Grade A), treatment (Grade A)]*** ARTG: Fosamax: 113482,120028,136846,157805, 161137, 53158, 54380, 67262, 68428, 73520, 73772, 76851, 93333, 98944; Dirrocal: 46852; Actonel: 117667, 138211, 141530, 150618, 166838, 166853, 166942,74135, 74136, 82746; Aclasta: 134664; Clodronate: 181921, 181922, 66703, 66704, 80125, 80130		
Indication	**Contraindication**	**Side effects**
Paget's disease of bone Prevention and treatment of osteoporosis (including postmenopausal and corticosteroid-induced) Hypercalcaemia of malignancy Prevention of skeletal-related events in patients with malignancies involving bone Prevention and treatment of heterotopic ossification due to spinal cord injury or complicating total hip replacement	Abnormalities of the oesophagus which delay oesophageal emptying, such as stricture or achalasia. Inability to stand or sit upright for at least 30 minutes. Hypersensitivity to any component of bisphosphonates. Hypocalcaemia. Severe hypercalciuria.	*Common* nausea, vomiting, diarrhoea, headache, hypocalcaemia, musculoskeletal pain (may rarely be severe and/or disabling) IV: fever, flu-like symptoms, injection site reaction, increased creatinine concentration, hypophosphataemia, myalgia, bone pain, hypertension *Infrequent* oesophagitis, oesophageal erosions and ulcers (mainly with alendronate), gastritis, duodenitis, glossitis, rash IV: hypotension, hypomagnesaemia, hypokalaemia *Rare* heart failure, renal impairment, ocular inflammation, osteonecrosis of the jaw, allergic reactions including angioedema IV: anaphylactic shock *Osteonecrosis of the jaw Risk appears to be associated with the potency, route and total dose of bisphosphonate and a history of dental surgery, trauma or disease. *Possible associations* Atypical low-energy femoral fractures have occurred rarely during long-term bisphosphonate treatment for osteoporosis. It is possible that bisphosphonates slightly increase the risk of AF, although this association was not found in all studies. Some epidemiological data suggest an association between long-term use of oral bisphosphonates and an increased risk of oesophageal cancer; further

		evidence is needed.

Hormone Replacement Therapy
[prevention (Grade A), treatment (Grade A)]

Indication	Contraindication	Side effects
Prevention of postmenopausal osteoporosis when there is a high risk of fractures and alternative treatment is inappropriate	Breast cancer or other oestrogen-dependent tumour. Unexplained vaginal bleeding. History of endometriosis Uterine fibroids Migraine—may be exacerbated or relieved. Diabetes—HRT may improve glycaemic control Epilepsy Treatment with enzyme-inducing drugs Smoking Systemic lupus erythematosus Hereditary angioedema	*Common* breast enlargement and tenderness, abnormal mammogram, headache, depression, change in libido, irregular or breakthrough bleeding, spotting, endometrial hyperplasia (oestrogen-only HRT; infrequent with combined HRT), leg cramps, dry eye syndrome (oestrogen-only HRT; infrequent with combined HRT) *Infrequent* benign proliferative breast disease, breast cancer, premenstrual-like syndrome, dementia, migraine, cardiovascular events, fluid retention, oedema, increased BP, exacerbation or recurrence of endometriosis, acne, itch, nausea, increased triglycerides, gall stones *Rare* cholestatic jaundice, pancreatitis, glucose intolerance, galactorrhoea, visual changes, chloasma, hypersensitivity (angioedema, urticaria), ovarian cancer, endometrial cancer, enlargement of uterine fibroids, enlargement of hepatic haemangiomas

Selective oestrogen receptor modulators (SERMs); *Raloxifene hydrochloride* (Evista*)*
[treatment (Grade A)]
ARTG: Evista: 64709; Femarelle: 161797

Indication	Contraindication	Side effects
For the symptomatic relief of menopause. Maintenance of bone health,indicated for the prevention and treatment of osteoporosis. Hormone receptor-positive breast cancer	Venous thromboembolism (VTE) — contraindicated in patients with a history of VTE or risk factors for VTE . Prolonged immobilisation—increases risk of VTE. Women with or at risk of coronary heart disease—increased risk of VTE or fatal stroke. History of hypertriglyceridaemia induced by oestrogens—increased risk of hypertriglyceridaemia. History of breast cancer—raloxifene is not indicated for treating, or reducing risk of recurrence of, breast cancer. hepatic impairment Surgery Pregnancy Breastfeeding Contraindicated.	*Common* hot flushes, sweating, leg cramps, peripheral oedema, sleep disorders *Infrequent* VTE

Monoclonal antibodies; *Denosumab (*Prolia)
ARTG: 159322,159323, 159324

Indication	Contraindication	Side effects
Treatment of postmenopausal osteoporosis	Hypocalcaemia Renal increased risk of hypocalcaemia if CrCl <30 mL/minute.	*Common* eczema, hypercholesterolaemia *Infrequent* skin infections (mainly cellulitis) *Rare* hypocalcaemia, osteonecrosis of the jaw

Teriparatide (Forteo) (parathyroid hormone) *[treatment – (Grade A)]*
ARTG: 80333

Indication	Contraindication	Side effects
Postmenopausal osteoporosis when there is a high risk of fractures and other agents are unsuitable Primary osteoporosis in men when there is a high risk of fractures and other agents are unsuitable Corticosteroid-induced osteoporosis in patients at high risk of fractures	Paget's disease of bone Hyperparathyroidism Urolithiasis, hypercalcaemia Skeletal malignancies, history of skeletal radiation treatment, unexplained increases in ALP—manufacturer discourages use. Treatment with alendronate—may reduce the effectiveness of teriparatide; combination not recommended. Effect of combination with other bisphosphonates is not known. Renal Limited clinical experience in renal impairment; avoid if CrCl <30mL/minute. manufacturer discourages use in children and young adults with open epiphyses. Avoid in women planning to conceive or who are not using adequate contraception. Pregnancy Breastfeeding	*Common* nausea, headache, dizziness, muscle cramp, arthralgia, hyperuricaemia, injection site reactions *Infrequent* hypercalcaemia, myalgia, increased ALP *Rare* allergic reactions

Strontium Ranelate *(*Protos)**
[treatment – (Grade A)]

Indication	Contraindication	Side effects
Treatment of postmenopausal osteoporosis to reduce the risk of fracture. Treatment of osteoporosis in men at increased risk of fracture.	Known hypersensitivity to strontium ranelate or to any of the excipients Severe renal impairment (see Pharmacokinetics – Special Populations) Current or previous venous thromboembolic events (VTE), including deep vein thrombosis and pulmonary embolism. Temporary or permanent immobilisation (e.g. post-surgical recovery or prolonged bed rest).um	*Common* Headache, disturbances in consciousness, memory loss, nausea, diarrhoea, loose stools, venous thromboembolism, blood creatinine phosphokinase (CPK) increase *Uncommon* Seizures.

	ranelate or to any of the excipients Severe renal impairment (see Pharmacokinetics – Special Populations) Current or previous venous thromboembolic events (VTE), including deep vein thrombosis and pulmonary embolism. · Temporary or permanent immobilisation (e.g. post-surgical recovery or prolonged bed rest).	

Calcium and vitamin D *[prevention (Grade C), treatment (Grade C)]*

Indication	Contraindication	Side effects
Calcium; Adjunctive treatment in osteoporosis Vitamin D; Treatment of osteoporosis, when vitamin D supplementation is recommended	Hypercalcaemia Hypercalciuria, history of nephrolithiasis Treatment with digoxin Treatment with calcitriol Decreased gastric acidity Phenylketonuria Sodium restriction Renal Monitor plasma calcium concentration in renal impairment; if necessary, reduce dosage or stop. Vitamin D; Hyperphosphataemia (Vitamin D only)	*Common* belching, flatulence, abdominal distension, constipation *Infrequent* hypercalcaemia, alkalosis, hypophosphataemia *Rare* renal calculi, milk-alkali syndrome IV skin necrosis (extravasation), irritation Vitamin D; hypercalcaemia, renal and cardiovascular damage may occur because of ectopic calcification.

All information obtained from the Australian Medicines Handbook (AMH), January 2012 or the NHMRC clinical guidelines 2010

Appendix 3 PBS listed pharmaceuticals (by drug) for the treatment of diseases of bone structure and mineralisation

Drug	strength	Indication code	Specific indication	BMD / T-score
Bisphosphonates				
Alendronate Sodium	40 mg alendronic acid	3256	Symptomatic Paget disease of bone	N/A
	70 mg alendronic acid	4122	Corticosteroid-induced osteoporosis in a patient currently on long-term (≥ 3 months), high-dose (7.5 mg/day prednisolone or equivalent) corticosteroid therapy. Patient must not receive concomitant treatment with any other PBS-subscribed anti-resorptive agent for this condition. Duration and dose of corticosteroid therapy together with the date, site (femoral neck or lumbar spine) and score of the qualifying BMD measurement must be documented in the patient's medical records when treatment is initiated.	≤-1.5
		4133	Osteoporosis in a patient aged 70 years or older. Patient must not receive concomitant treatment with any other PBS-subscribed anti-resorptive agent for this condition. Date, site (femoral neck or lumbar spine) and score of the qualifying BMD measurement must be documented in the patient's medical records when treatment is initiated.	≤-2.5
		4123	Established osteoporosis in a patient with fracture due to minimal trauma. Patient must not receive concomitant treatment with any other PBS-subscribed anti-resorptive agent for this condition. Fracture must have been demonstrated radiologically and the year of plain x-ray, CT or MRI scan must be documented in the patient's medical records when treatment is initiated. A vertebral fracture is defined as a ≥20% reduction in height of the anterior or mid portion of a vertebral body relative to the posterior height of that body or a ≥ 20% reduction in any of these heights compared to the vertebral body above or below the affected vertebral body.	N/A

Alendronate Sodium with Colecalciferol	70 mg alendronic acid + 70 micrograms colecalciferol	N/A	For preservation of bone mineral density in patients on long-term glucocorticoid therapy where patients are undergoing continuous treatment with a dose ≥7.5 mg of prednisone or equivalent per day. Prescribers need to demonstrate that the patient has been on continuous therapy for≥ 3 months and demonstrate that the patient is osteopenic.	<-1.0
		4070	Corticosteroid-induced osteoporosis in a patient currently on long-term (≥ 3 months), high-dose (7.5 mg/day prednisolone or equivalent) corticosteroid therapy. Patient must not receive concomitant treatment with any other PBS-subscribed anti-resorptive agent for this condition. Duration and dose of corticosteroid therapy together with the date, site (femoral neck or lumbar spine) and score of the qualifying BMD measurement must be documented in the patient's medical records when treatment is initiated.	≤-1.5
		4087	Osteoporosis in a patient aged 70 years or older. Patient must not receive concomitant treatment with any other PBS-subscribed anti-resorptive agent for this condition. Date, site (femoral neck or lumbar spine) and score of the qualifying BMD measurement must be documented in the patient's medical records when treatment is initiated.	≤-2.5
		4087	Established osteoporosis in a patient with fracture due to minimal trauma. Patient must not receive concomitant treatment with any other PBS-subscribed anti-resorptive agent for this condition. Fracture must have been demonstrated radiologically and the year of plain x-ray, CT or MRI scan must be documented in the patient's medical records when treatment is initiated. A vertebral fracture is defined as a ≥20% reduction in height of the anterior or mid portion of a vertebral body relative to the posterior height of that body or a ≥ 20% reduction in any of these heights compared to the vertebral body above or below the affected vertebral body.	N/A
	70 mg + 140 microg	N/A	For preservation of bone mineral density in patients on long-term glucocorticoid therapy where patients are undergoing continuous treatment with a dose ≥7.5 mg of prednisone or equivalent per day. Prescribers need to demonstrate that the patient has been on continuous therapy for≥ 3 months and demonstrate that the patient is osteopenic.	<-1.0
		4122	Corticosteroid-induced osteoporosis in a patient currently on long-term (≥ 3 months), high-dose (7.5 mg/day prednisolone or equivalent) corticosteroid therapy. Patient must not receive concomitant treatment with any other PBS-subscribed anti-resorptive agent for	≤-1.5

			this condition. Duration and dose of corticosteroid therapy together with the date, site (femoral neck or lumbar spine) and score of the qualifying BMD measurement must be documented in the patient's medical records when treatment is initiated.	
		4133	Osteoporosis in a patient aged 70 years or older. Patient must not receive concomitant treatment with any other PBS-subscribed anti-resorptive agent for this condition. Date, site (femoral neck or lumbar spine) and score of the qualifying BMD measurement must be documented in the patient's medical records when treatment is initiated.	≤-2.5
		4123	Established osteoporosis in a patient with fracture due to minimal trauma. Patient must not receive concomitant treatment with any other PBS-subscribed anti-resorptive agent for this condition. Fracture must have been demonstrated radiologically and the year of plain x-ray, CT or MRI scan must be documented in the patient's medical records when treatment is initiated. A vertebral fracture is defined as a ≥20% reduction in height of the anterior or mid portion of a vertebral body relative to the posterior height of that body or a ≥ 20% reduction in any of these heights compared to the vertebral body above or below the affected vertebral body	N/A
Alendronate Sodium with Colecalciferol and Calcium Carbonate	70 mg + 140 microg + 500 mg	N/A	For preservation of bone mineral density in patients on long-term glucocorticoid therapy where patients are undergoing continuous treatment with a dose ≥7.5 mg of prednisone or equivalent per day. Prescribers need to demonstrate that the patient has been on continuous therapy for≥ 3 months and demonstrate that the patient is osteopenic.	<-1.0
		4122	Corticosteroid-induced osteoporosis in a patient currently on long-term (≥ 3 months), high-dose (7.5 mg/day prednisolone or equivalent) corticosteroid therapy. Patient must not receive concomitant treatment with any other PBS-subscribed anti-resorptive agent for this condition. Duration and dose of corticosteroid therapy together with the date, site (femoral neck or lumbar spine) and score of the qualifying BMD measurement must be documented in the patient's medical records when treatment is initiated.	≤-1.5
		4133	Osteoporosis in a patient aged 70 years or older. Patient must not receive concomitant treatment with any other PBS-subscribed anti-resorptive agent for this condition.	≤-2.5

			Date, site (femoral neck or lumbar spine) and score of the qualifying BMD measurement must be documented in the patient's medical records when treatment is initiated.	
		4123	Established osteoporosis in a patient with fracture due to minimal trauma. Patient must not receive concomitant treatment with any other PBS-subscribed anti-resorptive agent for this condition. Fracture must have been demonstrated radiologically and the year of plain x-ray, CT or MRI scan must be documented in the patient's medical records when treatment is initiated. A vertebral fracture is defined as a ≥20% reduction in height of the anterior or mid portion of a vertebral body relative to the posterior height of that body or a ≥ 20% reduction in any of these heights compared to the vertebral body above or below the affected vertebral body.	N/A
Risedronate Sodium	5 mg	N/R	For preservation of bone mineral density in patients on long-term glucocorticoid therapy where patients are undergoing continuous treatment with a dose ≥7.5 mg of prednisone or equivalent per day. Prescribers need to demonstrate that the patient has been on continuous therapy for≥ 3 months and demonstrate that the patient is osteopenic.	<-1.0
		4122	Corticosteroid-induced osteoporosis in a patient currently on long-term (≥ 3 months), high-dose (7.5 mg/day prednisolone or equivalent) corticosteroid therapy.	≤-1.5
		4117	Osteoporosis in a patient aged 70 years or older. Patient must not receive concomitant treatment with any other PBS-subscribed anti-resorptive agent for this condition. Date, site (femoral neck or lumbar spine) and score of the qualifying BMD measurement must be documented in the patient's medical records when treatment is initiated.	≤-3.0
		4123	Established osteoporosis in a patient with fracture due to minimal trauma. Patient must not receive concomitant treatment with any other PBS-subscribed anti-resorptive agent for this condition. Fracture must have been demonstrated radiologically and the year of plain x-ray, CT or MRI scan must be documented in the patient's medical records when treatment is initiated. A vertebral fracture is defined as a ≥20% reduction in height of the anterior or mid portion of a vertebral body relative to the posterior height of that body or a ≥ 20% reduction in any of these heights compared to the vertebral body above or below the affected vertebral body	N/A
	30 mg	3256	Symptomatic Paget disease of bone	N/A
	35 mg	N/R	For preservation of bone mineral density in patients on long-term glucocorticoid therapy where patients are undergoing continuous treatment with a dose equal to or greater than 7.5 mg of prednisone or	<-1.0

			equivalent per day. Prescribers need to demonstrate that the patient has been on continuous therapy for 3 months or more and demonstrate that the patient is osteopenic.	
		4122	Corticosteroid-induced osteoporosis in a patient currently on long-term (≥ 3 months), high-dose (7.5 mg/day prednisolone or equivalent) corticosteroid therapy.	≤-1.5
		4117	Osteoporosis in a patient aged 70 years or older. Patient must not receive concomitant treatment with any other PBS-subscribed anti-resorptive agent for this condition. Date, site (femoral neck or lumbar spine) and score of the qualifying BMD measurement must be documented in the patient's medical records when treatment is initiated.	≤-3.0
		4123	Established osteoporosis in a patient with fracture due to minimal trauma. Patient must not receive concomitant treatment with any other PBS-subscribed anti-resorptive agent for this condition. Fracture must have been demonstrated radiologically and the year of plain x-ray, CT or MRI scan must be documented in the patient's medical records when treatment is initiated. A vertebral fracture is defined as a ≥20% reduction in height of the anterior or mid portion of a vertebral body relative to the posterior height of that body or a ≥ 20% reduction in any of these heights compared to the vertebral body above or below the affected vertebral body	N/A
	Tablet 35 mg (enteric coated)	N/A	For preservation of bone mineral density in patients on long-term glucocorticoid therapy where patients are undergoing continuous treatment with a dose equal to or greater than 7.5 mg of prednisone or equivalent per day. Prescribers need to demonstrate that the patient has been on continuous therapy for 3 months or more and demonstrate that the patient is osteopenic.	<-1.0
		4122	Corticosteroid-induced osteoporosis in a patient currently on long-term (≥ 3 months), high-dose (7.5 mg/day prednisolone or equivalent) corticosteroid therapy.	≤-1.5
		4117	Osteoporosis in a patient aged 70 years or older. Patient must not receive concomitant treatment with any other PBS-subscribed anti-resorptive agent for this condition. Date, site (femoral neck or lumbar spine) and score of the qualifying BMD measurement must be documented in the patient's medical records when treatment is initiated.	≤-3.0
		4123	Established osteoporosis in a patient with fracture due to minimal trauma. Patient must not receive concomitant treatment with any other PBS-subscribed anti-resorptive agent for this condition.	N/A

			Fracture must have been demonstrated radiologically and the year of plain x-ray, CT or MRI scan must be documented in the patient's medical records when treatment is initiated. A vertebral fracture is defined as a ≥20% reduction in height of the anterior or mid portion of a vertebral body relative to the posterior height of that body or a ≥ 20% reduction in any of these heights compared to the vertebral body above or below the affected vertebral body	
	150 mg	4122	Corticosteroid-induced osteoporosis in a patient currently on long-term (≥ 3 months), high-dose (7.5 mg/day prednisolone or equivalent) corticosteroid therapy.	≤-1.5
		4117	Osteoporosis in a patient aged 70 years or older. Patient must not receive concomitant treatment with any other PBS-subscribed anti-resorptive agent for this condition. Date, site (femoral neck or lumbar spine) and score of the qualifying BMD measurement must be documented in the patient's medical records when treatment is initiated.	≤-3.0
		4123	Established osteoporosis in a patient with fracture due to minimal trauma. Patient must not receive concomitant treatment with any other PBS-subscribed anti-resorptive agent for this condition. Fracture must have been demonstrated radiologically and the year of plain x-ray, CT or MRI scan must be documented in the patient's medical records when treatment is initiated. A vertebral fracture is defined as a ≥20% reduction in height of the anterior or mid portion of a vertebral body relative to the posterior height of that body or a ≥ 20% reduction in any of these heights compared to the vertebral body above or below the affected vertebral body	N/A
Risedronate Sodium and Calcium Carbonate	35 mg + 500 mg	N/R	For preservation of bone mineral density in patients on long-term glucocorticoid therapy where patients are undergoing continuous treatment with a dose equal to or greater than 7.5 mg of prednisone or equivalent per day. Prescribers need to demonstrate that the patient has been on continuous therapy for 3 months or more and demonstrate that the patient is osteopenic.	<-1.0
		4122	Corticosteroid-induced osteoporosis in a patient currently on long-term (≥ 3 months), high-dose (7.5 mg/day prednisolone or equivalent) corticosteroid therapy.	≤-1.5
		4117	Osteoporosis in a patient aged 70 years or older. Patient must not receive concomitant treatment with any other PBS-subscribed anti-resorptive agent for this condition. Date, site (femoral neck or lumbar spine) and score of the qualifying BMD measurement must be documented in the patient's medical records when treatment is initiated.	≤-3.0
		4123	Established osteoporosis in a patient with fracture due to minimal trauma.	N/A

			Patient must not receive concomitant treatment with any other PBS-subscribed anti-resorptive agent for this condition. Fracture must have been demonstrated radiologically and the year of plain x-ray, CT or MRI scan must be documented in the patient's medical records when treatment is initiated. A vertebral fracture is defined as a ≥20% reduction in height of the anterior or mid portion of a vertebral body relative to the posterior height of that body or a ≥ 20% reduction in any of these heights compared to the vertebral body above or below the affected vertebral body	
	35 mg + 1.25g (enteric coated)	N/A	For preservation of bone mineral density in patients on long-term glucocorticoid therapy where patients are undergoing continuous treatment with a dose equal to or greater than 7.5 mg of prednisone or equivalent per day. Prescribers need to demonstrate that the patient has been on continuous therapy for 3 months or more and demonstrate that the patient is osteopenic.	<-1.0
		4122	Corticosteroid-induced osteoporosis in a patient currently on long-term (≥ 3 months), high-dose (7.5 mg/day prednisolone or equivalent) corticosteroid therapy.	≤-1.5
		4117	Osteoporosis in a patient aged 70 years or older. Patient must not receive concomitant treatment with any other PBS-subscribed anti-resorptive agent for this condition. Date, site (femoral neck or lumbar spine) and score of the qualifying BMD measurement must be documented in the patient's medical records when treatment is initiated.	≤-3.0
		4123	Established osteoporosis in a patient with fracture due to minimal trauma. Patient must not receive concomitant treatment with any other PBS-subscribed anti-resorptive agent for this condition. Fracture must have been demonstrated radiologically and the year of plain x-ray, CT or MRI scan must be documented in the patient's medical records when treatment is initiated. A vertebral fracture is defined as a ≥20% reduction in height of the anterior or mid portion of a vertebral body relative to the posterior height of that body or a ≥ 20% reduction in any of these heights compared to the vertebral body above or below the affected vertebral body	N/A
Risedronate Sodium and Calcium Carbonate with Colecalciferol	35 mg + 2.5 g + 22 microg	N/R	For preservation of bone mineral density in patients on long-term glucocorticoid therapy where patients are undergoing continuous treatment with a dose equal to or greater than 7.5 mg of prednisone or equivalent per day. Prescribers need to demonstrate that the patient has been on continuous therapy for 3 months or more and demonstrate that the patient is osteopenic.	<-1.0
		4122	Corticosteroid-induced osteoporosis in a patient currently on long-term (≥ 3 months), high-dose (7.5	≤-1.5

			mg/day prednisolone or equivalent) corticosteroid therapy.	
		4117	Osteoporosis in a patient aged 70 years or older. Patient must not receive concomitant treatment with any other PBS-subscribed anti-resorptive agent for this condition. Date, site (femoral neck or lumbar spine) and score of the qualifying BMD measurement must be documented in the patient's medical records when treatment is initiated.	≤-3.0
		4123	Established osteoporosis in a patient with fracture due to minimal trauma. Patient must not receive concomitant treatment with any other PBS-subscribed anti-resorptive agent for this condition. Fracture must have been demonstrated radiologically and the year of plain x-ray, CT or MRI scan must be documented in the patient's medical records when treatment is initiated. A vertebral fracture is defined as a ≥20% reduction in height of the anterior or mid portion of a vertebral body relative to the posterior height of that body or a ≥ 20% reduction in any of these heights compared to the vertebral body above or below the affected vertebral body	N/A
Disodium Etidronate	200 mg	3257	Paget disease of bone when calcitonin has been found to be unsatisfactory due to lack of efficacy	N/A
		3258	Paget disease of bone when calcitonin has been found to be unsatisfactory due to unacceptable side effects	
		1153	Heterotopic ossification	
Disodium Etidronate and Calcium Carbonate	200 mg + 1.25g	2646	Established osteoporosis in patients with fracture due to minimal trauma	N/A
Dosodium Pamidronate	15 mg/5 mL injection, 1 x 5	3341	Hypercalcaemia of malignancy refractory to anti-neoplastic therapy	N/A
	30 mg/10 mL injection, 1 x 10 mL vial	3341	Hypercalcaemia of malignancy refractory to anti-neoplastic therapy	N/A
	60 mg/10 mL injection, 1 x 10 mL vial	3341	Hypercalcaemia of malignancy refractory to anti-neoplastic therapy	N/A
	90 mg	3341	Hypercalcaemia of malignancy refractory to anti-neoplastic therapy	N/A

		3342	Multiple myeloma	
		3343	Bone metastases from breast cancer	
	4 vials powder 15 mg + 4 ampoules solvent 5 ml	3341	Treatment of hypercalcaemia of malignancy refractory to anti-neoplastic therapy	N/A
	2 vials powder 30 mg + 2 ampoules solvent 10 ml	3256	Paget disease of bone	N/A
	Concentrated injection 15 mg in 5 mL	N/R 3256	Treatment of hypercalcaemia of malignancy refractory to anti-neoplastic therapy Symptomatic Paget disease of bone	N/A
	Concentrated injection 30 mg in 10 mL	N/R 3256	Treatment of hypercalcaemia of malignancy refractory to anti-neoplastic therapy Symptomatic Paget disease of bone	N/A
	Concentrated injection 60 mg in 10 mL	N/R 3256	Treatment of hypercalcaemia of malignancy refractory to anti-neoplastic therapy Symptomatic Paget disease of bone	N/A
	Concentrated injection 90 mg in 10 mL	N/R	Treatment of hypercalcaemia of malignancy refractory to anti-neoplastic therapy	N/A
	90 mg injection [1 x 90 mg vial] (&) inert substance diluent [1 x 10 mL ampoule], 1 pack	N/R	Hypercalcaemia of malignancy refractory to anti-neoplastic therapy Multiple myeloma Bone metastases from breast cancer	N/A
	30 mg injection [2 x 30 mg vials] (&) inert	N/R 3256	Treatment of hypercalcaemia of malignancy refractory to anti-neoplastic therapy Symptomatic Paget disease of bone	N/A

	substance diluent [2 x 10 mL ampoules], 1 pack			
	15 mg injection [4 x 15 mg vials] (&) inert substance diluent [4 x 5 mL ampoules]	N/R 3256	Treatment of hypercalcaemia of malignancy refractory to anti-neoplastic therapy Symptomatic Paget disease of bone	N/A
Clodronate sodium	400 mg	N/R	Maintenance treatment of hypercalcaemia of malignancy refractory to anti-neoplastic therapy; Multiple myeloma Bone metastases from breast cancer	N/A
	800 mg	N/R	Maintenance treatment of hypercalcaemia of malignancy refractory to anti-neoplastic therapy; Multiple myeloma Bone metastases from breast cancer	N/A
-Tiludronate Disodium	200 mg	3256	Symptomatic Paget disease of bone	N/A
-Ibandronic Acid	6 mg/6 mL injection, 1 x 6 mL vial	3343	Bone metastases from breast cancer	N/A
	50 mg	N/R	Bone metastases from breast cancer	N/A
Zoledronic Acid	4 mg/5 mL injection, 1 x 5 mL vial	N/R 3342 3343 4052 3341	Multiple myeloma Bone metastases from breast cancer Bone metastases from castration-resistant prostate cancer Treatment of hypercalcaemia of malignancy refractory to anti-neoplastic therapy	N/A
	5 mg/100 mL injection, 1 x 100 mL vial	4100	Corticosteroid-induced osteoporosis in a patient currently on (prednisolone or equivalent) corticosteroid therapy. The Clinical criteria is: Patient must currently be on long-term (at least 3 months), high-dose (at least 7.5 mg per day prednisolone or equivalent) corticosteroid therapy, AND the Clinical criteria is:	≤-1.5

			Patient must have a Bone Mineral Density (BMD) T-score of -1.5 or less, AND the Clinical criteria is: Patient must not receive concomitant treatment with any other PBS-subsidised anti-resorptive agent for this condition, AND the Clinical criteria is: Patient must not receive more than one PBS-subsidised treatment per year. The duration and dose of corticosteroid therapy together with the date, site (femoral neck or lumbar spine) and score of the qualifying BMD measurement must be documented in the patient's medical records when treatment is initiated.	
		4149	Osteoporosis The Population criteria is: Patient must be aged 70 years or older, AND the Clinical criteria is: Patient must have a Bone Mineral Density (BMD) T-score of -3.0 or less, AND the Clinical criteria is: Patient must not receive concomitant treatment with any other PBS-subsidised anti-resorptive agent for this condition, AND the Clinical criteria is: Patient must not receive more than one PBS-subsidised treatment per year. The date, site (femoral neck or lumbar spine) and score of the qualifying BMD measurement must be documented in the patient's medical records when treatment is initiated.	≤-3.0
		4157	Established osteoporosis The Clinical criteria is: Patient must have fracture due to minimal trauma, AND the Clinical criteria is: Patient must not receive concomitant treatment with any other PBS-subsidised anti-resorptive agent for this condition, AND the Clinical criteria is: Patient must not receive more than one PBS-subsidised treatment per year. The fracture must have been demonstrated radiologically and the year of plain x-ray or computed tomography (CT) scan or magnetic resonance imaging (MRI) scan must be documented in the patient's medical records when treatment is initiated. A vertebral fracture is defined as a 20% or greater reduction in height of the anterior or mid portion of a vertebral body relative to the posterior height of that body, or, a 20% or greater reduction in any of	N/R

			these heights compared to the vertebral body above or below the affected vertebral body.	
		N/R	Symptomatic Paget disease of bone. Only 1 treatment each year per patient will be PBS-subsidised	
		3947	Osteoporosis in a patient aged 70 years of age or older	≤-3.0
		3946	Established osteoporosis in a patient with fracture due to minimal trauma	N/A
		N/R	Symptomatic Paget disease of bone Only 1 treatment each year per patient will be PBS-subsidised	N/A
	4 mg/5 mL injection, 1 x 5 mL vial10 mg	3342	Multiple myeloma	N/A
		3343	Bone metastases from breast cancer	N/A
		4052	Bone metastases from castration-resistant prostate cancer	N/A
		3341	hypercalcaemia of malignancy refractory to anti-neoplastic therapy	N/A
Selective estrogen receptor modulator (SERM)				
raloxifene hydrochloride	60 mg	4071	Established post-menopausal osteoporosis The Clinical criteria is: Patient must have fracture due to minimal trauma, AND the Clinical criteria is: Patient must not receive concomitant treatment with any other PBS-subsidised anti-resorptive agent for this condition. The fracture must have been demonstrated radiologically and the year of plain x-ray or computed tomography (CT) scan or magnetic resonance imaging (MRI) scan must be documented in the patient's medical records when treatment is initiated. A vertebral fracture is defined as a 20% or greater reduction in height of the anterior or mid portion of a vertebral body relative to the posterior height of that body, or, a 20% or greater reduction in any of these heights compared to the vertebral body above or below the affected vertebral body.	N/A
Monoclonal antibody				
Denosumab	120 mg/1.7ml	4158 4150	Bone metastases from breast cancer Bone metastases from castration-resistant prostate cancer	N/A
	60 mg/ml	4094	Osteoporosis The Population criteria is: Patient must be female, AND the Population criteria is:	≤-2.5 N/A

			Patient must be aged 70 years or older, AND the Clinical criteria is: Patient must have a Bone Mineral Density (BMD) T-score of -2.5 or less, AND the Clinical criteria is: Patient must not receive concomitant treatment with any other PBS-subsidised anti-resorptive agent for this condition. The date, site (femoral neck or lumbar spine) and score of the qualifying BMD measurement must be documented in the patient's medical records when treatment is initiated.	
		4145	Established post-menopausal osteoporosis The Clinical criteria is: Patient must have fracture due to minimal trauma, AND the Clinical criteria is: Patient must not receive concomitant treatment with any other PBS-subsidised anti-resorptive agent for this condition. The fracture must have been demonstrated radiologically and the year of plain x-ray or computed tomography (CT) scan or magnetic resonance imaging (MRI) scan must be documented in the patient's medical records when treatment is initiated. A vertebral fracture is defined as a 20% or greater reduction in height of the anterior or mid portion of a vertebral body relative to the posterior height of that body, or, a 20% or greater reduction in any of these heights compared to the vertebral body above or below the affected vertebral body.	
Carbamazepine	200 mg		Continuing therapy only. For prescribing by nurse practitioners as continuing therapy only, where the treatment of, and prescribing of medicine for, a patient has been initiated by a medical practitioner. Further information can be found in the Explanatory Notes for Nurse Practitioners. Note For item codes 2419H and 1706T, pharmaceutical benefits that have the form tablet 200 mg are equivalent for the purposes of substitution.	N/A
		N/R	For item codes 5040G and 1724R, pharmaceutical benefits that have the form tablet 200 mg are equivalent for the purposes of substitution.	N/A
Parathyroid Hormone				

Teriparatide	20 microgram/dose injection, 1 x 2.4 mL cartridge		Initial treatment, as the sole PBS-subsidised agent, by a specialist or consultant physician, for severe, established osteoporosis in a patient with a very high risk of fracture who: (a) has a bone mineral density (BMD) T-score of -3.0 or less; and (b) has had 2 or more fractures due to minimal trauma; and (c) has experienced at least 1 symptomatic new fracture after at least 12 months continuous therapy with an anti-resorptive agent at adequate doses. A vertebral fracture is defined as a 20% or greater reduction in height of the anterior or mid portion of a vertebral body relative to the posterior height of that body, or, a 20% or greater reduction in any of these heights compared to the vertebral body above or below the affected vertebral body. If treatment with anti-resorptive therapy is contraindicated according to the relevant TGA-approved Product Information, details of the contraindication must be provided at the time of application. If an intolerance of a severity necessitating permanent treatment withdrawal develops during the relevant period of use of one anti-resorptive agent, alternate anti-resorptive agents must be trialled so that the patient achieves the minimum requirement of 12 months continuous therapy. Details of accepted toxicities including severity can be found on the Medicare Australia website at www.medicareaustralia.gov.au and must be provided at the time of application. Anti-resorptive therapies for osteoporosis and their adequate doses which will be accepted for the purposes of administering this restriction are alendronate sodium 10 mg per day or 70 mg once weekly, risedronate sodium 5 mg per day or 35 mg once weekly or 150 mg once monthly, raloxifene hydrochloride 60 mg per day (women only), denosumab 60 mg once every 6 months, disodium etidronate 200 mg with calcium carbonate 1.25 g per day, strontium ranelate 2 g per day and zoledronic acid 5 mg per annum. Details of prior anti-resorptive therapy, fracture history including the date(s), site(s), the symptoms associated with the fracture(s) which developed during the course of anti-resorptive therapy and the score of the qualifying BMD measurement must be provided to Medicare Australia at the time of application. Note No applications for increased maximum quantities and/or repeats will be authorised.	≤-3.0

			Continuing treatment for severe established osteoporosis where the patient has previously been issued with an authority prescription for this drug. Teriparatide must only be used for a lifetime maximum of 18 months therapy (18 pens). Up to a maximum of 18 pens will be reimbursed through the PBS. Note No applications for increased maximum quantities and/or repeats will be authorised. Continuing treatment for severe established osteoporosis where the patient has previously been issued with an authority prescription for this drug. Teriparatide must only be used for a lifetime maximum of 18 months therapy (18 pens). Up to a maximum of 18 pens will be reimbursed through the PBS. Note No applications for increased maximum quantities and/or repeats will be authorised.	
strontium ranelate	2 g	4117	Osteoporosis The Population criteria is: Patient must be aged 70 years or older, AND the Clinical criteria is: Patient must have a Bone Mineral Density (BMD) T-score of -3.0 or less, AND the Clinical criteria is: Patient must not receive concomitant treatment with any other PBS-subsidised anti-resorptive agent for this condition. The date, site (femoral neck or lumbar spine) and score of the qualifying BMD measurement must be documented in the patient's medical records when treatment is initiated.	≤-3.0
		4123	Established osteoporosis The Clinical criteria is: Patient must have fracture due to minimal trauma, AND the Clinical criteria is: Patient must not receive concomitant treatment with any other PBS-subsidised anti-resorptive agent for this condition. The fracture must have been demonstrated radiologically and the year of plain x-ray or computed tomography (CT) scan or magnetic resonance imaging (MRI) scan must be documented in the patient's medical records when treatment is initiated.	N/A

			A vertebral fracture is defined as a 20% or greater reduction in height of the anterior or mid portion of a vertebral body relative to the posterior height of that body, or, a 20% or greater reduction in any of these heights compared to the vertebral body above or below the affected vertebral body..	
Calcitriol	0.25 microg	1165	Hypocalcaemia due to renal disease.	N/A
		1166	Hypoparathyroidism.	N/A
		1167	Hypophosphataemic rickets.	N/A
		1467	Vitamin D-resistant rickets.	N/A
		2636	Established osteoporosis in patients with fracture due to minimal trauma.	N/A

1153 Heterotopic ossification.

1165 Hypocalcaemia due to renal disease.

1166Hypoparathyroidism.

1167 Hypophosphataemic rickets.

1467 Vitamin D-resistant rickets.

2636Treatment for established osteoporosis in patients with fracture due to minimal trauma. The fracture must have been demonstrated radiologically and the year of plain x-ray or CT-scan or MRI scan must be documented in the patient's medical records when treatment is initiated.
A vertebral fracture is defined as a 20% or greater reduction in height of the anterior or mid portion of a vertebral body relative to the posterior height of that body, or, a 20% or greater reduction in any of these heights compared to the vertebral body above or below the affected vertebral body.

2645 Treatment as the sole PBS-subsidised anti-resorptive agent for osteoporosis in a patient aged 70 years of age or older with a Bone Mineral Density (BMD) T-score of -3.0 or less. The date, site (femoral neck or lumbar spine) and score of the qualifying BMD measurement must be documented in the patient's medical records when treatment is initiated.

2646 Treatment as the sole PBS-subsidised anti-resorptive agent for established osteoporosis in patients with fracture due to minimal trauma. The fracture must have been demonstrated radiologically and the year of plain x-ray or CT-scan or MRI scan must be documented in the patient's medical records when treatment is initiated.
A vertebral fracture is defined as a 20% or greater reduction in height of the anterior or mid portion of a vertebral body relative to the posterior height of that body, or, a 20% or greater reduction in any of these heights compared to the vertebral body above or below the affected vertebral body.
Note
Anti-resorptive agents in established osteoporosis include alendronate sodium, risedronate sodium, denosumab, disodium etidronate, raloxifene hydrochloride, strontium ranelate and zoledronic acid.

2647 Treatment as the sole PBS-subsidised anti-resorptive agent for established post-menopausal osteoporosis in patients with fracture due to minimal trauma. The fracture must have been demonstrated radiologically and the year of plain x-ray or CT-scan or MRI scan must be documented in the patient's medical records when treatment is initiated.

A vertebral fracture is defined as a 20% or greater reduction in height of the anterior or mid portion of a vertebral body relative to the posterior height of that body, or, a 20% or greater reduction in any of these heights compared to the vertebral body above or below the affected vertebral body.

Note
Anti-resorptive agents in established osteoporosis include alendronate sodium, risedronate sodium, denosumab, disodium etidronate, raloxifene hydrochloride, strontium ranelate and zoledronic acid.

2758 Treatment as the sole PBS-subsidised anti-resorptive agent for osteoporosis in a woman aged 70 years or older with a bone mineral density (BMD) T-score of -3.0 or less.

The date, site (femoral neck or lumbar spine) and score of the qualifying BMD measurement must be documented in the patient's medical records when treatment is initiated.

3070 Treatment as the sole PBS-subsidised anti-resorptive agent for corticosteroid-induced osteoporosis in a patient currently on long-term (at least 3 months), high-dose (at least 7.5 mg per day prednisolone or equivalent) corticosteroid therapy with a Bone Mineral Density (BMD) T-score of -1.5 or less. The duration and dose of corticosteroid therapy together with the date, site (femoral neck or lumbar spine) and score of the qualifying BMD measurement must be documented in the patient's medical records when treatment is initiated.

3256 Symptomatic Paget disease of bone.

3257 Symptomatic Paget disease of bone when calcitonin has been found to be unsatisfactory due to lack of efficacy

3258 Symptomatic Paget disease of bone when calcitonin has been found to be unsatisfactory due to unacceptable side effects

3341Treatment of hypercalcaemia of malignancy refractory to anti-neoplastic therapy

3342 Multiple myeloma

3343 Bone metastases from breast cancer

3256 Symptomatic Paget disease of bone.

3257 Symptomatic Paget disease of bone when calcitonin has been found to be unsatisfactory due to lack of efficacy.

3258 Symptomatic Paget disease of bone when calcitonin has been found to be unsatisfactory due to unacceptable side effects.

3933 Treatment as the sole PBS-subsidised anti-resorptive agent for osteoporosis in a patient aged 70 years of age or older with a Bone Mineral Density (BMD) T-score of -2.5 or less. The date, site (femoral neck or lumbar spine) and score of the qualifying BMD measurement must be documented in the patient's medical records when treatment is initiated.

3945 Treatment as the sole PBS-subsidised anti-resorptive agent for corticosteroid-induced osteoporosis in a patient currently on long-term (at least 3 months), high-dose (at least 7.5 mg per day prednisolone or equivalent) corticosteroid therapy with a Bone Mineral Density (BMD) T-score of -1.5 or less.

3946 Treatment as the sole PBS-subsidised anti-resorptive agent for established osteoporosis in a patient with fracture due to minimal trauma.
A vertebral fracture is defined as a 20% or greater reduction in height of the anterior or mid portion of a vertebral body relative to the posterior height of that body, or, a 20% or greater reduction in any of these heights compared to the vertebral body above or below the affected vertebral body.
In all cases, the fracture must have been demonstrated radiologically and the year of plain x-ray or CT-scan or MRI scan must be documented in the patient's medical records when treatment is initiated.
Only 1 treatment each year per patient will be PBS-subsidised.

3947 Treatment as the sole PBS-subsidised anti-resorptive agent for osteoporosis in a patient aged 70 years of age or older with a Bone Mineral Density (BMD) T-score of -3.0 or less.
The date, site (femoral neck or lumbar spine) and score of the qualifying BMD measurement must be documented in the patient's medical records when treatment is initiated.
Only 1 treatment each year per patient will be PBS-subsidised.

3987
Treatment as the sole PBS-subsidised anti-resorptive agent for established post-menopausal osteoporosis in a woman with fracture due to minimal trauma. The fracture must have been demonstrated radiologically and the year of plain x-ray or CT-scan or MRI scan must be documented in the patient's medical records when treatment is initiated.
A vertebral fracture is defined as a 20% or greater reduction in height of the anterior or mid portion of a vertebral body relative to the posterior height of that body, or, a 20% or greater reduction in any of these heights compared to the vertebral body above or below the affected vertebral body.
Note
Anti-resorptive agents in established osteoporosis include alendronate sodium, risedronate sodium, denosumab, disodium etidronate, raloxifene hydrochloride, strontium ranelate and zoledronic acid.

4052Bone metastases from castration-resistant prostate cancer.

4054 Treatment as the sole PBS-subsidised anti-resorptive agent for osteoporosis in a woman aged 70 years of age or older with a Bone Mineral Density (BMD) T-score of -2.5 or less. The date, site (femoral neck or lumbar spine) and score of the qualifying BMD measurement must be documented in the patient's medical records when treatment is initiated.

Source: Pharmaceutical Benefits Scheme (PBS) as on 01/09/2012 <http://www.pbs.gov.au/browse/body-system?depth=3&codes=m05b>. Authority required to access details of indication for each drug.

Appendix 4 PBS listed pharmaceuticals (by indication) for treatment of diseases of bone structure and mineralisation

Indication	ARTG	PBS (indicated T-score)
Prevention and/or treatment of osteoporosis	Alendronate sodium:120028, 76851; Risedronate sodium: 141530, 150618, 166838, 166853, 166942, 74135, 82746	No drug specifically indicated
Treatment for established osteoporosis (T-score ≤-2.0) (MBS item 12321)	Alendronate sodium: 76851, 9333, 161137, 73520, 67262, 73772; Disodium etidronate: 46852	No drug specifically indicated
Risk factors for osteoporosis		
Postmenopausal women, with fracture	Alendronate sodium: 157805, 68428, 120028, 53158, 67262, 76851, 98944; Disodium etidronate: 46852; Zoledronic acid: 134664	Raloxifene hydrochloride , Raloxifene hydrochloride (with fractures), Denosumab (with fractures), Strontium ranelate (with fractures)
Previous fractures (including minimal trauma fractures)(MBS item 12306, 12321)	Alendronate sodium: 161137, 67262, 73772, 76851, 93333, 98944; Zoledronic acid: 134664	Alendronate sodium , Alendronate sodium with Colecalciferol , Alendronate sodium with Colecalciferol and Calcium carbonate , Risedronate sodium , Risedronate sodium and Calcium carbonate , Risedronate sodium and Calcium carbonate with Colecalciferol , Disodium etidronate and Calcium carbonate , Zolendronic acid , Denosumab (for postmenopausal women), Teriparatide (≤-3.0), Strontium ranelate (for postmenopausal women), Raloxifene hydrochloride (for postmenopausal women), Calcitriol .
70 years or over (MBS item 12323)	No drug specifically indicated	Alendronate sodium (≤-2.5), Alendronate sodium with Colecalciferol (≤-2.5), Alendronate sodium with Colecalciferol and Calcium carbonate (≤-2.5), Risedronate sodium (≤-3.0), Risedronate sodium and Calcium carbonate (≤-3.0), Risedronate sodium and Calcium carbonate with Colecalciferol (≤-3.0), Zolendronic acid (≤-3.0), Denosumab (≤-2.5), Strontium ranelate (≤-3.0 for women)
Corticosteroids use (MBS item 12312)	Alendronate sodium: 68428, 80333, 53158, 67262, 76851, 9333, 98944; Disodium etidronate: 46852; Risedronate	Alendronate sodium (≤-1.5), Alendronate sodium with Colecalciferol (≤-1.5), Alendronate sodium with

	sodium: 117667, 138211, 141530, 150618, 166838, 166853, 166942, 74135, 82746; Zoledronic acid: 134664;	Colecalciferol and Calcium carbonate (≤-1.5), Risedronate sodium (≤-1.0 if patients on steroids for > 3 months), Risedronate sodium (≤-1.5), Risedronate sodium and Calcium carbonate (NR), Risedronate sodium and Calcium carbonate with Colecalciferol (≤-1.5), Zolendronic acid (≤-1.5)
Male Hypogonadism (MBS item 12312)	No drug specifically indicated	No drug specifically indicated
Famale Hypogonadismlasting >6 months before age of 45 (MBS item 12312)	No drug specifically indicated	No drug specifically indicated
Primary Hyperparathyroidism (MBS item 12315)	No drug specifically indicated	No drug specifically indicated
Chronic renal disease (MBS item 12315)	No drug specifically indicated	No drug specifically indicated
Chronic liver disease (MBS item 12315)	No drug specifically indicated	No drug specifically indicated
Rheumatoid arthritis (MBS item 12315)	No drug specifically indicated	No drug specifically indicated
Conditions associated with thyroxine excess (MBS item 12315)	No drug specifically indicated	No drug specifically indicated
Proven malabsorptive disorders (MBS item 12315)	No drug specifically indicated	No drug specifically indicated
Breast cancer patients receiving aromatase inhibitor treatment	No drug specifically indicated	No drug specifically indicated
HIV	No drug specifically indicated	No drug specifically indicated
Paget's disease *	Risedronate sodium: 74136	Alendronate sodium, Risedronate sodium, Disodium etidronate, Disodium pamidronate, Zolendronic acid, Tiludronate disodium
Heterotopic ossification*	No drug specifically indicated	Disodium etidronate
hypercalcaemia of malignancy*	Sodium clodronate tetrahydrate: 181921, 181922, 66703, 66704,	Disodium pamidronate, Sodium clodronate tetrahydrate, Zolendronic acid
Multiple myeloma*	No drug specifically indicated	Disodium pamidronate, Sodium clodronate tetrahydrate, Zolendronic acid
Bone metastases from breast cancer*	No drug specifically indicated	Ibandronic acid, Disodium pamidronate, Sodium clodronate tetrahydrate, Zolendronic acid
Bone metastases from prostate cancer*	No drug specifically indicated	Zolendronic acid
*not considered as a risk factor for osteoporosis; NR: Not reported.		

Source: Pharmaceutical Benefits Scheme (PBS) as on 01/09/2012 <http://www.pbs.gov.au/browse/body-system?depth=3&codes=m05b>. Authority required to access details of indication for each drug (including indicated T-score)

Appendix 5 Medicare Benefits Schedule - Note D1.27

Category 2 - DIAGNOSTIC PROCEDURES AND INVESTIGATIONS D1.27 Bone Densitometry - (Items 12306 to 12323)

Item 12321 is intended to allow for bone mineral density measurement following a significant change in therapy - e.g. a change in the class of drugs - rather than for a change in the dosage regimen.

Item 12323 enables the payment of a Medicare benefit for a bone densitometry service performed on a patient aged 70 years or over. The Government has decided to expand access to Medicare subsidised bone mineral density testing to coincide with the expanded eligibility for the osteoporosis medication 'alendronate' under the Pharmaceutical Benefits Scheme.

An examination under any of these items covers the measurement of 2 or more sites, interpretation and provision of a report. Two or more sites must include the measurement of bone density of the lumbar spine and proximal femur. If technical difficulties preclude measurement at these sites, other sites can be used for the purpose of measurements. The measurement of bone mineral density at either forearms or both heels or in combination is excluded for the purpose of Medicare benefit.

Referrals

Bone densitometry services are available on the basis of referral by a medical practitioner to a specialist or consultant physician. However, providers of bone densitometry to whom a patient is referred for management may determine that a bone densitometry service is required in line with the provisions of Items 12306, 12309, 12312, 12315, 12318, 12321 and 12323.

For Items 12306 and 12309 the referral should specify the indication for the test, namely:

(a) 1 or more fractures occurring after minimal trauma; or

(b) monitoring of low bone mineral density proven by previous bone densitometry.

For Item 12312 the referral should specify the indication for the test, namely:

(a) prolonged glucocorticoid therapy;

(b) conditions associated with excess glucocorticoid secretion;

(c) male hypogonadism; or

(d) female hypogonadism lasting more than 6 months before the age of 45.

For Item 12315 the referral should specify the indication for the test, namely:

(a) primary hyperparathyroidism;

(b) chronic liver disease;

(c) chronic renal disease;

(d) proven malabsorptive disorders;

(e) rheumatoid arthritis; or

(f) conditions associated with thyroxine excess.

For Item 12318 the referral should specify the indication for the test, namely:

(a) prolonged glucocorticoid therapy;

(b) conditions associated with excess glucocorticoid secretion;

(c) male hypogonadism;

(d) female hypogonadism lasting more than 6 months before the age of 45;

(e) primary hyperparathyroidism;

(f) chronic liver disease;

(g) chronic renal disease;

(h) proven malabsorptive disorders;

(i) rheumatoid arthritis; or

(j) conditions associated with thyroxine excess.

Definitions

Low bone mineral density is present when the bone (organ) mineral density falls more than 1.5 standard deviations below the age matched mean or more than 2.5 standard deviations below the young normal mean at the same site and in the same gender.

For Items 12312 and 12318

(a) 'Prolonged glucocorticoid therapy' is defined as the commencement of a dosage of inhaled glucocorticoid equivalent to or greater than 800 micrograms beclomethasone dipropionate or budesonide per day; or

(b) a supraphysiological glucocorticoid dosage equivalent to or greater than 7.5 mg prednisolone in an adult taken orally per day;

for a period anticipated to last for at least 4 months.

Glucocorticoid therapy must be contemporaneous with the current scan. Patients no longer on steroids would not qualify for benefits.

For Items 12312 and 12318

(a) Male hypogonadism is defined as serum testosterone levels below the age matched normal range.

(b) Female hypogonadism is defined as serum oestrogen levels below the age matched normal range.

For Items 12315 and 12318

A malabsorptive disorder is defined as one or more of the following:

(a) malabsorption of fat, defined as faecal fat estimated at greater than 18 gm per 72 hours on a normal fat diet; or

(b) bowel disease with presumptive vitamin D malabsorption as indicated by a sub-normal circulating 25-hydroxyvitamin D level; or

(c) histologically proven Coeliac disease.

Related Items: 12306, 12309, 12312, 12315, 12318, 12321, 12323