
1248

Final decision analytic protocol (DAP) to guide the assessment of bone mineral density analyses using dual energy X-ray absorptiometry (DXA) or quantitative computerised tomography (QCT) for men and women aged 60 - 69 years to assess patient eligibility for alendronate

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Final

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

An application requesting MBS listing of bone mineral density analysis using dual energy X-ray absorptiometry (DXA) or quantitative computerised tomography (QCT) for men and women aged 60 - 69 was received from Merck Sharp & Dohme (Australia) Pty Ltd and Osteoporosis Australia by the Department of Health and Ageing in July 2012.

DXA or QCT for men and women aged 60 - 69 is currently not reimbursed through the MBS, although MBS item 12323 allows individuals 70 years and over access to DXA or QCT. This proposal relates to expanding public access to bone mineral density analyses by adding a new MBS item for men and women 60-69. Individuals with a T-score <-2.5 are proposed to become eligible for anti-osteoporotic treatment, specifically the bisphosphonate anti-resorptive agent alendronate.

This decision analytic protocol (DAP) was drafted to guide the assessment of safety, effectiveness and cost-effectiveness of bone mineral density analysis using DXA or QCT for men and women aged 60 - 69 in order to inform MSAC's decision-making regarding public funding of the intervention.

The original proposal was for a target population of men and women aged 60-69, with risk factors. PASC have expanded this population to all men and women aged 60-69.

Intervention

Description

The World Health Organisation (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 Reifstein 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, and diagnosis generally occurs following an incidence of a 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 (Center et al 2007). Predictors of minimal trauma fractures include age, muscle weakness, low bone mineral density, history of smoking, 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 per cent 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).

Table 1 Risk factors for the development of osteoporosis

Type of risk factor	Examples
Fixed (non-modifiable) risk factors	Age (increase with the age after 40-50) Sex (osteoporosis affects women at an earlier age) Menopause Family history of OP (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) Excessively high body mass index Anorexia/exercise induced amenorrhoea
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 (eg 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 treatment for prostate cancer

OP: osteoporosis; Source: AIHW 2008; AIHW 2010a; 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.

Maintenance of BMD relies upon equilibrium between bone formation and resorption. Bone formation refers to the deposition of bone matrix and the fixing of calcium in its mineral form. Bone resorption is the process of bone breakdown by osteoclasts and the release of minerals from bone. Coupled together, these two processes are referred to as bone remodelling. 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 number and activity of osteoclasts (Santen et al 2011).

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. This may reflect the increasing fracture rate with age, both in men and women (Figure 1, Figure 2).

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

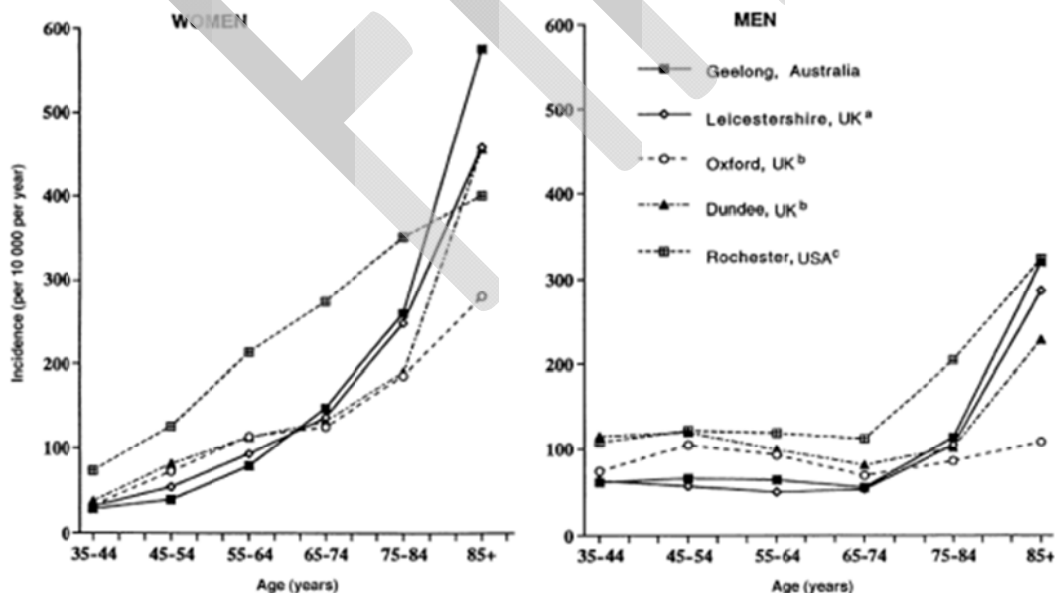
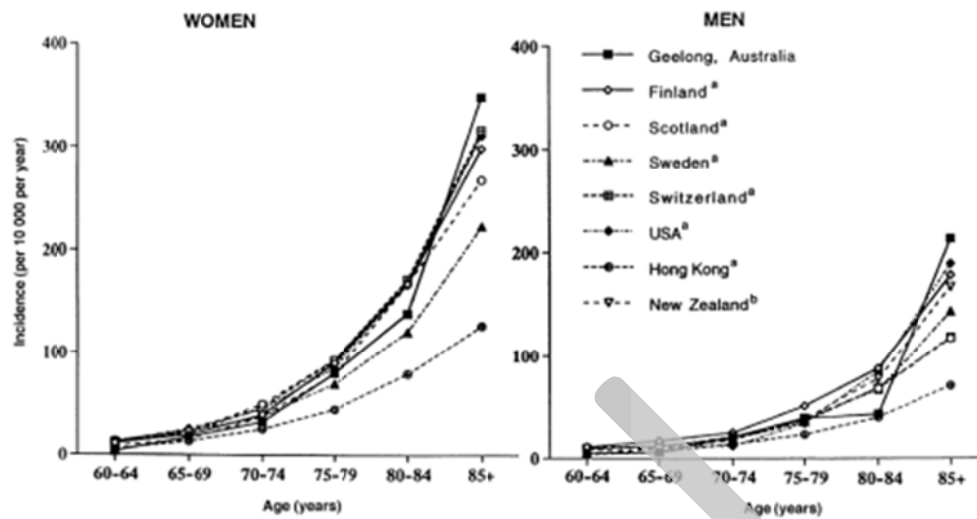


Figure 2 The rise in hip fracture rates with age in men and women (Sanders et al 1999b)



The rate of decline in bone mass is most rapid in women within two years of menopause and averages two per cent to four per cent a year during the first seven years after menopause. Bone mineral content may decline by 25 per cent to 33 per cent during this period. After this period, loss continues, albeit at a slower rate (1% to 2% a year). The areas of greatest loss include the femoral neck and lumbar vertebrae, sites rich in trabecular bone and subject to future fracture. Cortical bone, comprising 80 per cent of skeletal bone, is lost less rapidly. A similar phenomenon occurs in men; however, the rate of loss is lower compared to women. This reduction in bone density frequently remains unknown, and is most often clinically manifest as a skeletal fracture sustained with minimal trauma (WHO 2007).

Measurement of bone mineral density

DXA and QCT can be used in measuring BMD. DXA scanning is considered the gold standard for the purposes of identifying patients with low BMD, predominantly due to cost-effectiveness and accessibility. It documents small changes in bone mass and can also be used to examine both the spine and the extremities. DXA is more widely used, has better reproducibility, and is considered more appropriate in general use than QCT which delivers higher doses of radiation. The benefits of DXA over QCT include quicker scan time, which reduces issues with patient motion; lower radiation exposure compared to QCT, and a widely utilised T-score scale for the classification of low BMD (Bauer et al 2010).

QCT is often preferred when measuring BMD in the presence of fractures. QCT generates BMD information in Hounsfield units and requires calibration to obtain units used to measure BMD. Unlike DXA scanning, which provides area-adjusted results, QCT generates a volumetric density (mg/mm^3). It is the only technique that can directly measure bone density and volume, hence QCT is the most sensitive technique for the assessment of suspected local loss of BMD (WHO 2007).

Other tools may use in measuring BMD (eg quantitative ultrasound); however, they are less sensitive than DXA and QCT (Kumar and Clark 2009) and they are not a part of the current proposal.

The T-score is a comparison of a patient's BMD to that of peak BMD for the patient's gender. It is the number of standard deviations above or below the normal young adult mean (WHO 2007). BMD in OP is defined 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, Table 2). BMD reflects the amount of bone and, indirectly, the bone strength, its spatial distribution (ie shape and microarchitecture) and the intrinsic properties of the materials that comprise it, such as density, matrix mineralisation, collagen traits and micro-damage (Marcus et al 2008). 'Osteopenia' (low bone density) is a precursor to OP and according to WHO is defined as a T-score of between -1.0 and -2.5 (Table 2).

Table 2 Diagnosis of osteoporosis according to T-score

T-score	Diagnosis
Equal or greater than -1.0	Normal bone mineral density
Between -1.0 and -2.5	Low bone density ('osteopenia': at risk for developing OP and increasing fracture risk)
Equal to or less than -2.5	Osteoporosis

OP: osteoporosis; Source: WHO 2007, RACGP 2010b

Fracture risk

Ten-year fracture risk can be estimated through the use of on-line tools such as the FRAX tool developed by the University of Sheffield on behalf of the WHO (WHO 2007; WHO 2012). The assessment is likely to be less accurate for premenopausal women, young men (<50 years) and is not validated for children (Dasher et al 2010). A variation of FRAX supported with Australian data is available at: <http://www.shef.ac.uk/FRAX/tool.jsp?country=31>.

In terms of normative data, RACGP guidelines state: 'In Australia as a reference for fracture risk calculation in women, the T-scores calculated from the Geelong Osteoporosis Study database are used for the lumbar spine and the proximal femur. Normative data in Australian men are not currently available. Most BMD assessments currently report T-scores for men based on the US National Health and Nutrition Examination Survey (NHANES) normative data or reference ranges provided by densitometer manufacturers' (RACGP 2010b).

Administration, dose, frequency of administration, duration of treatment

Bone density scanning can be performed at any location which has both a DXA machine and qualified technician. A radiologist, nuclear medicine physician or other accredited specialist is required to interpret the results. The result is communicated to the patient through the referring practitioner.

Diagnosis of low bone mineral density is dependent on the measurement site and number of sites measured. According to local guidelines, bone mineral density should be measured by DXA scanning performed on two sites, preferably anteroposterior spine and hip (RACGP 2010b).

Absorbed radiation doses from using DXA are negligible for first-generation pencil beam scanners (well 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 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 with DXA usually takes up to a maximum of approximately 15-20 minutes (Dasher et al 2010).

A QCT scan involves higher doses of radiation than DXA. The effective dose is 50-100µSv for the spine and 500-1000µSv for the hip.

Current guidelines suggest general practitioners to evaluate patients at increased risk for osteoporotic fractures who are not receiving specific preventive anti-osteoporotic therapy in regard to future fracture risk at intervals adequate to the risk in question. BMD measurement can identify some non-fragility causes of fracture, for example T-score above -1.5. If a decision is made to not recommend specific preventive anti-osteoporotic therapy following evaluation of BMD, this must be formally reviewed in relation to future fracture risk at intervals relevant to the risk in question. In most cases BMD testing is recommended for intervals of 2 years or longer (RACGP 2010b).

In patients with confirmed OP and receiving anti-osteoporotic treatment, repeat DXA scans are recommended to be considered at 1 year if there is a change to anti-osteoporotic therapy, and recommended at 2 year intervals when BMD is likely to be approaching -2.5 (average decrease in T-score is 0.1/ year) (RACGP 2010b). The BMD at the time of screening is the most important factor in determining treatment and the time to repeat scan. The rates of change between scans are not as important in overall management decisions.

Additional question for the review:

- What is the diagnostic utility of DXA (sensitivity, specificity and accuracy) compared to QCT? Are both tests as safe and effective to identify patients with a T-score of ≤ -2.5 (osteoporotic)?

Summary of the approach to assessment for the test

The **proposed tests** are DXA and QCT.

Unconditional access to DXA or QCT scanning under the MBS is currently available to people aged 70 years and over (MBS item 12323). To align with this item, QCT included in the intervention in the

current submission. This will allow future decisions regarding the access to BMD testing to the proposed population to be considered as part of, or separate to, current item 12323.

In addition to the primary question of this assessment, evidence should also be provided on the comparative safety and diagnostic utility (sensitivity, specificity and accuracy) of DXA and QCT in relation to each other in classification of T-scores ≤ -2.5 .

Co-administered interventions

For people with OP, a variety of treatment options exist through which to reduce the rate of bone loss. In addition to maintenance of bone formation through supplementation (calcium and vitamin D), and reduction of bone resorption through lifestyle modification (exercise), Pharmaceutical medications are available for the treatment of osteoporosis in certain patient groups (RACGP 2010b). Bisphosphonates, teriparatide and strontium ranelate may be used. Postmenopausal women may also be treated with hormone therapy, monoclonal antibodies and selective oestrogen receptor modulators (SERMs) (Barlow et al 2010). Anti-osteoporotic medications on the ARTG are listed according to relatively broad indications (Appendix 1). For example, alendronate sodium is available to postmenopausal women and to men in the treatment of osteoporosis to help prevent fractures. Other medications are available confirmed by the finding of low bone mass, for patients on long-term corticosteroid therapy, or in the presence or history of osteoporotic fracture. Indications, contraindications and potential complications of the ARTG registered items are presented in below.

For the current submission, alendronate is proposed as the co-dependent drug for the treatment of OP. The active ingredient of the drug is alendronate sodium. The drug is also available as combinations with colecalciferol and calcium carbonate. A comprehensive list of alendronates listed in PBS for treatment of diseases of bone structure and mineralisation is provided in Appendix 3.

Threshold for therapy

The proposed threshold to therapy is any test result with a T-score ≤ -2.5 . However, the assessment phase should provide evidence to determine the best threshold for a test and address the issue of the criteria for, and timing of, initiation of therapy (alendronate).

Clinical research questions for the assessment relating to the intervention:

- What is the effect of alendronate on the rate of minimal trauma fracture in the target population (men and women aged 60-69 years of age)?
- What is the rate of bone loss over time in the proposed population who are not provided with this test and therapy regime? What is the rate of bone loss over time in the proposed population who are provided with this test and therapy regime? Evidence provided in response to these questions will inform the number and frequency of DXA/QCT re-testing and monitoring (respectively). The frequency of re-testing and monitoring should be justified by the submission of available evidence.

- The proposed target population are men and women aged 60-69. For the purposes of sensitivity analysis the assessment phase should consider different age ranges for testing (eg 60-69 years; 65-69 years) to initiate therapy (alendronate) to identify the optimal age range. The assessment phase should also consider 'rollout' in people who are in their 60s at the time of introduction (ie effectiveness in people who enter the test-and-treat regime when they are already in their 60s).
- What proportion of the population at each defined age group (ie over 60, over 65) will have a T-score of ≤ -2.5 ? This population will be provided with the proposed therapy (alendronate). Similar evidence should be provided for any other relevant thresholds identified as part of the assessment.
- What proportion of the population at each age group (ie over 60, over 65) will have a T-score of less than -2.5? This population will be eligible for repeat tests under existing items.

Summary of the approach to assessment for the intervention

Test

The proposed tests are DXA and QCT. PASC consider that testing for serum vitamin D sufficiency 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 alendronate.

The evaluation stage should provide evidence to determine the best **threshold for therapy**.

The assessment should address threshold to therapy as:

- A T-score of ≤ -2.5 (osteoporotic).
- The assessment should provide evidence on the appropriate threshold T-score(s) for access to alendronate so that MSAC can determine the best threshold for intervention.
- The assessment should undertake sensitivity analyses around T-scores of -1.0, -1.5, -2.0 and -2.5 as relevant thresholds for therapy.

Repeat test

According to the RACGP guidelines,

- Usually a decrease in bone density greater than the measurement error is not seen before two years; hence, follow up bone densitometry is not recommended at intervals of less than two years in most patients (RACGP 2010a).
- In patients with confirmed OP, repeat BMD is generally not required; however, it may be conducted before initiating a change in, or cessation of, anti-osteoporotic therapy (RACGP

2010a). They are eligible for repeat testing as required under MBS item 12306.

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 risk of minimal trauma fracture over time. The analysis of this evidence should identify 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 for patients with T-score greater than -1.0;
- Repeat test every 24 months for patients with T-scores less than or equal to -1.0 (noting that unlimited monitoring of patients with a T-score of ≤ -2.5 is available through a current MBS item);
- Sensitivity analysis should be undertaken for repeat tests using different threshold T-scores, as informed by the available evidence. Sensitivity analyses should also be undertaken on the frequency of the repeat test and monitoring tests, as informed by the available evidence.

For the population identified with low bone mineral density (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 **co-dependency** with alendronate.

Note that the final eligibility criteria including threshold T-score of the proposed population to alendronate would be defined by the Pharmaceutical Benefits Advisory Committee (PBAC).

Background

Current arrangements for public reimbursement

DXA scanning is not currently funded for men and women below the age of 70 unless they suffer from certain pre-defined conditions. Unconditional access to DXA or QCT scanning under the Medical Benefits Schedule is currently available to persons aged 70 years and over (MBS item number 12323). A variety of other patient populations are covered for DXA or QCT under the MBS (Table 3), including;

- Presumed low BMD following one 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

Relevant explanatory notes are in Appendix 5.

Several different MBS items cover a variety of indications for repeat scans every 12 or 24 months depending on the indication (See Table 3). According to current Australian guidelines, for patients with low risk factors and T-scores above osteopenic values (≥ -1.0), repeat scans are not required, unless substantial changes in circumstance (minimal trauma fracture or increased risk conditions). People diagnosed with osteoporosis (≤ -2.5) would be eligible for repeat testing as required under MBS item 12306; however, patients with confirmed osteoporosis and receiving anti-osteoporotic treatment, repeat DXA scans are not generally required unless there is a change in, or cessation of, anti-osteoporotic therapy (RACGP 2010b).

Table 3 Current MBS item descriptors for DXA and QCT

Category 2 – DIAGNOSTIC PROCEDURES AND INVESTIGATIONS	
<p>MBS 12306</p> <p>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:</p> <ul style="list-style-type: none"> • 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. <p>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).</p> <p>Fee: \$102.40 Benefit: 75% = \$76.80 85% = \$87.05</p> <p><u>Relevant explanatory notes: See Note D1.27</u></p>	
Category 2 – DIAGNOSTIC PROCEDURES AND INVESTIGATIONS	
<p>MBS 12309</p> <p>Bone densitometry (performed by a specialist or consultant physician where the patient is referred by another medical practitioner), using quantitative computerised tomography, for:</p> <ul style="list-style-type: none"> • 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. <p>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)</p> <p>Fee: \$102.40 Benefit: 75% = \$76.80 85% = \$87.05</p> <p><u>Relevant explanatory notes: see Note D1.27</u></p>	
Category 2 – DIAGNOSTIC PROCEDURES AND INVESTIGATIONS	

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: \$102.40 **Benefit:** 75% = \$76.80 85% = \$87.05

Relevant explanatory notes: See Note D1.27

Category 2 – DIAGNOSTIC PROCEDURES AND INVESTIGATIONS

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: \$102.40 **Benefit:** 75% = \$76.80 85% = \$87.05

Relevant explanatory notes: See Note D1.27

Category 2 – DIAGNOSTIC PROCEDURES AND INVESTIGATIONS

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: \$102.40 **Benefit:** 75% = \$76.80 85% = \$87.05

Relevant explanatory notes: see Note D1.27

Category 2 – DIAGNOSTIC PROCEDURES AND INVESTIGATIONS

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: \$102.40 **Benefit:** 75% = \$76.80 85% = 87.05

Relevant explanatory notes: See Note D1.27

Category 2 – DIAGNOSTIC PROCEDURES AND INVESTIGATIONS

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: \$102.40 **Benefit:** 75% = 76.80 85% = \$87.05

Relevant explanatory notes: See Note D1.27

Taken from <http://www9.health.gov.au/mbs/search.cfm>, accessed 08 July 2013

Table 4 provides data regarding the utilisation of DXA and QCT services between July 2009 and June 2010.

Table 4 MBS items utilised between July 2009 and June 2010 for DXA and QCT scanning

MBS item	45-54 years <i>(per 100,000)</i>	55-64 years <i>(per 100,000)</i>	65-74 years <i>(per 100,000)</i>	75-84 years <i>(per 100,000)</i>	≥85 years <i>(per 100,000)</i>	TOTAL – all ages <i>(per 100,000)</i>
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)
12309†	234 (8)	412 (16)	300 (19)	134 (14)	41 (11)	1,234 (6)
12318	301(0)	591 (2)	477 (0)	208 (0)	35 (0)	1,728 (8)
TOTAL	27,636	53,558	64,292	45,661	8,134	199,510

* this item include both DXA and QCT

† this item include QCT only

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: MBS item statistics were searched on 20/09/2012 < https://www.medicareaustralia.gov.au/statistics/mbs_item.shtml>.

A test for vitamin D sufficiency is available through MBS item 66608 (vitamin D or D fractions - 1 or more tests, Fee, \$33.20). In the financial year 2011-12, 3,481,966 services were provided under this item.

Regulatory status

DXA Scans

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 code 37661).

Table 5 TGA registered DXA 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 diagnosis 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 regeneration and loss.
158772	23/01/2009	Hologic Inc	Cytec 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

QCT scan

About 40 computed tomography systems are listed in the ARTG as of September 2012. These may include QCT devices.

Patient population

The proposal is to add a new MBS item for men and women 60-69 years who are not eligible for a test through existing MBS items, to have access to DXA or QCT scan. The clinical decision of whether to prescribe a test may be based on a patient's comorbidities and risk factors for OP, which are not covered by existing MBS items.

BMD is assessed using the T-score measurement and accordingly patients are stratified into one of the following three groups based on WHO guidelines, which determines the appropriate clinical management strategy.

- T-score \geq -1.0 (normal bone mineral density)

- T-score from -2.5 (excluded) to -1.0 (excluded) (osteopenia)
- T-score \leq -2.5 (osteoporosis)

Patients with a T-score \leq -2.5 are proposed to be eligible for treatment with alendronate. It has also been proposed that patients with T-score from -2.5 to -1.0 should be considered for treatment with alendronate.

During the assessment phase, the best age range threshold for testing (ie 60-69 years; 65-69 years) should be identified.

Risk factors

The specific risk factor associated with this population is age.

Baseline population

Men and women aged 70 years and older.

The proposal is to scan for bone mineral density and provide therapy to the target population in line with this baseline population. This baseline population is eligible for current MBS items for scanning for BMD, and may also be eligible for anti-resorptive treatment through the PBS.

Benchmark population

Men and women aged 70 years and older. Access to alendronate for the target population is proposed to be in line with access to alendronate currently available to the benchmark population.

Questions for the review relating to the population:

- What is the risk of minimal trauma fracture in the proposed population (with no intervention) compared to minimal trauma fracture in the baseline population (with no intervention)?
- What is the rate of bone mineral density loss in the proposed population (men and women aged 60-69 years of age)? What is the rate of bone mineral density loss in the benchmark population (men and women aged 70 years of age or older)? This will provide information regarding the frequency of re-testing and monitoring for the proposed population in light of evidence pertaining to the benchmark population who are already eligible for BMD scanning through the MBS.
- What proportion of men and women in the population would accept and receive a DXA scan as proposed?
- What risk factors, other than age between 60-69 years, are identified in the available evidence?

Summary of the approach to assessment for the population

The **population** is men and women 60-69 years. The **baseline population** and the **benchmark population** are men and women aged 70 years and older.

PASC advises that additional age groups for initial scanning for the sensitivity analysis should include:

- Men and women over 65 (65-69 years).

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

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

The assessment should provide evidence on the BMD threshold for testing and the frequency of re-testing in each BMD-defined group.

Excluded populations

- All men and women at age 70 and over are excluded, as they are eligible for current MBS items for DXA scanning.
- Men and women presenting with a minimal trauma fracture are excluded, as they are eligible for current MBS items for DXA scanning (12306, 12309).
- Men and 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 eligible for bone mineral density analysis.

The proposed MBS item is provided in the Table 6. Any non-age related risk factors for osteoporosis not covered by current MBS items (such as smoking, alcohol consumption and other shown in Table 1) are expected to be taken into account by medical practitioner prior to deciding if a BMD test is necessary. As such, the applicants propose that risk factors for osteoporosis other than age not be specifically included in the wording of the MBS item descriptor.

It is proposed that people with a T-score greater than or equal to -1.0 (normal bone mineral density) would not require repeat testing unless their risk factors change substantially. People with osteopenia (-1.0 > T-score > -2.5) would require retesting after 2 years. People identified with a T-score less than or equal to -2.5 would be eligible for repeat testing under item number 12306 (DXA) or 12309 (QCT). (Note that thresholds and frequency of repeat testing will form part of the assessment).

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.

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

Table 6 Proposed MBS item descriptor for men and women aged 60 years and over

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** or **quantitative computerised tomography**, for the measurement of hip and spine bone mineral density, for a person **aged 60 – 69 years**.

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, 12321 or 12323 applies.

Fee: \$102.40 Benefit: 75% = \$76.80 85% = \$87.05

[Relevant explanatory notes]

D1.27, Bone Densitometry – (Items 12306 to 12323)

Note that the proposed item shown in Table 6 aligns closely with current MBS item 12323, other than specifying the site of analysis and lowering the age of eligibility. Both the current and proposed item include testing by either DXA or QCT. Depending on the final decision, it may be that the proposed item shall be separate to current items, or item 12323 may be amended to include men and women aged 60 years or over. The consideration of evidence regarding DXA and QCT within this DAP and in the assessment phase will allow MSAC to make an informed decision regarding the final item listing.

Clinical place for proposed intervention

The current diagnosis and management algorithm for suspected or proven low bone mineral density follows in Figure 3. The current and proposed algorithms for the defined population (men and women 60-69 years) follow in Figure 4 and Figure 5.

Figure 3 Current clinical management algorithm for eligibility to MBS and PBS items for osteoporosis

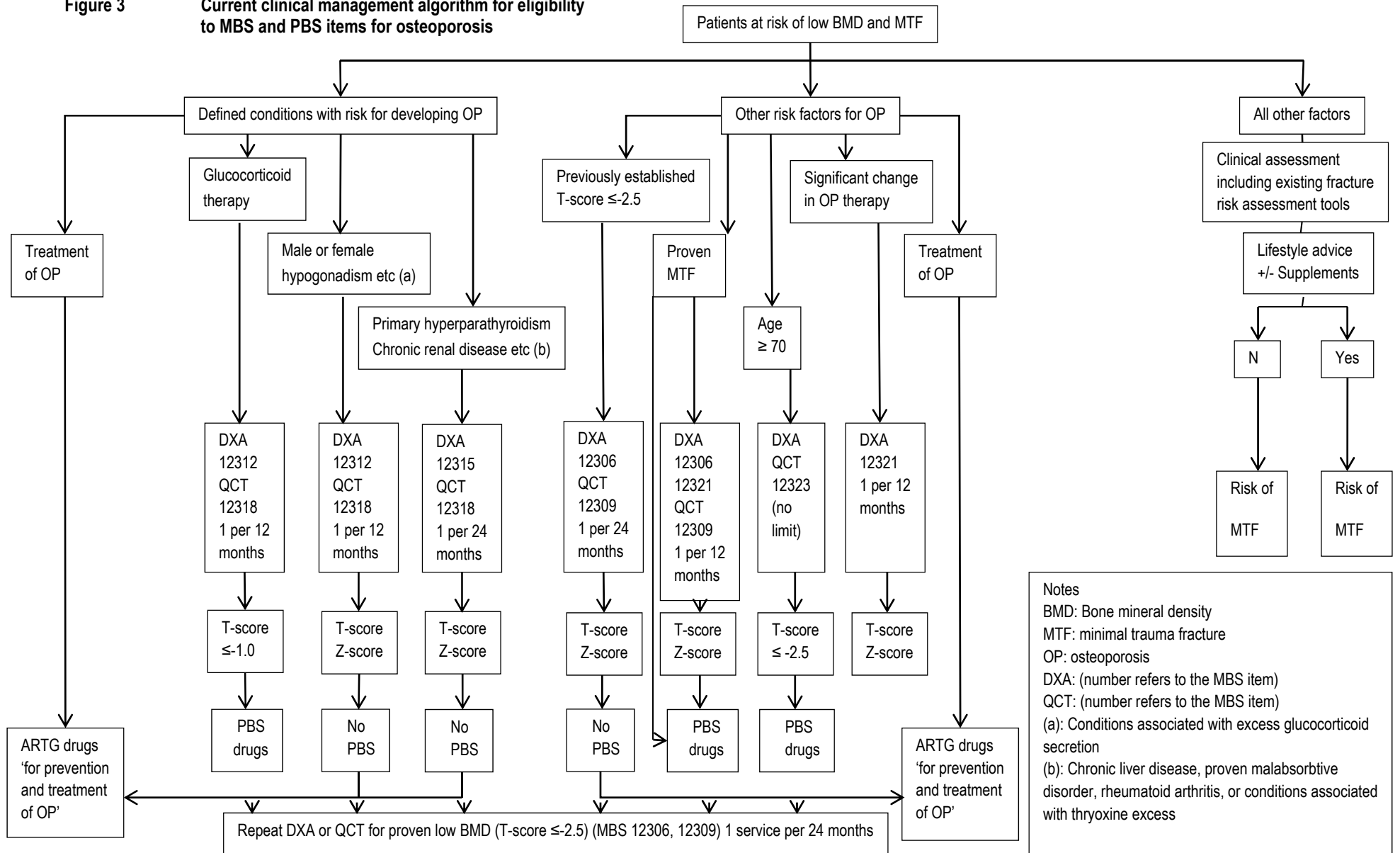


Figure 4 Current clinical management algorithm for the management of osteoporosis in men and women 60-69

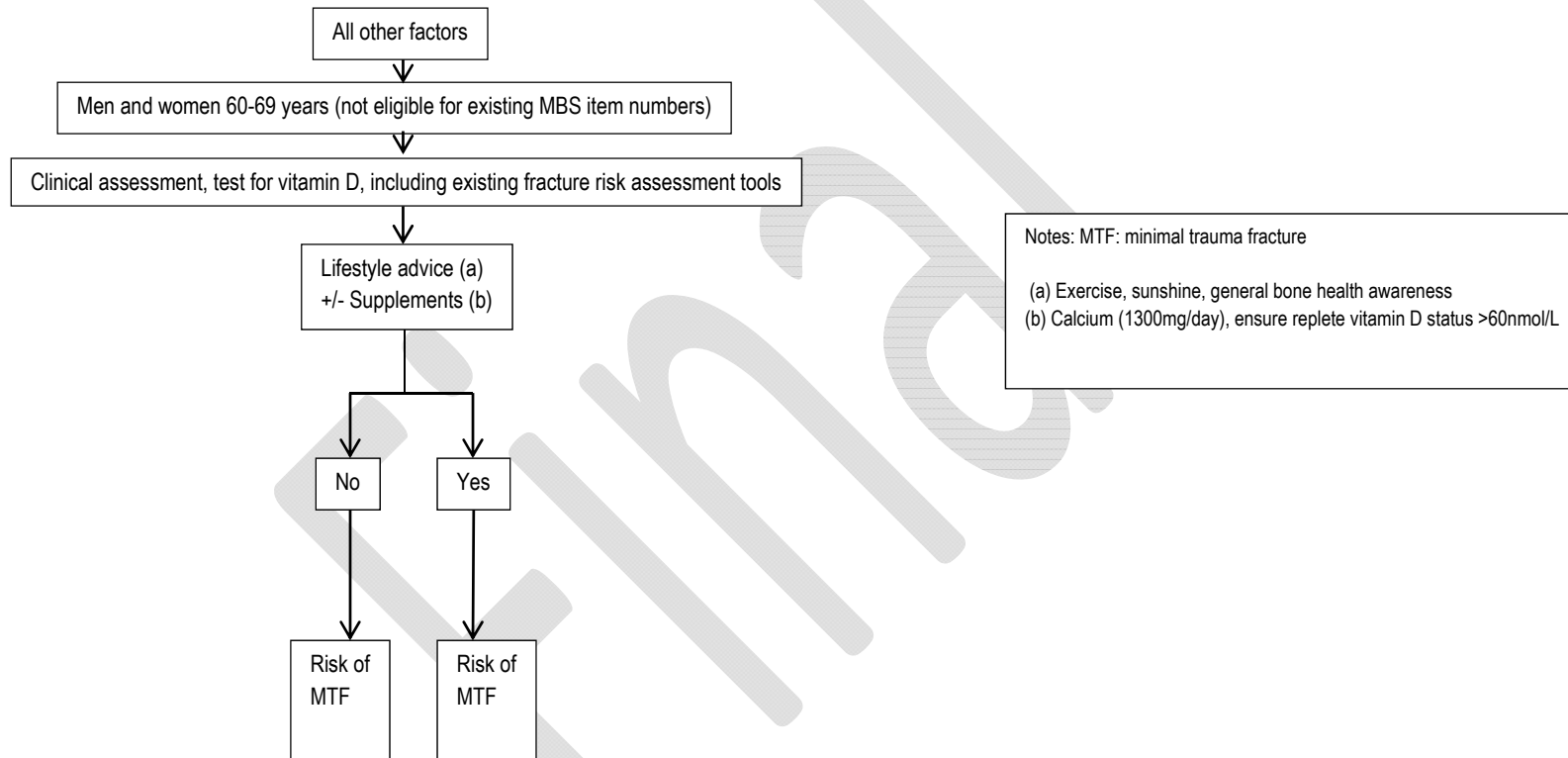
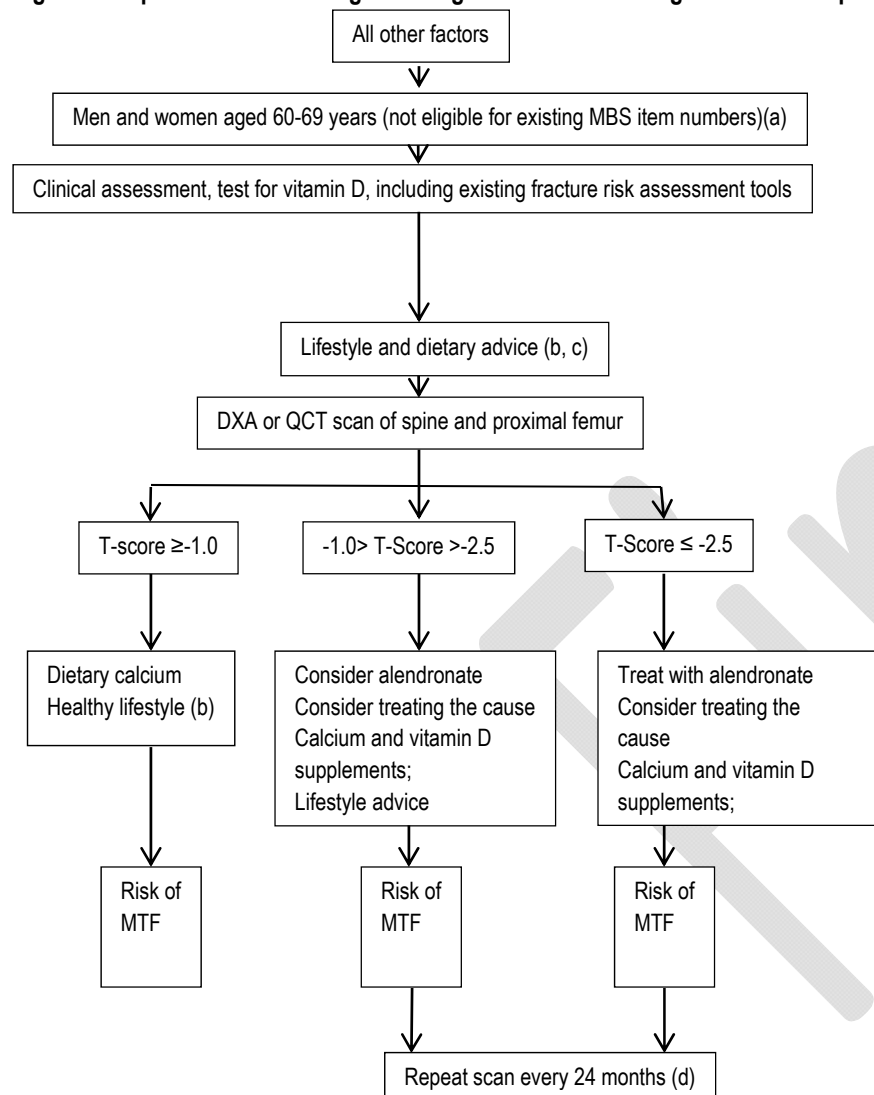


Figure 5 Proposed clinical management algorithm for the management of osteoporosis in men and women aged 60-69



Notes:
 (a) Options for a test to be provided to men and women 65-69 years
 (b) Exercise, sunshine, general bone health Awareness
 (c) Calcium (1300mg/day), ensure repeat vitamin D status >60nmol/L
 (d) For T-score ≤ -2.5, a repeat DXA would be available through existing MBS 12306, 12309, 12321 or 12318.
 MTF: minimal trauma fracture; OP: osteoporotic
 Key risk factors are to be determined as a part of the assessment.

Comparator

Presently, individuals 60-69 years will not routinely receive DXA or QCT scanning for osteoporosis. Vulnerability to the condition may be predicted through a clinical assessment, including a test for vitamin D sufficiency and the use of existing fracture determinant tools. Determining the probability of 10-year fracture risk can be estimated through use of the FRAX tool (WHO 2007). This tool can be used in combination with DXA results, or without DXA as a predictor of risk of fracture. Part of the population may take dietary and lifestyle measures to promote good bone health, including supplements (calcium and vitamin D), without a bone mineral density test. These supplements are available without prescription.

The comparator is:

- Lifestyle and dietary advice (calcium and vitamin D) based on a clinical assessment by a general practitioner using existing fracture risk assessment tools (for example the FRAX tool) 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

The DXA or QCT scanning, when applied to individuals aged 60-69 years, would identify patients with osteoporosis and provide an opportunity for early intervention with the anti-resorptive pharmaceutical, alendronate. The scan would therefore indirectly reduce the fracture rate in the target population.

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

		Comparative effectiveness versus comparator							
		Superior		Non-inferior	Inferior				
Comparative safety versus comparator	Superior	CEA/CUA		CEA/CUA	Net clinical benefit	CEA/CUA			
					Neutral benefit	CEA/CUA*			
					Net harms	None [^]			
	Non-inferior	CEA/CUA		CEA/CUA*	None [^]				
							Inferior	Net clinical benefit	CEA/CUA
								Neutral benefit	CEA/CUA*
Net harms	None [^]								
None [^]		None [^]		None [^]					

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 (ie, 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

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.
- To account for all patients in the target population who become eligible to current MBS items (for example through age, history of minimal trauma fracture, or other reimbursable risk factors).

Outcomes and health care resources affected by introduction of proposed intervention

Outcomes

Several outcomes are highlighted in the clinical pathway algorithms (Figure 4, Figure 5). It is suggested that a difference in outcomes between proposed and current pathways will occur as a result of there being a greater number of patients identified early and treated early, thus delaying the progression of the disease and reducing the incidence of minimal trauma fractures.

Effectiveness

Primary outcome;

- Incidence of minimal trauma fracture
- Incidence of all fractures
- Patient-related quality of life

Secondary outcomes;

- Change in mortality/morbidity
- Bone mineral density (for example as determined by the T-score)

Safety

- Any adverse event or complication related to the intervention (DXA, QCT or alendronate). This includes any adverse event arising from exposure to ionising radiation.

Please note:

- 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/QCT 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 patients 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. This is to account for any variability of test results between machines.
- PASC acknowledges that DXA is associated with low radiation doses compared to QCT, but that increasing the availability of DXA and QCT may significantly increase the exposure of the proposed population to ionising radiation. This issue should be addressed in the assessment of evidence.
- Evidence related to DXA should be provided separately to evidence related to QCT.

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					Fee \$33.20					
- Dietary supplements			TBA						Patient cost	
Resources provided in association with comparator 1 (eg, 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 comparator 2, etc										
- N/A										
-										
Resources provided in association with comparator 2, etc										
- N/A										
-										
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	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 test			TBA		Fee \$33.20					
- Alendronate					\$37.38 to \$589.17	\$5.60 to \$34.20				
- Costs associated with fracture	Public and private hospitals									
- Cost 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)

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
Men and women aged 60-69 years ^a	Dual energy X-ray absorptiometry (DXA) OR	Clinical assessment including the use of existing fracture risk assessment tools and vitamin D test, with lifestyle and dietary advice.	<u>Effectiveness</u> Primary: •Incidence of MTF •Incidence of all fractures •Patient-related quality of life	GP consultation (clinical examination and use of existing fracture risk tools). Vitamin D test. Use of dietary supplements. Alendronate
Additional groups for consideration for the sensitivity analysis: Men and women 65-69 (over 65)	Quantitative Computer Tomography (QCT)	DXA and QCT are excluded. Alendronate and any other anti-resorptive prescription medication are excluded.	Secondary: •change in morbidity/mortality •BMD (as determined by T-score)	Costs associated with a fracture Costs associated with recovery from a fracture DXA/QCT test Follow-up GP consultation for advice
Exclude: All women at age 70 and over, women with a previous minimal trauma fracture, all men and women currently eligible for MBS items for scanning for bone mineral density.	Treatment with alendronate for men and women with a T-score \leq -2.5. The evidence should be used to determine the best threshold (measured as T-score) for therapy.		<u>Safety</u> Any adverse event or complication related to the treatments for OP after diagnosing the disease. See also 'Outcomes' section above.	See Table 16.

MTF: minimal trauma fracture; OP: osteoporosis

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 below (Table 10).

Table 10 Summary of issues relating to the approach to assessment

Population	Men and women 60-69 years
Context	The population consists of men and women over 60 years. . PASC advises that alternative ages for initial scanning for the sensitivity analysis should include: <ul style="list-style-type: none"> Men and women 65-69. The assessment should provide the best age range threshold for testing. Excluded: All men and women at age 70 and over are excluded, as these are eligible for current MBS items for DXA/QCT scanning and testing for low bone mineral density. Men and women presenting with a minimal trauma fracture are excluded, as these are eligible for current MBS items for DXA scanning and testing for low bone mineral density (12306, 12309). All men and women currently eligible for MBS items for scanning for bone mineral density are also excluded.
Baseline population	Men and women aged 70 years and over.

Benchmark population	Men and women aged 70 years and over as these are eligible for current MBS items may be eligible for certain PBS anti-resorptive medications.
Approach to assessment	<p>The assessment should provide evidence regarding what age the test should be performed. The assessment should consider any impact of patients receiving the test at other ages within the defined range, and what impact this may have on the rollout and use of the proposed item.</p> <p>Not all men and women in the target population will choose to receive the test. The assessment should provide evidence regarding the proportion of men and women who would be expected to undertake DXA/QCT testing as proposed.</p>

Intervention	DXA or QCT for bone densitometry. Treatment with alendronate for men and women with a T-score less than or equal to -2.5.
Context	The proposed tests are DXA and QCT.
Co-dependency	The proposed therapy is alendronate.
Treatment threshold	The proposed threshold for therapy is a T-score ≤ 2.5 . Evidence regarding any other T-scores as thresholds to therapy should be provided.
Context	PASC identified a need to define the best threshold for intervention and to explore multiple thresholds.
Approach to assessment	<p>The evaluation stage should provide evidence to determine the best threshold for intervention.</p> <p>The assessment should address threshold to therapy as:</p> <ul style="list-style-type: none"> • A T-score ≤ 2.5. • The assessment should provide evidence to inform on any other appropriate threshold T-score(s) for access to therapy, noting that the final decision on access to alendronate will be informed by PBAC. • The assessment should undertake sensitivity analyses around various relevant thresholds for therapy.
Re-testing and monitoring	<p>Should repeat testing be conducted in men and women with a known T-score?</p> <p>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.</p> <p>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.</p> <p>Similar information should be provided for the Benchmark population so that re-testing and monitoring can be established in line with current eligibility.</p>
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	<p>For sensitivity analysis the following options should be evaluated regarding re-testing and monitoring of the population:</p> <ul style="list-style-type: none"> • Repeat test each 24 months for men and women with T-scores from -2.5 (excluded) to -1.0 (excluded), up to the age of 70 years when they will become eligible for an existing MBS item; • Monitoring tests each 24 months for men and women with T-scores less than or equal to -2.5 (this population will be eligible for existing MBS item 12306). • The frequency of re-testing and monitoring should also be informed by the available evidence.
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 tool) without the results of a bone mineral density test. This clinical assessment would include a test for vitamin D sufficiency (MBS item 66608).
Outcomes	<p>Outcomes include primary effectiveness, secondary effectiveness and safety outcomes.</p> <p>Primary effectiveness outcomes:</p> <ul style="list-style-type: none"> • Incidence of minimal trauma fracture • Incidence of all fractures • Patient-related quality of life. <p>Secondary effectiveness outcomes:</p> <ul style="list-style-type: none"> • Change in morbidity/mortality • Bone mineral density (for example as determined by the T-score)

Safety outcomes and adverse events:	<ul style="list-style-type: none"> • Any adverse event or complication related to the DXA/QCT scanning or therapy (alendronate) • Any adverse event arising from exposure to ionising radiation
Approach to assessment	<p>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.</p> <p>The location of the DXA/QCT exam (for example, proximal femur, lumbar spine, hip, distal radius) should be reported for all studies where possible.</p> <p>Where men and 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.</p> <p>PASC acknowledges that DXA/QCT are associated with radiation doses. Increasing the availability of DXA/QCT may significantly increase the exposure of the proposed population to ionising radiation. This issue should be addressed in the assessment of evidence.</p> <p>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.</p> <p>Any evidence relating to the proportion of women in the target population who will have a T-Score of ≤ -2.5 should be presented.</p>

Clinical research questions for public funding

1. What is the safety of DXA or QCT and treatment of low bone mineral density with alendronate compared with clinical evaluation, lifestyle and dietary advice for individuals aged 60-69 years?
2. What is the effectiveness of DXA or QCT and treatment of low bone mineral density with alendronate compared with clinical evaluation, lifestyle and dietary advice for individuals aged 60-69 years?
 - Does the treatment (alendronate) reduce the incidence of minimal trauma fractures?
3. What is the cost effectiveness of DXA or QCT and treatment of low bone mineral density with alendronate compared with clinical evaluation, lifestyle and dietary advice (or non-prescription bone loss management) for individuals aged 60-69 years?
 - Sensitivity analysis should be undertaken to provide information on the range of variables identified throughout the DAP.

Secondary clinical research questions identified as relevant to this DAP:

4. What is the safety and diagnostic effectiveness (sensitivity, specificity, accuracy) of QCT compared to DXA for the measurement of bone mineral density?
5. Are there any specific risk factors not currently covered by current MBS items for bone mineral density testing (such as smoking, alcohol, lack of exercise) that have been shown to be particularly relevant to this population?
6. At what threshold should the therapy be made available to the population?
7. At what frequency should re-testing be made available to the population?

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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; Fosamax, Didrocal, Actonel, Aclasta, Clodronate <i>[prevention (Grade A), treatment (Grade A)]</i>		
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
<p>Paget's disease of bone</p> <p>Prevention and treatment of osteoporosis (including postmenopausal and corticosteroid-induced)</p> <p>Hypercalcaemia of malignancy</p> <p>Prevention of skeletal-related events in patients with malignancies involving bone</p> <p>Prevention and treatment of heterotopic ossification due to spinal cord injury or complicating total hip replacement</p>	<p>Abnormalities of the oesophagus which delay oesophageal emptying, such as stricture or achalasia.</p> <p>Inability to stand or sit upright for at least 30 minutes.</p> <p>Hypersensitivity to any component of bisphosphonates.</p> <p>Hypocalcaemia.</p> <p>Severe hypercalciuria.</p>	<p><i>Common</i></p> <p>nausea, vomiting, diarrhoea, headache, hypocalcaemia, musculoskeletal pain (may rarely be severe and/or disabling)</p> <p>IV: fever, flu-like symptoms, injection site reaction, increased creatinine concentration, hypophosphataemia, myalgia, bone pain, hypertension</p> <p><i>Infrequent</i></p> <p>oesophagitis, oesophageal erosions and ulcers (mainly with alendronate), gastritis, duodenitis, glossitis, rash</p> <p>IV: hypotension, hypomagnesaemia, hypokalaemia</p> <p><i>Rare</i></p> <p>heart failure, renal impairment, ocular inflammation, osteonecrosis of the jaw, allergic reactions including angioedema</p> <p>IV: anaphylactic shock</p> <p><i>*Osteonecrosis of the jaw</i></p> <p>Risk appears to be associated with the potency, route and total dose of bisphosphonate and a history of dental surgery, trauma or disease.</p> <p><i>Possible associations</i></p> <p>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.</p>
Hormone Replacement Therapy <i>[prevention (Grade A), treatment (Grade A)]</i>		
Indication	Contraindication	Side effects
Prevention of postmenopausal	Breast cancer or other oestrogen-	<i>Common</i>

osteoporosis when there is a high risk of fractures and alternative treatment is inappropriate	<p>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</p>	<p>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)</p> <p><i>Infrequent</i> 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</p> <p><i>Rare</i> cholestatic jaundice, pancreatitis, glucose intolerance, galactorrhoea, visual changes, chloasma, hypersensitivity (angioedema, urticaria), ovarian cancer, endometrial cancer, enlargement of uterine fibroids, enlargement of hepatic haemangiomas</p>
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Selective oestrogen receptor modulators (SERMs); *Evista; Femarelle*
[treatment (Grade A)]

ARTG: Evista: 64709; Femarelle: 161797

Indication	Contraindication	Side effects
For the symptomatic relief of menopause.	Venous thromboembolism (VTE) — contraindicated in patients with a history of VTE or risk factors for VTE.	<i>Common</i> hot flushes, sweating, leg cramps, peripheral oedema, sleep disorders
Maintenance of bone health, indicated for the prevention and treatment of osteoporosis.	Prolonged immobilisation—increases risk of VTE. Women with or at risk of coronary heart disease—increased risk of VTE or fatal stroke.	<i>Infrequent</i> VTE
Hormone receptor-positive breast cancer	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.	

Monoclonal antibodies; *Denosumab*

ARTG: 159322, 159323, 159324

Indication	Contraindication	Side effects
Treatment of postmenopausal	Hypocalcaemia	<i>Common</i>

osteoporosis	Renal increased risk of hypocalcaemia if CrCl <30 mL/minute.	eczema, hypercholesterolaemia <i>Infrequent</i> skin infections (mainly cellulitis) <i>Rare</i> hypocalcaemia, osteonecrosis of the jaw
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Teriparatide (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	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.	<i>Common</i> nausea, headache, dizziness, muscle cramp, arthralgia, hyperuricaemia, injection site reactions
Primary osteoporosis in men when there is a high risk of fractures and other agents are unsuitable	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.	<i>Infrequent</i> hypercalcaemia, myalgia, increased ALP
Corticosteroid-induced osteoporosis in patients at high risk of fractures	Pregnancy Breastfeeding	<i>Rare</i> allergic reactions

Strontium Ranelate (Protos)

[treatment – (Grade A)]

Indication	Contraindication	Side effects
Treatment of postmenopausal osteoporosis to reduce the risk of fracture.	Known hypersensitivity to strontium ranelate or to any of the excipients	<i>Common</i> Headache, disturbances in consciousness, memory loss, nausea, diarrhoea, loose stools, venous thromboembolism, blood creatinine phosphokinase (CPK) increase
Treatment of osteoporosis in men at increased risk of fracture.	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 (eg post-surgical recovery or prolonged bed rest).um ranelate or to any of the excipients Severe renal impairment (see Pharmacokinetics – Special Populations)	<i>Uncommon</i> Seizures.

Current or previous venous thromboembolic events (VTE), including deep vein thrombosis and pulmonary embolism.

· Temporary or permanent immobilisation (eg 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	Hypercalcaemia Hypercalciuria, history of nephrolithiasis	<i>Common</i> belching, flatulence, abdominal distension, constipation
Vitamin D; Treatment of osteoporosis, when vitamin D supplementation is recommended	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.	<i>Infrequent</i> hypercalcaemia, alkalosis, hypophosphataemia
	Vitamin D; Hyperphosphataemia (Vitamin D only)	<i>Rare</i> 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 RACGP clinical guidelines 2010

Appendix 3 Alendronates registered in the TGA as of September 2012

ARTG number	Approval date	Description	Specific Indication
123866	28/08/2006	TERRY WHITE CHEMISTS ALENDRONATE alendronate sodium (equivalent to 70 mg alendronic acid) ^b	Treatment of osteoporosis ^a
17781	18/06/2012	STEOVESS alendronic acid (as sodium) 70mg effervescent tablet blister pack ^c	Treatment of osteoporosis ^a
161445	18/10/2010	PHARMACOR ALENDRONATE 10 alendronic acid (as alendronate sodium) 10 mg tablet blister pack ^d	Treatment of osteoporosis ^a Treatment and prevention of glucocorticoid-induced osteoporosis in postmenopausal women not receiving oestrogen and who are on long term corticosteroid therapy.
129378	25/07/2007	OSSMAX 70mg alendronic acid 70mg (as sodium alendronate anhydrous) tablets blister pack ^e	Treatment of osteoporosis ^a
129363	25/07/2007	OSSMAX 5mg alendronic acid 5mg (as sodium alendronate anhydrous) tablets blister pack ^e	Prevention of osteoporosis in postmenopausal women with low bone mass (at least 1 standard deviation below the mean for young adults). Treatment and prevention of glucocorticoid-induced osteoporosis in those patients on long term corticosteroid therapy.
129364	25/07/2007	OSSMAX 10mg alendronic acid 10mg (as sodium alendronate anhydrous) tablets blister pack ^e	Treatment of osteoporosis ^a Treatment and prevention of glucocorticoid-induced osteoporosis in postmenopausal women not receiving oestrogen and who are on long term corticosteroid therapy.
123864	28/08/2006	GENRX ALENDRONATE alendronate sodium (equivalent to 70 mg alendronic acid) tablet blister pack ^b	Treatment of osteoporosis ^a
147753	15/10/2008	FONAT alendronic acid 70mg tablet bottle ^f	Treatment of osteoporosis ^a , including glucocorticoid-induced osteoporosis. Prevention of Glucocorticoid-induced osteoporosis ^a in those patients on long term corticosteroid therapy.
134702	15/10/2008	FONAT alendronic acid 70mg tablet blister pack ^f	Treatment of osteoporosis ^a , including glucocorticoid-induced osteoporosis. Prevention of Glucocorticoid-induced osteoporosis in those patients on long term corticosteroid therapy.
161182	25/03/2010	DRONALEN PLUS D-CAL alendronic acid 70mg/colecalciferol 140 microgram tablet and 1250mg	Osteoporosis ^a in select patients where vitamin D and calcium supplementation is recommended.

153488	20/03/2009	calcium carbonate tablet composite pack ⁹ DRONALEN PLUS 70 mg/140 microgram alendronic acid 70 mg (as alendronate sodium) and colecalfiferol 140 micrograms tablet blister pack ⁹	The treatment of osteoporosis in select patients where vitamin D supplementation is recommended.
113482	08/03/2006	FOSAMAX PLUS* once weekly alendronic acid 70 mg (as alendronate sodium) and colecalfiferol 70 micrograms tablet blister pack ⁹	Treatment of osteoporosis in select patients where vitamin D supplementation is recommended.
136846	14/05/2008	FOSAMAX PLUS* 70 mg/140 ug alendronic acid 70 mg (as alendronate sodium) and colecalfiferol 140micrograms tablet blister pack ⁹	Treatment of osteoporosis in select patients where vitamin D supplementation is recommended.
157805	12/12/2008	FOSAMAX PLUS* 70 mg/140 ug alendronic acid 70 mg and colecalfiferol 140 micrograms tablet blister pack export ⁹	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.
161137	25/03/2010	FOSAMAX PLUS D-CAL* alendronic acid 70mg/colecalfiferol 140 microgram tablet and 1250mg calcium carbonate tablet composite pack ⁹	Osteoporosis ^a in selected patients where vitamin D and calcium supplementation is recommended.
54380	10/07/1996	FOSAMAX ^A alendronic acid 40mg (as sodium) tablet blister pack (New dosage regimen 16/4/03) ⁹	Treatment of Paget's disease.
68428	22/09/1999	FOSAMAX ^A alendronic acid 5mg (as sodium) tablet blister pack ⁹	Prevention of osteoporosis in postmenopausal women with low bone mass (at least 1 standard deviation below the mean for young adults). Treatment and prevention of glucocorticoid-induced osteoporosis in those patients on long term corticosteroid therapy.
73520	03/04/2000	FOSAMAX ^A alendronic acid 10mg (as sodium) tablet blister pack ⁹	Treatment of Osteoporosis ^a . Treatment and prevention of glucocorticoid-induced osteoporosis in postmenopausal women not receiving oestrogen and who are on long term corticosteroid therapy.
73772	09/02/2001	FOSAMAX ^A once weekly alendronic acid 70mg (as sodium) tablet blister pack ⁹	Treatment of Osteoporosis. Osteoporosis must be confirmed by: the finding of low bone mass of at least 2 standard deviations below the gender specific mean for young adults or by the presence of osteoporotic fracture.

93333	06/03/2003	FOSAMAX ^a (Alendronate sodium) 70 mg tablet - uncoated bulk ^g	Treatment of: Osteoporosis, including glucocorticoid-induced osteoporosis. Osteoporosis must be confirmed by: - the finding of low bone mass of at least 2 standard deviations below the gender specific mean for young adults or by - the presence of osteoporotic fracture - Paget's disease of bone. Also indicated for the prevention of glucocorticoid-induced osteoporosis in those patients on long term corticosteroid therapy.
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* active ingredient is Alendronate sodium

† active ingredients are Alendronate sodium with Colecalciferol

‡ active ingredient is alendronate with colecalciferol and calcium carbonate.

Note: export only drugs have not been considered.

a confirmed by the finding of low bone mass of at least two standard deviations below the gender specific mean for young adults, or by the presence of osteoporotic fracture.

b sponsor Apotex Pty Ltd.

c sponsor Nycomed Pty Ltd

d sponsor Accord Healthcare Pty Ltd

e sponsor Ranbaxy Australia Pty Ltd

f sponsor Alphapharm Pty Ltd

g sponsor is Merck Sharp & Dohme Australia Pty Ltd

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

Appendix 4 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 $\geq 20\%$ reduction in height of the anterior or mid portion of a vertebral body relative to the posterior height of that body or a $\geq 20\%$ 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 $\geq 20\%$ reduction in height of the anterior or mid portion of a vertebral body relative to the posterior height of that body or a $\geq 20\%$ 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

			<p>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.</p>	
		4133	<p>Osteoporosis in a patient aged 70 years or older.</p> <p>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.</p>	≤-2.5
		4123	<p>Established osteoporosis in a patient with fracture due to minimal trauma.</p> <p>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</p>	N/A
Alendronate Sodium with Colecalciferol and Calcium Carbonate	70 mg + 140 microg + 500 mg	N/A	<p>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.</p>	<-1.0
		4122	<p>Corticosteroid-induced osteoporosis in a patient currently on long-term (≥ 3 months), high-dose (7.5 mg/day prednisolone or equivalent) corticosteroid therapy.</p> <p>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.</p>	≤-1.5
		4133	<p>Osteoporosis in a patient aged 70 years or older.</p> <p>Patient must not receive concomitant treatment with any other PBS-subscribed anti-resorptive agent for this condition.</p>	≤-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 $\geq 20\%$ reduction in height of the anterior or mid portion of a vertebral body relative to the posterior height of that body or a $\geq 20\%$ 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 $\geq 20\%$ reduction in height of the anterior or mid portion of a vertebral body relative to the posterior height of that body or a $\geq 20\%$ 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 $\geq 20\%$ reduction in height of the anterior or mid portion of a vertebral body relative to the posterior height of that body or a $\geq 20\%$ 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 $\geq 20\%$ reduction in height of the anterior or mid portion of a vertebral body relative to the posterior height of that body or a $\geq 20\%$ 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 $\geq 20\%$ reduction in height of the anterior or mid portion of a vertebral body relative to the posterior height of that body or a $\geq 20\%$ 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

			<p>Patient must not receive concomitant treatment with any other PBS-subscribed anti-resorptive agent for this condition.</p> <p>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.</p> <p>A vertebral fracture is defined as a $\geq 20\%$ reduction in height of the anterior or mid portion of a vertebral body relative to the posterior height of that body or a $\geq 20\%$ reduction in any of these heights compared to the vertebral body above or below the affected vertebral body</p>	
	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	<p>Osteoporosis in a patient aged 70 years or older.</p> <p>Patient must not receive concomitant treatment with any other PBS-subscribed anti-resorptive agent for this condition.</p> <p>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.</p>	≤ -3.0
		4123	<p>Established osteoporosis in a patient with fracture due to minimal trauma.</p> <p>Patient must not receive concomitant treatment with any other PBS-subscribed anti-resorptive agent for this condition.</p> <p>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.</p> <p>A vertebral fracture is defined as a $\geq 20\%$ reduction in height of the anterior or mid portion of a vertebral body relative to the posterior height of that body or a $\geq 20\%$ reduction in any of these heights compared to the vertebral body above or below the affected vertebral body</p>	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
Disodium 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 substance	N/R 3256	Treatment of hypercalcaemia of malignancy refractory to anti-neoplastic therapy Symptomatic Paget disease of bone	N/A

	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: Patient must have a Bone Mineral Density (BMD) T-score of -1.5 or less,	≤-1.5

		<p>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.</p>	
4149	<p>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.</p>	≤-3.0	
4157	<p>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 these heights compared to the vertebral body above or below the affected vertebral body.</p>	N/R	

		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 vial 10 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: Patient must be aged 70 years or older, AND the Clinical criteria is:	≤-2.5 N/A

			<p>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.</p>	
		4145	<p>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.</p>	
Carbamazepine	200 mg		<p>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.</p>	N/A
		N/R	<p>For item codes 5040G and 1724R, pharmaceutical benefits that have the form tablet 200 mg are equivalent for the purposes of substitution.</p>	N/A
Parathyroid Hormone				

Teriparatide	20 microgram/dose injection, 1 x 2.4 mL cartridge		<p>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:</p> <p>(a) has a bone mineral density (BMD) T-score of -3.0 or less; and</p> <p>(b) has had 2 or more fractures due to minimal trauma; and</p> <p>(c) has experienced at least 1 symptomatic new fracture after at least 12 months continuous therapy with an anti-resorptive agent at adequate doses.</p> <p>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.</p> <p>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.</p> <p>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.</p> <p>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.</p> <p>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.</p> <p>Note</p> <p>No applications for increased maximum quantities and/or repeats will be authorised.</p>	≤-3.0
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			<p>Continuing treatment for severe established osteoporosis where the patient has previously been issued with an authority prescription for this drug.</p> <p>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.</p> <p>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.</p> <p>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.</p> <p>Note No applications for increased maximum quantities and/or repeats will be authorised.</p>	
strontium ranelate	2 g	4117	<p>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.</p>	≤-3.0
		4123	<p>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.</p>	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
<p>1153 Heterotopic ossification.</p> <p>1165 Hypocalcaemia due to renal disease.</p> <p>1166 Hypoparathyroidism.</p> <p>1167 Hypophosphataemic rickets.</p> <p>1467 Vitamin D-resistant rickets.</p> <p>2636 Treatment 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.</p> <p>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.</p> <p>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.</p> <p>Note Anti-resorptive agents in established osteoporosis include alendronate sodium, risedronate sodium, denosumab, disodium etidronate, raloxifene hydrochloride, strontium ranelate and zoledronic acid.</p>				

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

3341 Treatment 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.

4052 Bone 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.

Finda

Appendix 5 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 \leq -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 , Zoledronic acid , Denosumab (for postmenopausal women), Teriparatide (\leq -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 (\leq -2.5), Alendronate sodium with Colecalciferol (\leq -2.5), Alendronate sodium with Colecalciferol and Calcium carbonate (\leq -2.5), Risedronate sodium (\leq -3.0), Risedronate sodium and Calcium carbonate (\leq -

		3.0), Risedronate sodium and Calcium carbonate with Colecalciferol (\leq -3.0), Zoledronic acid (\leq -3.0), Denosumab (\leq -2.5), Strontium ranelate (\leq -3.0 for women)
Corticosteroids use (MBS item 12312)	Alendronate sodium: 68428, 80333, 53158, 67262, 76851, 9333, 98944; Disodium etidronate: 46852; Risedronate sodium: 117667, 138211, 141530, 150618, 166838, 166853, 166942, 74135, 82746; Zoledronic acid: 134664;	Alendronate sodium (\leq -1.5), Alendronate sodium with Colecalciferol (\leq -1.5), Alendronate sodium with Colecalciferol and Calcium carbonate (\leq -1.5), Risedronate sodium (\leq -1.0 if patients on steroids for > 3 months), Risedronate sodium (\leq -1.5), Risedronate sodium and Calcium carbonate (NR), Risedronate sodium and Calcium carbonate with Colecalciferol (\leq -1.5), Zoledronic acid (\leq -1.5)
Male Hypogonadism (MBS item 12312)	No drug specifically indicated	No drug specifically indicated
Female Hypogonadism lasting >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, Zoledronic acid, Tiludronate disodium
Heterotopic ossification*	No drug specifically indicated	Disodium etidronate
hypercalcaemia of malignancy*	Sodium clodronate tetrahydrate: 181921, 181922,	Disodium pamidronate, Sodium clodronate

	66703, 66704,	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 6 Explanatory notes applicable for MBS items 12306 to 12323

Category 2 – DIAGNOSTIC PROCEDURES AND INVESTIGATIONS

Note 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 - eg 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;
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- (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

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