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Final decision analytic protocol (DAP) to guide the assessment of bone mineral density analyses using dual energy X-ray absorptiometry (DXA) for women and men aged 50-69 years with risk factors for osteoporosis

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MSAC and PASC

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

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

Purpose of this document

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

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

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

Purpose of application

The Department of Health and Ageing received a proposal for the listing of dual energy X-ray absorptiometry (DXA) on the Medicare Benefits Schedule (MBS) in June 2011. Osteoporosis Australia subsequently became involved in the preparation of the draft Decision Analytic Protocol (DAP) in March 2012.

This proposal is for the provision of an MBS item for bone densitometry by DXA scan to women and men over the age of 50 years who have significant risk factors for osteoporosis. This submission was originally formulated as a proposed Decision Analytic Protocol (DAP) by Osteoporosis Australia in conjunction with the Department of Health and Ageing.

Intervention

Description

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

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

Fractures are defined as minimal trauma fractures when the trauma is a result of a fall from standing height or less, and comprise a significant portion of the health burden caused by osteoporosis. Patients with minimal trauma fractures experience increased morbidity, complications, and increased mortality compared to age- and gender-matched peers. Predictors of minimal trauma fracture include age, muscle weakness, low bone mineral density, history of smoking, increased body sway and less physical activity (Center et al 2007). Common sites of minimal trauma fracture are the hip, pelvis, wrist, forearm and spine. Some fractures may not come to medical attention, for example it has been estimated that 50-75% of vertebral fractures are not diagnosed (Sanders et al 1999a). While the disease is not usually recorded as the primary cause of death, osteoporosis 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 osteoporosis (Table 1). The prevalence of osteoporosis is high in women, due to the decrease in oestrogen levels after menopause which result in higher rates of bone loss per year than in men. Low body mass index (BMI) (<18.5 kg/m^2) is also considered a risk factor for osteoporosis as it is often associated with lower levels of oestrogen.

Table 1 Risk factors for the development of osteoporosis

Type of risk factor	Examples
Fixed (non-modifiable) risk factors	Age (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
	Hyperparathyroisism
	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 2010b; Osteoporosis Australia 2011; Smith 2006.

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

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

The dynamics of bone remodelling require appropriate balance between bone formation and resorption. In a healthy individual, from birth until the age of approximately 20 years, bone formation exceeds resorption. At the end of this period, peak bone mass is achieved and between the ages of 20 and 40 is roughly maintained through the balance of bone formation and resorption (Marcus et al 2008). Following this period of equilibrium and with increasing age, bone resorption exceeds bone formation resulting in net bone loss. 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)

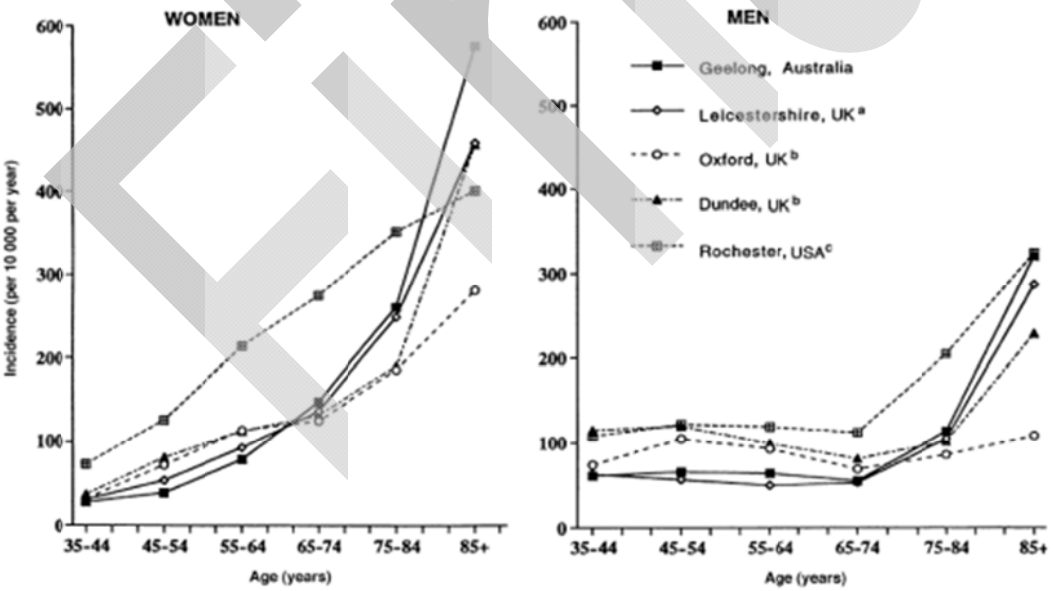
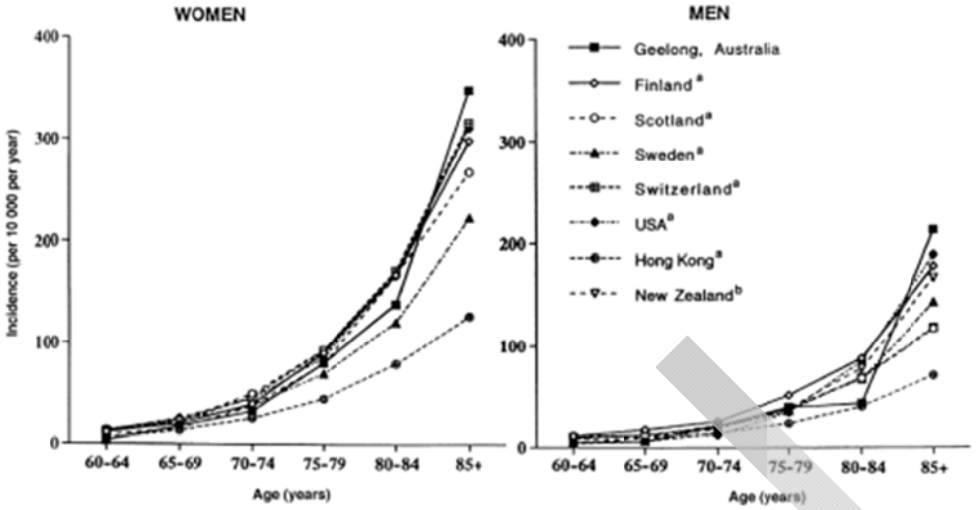


Figure 2 The rise in hip fracture rates with age in men and women (Sanders et al 1999b)



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

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

As a result of these changes, bone strength is affected, increasing the risk of developing osteoporosis (Riggs 2000). Prior to menopause in women, approximately at the age of 40, net bone loss proceeds at an initial rate of approximately 0.3-0.5 per cent per annum. In the first five years post-menopause the rate of bone loss increases to 2-3 per cent per annum, and may exceed 5 per cent per annum (Elders et al 1988). Following this the bone loss rate slows to around one per cent per annum.

A similar phenomenon occurs in men, but often does not occur until later in life or in association with other conditions. The three major causes of osteoporosis in men are alcohol abuse, glucocorticoid excess (either endogenous Cushing's syndrome or, more commonly, chronic glucocorticoid therapy), and hypogonadism (Bilezikian 1999). Osteoporosis is also of particular concern for men with prostate

cancer (Smith 2006). This net loss of the 'bone in bone', in other words the bone mineral density (BMD), frequently remains undiagnosed, and is most often clinically manifest as a skeletal fracture sustained with minimal trauma (WHO 2007).

Measurement of bone mineral density

DXA and quantitative computed tomography (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 has better reproducibility, and is considered more appropriate in general use than QCT which delivers higher doses of radiation. QCT may be preferred when measuring BMD in the presence of fractures, but has been excluded from this DAP (see Summary box below). Another tool for measuring BMD is quantitative ultrasound (QUS).

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

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

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, **Error! Reference source not found.**). 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 (**Error! Reference source not found.**).

Table 2 Diagnosis of osteoporosis according to T-score

T-score	Diagnosis
Equal or greater than -1.0	Normal bone density
Between -1.0 and -2.5	Low bone mass ("osteopenia": at risk for developing osteoporosis and increasing fracture risk)
Equal to or less than -2.5	Osteoporosis

Source: WHO 2007, RACGP 2010b

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 the intervention

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

Although the DXA device measures total density, the use of both high- and low-energy X-rays facilitates the separation of soft tissue and bone contributions to overall density (Dasher et al 2010). Scanning of the hip and spine usually takes up to a maximum of approximately 15-20 minutes (Dasher et al 2010).

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, 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 osteoporosis 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 rate of change between scans is not as important in overall management decisions.

Summary of the approach to assessment for the test

The **proposed test** is DXA.

Bone density testing with QCT is excluded for the following reasons:

- QCT results are less reproducible than DXA
- There is less robust evidence currently available to support the use of QCT
- Although QCT radiation doses are reducing over time, currently the use of QCT involves a higher dose of radiation than DXA so exposes patients to a greater degree of potential harm.
- There are no standardised Australian normative data for QCT.
- QCT assessment of the spine may overestimate osteoporosis compared to DXA using the WHO standard definitions.
- PASC recognise that QCT may be considered an alternative to DXA in the future.

Co-administered interventions

A variety of options exist for the prevention and treatment of osteoporosis. Preventive options include calcium and vitamin D supplementation, exercise and education (awareness). Additionally, prescription medication is available for certain conditions (RACGP 2010b).

Different preventive and treatment modalities include:

- Exercise - regular, progressive weight-bearing and resistance exercise aids in the preservation and increase of bone density
- Calcium and vitamin D – it is recommended that to optimise clinical efficacy, adequate calcium and vitamin D are required. If sufficient calcium cannot be obtained from diet, and adequate Vitamin D levels are not achieved by sun exposure, supplements may be required. Total calcium intake of 1000-1300 mg/day (combination of food and supplement) is recommended (RACGP 2010b). Where sun exposure is not adequate to generate sufficient Vitamin D levels, supplementation of vitamin D 700-800 IU/day is recommended (Nowson et al 2012).
- Selective oestrogen receptor modulators (SERMs) – decrease bone resorption via binding to oestrogen receptors and may best be used as an alternative to hormone therapy in women with contraindications (RACGP 2010b).
- Bisphosphonates–The bisphosphonates currently used in Australia include alendronate, disodium etidronate, risedronate, and zoledronic acid. These drugs reduce the risk of fractures by

increasing bone density through the reduction of osteoclast activity. On average, these drugs lead to an increase in bone density by approximately 4-8% at the spine and 1-3% at the hip over the first 3-4 years of treatment.

- Monoclonal antibodies (Denosumab) – the RANK Ligand inhibitor, monoclonal antibody Denosumab binds to a specific ligand which is required for osteoclast formation. This inhibition of osteoclast formation results in decreased bone resorption and increased bone mass and strength in both cortical and trabecular bone.
- Teriparatide (parathyroid hormone) – Teriparatide increases new bone formation through a reduction in osteoblast apoptosis. Due to its great expense and potentially deleterious side effects (including a potential increased risk of osteogenic sarcoma), teriparatide is only reimbursed by the PBS for severe established osteoporosis in patients with a very high risk of fracture (RACGP 2010b).

Anti-osteoporotic medications on the ARTG are listed according to relatively broad indications (Appendix 1 Examples of treatments currently listed on the ARTG for the treatment of osteoporosis). For example, alendronate sodium is available to post-menopausal 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 anti-osteoporotic medication are presented in Appendix 2 Indications, contraindications and potential complications of the co-administered interventions. PBS-listed anti-resorptive pharmaceuticals are listed by drug in Appendix 3 PBS listed pharmaceuticals (by drug) for the treatment of diseases of bone structure and mineralisation and by indication in Appendix 4 PBS listed pharmaceuticals (by indication) for treatment of diseases of bone structure and mineralisation.

<u>Clinical research questions for the assessment relating to the intervention:</u>

- What is the effect of prescription anti-resorptive medication on the rate of minimal trauma fracture in the target population?
- What is the rate of bone loss over time in the proposed population who are not provided test and therapy? What is the rate of bone loss over time in the proposed population who are provided test and therapy? Evidence provided in response to these questions will inform the number and frequency of DXA re-testing and monitoring (respectively). The frequency of re-testing and monitoring should be justified by the submission of available evidence.
- The proposed target population are men and women aged 50-69, with risk factors. For the purposes of sensitivity analysis the assessment phase should consider different age ranges (eg 55-69 years; 60-69 years; 65-69 years) for testing men and women. The assessment should also consider 'rollout' in people who are 55 years at the introduction (eg effectiveness in people who enter the proposed pathway after their 55th birthday).
- What proportion of the population at each defined age group will have a T-score of less than or equal to -2.5? This population will be provided with the proposed therapy (anti-resorptive medication). Similar evidence should be provided for any other relevant thresholds identified as part of the assessment.

- **NOTE**: As detailed under 'Population', there are a range of potential risk factors, combination of risk factors, and other prognostic factors that will define eligibility to this service.
    - Data for all elements of the assessment should be provided in terms of each specific risk factor or combination of risk factors.

Summary of the approach to assessment for the intervention

Test

The proposed test is DXA. 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 management informed by the result of a BMD test. The proposed thresholds are:

- For -1.0> T-score >-2.5, management would be through lifestyle and dietary advice;
- For T-score ≤-2.5, management would involve treatment with anti-resorptive medications in addition to lifestyle and dietary advice.

No specific PBS-listed medication is associated with this proposal.

The evaluation phase should provide evidence to determine the best **threshold for therapy** for anti-resorptive drug therapy. The assessment phase should address threshold to therapy as:

- The proposed T-score of ≤-2.5.
- The assessment should provide evidence on the appropriate threshold T-score(s) for access to therapy, including consideration of threshold T-score dependent on specific risk factors for osteoporosis.
- 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 re-testing** should be informed by evidence of the risk of minimal trauma fracture over time. PASC agreed that the submission of evidence needs to include information on the rate of bone loss in individuals who do not reach the nominated BMD threshold T-score to trigger anti-resorptive treatment to determine the appropriate frequency of BMD retesting in patients who do not reach this threshold. The frequency of re-testing should also be advised by the evidence of bone mineral density loss associated with specific risk factors for osteoporosis.

PASC noted one option might be retesting every 5 years, but are also aware that the Royal Australasian College of GP guidelines do not recommend retesting in 5-10 yrs.

For sensitivity analyses the following options should be evaluated regarding re-testing of the proposed population:

- T-score ≥-1.0: no repeat test; every 5 years; every 10 years
- -1.0 > T-score >-2.5: repeat test every 24 months
- T-score ≤-2.5: repeat test every 12-24 months (MBS item 12306)
- Re-testing using thresholds as advised by the evidence dependent on the specific risk factor(s) for osteoporosis.

PASC indicated that BMD test results should **not be used to monitor** treatment response in patients reaching the threshold for therapy.

Co-dependency

This DAP has a **co-dependency** with pharmaceutical agent(s) involving prescription medicines not currently PBS subsidised for the patient population in question. However, at this stage there is no concurrent co-dependent application.

As the use of prescription medicines is essential to the overall cost-effectiveness of this proposal, the necessary co-dependencies will need to be addressed for PBS listing as well as MBS listing purposes.

Note that the final eligibility criteria including threshold T-score of the proposed population to any co-dependent anti-resorptive drug would be defined by the Pharmaceutical Benefits Advisory Committee (PASC).

PASC agreed that the assessment of evidence will need to report the effectiveness of the co-dependent medicines in the proportion of the target population for BMD testing who achieve a threshold result to trigger the initiation of prescribed medication.

Background

Current arrangements for public reimbursement

Several different MBS items provide bone density scanning services on a variety of indications with repeat scans dependent on the indication. DXA scanning is not currently funded for the proposed patient population of women and men over the age of 50 and below the age of 70 unless they suffer from certain pre-defined conditions. Unconditional access to DXA scanning under the schedule is currently available to persons aged 70 years and over (MBS item number 12323). A variety of other patient populations are covered for DXA or QCT under the MBS (Table 3), including:

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

Relevant explanatory notes are in the Appendix 5 Medicare Benefits Schedule - Note D1.27.

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 SD), 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).

[1] It is recognized that an unintended knock on effect of this proposal is that there may be situation where there are individuals aged between 45-50 with hypogonadism who are not eligible for DXA. This will be addressed in the submission.

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

Category 2 – DIAGNOSTIC PROCEDURES AND INVESTIGATIONS, Bone Densitometry MBS 12306 Bone densitometry (performed by a specialist or consultant physician where the patient is referred by another medical practitioner), using dual energy X-ray absorptiometry, for: • The confirmation of a presumptive diagnosis of low bone mineral density made on the basis of 1 or more fractures occurring after minimal trauma; or • For the monitoring of low bone mineral density proven by bone densitometry at least 12 months previously. Measurement of 2 or more sites – 1 service only in a period of 24 months – including interpretation and report; not being a service associated with a service to which item 12309, 12312, 12315, 12318 or 12321 applies (Ministerial Determination). Fee: $102.40 Benefit: 75% = $76.80 85% = $87.05 Relevant explanatory notes: See Note D1.27
Category 2 – DIAGNOSTIC PROCEDURES AND INVESTIGATIONS, Bone Densitometry MBS 12309 Bone densitometry (performed by a specialist or consultant physician where the patient is referred by another medical practitioner), using quantitative computerised tomography, for: • the confirmation of a presumptive diagnosis of low bone mineral density made on the basis of 1 or more fractures occurring after minimal trauma; or • for the monitoring of low bone mineral density proven by bone densitometry at least 12 months previously. Measurement of 2 or more sites - 1 service only in a period of 24 months - including interpretation and report; not being a service associated with a service to which item 12306, 12312, 12315, 12318 or 12321 applies (Ministerial Determination) Fee: $102.40 Benefit: 75% = $76.80 85% = $87.05 Relevant explanatory notes: See Note D1.27
Category 2 – DIAGNOSTIC PROCEDURES AND INVESTIGATIONS, Bone Densitometry MBS 12312 Bone densitometry (performed by a specialist or consultant physician where the patient is referred by another medical practitioner), using dual energy X-ray absorptiometry, for the diagnosis and monitoring of bone loss associated with 1 or more of the following conditions: • Prolonged glucocorticoid therapy; • Conditions associated with excess glucocorticoid secretion; • Male hypogonadism; or • Female hypogonadism lasting more than 6 months before the age of 45 Where the bone density measurement will contribute to the management of a patient with any of the above conditions – measurement of 2 or more sites – 1 service only in a period of 12 consecutive months – including interpretation and report; not being a service associated with a service to which item 12306, 12309, 12315, 12318 or 12321 applies (Ministerial Determination) Fee: $102.40 Benefit: 75% = $76.80 85% = $87.05 *Relevant explanatory notes: See Note D1.27*
Category 2 – DIAGNOSTIC PROCEDURES AND INVESTIGATIONS, Bone Densitometry

MBS 12315

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

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

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

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

Relevant explanatory notes: See Note D1.27

Category 2 – DIAGNOSTIC PROCEDURES AND INVESTIGATIONS, Bone Densitometry

MBS 12318

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

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

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

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

Relevant explanatory notes: See Note D1.27

Category 2 – DIAGNOSTIC PROCEDURES AND INVESTIGATIONS, Bone Densitometry

MBS 12321

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

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

Measurement of 2 or more sites – 1 service only in a period of 12 consecutive months – including interpretation and report; not being a service associated with a service to which item 12306, 12309, 12312, 12315 or 12318 applies (Ministerial Determination)
Fee: $102.40 Benefit: 75% = $76.80 85% = $87.05

Relevant explanatory notes: See Note D1.27

Category 2 – DIAGNOSTIC PROCEDURES AND INVESTIGATIONS, Bone Densitometry
MBS 12323
Bone densitometry (performed by a specialist or consultant physician where the patient is referred by another medical practitioner), using dual energy X-ray absorptiometry or quantitative computerised tomography, for the measurement of bone mineral density, for a person aged 70 years or over.
Measurement of 2 or more sites – including interpretation and report; not being a service associated with a service to which item 12306, 12309, 12312, 12315, 12318 or 12321 applies (Ministerial Determination)
Fee: $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

A test for vitamin D sufficiency is available through MBS item 66608 (Vitamin D or D fractions – 1 or more tests, Fee $33.20). Anti-osteoporotic medication on the PBS is shown in Appendix 3 PBS listed pharmaceuticals (by drug) for the treatment of diseases of bone structure and mineralisation (by drug) and Appendix 4 PBS listed pharmaceuticals (by indication) for treatment of diseases of bone structure and mineralisation (by indication). PBS eligibility is in general focused to specific indications. A T-score is required for most indications, other than where patients have a fracture due to minimal trauma, where the fracture has been established using radiology.

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

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

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

* this item include both DXA and QCT

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: http://www9.health.gov.au/mbs/search.cfm, August 2012

Regulatory status

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

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

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

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

Patient population

DXA scanning is proposed for women and men with risk factors for osteoporosis (see Table 1) aged 50-69 years, who are not eligible for a test through existing MBS items. The clinical decision of whether to prescribe a test may be based on patients' comorbidities and risk factors (or combination of risk factors) for osteoporosis which are not covered by existing MBS items.

Risk factors

The specific risk factors associated with this population are:

- Age (men and women aged 50-69 years)
- During the assessment phase, the best age range threshold for testing and to initiate therapy should be identified.
- Risk factors associated with osteoporosis (as shown in Table 1), which are not covered by current MBS items.

Baseline population

The baseline population for this application is age and gender matched patients without specific risk factors for osteoporosis (aged 50-69 years).

Benchmark population

The benchmark population for this population is people aged 70 years and older. These are currently eligible for DXA scanning through the MBS and also eligible for PBS subsidy of anti-resorptive medication.

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)? This will confirm the clinical need for testing for bone mineral density in this population.
- What is the effect of different risk factors for osteoporosis on minimal trauma fracture or bone mineral density?
- What is the effect of combinations of more than one risk factor for osteoporosis on minimal trauma fracture or bone mineral density?
- Are there any prognostic factors such as patient age, or specific risk factors which impact on the rate of bone mineral density loss or elevate the risk of minimal trauma fracture in this population? This may inform the frequency of re-testing.
- For each relevant risk factor or combination, what threshold should be used for eligibility for a DXA test?
- What is the rate of bone mineral density loss in the proposed population? What is the rate of bone mineral density loss in the benchmark population? This will provide information regarding the frequency of re-testing for the proposed population in light of evidence pertaining to the benchmark population who are already eligible for BMD scanning through the MBS. For the benchmark population (people aged 70 years and older) re-testing is supported by MBS item 12323.

Summary of the approach to assessment for the population

The **population** is women and men with risk factors for osteoporosis aged 50-69 years.

The **baseline population** for this DAP is age and gender matched patients without specific risk factors for osteoporosis (aged 50-69 years).

The **benchmark population** for this DAP is people aged 70 years and older.

The assessment of evidence should attempt to inform on:

- The risk of minimal trauma fracture (or the extent of bone mineral density loss for baseline risk of minimal trauma fracture) in an individual aged 50-69 years with specific risk factors for osteoporosis.
- The rate of bone loss in the baseline population and the benchmark population.
    - Relevant risk factors should be provided separately.
    - Any cumulative effect of multiple risk factors.
    - Other prognostic factors such as age and gender should be reported.

This will be used to identify the baseline risk levels of minimal trauma fracture in the proposed population as compared to the baseline and benchmark populations. This will also inform questions of what specific risk factors for osteoporosis should be considered and how they will be used to form a preliminary assessment of the risk of minimal trauma fracture. This information will also provide an evidence base for the appropriate criteria for BMD testing eligibility

Note that a comparison of the rate of bone loss in the target population to the baseline and benchmark populations will need to take into account the age and gender of persons within those populations.

Excluded populations

- All men and women at age 70 and over are excluded, as these are eligible for current MBS items for DXA scanning.
- Men and women presenting with a minimal trauma fracture are excluded, as these 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

The proposed MBS item is shown in Table 6. For patients with T-scores less than or equal to -2.5 repeat scans would be available through the existing item 12306.

The applicant proposes making available, under a new MBS item, an initial DXA scan to women and men from the age of 50 who have recognised risk factors. The eligibility in relation to the risk factors present would be dependant of the number and the seriousness of the risk factors. The submission will address the optimal means of ranking or weighting the risk factors to ensure that the test is made available only to those with a real risk of having low bone density. Additional scans would be dependent on individual T-scores, ie individuals with high T-scores (≥-1.0) would not require any additional scans, whereas individuals with low T-scores (≤-2.5) would be eligible for additional scans every two years under MBS item number 12306 (Figure 3).

At present, neither normal healthy individuals, nor those individuals under the age of 70 with other risk factors groups (low BMI, family history, smoking, alcohol, low level of physical activity etc.) are covered for DXA analysis. The applicant proposes reducing the age of eligibility for DXA MBS

reimbursement to women and men with risk factors for osteoporosis over 50 years of age. Table 6 shows the proposed MSB item descriptor for bone densitometry in women and men with risk factors for osteoporosis over 50 years of age. A recommendation for use of an algorithm or risk calculator to weight the relative risk factors should be addressed in the submission. The proposed MBS item descriptor may need to be amended accordingly.

It is envisaged that people with a T-score which ≥-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 ≤-2.5 would be eligible for repeat testing under item Number 12306. (Note that thresholds and the 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

Category 2 – DIAGNOSTIC PROCEDURES AND INVESTIGATIONS, Bone Densitometry
MBS XXXXX
Bone densitometry (performed by a specialist or consultant physician where the patient is referred by another medical practitioner), using dual energy X-ray absorptiometry, for the measurement of bone mineral density in women and men aged 50-69 years or over with recognised risk factors for osteoporosis.
Measurement of 2 or more sites –1 service only in a period of 24 - 60 consecutive months –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]
(a) D1.27, Bone Densitometry – (Items 12306 to 12323)

Currently, no specific medication has been identified for use in the proposed population.

Clinical place for proposed intervention

The current diagnosis and management algorithm for suspected or proven low bone mineral density follows in Figure 3. The current and proposed algorithms for men and women aged 50-69, with risk factors follows in Figure 4 and Figure 5.

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

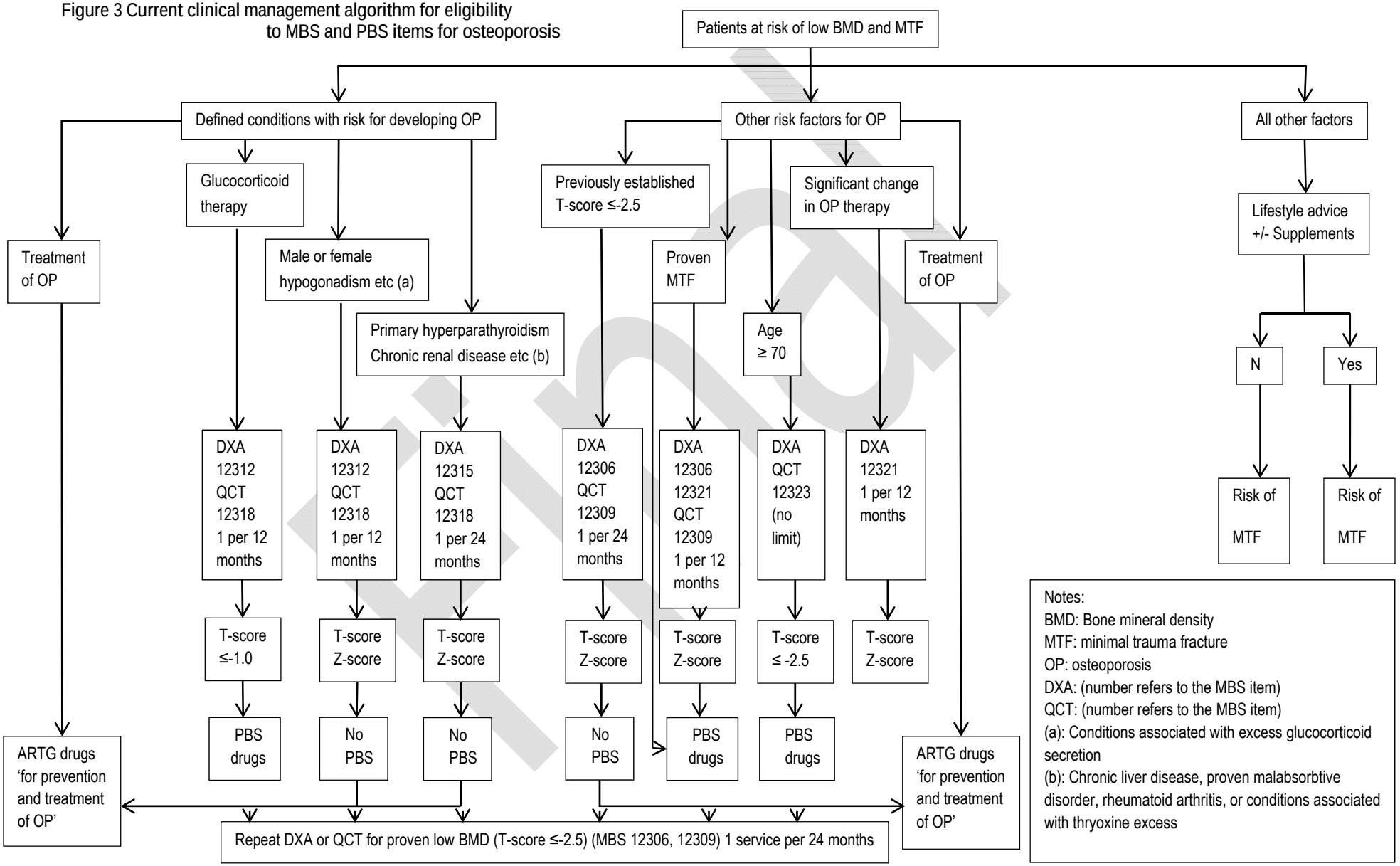


Figure 4 Current clinical management algorithm osteoporosis management of men and women aged 50-69, with risk factors

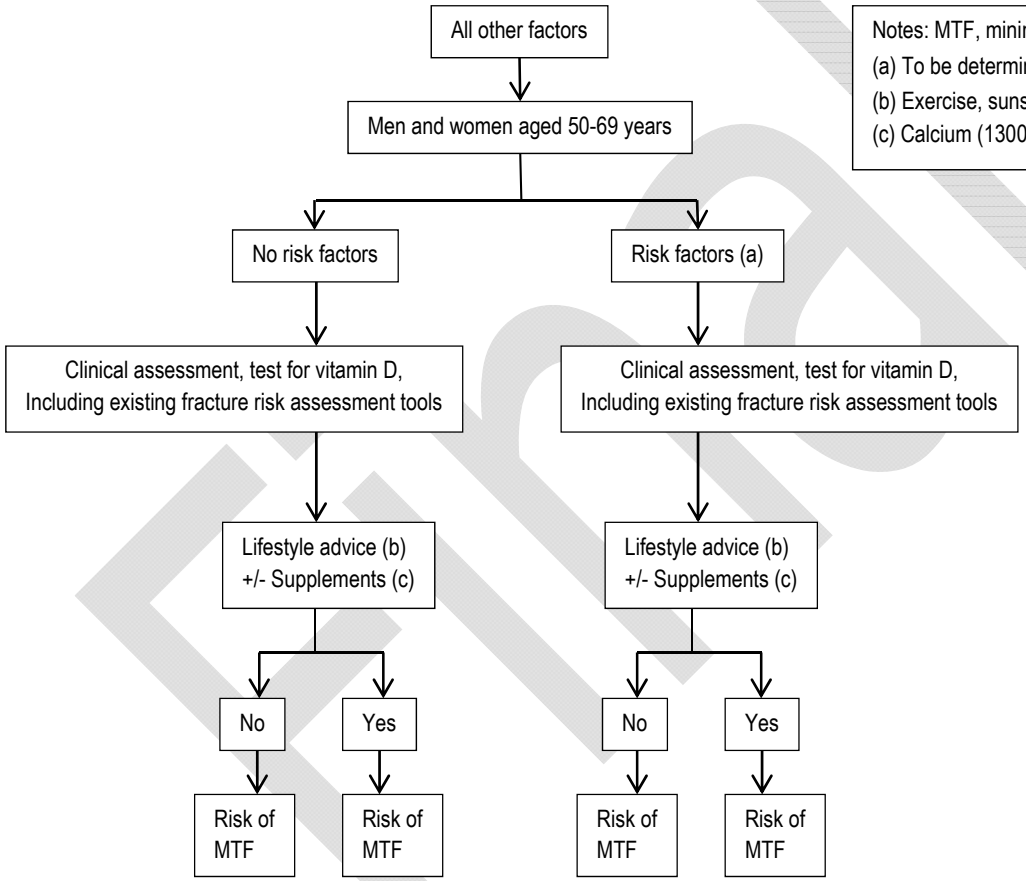
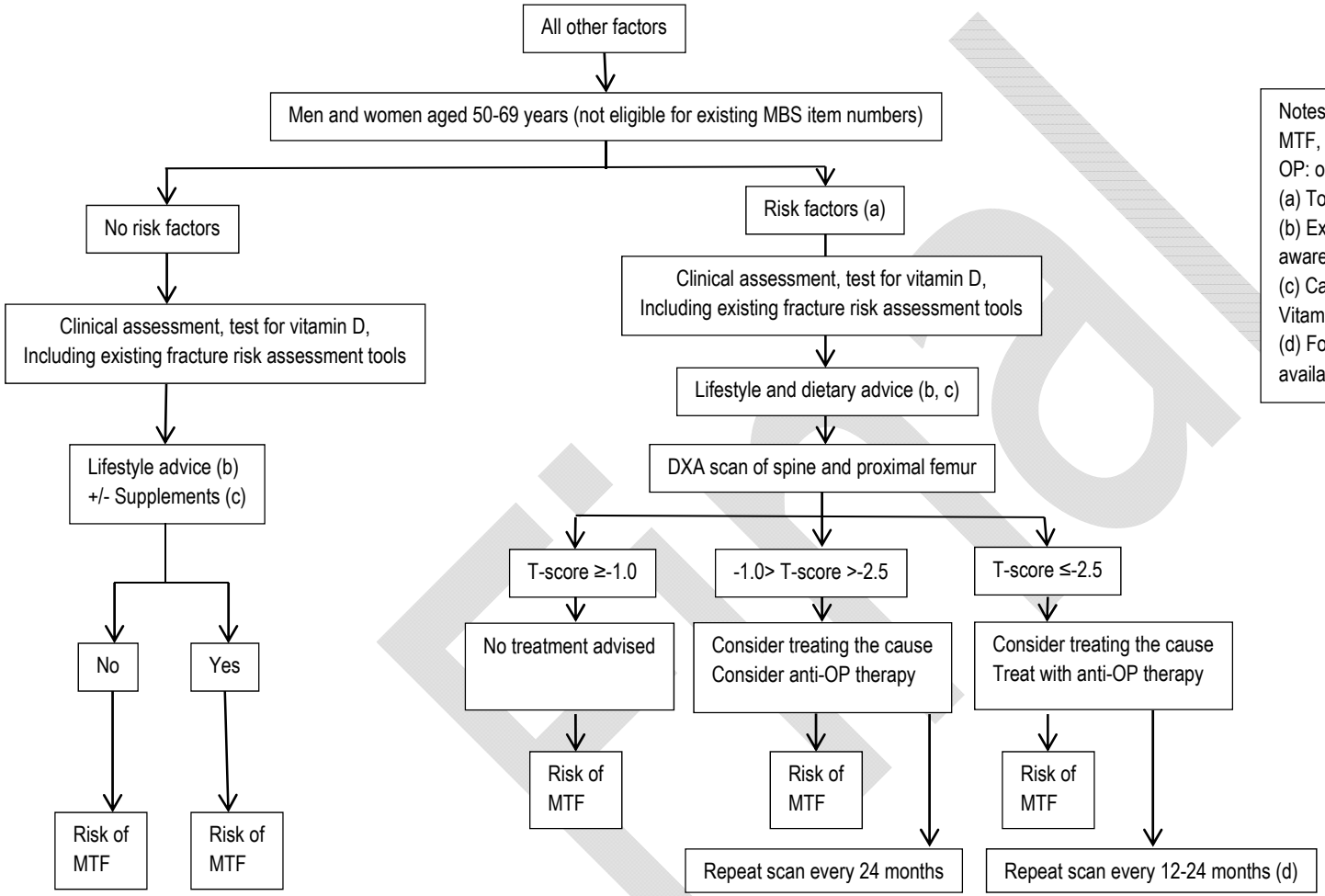


Figure 5 Proposed clinical management algorithm for osteoporosis management of men and women aged 50-69, with risk factors



Notes:
MTF, minimal trauma fracture
OP: osteoporotic
(a) To be determined
(b) Exercise, sunshine, general bone health awareness
(c) Calcium (1000-1300mg/d), ensure replete Vitamin D status >60nmol/L
(d) For T-score ≤-2.5, a repeat DXA would be available through existing MBS 12306 or 12321

Comparator

Currently people aged 50-69 years do not routinely receive DXA scanning, unless they have a specific condition associated with a current MBS item number. Vulnerability to the condition may be predicted through a clinical assessment, including a test for vitamin D and the use of existing fracture determinant tools. Ten-year fracture risk can be estimated through the use of on-line tools such as the FRAX tool (WHO 2007; WHO 2012). The 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 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 applicant claims that DXA scanning, when applied to women and men over the age 50-69 years and with risk factors for osteoporosis, may facilitate in the identification of those with low bone density who may otherwise have gone on to experience fractures.

While part of the population may be readily able to adapt their diet and lifestyle to have an adequate calcium intake and/or sufficient sun exposure to ensure adequate vitamin D levels the patient may be less likely to maintain motivation and persistence with such therapies in the absence of diagnosis. This may also be an issue when supplements are recommended by a GP to maintain bone health.

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

		Comparative effectiveness (DXA scanning) 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	None^	None^		
		Neutral benefit	CEA/CUA*				
		Net harms	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

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

Questions for the review relating to the economic evaluation

Cost effectiveness models should be undertaken:

- To establish the baseline scenario: What are the downstream costs and outcomes without the proposed intervention?
- To assess the proposed scenario: What are the downstream costs and outcomes with the proposed intervention?
- As noted throughout the DAP, sensitivity analyses should be undertaken around:
    - The factors, ages and eligibility criteria as specified in the proposal;
    - The variables as advised by the available evidence;
    - The variables as advised by PASC as being informative for sensitivity analyses to inform the final decision making.
- The economic analysis should account for different thresholds for therapy and re-treatment as advised by the available evidence.
- The economic evaluation should account for any prognostic factors and their impact on lowering bone mineral density, such as specific risk factors, age or gender.
- The economic evaluation should account for all patients in the target population who become eligible for current MBS items (for example through age or minimal trauma fracture).

Outcomes and health care resources affected by introduction of proposed intervention

Outcomes

Several outcomes are highlighted in the clinical pathway algorithms. It is proposed that a difference in outcomes 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.

Primary effectiveness outcomes:

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

Secondary effectiveness outcomes:

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

Safety outcomes and adverse events:

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

Please note:

- It is important to note all risk factors and their impact on loss of bone mineral density or minimal trauma fractures.
- All other prognostic factors for bone mineral density loss and minimal trauma fracture should be noted (such as age or gender).
- Where possible, the outcome of minimal trauma fracture should be disaggregated to type and location of fracture (eg hip vs. non-hip) as this is important to translate to any possible effects on life-years and quality-adjusted life-years.
- The site of the DXA exam (for example, proximal femur, lumbar spine, hip, distal radius) should be reported for all studies where possible. This is to account for any variability related to the site of the body where the testing is conducted.
- Where 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. This is to account for any variability of test results between machines.
- PASC acknowledges that DXA is associated with low radiation doses, but that increasing the

availability of DXA may significantly increase the exposure of the proposed population of otherwise healthy men and women to ionising radiation. This issue should be addressed in the assessment of evidence.

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 proposed intervention										
- Dual-Energy X-ray absorptiometry device	Technician	Mainly private, but there may be some public	TBA	1 per patient	MBS					
- GP visit for referral to DXA	GP				MBS					
- GP visit to discuss results and to provide advice	GP				MBS					
Resources provided in association with proposed intervention										
- Dietary supplements									Patient cost	
- Vitamin D test			TBA		Fee $33.20					
- Treatment	Pharmacy	Private	Unknown	Variable**	$37.38 to $589.17	$5.60 to $34.20				
- Costs associated with a fracture	Public or private hospital									

	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
- Costs associated with recovery from a fracture									Patient cost	

*eligible patients will be referred to have a DXA scan performed through their GP or other health professional in each case **although the duration of treatment per prescription varies, prescriptions usually contain sufficient medicine to treat the patient for 28 days.

Proposed structure of economic evaluation (decision-analytic)

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 age 50-69 with risk factors for osteoporosis (risk factors undefined). Subgroups of interest: • Data for each risk factor should be reported separately • Data corresponding to any other prognostic factor for low mineral density (such as age or gender) should be reported separately. Follow-up options: • T-score ≥-1.0, no re-test required. • -1.0> T-score >-2.5, re-test every 24 months. • T-score ≤-2.5, re-test every 12-24 months (repeat test available through MBS item 12306). Exclude: All women at age 70 and over, women with a previous minimal trauma fracture, all women currently eligible for MBS items for scanning for bone mineral density.	Dual energy X-ray absorptiometry (DXA) scanning and treatment at the following thresholds: • T-score ≥-1.0, no treatment required • -1.0> T-score >-2.5, lifestyle and dietary advice, consider anti-resorptive medication • T-score≤-2.5, anti-resorptive medication Sensitivity analysis should investigate other options of threshold to therapy as advised by the evidence. QCT is excluded.	Clinical assessment including the use of existing fracture risk assessment tools (including vitamin D test) with lifestyle and dietary advice. DXA and QCT scanning are excluded	Primary effectiveness outcomes: •Incidence of minimal trauma fractures •Incidence of all new fractures •Patient-related quality of life Secondary effectiveness outcomes: •Change in morbidity/mortality •Bone mineral density (as determined by T-score) Safety outcomes and adverse events: • Any adverse event or complication related to the DXA scanning or treatments for osteoporosis • Any adverse event arising from exposure to ionising radiation.	See Table 8.

Please note:

It will be important to report all outcomes according to risk factor, or combination of risk factors.

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

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

Table 10 Summary of issues relating to the approach to assessment

Population	Women and men with risk factors for osteoporosis aged 50-69 years.
Context	DXA scanning is proposed for women and men with risk factors for osteoporosis aged 50-69 years. PASC has identified a need to inform questions of what specific risk factors for osteoporosis should be considered and how they will be used to form a preliminary assessment of the risk of minimal trauma fracture. An initial list of risk factors is shown in Table 1. PASC has also recognised the need to identify criteria of eligibility for access to BMD testing.
Baseline population	The baseline population for this application is age and gender matched patients without specific risk factors for osteoporosis (aged 50-69 years).
Benchmark population	The benchmark population for this population is people aged 70 years and older. These are currently eligible for DXA scanning through the MBS and also eligible for PBS subsidy of anti-resorptive medication.
Approach to assessment	The assessment phase should identify: • Specific risk factors for OP and the baseline risk of MTF associated with each risk factor • Threshold scores for re-testing and for therapy for each identified risk factor • Interrelationships between multiple risk factors for OP • Any other prognostic factors associated with bone mineral density loss such as age or gender.
Intervention	DXA test for bone mineral density with lifestyle and dietary advice. Therapy with anti-resorptive drugs when a threshold T-score is reached.
Context	The proposed test is DXA. The proposed therapy is anti-resorptive drugs. This is a co-dependent application involving prescription medicines which are not currently PBS-subsidised for this purpose. PBAC would need to consider whether to subsidise the subsequent anti-resorptive treatment when indicated by the BMD test result.
Co-dependency	There is a co-dependency for this DAP. The assessment of evidence will be required to present evidence with regards to the efficacy of the co-dependent medicine in the proportion of the target population for BMD testing who achieve a threshold result to trigger the initiation of prescribed medication. At this stage no co-dependent submission has been received.
Treatment threshold	The proposed threshold is a T-score of less than or equal to -2.5 for the initiation of anti-osteoporotic treatment. For -1.0> T-score > -2.5 lifestyle and dietary advice would be provided, and consideration would be given to treatment with anti-resorptives.
Context	PASC considered that different BMD thresholds should be examined as the trigger for therapy, as advised by the evidence.
Approach to assessment	The assessment phase should provide evidence to support the proposed threshold for initiating treatment. As part of this the assessment phase should inform on: • The extent of bone loss in an individual aged 50-69 years with specific risk factors for osteoporosis, but not taking anti-resorptive agents. To support the nominated BMD threshold T-score to trigger anti-resorptive treatment. Each threshold should be reported in the context of the risk factor or combination of risk factors, or other prognostic factors associated with bone mineral density loss. The assessment phase should also undertake sensitivity analyses to examine T-score thresholds of: • T-score <-1.5 • T-score <-2.0 • Sensitivity analyses around T-scores of -1.0, -2.0 and -2.5
Re-testing and monitoring	The submissions should present evidence to inform questions of re-testing. BMD testing should not be used for the purposes of monitoring in this population.
Context	PASC considers that the timing and frequency of re-testing should be informed by evidence. PASC noted that guidelines from the College of GPs do not recommend retesting within 5-10 years of the initial test.
Approach to assessment	The assessment phase should address questions regarding the rate of bone loss in individuals who do not reach the nominated BMD threshold T-score to trigger anti-resorptive treatment. This should be done with respect to specific risk factors for osteoporosis. Sensitivity analyses should investigate the following options of re-testing: T-score ≥-1.0: no re-test; re-test every 5 years; re-test every 10 years T-score between -1.0 and -2.5: re-test every 24 months T-score ≤-2.5: re-test every 12-24 months (MBS item 12306) Re-testing as advised by the 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	Outcomes include primary effectiveness, secondary effectiveness and safety outcomes. Minimal trauma fracture is a primary effectiveness outcome.

	Primary effectiveness outcomes: • Incidence of minimal trauma fractures • Incidence of all new fractures • Patient-related quality of life Secondary effectiveness outcomes: • Change in morbidity/mortality • Bone mineral density (for example as provided by T-score). Safety outcomes and adverse events: • Any adverse event or complication related to the DXA scanning or treatments for OP • Any adverse event arising from exposure to ionising radiation.
Approach to assessment	It is important to note all risk factors and their impact on loss of bone mineral density or minimal trauma fractures. All other prognostic factors for bone mineral density loss and minimal trauma fracture should be noted (such as age or gender). Where possible, the outcome of minimal trauma fracture should be disaggregated to type and location of fracture (eg hip vs non-hip) as this is important to translate to any possible effects on life-years and quality-adjusted life-years. The location of the DXA exam (for example, proximal femur, lumbar spine, hip, distal radius) should be reported for all studies where possible. Where 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. PASC acknowledges that DXA is associated with low radiation doses, but that increasing the availability of DXA may significantly increase the exposure of the proposed population of otherwise healthy men and women to ionising radiation. This issue should be addressed in the assessment of evidence. Outcomes should be separated according to sub-populations where possible.

OP: osteoporosis

Clinical research questions for public funding

- What is the safety of DXA and management of bone mineral density compared with no DXA and no bone loss management (or non-prescription bone loss management) for individuals aged 50-69 years with risk factors?
- What is the effectiveness of DXA and management of bone mineral density compared with no DXA and no bone loss management (or non-prescription bone loss management) for individuals aged 50-69 years with risk factors?
- What is the cost effectiveness of DXA and management of bone mineral density compared with no DXA and no bone loss management (or non-prescription bone loss management) for individuals aged 50-69 years with risk factors?
    - Sensitivity analyses should be undertaken to provide information on the range of variables identified throughout this DAP.
- The response to each question should account for:
    - What risk factors currently not reflected in the MBS are most relevant for osteoporosis?
    - For each risk factor identified, what should the threshold be for treatment with anti-resorptive medication?
    - How should multiple risk factors and their interactions be considered in terms of treatment with anti-resorptive medication?
    - What should be the frequency of re-testing in each identified 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; Alendronate (Fosamax), Disodium etidronate (Didrocal), Risedronate（Actonel), Zoledronic Acid (Aclasta) ***[prevention (Grade A), treatment (Grade A)]*** ARTG: Fosamax: 113482,120028,136846,157805, 161137, 53158, 54380, 67262, 68428, 73520, 73772, 76851, 93333, 98944; Dirrocal: 46852; Actonel: 117667, 138211, 141530, 150618, 166838, 166853, 166942,74135, 74136, 82746; Aclasta: 134664; Clodronate: 181921, 181922, 66703, 66704, 80125, 80130		
Indication	**Contraindication**	**Side effects**
Paget's disease of bone Prevention and treatment of osteoporosis (including postmenopausal and corticosteroid-induced) Hypercalcaemia of malignancy Prevention of skeletal-related events in patients with malignancies involving bone Prevention and treatment of heterotopic ossification due to spinal cord injury or complicating total hip replacement	Abnormalities of the oesophagus which delay oesophageal emptying, such as stricture or achalasia. Inability to stand or sit upright for at least 30 minutes. Hypersensitivity to any component of bisphosphonates. Hypocalcaemia. Severe hypercalciuria.	*Common* nausea, vomiting, diarrhoea, headache, hypocalcaemia, musculoskeletal pain (may rarely be severe and/or disabling) IV: fever, flu-like symptoms, injection site reaction, increased creatinine concentration, hypophosphataemia, myalgia, bone pain, hypertension *Infrequent* oesophagitis, oesophageal erosions and ulcers (mainly with alendronate), gastritis, duodenitis, glossitis, rash IV: hypotension, hypomagnesaemia, hypokalaemia *Rare* heart failure, renal impairment, ocular inflammation, osteonecrosis of the jaw, allergic reactions including angioedema IV: anaphylactic shock *Osteonecrosis of the jaw Risk appears to be associated with the potency, route and total dose of bisphosphonate and a history of dental surgery, trauma or disease. *Possible associations* Atypical low-energy femoral fractures have occurred rarely during long-term bisphosphonate treatment for osteoporosis. It is possible that bisphosphonates slightly increase the risk of AF, although this association was not found in all studies. Some epidemiological data suggest an association between long-term use of oral bisphosphonates and an increased risk of oesophageal cancer; further evidence is needed.
Hormone Replacement Therapy		

[prevention (Grade A), treatment (Grade A)]

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

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

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

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

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

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

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

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

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

	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).	

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

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

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

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

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

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

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

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

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

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

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

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

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

			AND the Clinical criteria is: Patient must not receive concomitant treatment with any other PBS-subsidised anti-resorptive agent for this condition, AND the Clinical criteria is: Patient must not receive more than one PBS-subsidised treatment per year. The duration and dose of corticosteroid therapy together with the date, site (femoral neck or lumbar spine) and score of the qualifying BMD measurement must be documented in the patient's medical records when treatment is initiated.	
		4149	Osteoporosis The Population criteria is: Patient must be aged 70 years or older, AND the Clinical criteria is: Patient must have a Bone Mineral Density (BMD) T-score of -3.0 or less, AND the Clinical criteria is: Patient must not receive concomitant treatment with any other PBS-subsidised anti-resorptive agent for this condition, AND the Clinical criteria is: Patient must not receive more than one PBS-subsidised treatment per year. The date, site (femoral neck or lumbar spine) and score of the qualifying BMD measurement must be documented in the patient's medical records when treatment is initiated.	≤-3.0
		4157	Established osteoporosis The Clinical criteria is: Patient must have fracture due to minimal trauma, AND the Clinical criteria is: Patient must not receive concomitant treatment with any other PBS-subsidised anti-resorptive agent for this condition, AND the Clinical criteria is: Patient must not receive more than one PBS-subsidised treatment per year. The fracture must have been demonstrated radiologically and the year of plain x-ray or computed tomography (CT) scan or magnetic resonance imaging (MRI) scan must be documented in the patient's medical records when treatment is initiated. A vertebral fracture is defined as a 20% or greater reduction in height of the anterior or mid portion of a vertebral body relative to the posterior height of that body, or, a 20% or greater reduction in any of these heights compared to the vertebral body above or below the affected vertebral body.	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 vial10 mg	3342	Multiple myeloma	N/A
		3343	Bone metastases from breast cancer	N/A
		4052	Bone metastases from castration-resistant prostate cancer	N/A
		3341	hypercalcaemia of malignancy refractory to anti-neoplastic therapy	N/A
Selective estrogen receptor modulator (SERM)				
raloxifene hydrochloride	60 mg	4071	Established post-menopausal osteoporosis The Clinical criteria is: Patient must have fracture due to minimal trauma, AND the Clinical criteria is: Patient must not receive concomitant treatment with any other PBS-subsidised anti-resorptive agent for this condition. The fracture must have been demonstrated radiologically and the year of plain x-ray or computed tomography (CT) scan or magnetic resonance imaging (MRI) scan must be documented in the patient's medical records when treatment is initiated. A vertebral fracture is defined as a 20% or greater reduction in height of the anterior or mid portion of a vertebral body relative to the posterior height of that body, or, a 20% or greater reduction in any of these heights compared to the vertebral body above or below the affected vertebral body.	N/A
Monoclonal antibody				
Denosumab	120 mg/1.7ml	4158 4150	Bone metastases from breast cancer Bone metastases from castration-resistant prostate cancer	N/A
	60 mg/ml	4094	Osteoporosis The Population criteria is: Patient must be female, AND the Population criteria is: Patient must be aged 70 years or older, AND the Clinical criteria is:	≤-2.5 N/A

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

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

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

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

1153 Heterotopic ossification.

1165 Hypocalcaemia due to renal disease.

1166Hypoparathyroidism.

1167 Hypophosphataemic rickets.

1467 Vitamin D-resistant rickets.

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

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

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

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

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

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

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

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

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

3256 Symptomatic Paget disease of bone.

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

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

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

3342 Multiple myeloma

3343 Bone metastases from breast cancer

3256 Symptomatic Paget disease of bone.

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

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

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

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

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

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

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

4052Bone metastases from castration-resistant prostate cancer.

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

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

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

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

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

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

Appendix 5 Medicare Benefits Schedule - Note D1.27

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

Item 12321 is intended to allow for bone mineral density measurement following a significant change in therapy - 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;

(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