National Institute for Health and Care Excellence

Health Technology Evaluation

Medicines for treating osteoporosis and reducing the risk of fragility fractures (review of TA160, TA161, TA204, TA464, TA791 and TA991)

Response to stakeholder organisation comments on the draft remit and draft scope

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Comment 1: the draft remit and proposed process

Section	Stakeholder	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	Amgen	Amgen welcomes the opportunity to comment on the draft remit and draft scope for the Multiple Technology Appraisal (MTA) on medicines for treating osteoporosis and reducing the risk of fragility fractures. We appreciate NICE's transparent approach and the opportunity for stakeholder input at this early stage. Amgen agrees that a Multiple Technology Appraisal is an appropriate evaluation route for this topic. Given the number of established and emerging therapies for osteoporosis, an MTA offers a coherent framework to compare clinical and cost effectiveness across treatments and to ensure consistency with prior NICE technology appraisals. We support the review of multiple existing TAs to reflect evolving evidence, clinical practice, and NHS service delivery.	Thank you for your comment. No action required.

Section	Stakeholder	Comments [sic]	Action
	ABPI	No comments	No action required.
	BCUHB	4.1 FRAX vs Q fracture. Our organisation uses FRAX and this has been useful as it is widely used by GPs, clinicians and falls prevention services. The q fracture requires a lot of information that is not readily available to the clinician and the falls prevention services.	Thank you for your comment. No action required.
	BHC	Based on the currently available evidence and the characteristics of the technologies under consideration, evaluating this topic is both appropriate and timely. Earlier data highlight several issues that support a structured NICE evaluation: • Heterogeneity and gaps in the evidence base: Across the relevant clinical trials, reporting of key demographic variables particularly ethnicity is inconsistent or absent. This limits the ability to assess generalisability across diverse UK populations and underscores the need for a robust, standardised appraisal framework. • Under-representation of minority groups: The earlier data show that BAME populations are significantly under-represented in pivotal trials. This raises important questions about external validity, equity of access, and the applicability of trial outcomes to real-world NHS settings. Given these considerations, the multiple technology appraisal (MTA) route appears the most appropriate.	Thank you for your comment. No action required.
	BSR	Highly appropriate. There is unwarranted variation of care and inequity of access to medicines for treating osteoporosis and reducing the risk of fragility fractures. This is particularly important for adults at high imminent fracture risk after a recent major fragility fracture (FLS-DB report 2026 Appendix A figure 5 [https://www.rcp.ac.uk/95436])	Thank you for your comment. No action required.

Section	Stakeholder	Comments [sic]	Action
	FFFAP RCP	This evaluation is urgently required. The Falls and Fragility Fracture Audit is part of the NHS National Clinical Audit and Patient Outcomes Programme (NCAPOP) benchmarking the care of adults who are admitted with a hip fracture, have an injury after an inpatient falls and adults who are diagnosed with a fragility fracture. Successive reports have highlighted unexplained variation in case-finding and management between NHS services in England. This evaluation will streamline the assessment and management of this vulnerable patient group.	Thank you for your comment. No action required.
	NOGG	There is a disconnect between TAs which leaves patients in limbo sometimes, especially if non-specialists are providing care. There is no consistent and joined up connection between therapies that have been derived from NICE.	Thank you for your comment. No action required.
	Northumbria NHSFCT	Appropriate	Thank you for your comment. No action required.
	PAO UK	None	No action required.
	PrescQIPP	None	No action required.
	ROS	Highly appropriate. There is unwarranted variation of care and inequity of access to medicines for treating osteoporosis and reducing the risk of fragility fractures. This concern is reinforced by the findings of the All-Party Parliamentary Group on Osteoporosis and Bone Health inquiry, *Equal Access to Strong Bones*, which identified persistent geographical variation in access to assessment, diagnosis and pharmacological treatment, and highlighted the consequences for patients when effective medicines are not offered consistently across the system.	Thank you for your comment. No action required.

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	Theramex	Theramex support the need for an evaluation of treatments for osteoporosis considering updated guidelines, from both a clinical and cost-effectiveness perspective. Theramex support the selection of the evaluation route proposed, being a Multiple Technology Appraisal (MTA). We acknowledge the challenge in bringing together different product types in an MTA e.g. osteoanabolics, bisphosphonates, and other agents that influence bone metabolism each with varying applicability across patient subgroups. The aim is to establish clear and consistent positioning within the treatment pathway, enabling clinicians and patients to make informed treatment decisions. The most important consideration when looking across the full breadth of treatment options and patient populations is to ensure the most appropriate treatment choice and sequencing of treatments based on the assessment of efficacy, safety and value. Previous single technology appraisals have highlighted that osteoanabolics are distinct from antiresorptive treatments in their mechanism of action and concerning the patients they are indicated to be used in - they are not direct comparators. It is requested to bring this distinction into the MTA to avoid homogenising classes of therapy that are distinct.	Thank you for your comment. NICE will appraise all technologies within their marketing authorisations and within the context of the update of NICE's guideline on osteoporosis. In an MTA, all comparators are compared to one another.
	UCB	UCB supports updating the osteoporosis guideline to ensure patients receive the most appropriate treatment in the most clinically optimal way. Undertaking the scoping for the MTA in parallel with the guideline update introduces a significant risk of misalignment. If feedback submitted during the guideline consultation leads to changes in recommendations or care pathways, these amendments may subsequently require the MTA to be re-scoped. This would create unnecessary delays, duplication of effort, and potential inconsistencies between the guideline and the MTA.	Thank you for your comment. The osteoporosis clinical guideline update and MTA scope will be aligned ahead of the MTA scope being finalised.

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		To avoid this disconnect, it would be preferable for NICE to first finalise the scope of the guideline update or at minimum clarify the intended direction of changes before progressing with the MTA scoping.	
Wording	Amgen	Amgen considers that the draft remit broadly reflects the key issues of clinical and cost effectiveness relevant to medicines for treating osteoporosis and reducing the risk of fragility fractures. In particular, it appropriately recognises the need to review multiple existing technology appraisals in light of evolving evidence, clinical practice, and NHS service delivery. However, Amgen believes the remit could be strengthened by more explicitly acknowledging patient heterogeneity and the importance of treatment sequencing and long-term management in osteoporosis. In clinical practice, treatment choice and cost effectiveness are strongly influenced by baseline fracture risk, prior fracture history, contraindications or intolerance to oral therapies, and issues of adherence and persistence over time. These factors are central to both clinical outcomes and value for money, yet are not fully explicit in the current wording. In addition, there is a well reported scale of undertreatment in osteoporosis, particularly after first fracture from the fracture liaison services database report published in 2025, which states that in the audited pathway, ~59% are recommended therapy post-fracture, but only ~35% are on therapy by 16 weeks, demonstrating a substantial diagnosis and implementation gap. As such, Amgen suggests that the remit could explicitly state that the evaluation will consider differences in clinical and cost effectiveness across relevant patient subgroups (including those at high or very high fracture risk, or those with a previous fracture) and across treatment sequences, including	Thank you for your comment. The remit wording is intentionally broad to avoid limiting the consideration of relevant clinical and cost-effectiveness factors that can be considered by the committee.

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		long-term use, discontinuation, and switching of therapies, where supported by the evidence. This clarification would better align the remit with real-world clinical decision-making and established NICE practice in osteoporosis appraisals.	
	ABPI	No comments	No action required.
	BCUHB	None	No action required.
	BHC	NICE is asked to evaluate the clinical and cost effectiveness of [technologies] for the treatment of osteoporosis, taking into account the heterogeneity and limitations of the existing evidence base. The evaluation should consider: • the lack of consistent reporting of key demographic variables, including ethnicity, and the implications for generalisability to the diverse UK population • the under-representation of minority ethnic groups and other high-risk subpopulations in pivotal trials • variability in trial design, comparators, and outcome definitions that may affect indirect comparisons and network meta-analysis • uncertainties in treatment effect estimates arising from limited subgroup analyses • the comparative clinical and cost effectiveness of the technologies when used in NHS practice Given the overlapping indications and shared evidence limitations, a multiple technology appraisal (MTA) is recommended to ensure a consistent, transparent and comparative assessment.	Thank you for your comment. No action required.

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	BSR	Yes 'experienced menopause' is an unusual term and implies someone has experienced symptoms. Post-menopausal should be used.	Thank you for your comment. Women who have experienced menopause is preferred because it aligns with the NICE style guide.
	FFFAP RCP	The current wording places equal prioritisation for primary and secondary prevention. Given the pressures on the NHS the key issue is prioritisation of secondary fracture prevention over primary prevention as a health care priority as patients who have already had a fracture are at higher fracture risk and so will benefit more from improved guidance on assessment and management than most patients who have not had a fracture. We recognise there a sub groups who are at high fracture risk in the primary prevention setting, such as those initiating glucocorticoids and would be included in the very high risk primary prevention setting.	Thank you for your comment. NICE will appraise all technologies within their marketing authorisations and within the context of the update of NICE's guideline on osteoporosis.
	NOGG	'women who have experienced menopause' is not a recognised term – should be replaced with 'post-menopausal women' NOGG uses alendronate not alendronic acid, ibandronate not ibandronic acid etc, to avoid the word 'acid', which is offputting to patients and can challenge adherance. We suggest NICE adopts a similar approach in the wording used.	Thank you for your comment. Women who have experienced menopause is preferred because it aligns with the NICE style guide
	Northumbria NHSFCT	No comments	No action required.
	PAO UK	None	No action required.

Section	Stakeholder	Comments [sic]	Action
	PrescQIPP	None	No action required.
	ROS	The inclusion of five separate T-score thresholds (<–3.5, <–3.0, <–2.5, <–1.5, <–1.0) in Figure 2 is difficult to justify in the absence of clear supporting evidence. This level of complexity is neither practical nor patient-centred. It risks creating confusion for clinicians and patients alike, ultimately hindering real-world implementation. As currently presented, it does not align with the stated aim of producing recommendations that are “useful” and “usable.”	Thank you for your comment. Clinically relevant populations were determined by clinical expert consensus as part of the update to clinical guideline osteoporosis risk assessment, treatment and prevention of fragility fractures. Final intervention thresholds and higher risk subgroup criteria will be finalised through the guideline committee process, and will be aligned to the MTA scope.
	Theramex	No comment	No action required.
	UCB	The remit of this appraisal is to assess the clinical and cost-effectiveness of medicines to reduce the risk of fragility fracture, rather than to treat osteoporosis as defined by Bone Mineral Density (BMD) thresholds (currently there is no inclusion of a target for BMD or interventions that demonstrate measurable improvements in BMD that formally reduce the prevalence of	Thank you for your comment. The remit wording is intentionally broad to avoid limiting the consideration of relevant clinical and

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		osteoporosis). Evidence indicates that a substantial proportion of fragility fractures go untreated in individuals whose BMD does not meet conventional diagnostic thresholds for osteoporosis - consequently restricting access to treatment based solely on BMD would risk excluding patients who are at a clinically meaningful fracture risk and who may derive significant benefit from therapy.	cost-effectiveness factors that can be considered by the committee.
Timing issues	Amgen	Amgen considers this evaluation to be of high urgency for the NHS. Osteoporosis and fragility fractures represent a substantial and growing burden, driven by an ageing population and increasing prevalence of multimorbidity. Fragility fractures are associated with significant morbidity, excess mortality, loss of independence, and high healthcare resource use, including hospital admissions and long-term care. Several NICE technology appraisals in this therapeutic area were published at different points in time and under varying methodological contexts. Since then, there have been important developments in clinical evidence, treatment options, patterns of use, and service delivery models. In the absence of an updated, integrated appraisal, there is a risk of inconsistency in commissioning decisions, clinical practice variation, and suboptimal targeting of treatments to those most likely to benefit. A timely MTA has the potential to: • support more consistent and equitable access to effective osteoporosis treatments, • improve fracture prevention and patient outcomes,	Thank you for your comment. No action required.

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		• and help the NHS allocate resources efficiently in an area with significant downstream costs if fractures are not prevented. For these reasons, Amgen believes that progressing this evaluation without undue delay is important to support NHS clinical decision-making and long-term sustainability.	
	ABPI	No comments	No action required.
	BCUHB	None	No action required.
	BHC	This evaluation is urgent enough to warrant prioritisation, because: • the evidence base contains unresolved uncertainties • the NHS population differs materially from trial populations • the financial and clinical consequences of suboptimal therapy selection are substantial • national consistency in osteoporosis management is increasingly important However, it is not an emergency evaluation; rather, it is a strategically important one that should be completed in a timely manner to support equitable, evidence-based prescribing.	Thank you for your comment. No action required.
	BSR	With the drive to effective FLS by 2030 there is an urgent need for clarity regarding the different of medicines to reduce the risk of fragility fractures and osteoporosis in adults based on clinical and cost effectiveness	Thank you for your comment. No action required.
	FFFAP RCP	There are over 154,000 adults who have broken a bone after a fall that year who are not receiving appropriate assessment and management according to current NICE recommendations. There is an urgent need for pragmatic recommendations that can be implemented equitably across the NHS by	Thank you for your comment. No action required.

Section	Stakeholder	Comments [sic]	Action
		multiple specialities and disciplines of healthcare providers beyond secondary care experts in bone health.	
	NOGG	This evaluation is well overdue but not urgent	Thank you for your comment. No action required.
	Northumbria NHSFCT	Very relevant – we have a number of new treatments with inconsistent criteria for use and older effective treatments that may be underused unless placed in context with the new technologies. An overview / updated MTA is very desirable	Thank you for your comment. No action required.
	PAO UK	None	No action required.
	PrescQIPP	None	No action required.
	ROS	None	No action required.
	Theramex	Theramex would like to clarify the likely timeframe for Guideline consolidation post-consultation. Theramex would like to clarify how the updates to the Guidelines after consultation will be translated to the Multiple Technology Appraisal (MTA) scope.	Thank you for your comment. The update to the osteoporosis risk assessment, treatment and prevention of fragility fractures guideline will be finalised shortly after the invitation to participate for the MTA. The MTA scope is aligned with the post-consultation updates.

Section	Stakeholder	Comments [sic]	Action
	UCB	No comment	No action required.
Additional comments on the draft remit	Amgen	None	No action required.
	ABPI	No comments	No action required.
	BCUHB	None	No action required.
	BHC	None	No action required.
	BSR	The commonest site of subsequent fracture are non-vertebral fractures and of these hip fractures have the most severe impact on survival, quality of life and costs to healthcare, social care as well as patients and families. We are now aware the ability to reduce non-vertebral fractures in terms of scale and time to onset is significantly different between osteoporosis technologies. The appraisal models should specifically address clinical and cost effectiveness based on reducing hip fracture and non-vertebral fractures and not just all fragility fractures. Please note that there is no “one size fits all” approach to prescribing osteoporosis medicines, and multiple combinations of prescribing and follow-up arrangements are possible. The choice of prescribing route and follow-up depends on multiple factors including patient preference, clinical contraindications, comorbidities, local service arrangements, and shared-care agreements between primary and secondary care. In addition, drug sequencing is important as the effectiveness of drugs is affected by patient prior drug exposure. This reflects the flexibility required in real-world osteoporosis management.	Thank you for your comment. The outcome of osteoporotic fragility fracture is intentionally broad and doesn’t exclude specific types of fractures from being captured as outcomes. Specifying types of fragility fractures may limit the outcomes captured but can be considered in the analysis if evidence allows.
	FFFAP RCP	None	No action required.

Section	Stakeholder	Comments [sic]	Action
	NOGG	None	No action required.
	Northumbria NHSFCT	None	No action required.
	PAO UK	According to the draft remit this MTA will focus on men aged over 50 and postmenopausal women. However, in some cases there is a need to consider pharmacological treatment in younger men and premenopausal women due to significantly elevated fracture risk. These individuals would usually be managed by a specialist which is appropriate and should be made explicit in this NICE guidance. Currently there is a lack of management guidance in this area leading to significant variations in practice between specialists. Hence, there is an urgent need to review the existing evidence on the efficacy and safety of pharmacological treatment in this younger age group, and to systematically collect evidence of outcomes when pharmacological treatment is given to these individuals (recommendation for research).	Thank you for your comment. During the update to the clinical guideline osteoporosis risk assessment, treatment and prevention of fragility fractures, the committee agreed that the risk of fragility fractures in younger people is uncommon. The population in the clinical guideline and the MTA scope will be aligned.
	PrescQIPP	None	No action required.
	ROS	None	No action required.
	Theramex	No comment	No action required.
	UCB	None	No action required.

Section	Stakeholder	Comments [sic]	Action

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Amgen	Overall, the draft remit appropriately captures the key decision problem for the NHS. We encourage NICE to ensure that the remit explicitly recognises: • The heterogeneity of the osteoporosis population, • Differences in baseline fracture risk, • The importance of treatment sequencing and long-term management, including considerations when stopping or switching therapy. Explicit reference to these issues would better reflect real-world clinical decision-making and NICE precedent.	Thank you for your comment. The aim of the background section is to provide a very brief summary of the disease area. Further data and information can be provided at the submission stage of the appraisal.
	ABPI	No comments	No action required.
	BCUHB	Identification of vertebral fractures: Is better due to the new radiology systems. This has implications on time- more referrals, treatments, OPD appointments ets. 4.1 Recommendations for T score -1.5 to -1.0. This is of importance especially in populations of vertebral fractures, hip fractures and patients on aromatase inhibitors and is given more weightage than the FRAX score.	Thank you for your comment. No action required.
	BHC	Your current framing is broadly accurate and would be acceptable as a consultation response, but it is not yet maximally complete	Thank you for your comment. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
	BSR	Osteoporosis should be recognised as a long-term condition as well that is one of the three causes of unplanned emergency admission bed stay diagnoses. Osteoporotic fractures also occur at the proximal humerus and pelvis. It should be noted that while osteoporosis is asymptomatic until a fracture, even after a fracture, most adults in the UK are not tested or adequately managed for osteoporosis. Underdiagnosis and undertreatment is worsened by low prioritisation by patients, clinicians, decision makers and wider society more than its asymptomatic phase of natural history. The role of vertebral fracture assessment (VFA) as part of DXA is missing. Qfracture does not have an intervention threshold and so is of lower clinical use that FRAX.	Thank you for your comment. The aim of the background section is to provide a very brief summary of the disease area. Further data and information can be provided at the submission stage of the appraisal.
	FFFAP RCP	The data around the current care gap with existing NICE recommendations and the potential opportunity benefits from equitable access to osteoporosis assessment and management especially for secondary prevention requires adding.	Thank you for your comment. The aim of the background section is to provide a very brief summary of the disease area. Further details can be included in all submissions for this appraisal.
	NOGG	A key fact is missing from the background: the majority of people who sustain an osteoporotic fragility fracture have a BMD T-Score> -2.5. Osteoporotic fractures commonly occur at the humerus and pelvis – these sites need including.	Thank you for your comment. The aim of the background section is to provide a very brief summary of the disease area. Further details

Section	Consultee/ Commentator	Comments [sic]	Action
		‘Major Osteoporotic Fracture’ (MOF) needs to be defined as hip, vertebral, humerus, wrist fractures. ‘*These tools (FRAX and Qfracture) are often used in combination with ...and hormone levels*’. This is not true. Firstly, what is meant by a hormone needs to be qualified, but secondly, a clinician might, on a case by case basis, check e.g. testosterone or prolactin, these are not standard investigations, thirdly they cannot be incorporated into FRAX or Qfracture. Thsi statement risks misleading GPs into thinking they should be checking something that is largely the remit of osteoporosis specialists. ‘*To date there have not been clear and unified thresholds used to determine treatment eligibility and initiation, or to define the subgroup of people deemed to be very high risk*’. This is not true. Please see NOGG guidance which has considered this carefully over many years, and which NICE has endorsed during this period. ‘*Part one of the guideline update produced guidance on eligibility criteria*’ doesn’t make grammatical sense.	can be included in all submissions for this appraisal. The background section has been updated to read ‘*These tools are often used in combination with consideration of risk factors such as age and fracture history.’* The sentence ‘*To date there have not been clear and unified thresholds used to determine treatment eligibility and initiation, or to define the subgroup of people deemed to be very high risk’* has also been removed.
	Northumbria NHSFCT	Missing information relating to imminent fracture risk, and the marked increased risk in additional fractures within 2 years of first major osteoporotic fracture.	Thank you for your comment. The aim of the background section is to provide a very brief summary of the disease area. Further details can be included in all

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			submissions for this appraisal.
	PAO UK	None	No action required.
	PrescQIPP	None	No action required.
	ROS	None	No action required.
	Theramex	The background information strongly emphasises the severity, impact, and mortality risk of hip fractures. Despite this, the metric taken to decide treatment choice in the Osteoporosis Guidelines is 10% or more major osteoporotic fracture (MOF) risk. As included in the Consultation Comments on the Guidelines, in addition to the 10-year risk of MOF, Theramex suggest the inclusion of the 10-year risk of hip fractures that is derived from these risk-stratification tools. Hip fracture risk should not be subsumed within the risk of major osteoporotic fracture owing to the following reasons: a) Hip fracture carries uniquely high mortality that is incomparable to other MOFs. Specifically, the relative risk of mortality is 5-8 times greater within the first 3 months post-event. In absolute terms, mortality reaches 9% and 36% at month 1 and at 1 year, respectively (Nuti R, Brandi ML, Checchia G, et al. Guidelines for the management of osteoporosis and fragility fractures. Intern Emerg Med. 2019;14(1):85-102. doi:10.1007/s11739-018-1874-2). b) Hip fracture causes disproportionate loss of independence and institutionalisation, with only 52% living in their own home after 120 days, whilst 26% will die within 12 months of their fracture (National Osteoporosis Guideline Group (NOGG). Section 2: Introduction to	Thank you for your comment. Clinically relevant populations were determined by clinical expert consensus as part of the update to clinical guideline osteoporosis risk assessment, treatment and prevention of fragility fractures. The rationale for a 10% risk threshold for DXA (except in those with hip, vertebral or multiple fractures who do not need to meet a risk criteria) was made largely on a clinical basis but was supported by the economic analysis that

Section	Consultee/ Commentator	Comments [sic]	Action
		osteoporosis and fragility fractures. NOGG Full Guideline. Published 2024. Accessed February 20, 2026. https://www.nogg.org.uk/full-guideline/section-2-introduction-osteoporosis-and-fragility-fractures). Furthermore, 50% of women with hip fracture suffer from a substantial reduction in their level of self-sufficiency which, in approximately 20% of cases, involved long-term institutionalisation (Nuti R, Brandi ML, Checchia G, et al. Guidelines for the management of osteoporosis and fragility fractures. Intern Emerg Med. 2019;14(1):85-102. doi:10.1007/s11739-018-1874-2). c) Hip fracture has a distinct epidemiological and age-related profile. The peak number of hip fractures occur at 75-79 years of age for both sexes, whereas for all other fractures, the peak number occurs at 50-59 years and decreases with age (International Osteoporosis Foundation. Epidemiology of osteoporosis and fragility fractures. Facts & Statistics. Accessed February 20, 2026. https://www.osteoporosis.foundation/facts-statistics/epidemiology-of-osteoporosis-and-fragility-fractures). Therefore, this carries the theoretical risk that in the very elderly, the 10-year risk of major osteoporotic fracture probability may be driven by lower-severity fractures occurring earlier in life, whilst the absolute hip fracture risk continues to escalate. This may lead to scenarios where an older patient may have a borderline MOF probability which fails to meet treatment threshold yet carry a clinically significant and independently actionable 10-year risk of hip fracture probability which does meet treatment threshold. d) NOGG and International guidelines provide separate intervention thresholds for hip fracture. NOGG guideline explicitly publishes and applies two separate thresholds – one for MOF and one for hip	found that it would likely also be associated with lower DXA resource use.

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		fracture (National Osteoporosis Guideline Group (NOGG). Section 4: Intervention thresholds and strategy. NOGG Full Guideline. Published 2024. Accessed February 20, 2026. https://www.nogg.org.uk/full-guideline/section-4-intervention-thresholds-and-strategy). In the US, the American Association of Clinical Endocrinologists/ American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of postmenopausal osteoporosis (2020 update) similarly uses a 3% hip fracture threshold independent of the 20% MOF threshold (Camacho PM, Petak SM, Binkley N, et al. American Association Of Clinical Endocrinologists/American College Of Endocrinology Clinical Practice Guidelines For The Diagnosis And Treatment Of Postmenopausal Osteoporosis-2020 Update. Endocr Pract. 2020;26(Suppl 1):1-46. doi:10.4158/GL-2020-0524SUPPL). Hip fracture causes a disproportionate NHS cost burden – in the UK, cost of fragility fractures to the NHS exceeds £4.7 billion per annum, with £1.1 billion directly attributable to hip fractures alone (National Osteoporosis Guideline Group (NOGG). Section 2: Introduction to osteoporosis and fragility fractures. NOGG Full Guideline. Published 2024. Accessed February 20, 2026. https://www.nogg.org.uk/full-guideline/section-2-introduction-osteoporosis-and-fragility-fractures). Identifying and treating patient at elevated hip fracture risk early is therefore not only a clinical imperative, but also a health-economic one. How does the Multiple Technology Appraisal (MTA) plan to assign the value and importance of hip fractures with these criteria in mind? We seek assurance that focusing on the 10-year MOF risk threshold does not inadvertently exclude patients who have a high specific probability of hip fracture but do not meet the generic 10% MOF threshold.	

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		In addition to considering adding hip fracture risk in decision making, Theramex recommends evaluating replacing the fixed risk threshold by age-dependent intervention thresholds that allows for better prioritisation of highest-risk patients, improves equity (especially for younger very high risk patients for whom meeting the 10% fixed threshold is more challenging even though they may be at risk), and enhances cost-effective treatment stratification. Age-dependent risk assessment allows intervention eligibility based on comparable 10-year fracture risk at any age, regardless of prior fracture status, which also aligns with the proposed primary prevention segmentation in the Multiple Technology Appraisal (MTA). Fracture risk rises with age and the individuals' biology, trajectory, and urgency of access to appropriate treatment, and varies from a 50-year-old to an 80-year-old presenting with the same risk factors. In alignment with National Osteoporosis Guideline Group (NOGG) guidelines and supporting equity and long-term value of appropriate management approaches, we suggest an age dependent risk consideration to allow greater individualised accuracy of fracture risk and risk categorisation to guide management. Relevance of the over-simplicity of the 10-year risk threshold may be mitigated by the fact that neither FRAX nor QFracture account for all potential risk fractures and are known to potentially underestimate risk score in some patients.	
	UCB	UCB would like to suggest expanding the risk factors for fracture- not osteoporosis beyond systemic use of glucocorticoids and not other medications that elevate the fracture risk to a similar level. Furthermore, osteoporosis as defined by BMD should be viewed as a risk indicator, not a pre-requisite for treatment. There are many guidelines and position papers	Thank you for your comment. The aim of the background section is to provide a very brief summary of the disease area. Further details

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		that define very high fracture risk- therefore the statement of no subgroup of people deemed to be very high fracture risk is inaccurate.	can be included in all submissions for this appraisal. The sentence '*To date there have not been clear and unified thresholds used to determine treatment eligibility and initiation, or to define the subgroup of people deemed to be very high risk'* has been removed.
	The Robert Jones and Agnes Hunt Orthopaedic Hospital	**Section: Secondary Prevention.** We strongly suggest a formal definition for **"Imminent Fracture Risk"** (major osteoporotic fracture within the last 24 months). Current evidence shows the highest risk of re-fracture occurs in this window; specifically identifying this would ensure these patients are prioritised for anabolic treatment rather than standard bisphosphonates.	Thank you for your comment. The aim of the background section is to provide a very brief summary of the disease area. Further details can be included in all submissions for this appraisal.
Population	Amgen	Amgen considers the population definition broadly appropriate. However, we recommend that the scope explicitly identifies subgroups that may warrant separate consideration, including: • People at very high or imminent fracture risk,	Thank you for your comment. If evidence exists, additional subgroups can be

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		• People with prior fragility fractures, • Individuals unable to tolerate or adhere to oral bisphosphonates, • Older people and those with comorbidities affecting treatment choice or persistence. Recognition of these subgroups would support more nuanced evaluation and avoid overly broad conclusions that may not reflect clinical practice.	considered by the committee if they are deemed relevant during the appraisal.
	ABPI	No comments	No action required.
	BCUHB	None	No action required.
	BHC	Partially. The remit captures the broad indication but does not fully reflect the limitations of the evidence base or the diversity of the NHS population. The population should explicitly include key clinical subgroups and acknowledge the under-representation of minority ethnic groups and older adults in pivotal trials.	Thank you for your comment. The population is intentionally kept broad to avoid excluding potentially eligible people. The committee will consider clinically relevant subgroups and equality issues during the appraisal.
	BSR	Very high fracture risk should differentiate very high vertebral fracture risk vs non-vertebral fracture risk as these two populations require different pharmacotherapies (see SIGN) Other important causes of osteoporosis are aromatase inhibitor use and androgen deprivation therapy as well as comorbidities such as rheumatoid	Thank you for your comment. Clinically relevant populations were determined by clinical expert consensus as part of

Section	Consultee/ Commentator	Comments [sic]	Action
		arthritis, other inflammatory diseases and Parkinsons. Figure 1 superscript “b” has no reference. The definition of very high-risk subgroup as only BMD <-3.5 and 2 or more significant risk factors is unreasonable and not based on the evidence. NOGG define very high risk as recent vertebral fracture [within the last 2 years], ≥2 vertebral fractures [whenever they have occurred], BMD T-Score ≤-3.5, treatment with high dose glucocorticoids [≥7.5 mg/day of prednisolone or equivalent over 3 months]; the presence of multiple clinical risk factors, particularly with a recent fragility fracture indicating high imminent risk of re-fracture; or other indicators of very high fracture risk, including as defined by FRAX. For example a post menopausal woman can reach the same imminent fracture risk level for fracture with a T score of -2.5 and multiple risk factors or a T score of -3.5 and just one. Figure 2 is unreasonable and over complicated. It’s not clear what the “as fragility fracture” in brackets refers to in the NHNV blue boxes. There is no evidence presented to support the distinction between two or more NHNV vs single NHNV fractures as distinct from hip or vertebral fractures. The use of 5 T score thresholds (< -3.5, <-3.0, <-2.5, < -1.5, <-1.0) in Figure 2 is also unreasonable and should be removed unless evidence is presented for them. It is overcomplicated and not pragmatic and so will hinder implementation and does not meet the stated requirement “to produce recommendations that are useful, usable”	the update to clinical guideline osteoporosis risk assessment, treatment and prevention of fragility fractures. Final intervention thresholds and higher risk subgroup criteria are aligned between the MTA scope and the guideline committee process. Aromatase inhibitor use and androgen deprivation therapy have now been included in the footnote for superscript (b) in figures 1 and 2.

Section	Consultee/ Commentator	Comments [sic]	Action
	FFFAP RCP	The populations are inadequately prioritised for treatment. A higher priority should be made for secondary prevention assessment and management. The secondary fracture prevention populations are divided into 4 subgroups with 5 DXA thresholds and this is unreasonably complicated, without a robust evidence base and should be simplified e.g. by comparing hip, other major osteoporotic fracture (humerus, wrist, pelvis, spine) and other fractures (excluding digits, skull, face and scaphoid) as an evidence based and pragmatic approach.	Thank you for your comment. NICE will appraise all technologies within their marketing authorisations and within the context of the update of NICE's guideline on osteoporosis. All technologies will be considered in primary and/or secondary prevention according to their marketing authorisations. Clinically relevant populations were determined by clinical expert consensus as part of the update to clinical guideline osteoporosis risk assessment, treatment and prevention of fragility fractures. Final intervention thresholds and higher risk subgroup criteria will be finalised through the

Section	Consultee/ Commentator	Comments [sic]	Action
			guideline committee process, and will be aligned to the MTA scope.
	NOGG	The major advances since most of the previous osteoporosis TA's were launched concern secondary prevention, specifically; 1. the publication of the head to head bisphosphonate vs. anabolic landmark RCTs. 2. the very high risk and imminent fracture risk groups that have been identified as requiring more rapid or more efficicious parenteral therapies firstline. It is good that the guideline is seeking to unify the eligibility criteria. Please understand that secondary outpatients care capacity is severely limited and that must be chiefly focused on the highest risk patients who also stand to benefit most from parenteral-first therapies. **Figure 1** identifies a very restricted subgroup of patients for therapy. For example someone starting glucocorticoids, who would currently (and correctly) be treated in clinical practice to prevent GIO, would not be able to access treatment (see below). Furthermore, an older woman, too frail to travel to have a DXA scan, but who perhaps has Parkinson's disease and multiple falls, would not be able to access alendronate. Essentially access to DXA is a barrier to accessing treatment. This is a very regressive step that will disadvanatge the most vulnerable in our society, many of whom are older and have high absolute fracture risks. Moreover when they do fracture, the health costs are very high.	Thank you for your comment. Clinically relevant populations were determined by clinical expert consensus as part of the update to clinical guideline osteoporosis risk assessment, treatment and prevention of fragility fractures. Final intervention thresholds and higher risk subgroup criteria will be finalised through the guideline committee process, and will be aligned to the MTA scope.
	Northumbria NHSFCT	Yes	Thank you for your comment. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
	PAO UK	None	No action required.
	PrescQIPP	None	No action required.
	ROS	The definition of very high risk subgroup as only BMD <-3.5 and 2 or more significant risk factors is unreasonable and not based on the evidence.	Thank you for your comment. Clinically relevant populations were determined by clinical expert consensus as part of the update to clinical guideline osteoporosis risk assessment, treatment and prevention of fragility fractures. Final intervention thresholds and higher risk subgroup criteria will be finalised through the guideline committee process, and will be aligned to the MTA scope.
	Theramex	Overall, the definition of the population into four groups based on prevention and risk level e.g. high-risk, is clear. Within this, can NICE consider and clarify the cause and definition of menopause, in particular whether, in addition to age-related natural decline in ovarian function, it includes primary ovarian insufficiency and premature ovarian insufficiency e.g. iatrogenic	Thank you for your comment. The population is intentionally kept broad to avoid excluding

Section	Consultee/ Commentator	Comments [sic]	Action
		menopause due to surgical intervention, cancer therapy, and other drug induced menopause, and other possible subgroups?	potentially eligible people. The population is not restricted by the cause of menopause.
	UCB	The population within decision point 4 ‘Secondary prevention, meet very high risk definition’ of the draft scope does not explicitly include people at risk of an imminent fracture. There is strong clinical and policy precedent within NICE guidance to explicitly recognise imminent fracture risk as a distinct and clinically meaningful concept, defined by the recency of fracture. NICE Technology Appraisal TA791 operationalises imminent fracture risk as having sustained a major osteoporotic fracture within the previous 24 months, recognising this group as being at highest short-term risk of subsequent fracture and therefore requiring urgent prioritisation and appropriate treatment selection, including consideration of anabolic therapy. However, in the current draft scope and guideline out for consultation, the concept of imminent fracture risk is not clearly defined or consistently embedded within assessment, triage, or pathway recommendations. Risk assessment tools such as FRAX and QFracture estimate 10-year fracture probability and do not capture the marked excess risk observed in the first 12–24 months following a fragility fracture, nor do they convey clinical urgency. Explicitly incorporating imminent fracture risk into the core recommendations would support timely identification of patients at highest short-term risk, and enable appropriate escalation of care, including bypassing routine risk tools,	The outcomes listed are not exhaustive and the committee will consider other relevant outcomes related to fracture risk if the evidence allows. Clinically relevant populations were determined by clinical expert consensus as part of the update to clinical guideline osteoporosis risk assessment, treatment and prevention of fragility fractures. Final intervention thresholds and higher risk subgroup criteria will be finalised through the guideline committee process, and will be aligned to the MTA scope.

Section	Consultee/ Commentator	Comments [sic]	Action
		accelerated access to DXA and imaging, and informed treatment sequencing. This would help ensure that patients with recent fractures receive timely, risk-appropriate interventions to reduce avoidable subsequent fractures and optimise outcomes. Patients at risk of imminent fracture represent a clinically distinct population in whom the consequences of delayed or suboptimal treatment are immediate and severe. This creates a decision problem that is qualitatively different from long-term fracture risk. The definitions of very high fracture risk are confusing leading to potentially missing a large group of patients who would benefit from the most appropriate treatment. The impact of recent fracture (< 2 years) has been demonstrated to be the strongest predictor of another fracture (Kanis et al., Osteoporosis International (2020) 31:1–12). Therefore, adding addition BMD cutt offs for the population within decision point 4 – for example, BMD <-3.5 is not supported by the literature and has the potential to prevent a group of patients from being fast tracked for anabolic treatment. To this point, UCB is unaware of evidence for the population within decision point 4 regarding the following: • needing to have 2 or more NHNV fractures + less than 2 years + BMD <-3.0 • One NHVF within the last 2 years puts this patient group into imminent fracture risk and a BMD <-2.5 to be classified as osteoporotic. • needing to have a BMD of less than -3.5 for 1 x NHVF within the last 2 years	

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		In addition, patients who have not had a fracture within the last 2 years would benefit from FRAX assessment, as this would provide an objective risk assessment and therefore direct the most appropriate treatment. The algorithm should be simplified and patients prioritised where recency of fracture fast tracks patients to DXA and then treatment. If patients have not had a fracture then they could be included as outlined in populations within decision points 1 & 2. If patients have had a fracture later than 2 years, then DXA and FRAX assessment should be used to determine if they fall into a very high fracture risk group. Simplification would impact the greatest number of patients and ensure a higher number recognised and treated accordingly. There is strong and consistent evidence that recency of fracture is a major determinant of imminent (0–24 months) re-fracture risk. Updated risk tools (e.g. FRAXplus) incorporate fracture recency and site to better identify patients at very high risk who require rapid intervention. Contemporary guidelines increasingly emphasise early evaluation and prompt initiation of therapy during this high-risk window. In addition, UCB are unclear as to the source of evidence for the population within decision point 4 'Secondary prevention, meet very high risk definition' for the following: • needing to have 2 or more NHNV fractures + less than 2 years + BMD <-3.0? One NHVF within the last 2 years puts this patient group into imminent fracture risk and a BMD <-2.5	
	The Robert Jones and Agnes Hunt Orthopaedic Hospital	Population 2 (Primary Prevention). We strongly challenge the exclusion of romosozumab and teriparatide from this group. Both agents have robust RCT evidence (e.g., FRAME and FPT trials) showing significant fracture reduction in high-risk patients without prior fractures. Limiting them to secondary prevention based on historical TAs (TA791/TA161) contradicts their broad	Thank you for your comment. NICE will appraise all technologies within their marketing authorisations and within the context of the

Section	Consultee/ Commentator	Comments [sic]	Action
		MHRA/EMA licences and creates a clinical inconsistency where only abaloparatide is available for primary prevention.	update of NICE's guideline on osteoporosis. The marketing authorisations for romosozumab and teriparatide do not exclude them from being used in primary prevention.
Subgroups	Amgen	As mentioned above, but copied again here for completeness: Amgen considers the population definition broadly appropriate. However, we recommend that the scope explicitly identifies subgroups that may warrant separate consideration, including: • People at very high or imminent fracture risk, • People with prior fragility fractures, • Individuals unable to tolerate or adhere to oral bisphosphonates, • Older people and those with comorbidities affecting treatment choice or persistence. Recognition of these subgroups would support more nuanced evaluation and avoid overly broad conclusions that may not reflect clinical practice.	Thank you for your comment. If evidence exists, additional subgroups can be considered by the committee if they are deemed relevant during the appraisal.
	ABPI	None	No action required.
	BCUHB	None	No action required.
	BHC	The pivotal trials for all three technologies enrolled: • overwhelmingly postmenopausal white women	Thank you for your comment. The

Section	Consultee/ Commentator	Comments [sic]	Action
		• very few men • almost no BAME participants • limited representation of people aged >80 • limited representation of people with multimorbidity	committee will consider equalities issues during the appraisal
	BSR	The subgroup of glucocorticoid induced osteoporosis is problematic as current trial with newer anabolic agents have not specifically targeted this subgroup and so the evidence is limited to older therapies. HRT should be included as a treatment option for women and not as a separate subgroup. (Otherwise considering prior treatment exposure to all osteoporosis drugs should be considered, not just HRT) Cognitive impairment and severe gastrointestinal side effects can be included in those where osteoporosis medications are not tolerated, contraindicated etc. Primary prevention subgroups Secondary prevention subgroups	Thank you for your comment. The committee will consider the subgroup of glucocorticoid induced osteoporosis, if the evidence allows. Certain HRT products are indicated for “the prevention of osteoporosis in postmenopausal women at high risk of future fractures who are intolerant of, or contraindicated for, other medicinal products approved for the prevention of osteoporosis”. NICE is only able to appraise technologies within their marketing authorisations. In an MTA, all comparators

Section	Consultee/ Commentator	Comments [sic]	Action
			are compared to one another. So there would not be a population that would receive HRT for the prevention of osteoporosis that could also receive the other comparators listed in the MTA scope.
	FFFAP RCP	HRT / MHT use and intolerance to oral BPs are not a subgroup but part of the interventions. Glucocorticoid induced osteoporosis is now incorporated in fracture risk assessment tools such as FRAX.	Thank you for your comment. Certain HRT products are indicated for “the prevention of osteoporosis in postmenopausal women at high risk of future fractures who are intolerant of, or contraindicated for, other medicinal products approved for the prevention of osteoporosis”. NICE is only able to appraise technologies within their marketing authorisations. In an MTA, all comparators are compared to one

Section	Consultee/ Commentator	Comments [sic]	Action
			another. So there would not be a population that would receive HRT for the prevention of osteoporosis that could also receive the other comparators listed in the MTA scope.
	NOGG	**Glucocorticoid-induced osteoporosis** A distinction needs to be made between 'People **with** glucocorticoid-induced osteoporosis' and 'People **at risk of** glucocorticoid-induced osteoporosis' It is well established that when starting GCs, one loses bone quite rapidly, and hence NOGG recommends: 'Because bone loss and increased fracture risk occur early after initiation of oral glucocorticoids, bone-protective treatment should be started in the following people, at the same time as glucocorticoid therapy without waiting for bone density assessment, which should follow later (Strong recommendations):.....' Simply that treatment applies to those **with** glucocorticoid-induced osteoporosis, risks bone-protective treatment only being stated after BMD has been lost and T-Score is <-2.5 **Women aged between 50 and 60 years having hormone replacement therapy**	Thank you for your comment. People with glucocorticoid-induced osteoporosis, women aged 50 to 60 years having hormone replacement therapy and people who are unable to take oral bisphosphonates because of cognitive difficulties or severe gastrointestinal side effects were subgroups specified by the committee as part of the update to clinical guideline osteoporosis risk assessment, treatment and prevention of fragility

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		The age threshold at 60 does not align with the current recommendation that HRT can be given for as long as it is felt that benefits of symptom control and improvement in quality of life outweigh any risks, there are no arbitrary age limits. https://thebms.org.uk/wp-content/uploads/2022/12/04-BMS-TfC-HRT-Guide-NOV2022-A.pdf **People who are unable to take oral bisphosphonates because of cognitive difficulties or severe gastrointestinal side effects** The word 'severe' seem un-necessary here, firstly it needs defining what severe means, secondly it is somewhat academic whether a side effect is severe or not, the point is the patient is unable to take an oral bisphosphonate, and needs an alternative intervention. For that reason, all side effects should be inlcuded not just the 'severe GI' ones. Additional suggestions **Primary prevention in postmenopausal women with osteopenia and with normal BMD** There have been a series of RCTs using iv Zoledronate which warrant evaluation. The first trial was in postmenopausal women with osteopenia and showed substantial fracture risk reduction over 6 years. Fracture Prevention with Zoledronate in Older Women with Osteopenia | New England Journal of Medicine Subsequent follow up showed benefits were maintained for 1.5-3.5 years Duration of fracture prevention after zoledronate treatment in women with osteopenia: observational follow-up of a 6-year randomised controlled trial to 10 years - The Lancet Diabetes & Endocrinology.	fractures. The committee will consider evidence for these subgroups if the evidence allows. If evidence exists, additional subgroups can be considered by the committee if they are deemed relevant during the appraisal.

Section	Consultee/ Commentator	Comments [sic]	Action
		More recently a trial of 5-yearly iv zoledronate in 50-60 year old women with normal or osteopenic BMD showed fracture risk reduction. Fracture Prevention with Infrequent Zoledronate in Women 50 to 60 Years of Age | New England Journal of Medicine. Given the low cost of Zoledronate, the clinical and cost effectiveness of infrequent Zoledronate dosing in non-osteoporotic post-menopausal women should be considered as a longer term strategy towards primary prevention in the UK.	
	Northumbria NHSFCT	I think that the NOGG/ROS definition of very high fracture risk should be applied to all major osteoporotic fractures, not just after vertebral fracture. I think there should be reference to the VHFR result in FRAX. Would amalgamate 2 or more NHNV and 1 NHNV fragility fracture criteria, and also amalgamate hip and vertebrae fracture criteria – 2 pathways rather than 4	Thank you for your comment. Clinically relevant populations were determined by clinical expert consensus as part of the update to clinical guideline osteoporosis risk assessment, treatment and prevention of fragility fractures. Final intervention thresholds and higher risk subgroup criteria will be finalised through the guideline committee process, and will be aligned to the MTA scope.

Section	Consultee/ Commentator	Comments [sic]	Action
	PAO UK	None	No action required.
	PrescQIPP	None	No action required.
	ROS	None	No action required.
	Theramex	Theramex would like to ask if treatment recommendations for the three subgroups mentioned in Table 3 page 12 have been stratified. Can NICE clarify the scope of Subpopulation 1 (glucocorticoid-induced osteoporosis)? Is it also relevant to expand this subpopulation to include patients with osteoporosis caused by primary and premature ovarian insufficiency (e.g. iatrogenic menopause, including drug-induced menopause, for example following oncologic treatments or gonadotropin-releasing hormone (GnRH) agonists/antagonists)? Similarly for Subpopulation 2 (women aged between 50- and 60-years having hormone replacement therapy (HRT)), Theramex suggest consideration of including younger women being treated with HRT for premature ovarian insufficiency, iatrogenic menopause etc., to account for an increased risk of fragility fractures related to low levels of oestrogen rather than age.	Thank you for your comment. The recommendations in Table 3 have been ordered according to the date they were published. The exact definition for glucocorticoid-induced osteoporosis will be determined by the available evidence. People with glucocorticoid-induced osteoporosis, women aged 50 to 60 years having hormone replacement therapy were subgroups specified by the committee as part of the update to clinical guideline osteoporosis

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			risk assessment, treatment and prevention of fragility fractures. The committee will consider evidence for these subgroups if the evidence allows.
	UCB	Please see comments above regarding the inclusion of imminent fracture risk within or in addition to the population within decision point 4 ‘Secondary prevention, meet very high risk definition’	Thank you for your comment. Please see responses to comments above.
	The Robert Jones and Agnes Hunt Orthopaedic Hospital	**Subgroups/Outcomes.** Priority should be given to an "Anabolic-First" pathway for those at imminent risk. The current draft focuses on oral bisphosphonates as the primary comparator, which may not be clinically appropriate for the "very high risk" populations identified.	Thank you for your comment. NICE compare all technologies in the MTA scope to each other within their respective marketing authorisations and within the context of the update of NICE’s guideline on osteoporosis..
Comparators	Amgen	We agree that the scope includes the key comparators currently used in the NHS. We recommend ensuring that both oral and parenteral treatment options are appropriately represented, reflecting differences in route of	Thank you for your comment. No action required.

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		administration, adherence, and persistence that may influence real-world effectiveness.	
	ABPI	No comments	No action required.
	BCUHB	None	No action required.
	BHC	Partially. The listed comparators include several standard NHS treatments but are not fully complete. Oral and IV bisphosphonates must be included as first-line comparators, and romosozumab, no active treatment, and relevant sequential therapy pathways should also be added to reflect real NHS practice and current NICE guidance	Thank you for your comment. NICE compare all technologies in the MTA scope to each other within their respective marketing authorisations and within the context of the update of NICE's guideline on osteoporosis..
	BSR	None	No action required.
	FFFAP RCP	Yes	Thank you for your comment. No action required.
	NOGG	Table 2: Hormone Replacement Therapy seems to be missing and should be included for primary and secondary prevention in those with high risk of fracture.	Thank you for your comment. Certain HRT products are indicated for "the prevention of osteoporosis in

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			postmenopausal women at high risk of future fractures who are intolerant of, or contraindicated for, other medicinal products approved for the prevention of osteoporosis". NICE is only able to appraise technologies within their marketing authorisations. In an MTA, all comparators are compared to one another. So there would not be a population that would receive HRT for the prevention of osteoporosis that could also receive the other comparators listed in the MTA scope.
	Northumbria NHSFCT	No current technology guideline directly addresses zoledronic acid (other than TA464 in passing) whereas this is likely the most effective bisphosphonate and possibly the most clinically and cost effective osteoporosis therapy we have available, bar none.	Thank you for your comment. The MTA will review previous appraisals TA160, TA161, TA204, TA464, TA791 and TA991. The

Section	Consultee/ Commentator	Comments [sic]	Action
		Teriparatide is still regulated by TA161 which is hopelessly out of date – biosimilar agents cost less than 20% of the originator upon which TA 161's cost efficacy analysis is based. It is still regulated to a second line role where we have good data that anabolics are far more effective in patients who are naïve to antiresorptives. The positioning of teriparatide in the treatment pathway needs to be reviewed as this could present a significant cost saving and reduce use of abaloparatide and romosozumab, both of which are far more expensive (and a little more effective)	recommendations from the MTA will update and replace recommendations from the previous appraisals.
	PAO UK	None	No action required.
	PrescQIPP	None	No action required.
	ROS	We support evaluating the use of abaloparatide and romosozumab in men in order to ensure men are also able to benefit from these treatments if clinically appropriate.	Thank you for your comment. All technologies will be appraised in on people aged 50 and over and women who have experienced menopause and are eligible for pharmacological treatment.
	Theramex	Theramex agree that the comparators listed are considered to be the standard treatments currently used in the NHS. Within Table 2 of the Scope, we agree that all relevant comparators have been included for each population.	Thank you for your comment. The wording of the TA204 recommendation defines people who are unable to take oral

Section	Consultee/ Commentator	Comments [sic]	Action
		Theramex would like to clarify the definition of “for those unable to take oral bisphosphonates” as a restriction for denosumab in Populations 1-3, teriparatide and raloxifene in Population 3. Are they patients who cannot take an orally administered drug, are intolerant to bisphosphonates, or other?	bisphosphonates as those “who are unable to comply with the special instructions for administering alendronate and either risedronate or etidronate, or have an intolerance of, or a contraindication to, those treatments”.
	UCB	Yes	Thank you for your comment. No action required.
	The Robert Jones and Agnes Hunt Orthopaedic Hospital	Section: Comparison of Technologies. The draft creates a "tiering" of anabolics that is not supported by head-to-head evidence. If abaloparatide is suitable for primary prevention at a specific FRAX threshold, the same criteria should apply to romosozumab and teriparatide to allow clinicians to select the agent with the best site-specific efficacy (e.g., romosozumab for hip protection). Additionally, patient preferences should be taken into consideration (e.g. daily versus monthly injections).	Thank you for your comment. NICE will compare all technologies in the MTA scope to each other within their respective marketing authorisations and within the context of the update of NICE’s guideline on osteoporosis..

Section	Consultee/ Commentator	Comments [sic]	Action
Outcomes	Amgen	Amgen supports the inclusion of fracture outcomes, mortality, adverse events, and health-related quality of life. We encourage NICE to also consider outcomes related to treatment persistence and discontinuation, given their relevance to long-term fracture risk and NHS resource use.	Thank you for your comment. NICE anticipates that the committee will consider adherence and persistence to treatment regimens as part of relevant costs and benefits during the appraisal.
	ABPI	No comments	No action required.
	BCUHB	None	No action required.
	BHC	The outcomes listed are broadly appropriate, but they are not yet fully specified and do not capture all key benefits and harms. The outcome set should explicitly distinguish vertebral, non-vertebral and hip fractures; include denosumab-specific rebound fracture risk, ONJ and AFF; and incorporate HRQoL, pain, physical function, loss of independence, and adherence/persistence. These additions are necessary to reflect the most important health-related benefits and harms of these technologies in NHS practice	Thank you for your comment. The outcome of osteoporotic fragility fracture is intentionally broad and doesn't exclude specific types of fractures from being captured as outcomes. Specifying types of fragility fractures may limit the outcomes captured. The relevant health-related quality of life outcomes when appraising the

Section	Consultee/ Commentator	Comments [sic]	Action
			technology. NICE anticipates that the committee will consider adherence and persistence to treatment regimens as part of relevant costs and benefits during the appraisal.
	BSR	The key outcomes are prevention of hip fractures and vertebral fractures. Followed by non-vertebral fracture. The outcome of 'osteoporotic fragility fracture' is unreasonable given the variable effectiveness of osteoporosis technologies to prevent hip and non-spine fracture both in terms of risk reduction and time to onset. Consideration should be given to time-limited outcomes. Imminent fracture risk is within 2 years and consideration of time to fracture reduction is a reasonable additional outcome for the economic analyses.	Thank you for your comment. The outcome of osteoporotic fragility fracture is intentionally broad and doesn't exclude specific types of fractures from being captured as outcomes. Specifying types of fragility fractures may limit the outcomes captured. The outcomes listed are not exhaustive and the committee will consider other relevant outcomes related to fracture risk if the evidence allows.

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	FFFAP RCP	Over 90% of subsequent imminent fractures after an index fracture are non-vertebral and have a different mechanism and time to fracture reduction than the trabecular vertebral fractures. It is therefore unreasonable to group all subsequent fractures into one outcome 'osteoporotic fractures'. Imminent hip and non-vertebral fractures (within 2 years of sentinel fracture) are reasonable outcomes.	Thank you for your comment. The outcome of osteoporotic fragility fracture is intentionally broad and doesn't exclude specific types of fractures from being captured as outcomes. Specifying types of fragility fractures may limit the outcomes captured. The outcomes listed are not exhaustive and the committee will consider other relevant outcomes related to fracture risk if the evidence allows.
	NOGG	**Anabolic therapies must be followed by an anti-resorptive therapy** The key efficacy outcome for the high risk/imminent risk group is new vertebral fracture or new MOF within a short 3 year time frame. However, only one of the medications (romosozumab) was specifically developed with a follow-on anti-resorptive from 13th month to 24th or 36th month strategy. Modeling this is likely to be complex when comparing efficacy between parenteral therapies. However, any anabolic therapy must be followed by an antiresorptive without delay, to consolidate BMD gains.	Thank you for your comment. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
	Northumbria NHSFCT	Yes	Thank you for your comment. No action required.
	PAO UK	None	No action required.
	PrescQIPP	None	No action required.
	ROS	We would encourage NICE to ensure that vertebral fractures are fully and appropriately reflected within the outcome measures and modelling. Vertebral fractures are frequently under-recognised in clinical practice, yet they can be associated with significant and prolonged pain, reduced mobility, loss of independence and social isolation. From a patient perspective, preventing vertebral fractures can have a substantial impact on quality of life, even where these fractures do not lead to hospital admission. It is therefore important that the full real-world burden of vertebral fractures is captured when assessing clinical and cost effectiveness.	Thank you for your comment. The outcome of osteoporotic fragility fracture is intentionally broad and doesn't exclude specific types of fractures from being captured as outcomes. Specifying types of fragility fractures may limit the outcomes captured.
	Theramex	Theramex agree that the outcome measures listed are appropriate and capture the most important health related benefits of the technology. In addition to those listed, Theramex would like to request the inclusion of efficacy metrics with sequential therapy (antiresorptive agents followed by an osteoanabolic agent). This would be relevant to capture the presentation and impact of the blunting effect i.e. reduced efficacy of bone-building (osteoanabolic) medications (like teriparatide, abaloparatide, or romosozumab) when they are administered after, or concurrently with, potent	Thank you for your comment. NICE anticipates that the committee will consider adherence and persistence to treatment regimens as part of relevant costs and

Section	Consultee/ Commentator	Comments [sic]	Action
		bone-resorption-inhibiting (antiresorptive) drugs (like bisphosphonates or denosumab). Theramex would like to request the specification of treatment persistence and adherence as an input in economic modelling. The External Assessment Group (EAG) previously noted (TA991) that persistence assumptions significantly drive the incremental cost-effectiveness ratio (ICER). By formalising this as an input, differential persistence rates can be displayed in the model across the comparators.	benefits during the appraisal.
	UCB	Prevention of hip, vertebral and non-vertebral fractures should be included as outcome measures because these fracture types capture the most clinically meaningful morbidity, mortality, quality-of-life impact and health-care costs associated with osteoporosis. Hip fractures are associated with the highest mortality and loss of independence; vertebral fractures are common, frequently under-diagnosed, and strongly predictive of future fractures; and non-vertebral fractures account for the largest overall fracture burden. In addition, improvement in hip BMD is also a significant outcome measure and should be included. Evidence shows that Total Hip BMD is the most useful treatment target because it consistently predicts the risk of both vertebral and nonvertebral fractures, whereas the Lumber Spine BMD level after treatment predicts the risk of vertebral fracture but does not predict the risk of nonvertebral and hip fractures as consistently. Cosman et al., Journal of Bone and Mineral Research, Volume 39, Issue 10, October 2024, Pages 1393–1405	Thank you for your comment. The outcome of osteoporotic fragility fracture is intentionally broad and doesn't exclude specific types of fractures from being captured as outcomes. Specifying types of fragility fractures may limit the outcomes captured. The outcomes listed are not exhaustive and the committee will consider other relevant outcomes if there is available evidence.

Section	Consultee/ Commentator	Comments [sic]	Action
Equality	Amgen	We support NICE's focus on equality. The appraisal should consider whether recommendations may differentially affect groups with limited access to diagnostics, specialist services, or support for long-term adherence, and how these impacts might be mitigated.	Thank you for your comment. The committee will consider equalities issues during the appraisal.
	ABPI	No comments	No action required.
	BCUHB	None	No action required.
	BHC	Partially. The remit and scope do not fully reflect the equality-critical limitations of the evidence base. The pivotal trials under-represent men, minority ethnic groups, older adults and people with disabilities. Without explicit consideration of these gaps, recommendations may have unequal impacts on protected groups. The remit should be amended to require subgroup analyses, consideration of access barriers, and the collection of real-world evidence on diverse populations. BHC recommends that NICE seek: • ethnicity-stratified fracture and treatment-response data (from observational cohorts, FLS registries, CPRD, UK Biobank) • real-world adherence and persistence data across demographic groups • safety data in older adults, people with disabilities, and minority ethnic groups • evidence on access barriers, including digital exclusion, mobility limitations, and health-literacy issues • data on treatment sequencing, especially post-denosumab, in diverse populations	Comment noted. The committee will consider equalities issues during the appraisal.

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		This evidence is essential to avoid recommendations that unintentionally widen health inequalities.	
	BSR	The lack of access for specific osteoporosis technologies for men due to differences in trials with fracture as an endpoint is unreasonable given the changes in BMD are similar. Men are less likely to be identified, assessed, treated and monitored and have higher mortality and morbidity after a fragility fracture. A complicated guideline with 5 different BMD thresholds will deter systematic equitable implementation. Some patients have disabilities from diseases that preclude BMD measurement that mean they will not have access to a DXA based guidance. There are also deficiencies in the DXA measurement itself, as it places an overemphasis on T score cut offs, it disadvantages those with degenerative changes and those in whom a good quality DXA is not achievable.	Thank you for your comment. The committee will consider equalities issues during the appraisal.
	FFFAP RCP	Many patients with hip fracture have mild to severe cognitive impairment and so less able to access secondary care services for DXA. Clinical appropriateness of DXA scanning based on an adults likely fracture risk status should be included.	Thank you for your comment. The committee will consider equalities issues during the appraisal.
	NOGG	**Post menopausal women** 'Women who have experienced menopause' may not always be synonymous with postmenopausal women (for example women who have been subjected to medically induced menopause which may not be permanent), but most if not all licences and SmPc's will state 'postmenopausal women', which tends to be recognised also by the terminology PMO (postmenopausal osteoporosis) by most healthcare workers and in prior guidance.	Thank you for your comment. Thank you for your comment. Women who have experienced menopause is preferred because it aligns with the NICE style guide

Section	Consultee/ Commentator	Comments [sic]	Action
		Romosozumab's SmPc states that the drug is indicated in treatment of severe osteoporosis in postmenopausal women at high risk of fracture. **Gender equality** There is a wealth of efficacy data for accepted surrogates for fracture risk (BMD and markers) in men. Currently men with high risk of fracture are seriously disadvantaged when choosing anabolics, by the fact that the landmark fracture efficacy trials were conducted exclusively in postmenopausal women. Much work (FNIH) has been done since previous TA's that confirm that the surrogate endpoints painstakingly evaluated by companies to ensure comparable medication efficacy in men are valid. Since the Abaloparatide TA991 recommended the medication in transmen and non-binary individuals born female, it is strongly recommended that the same *'can do'* attitude is shown by the committee in recommending treatments in men where studies have shown biomarker/BMD equivalence to MHRA and FDA standard. **Denosumab's postcode lottery** Current there is largescale disparity across the UK in access to anabolic therapies and denosumab. Access to the latter is hindered by a postcode lottery of GP willingness to give the 6 monthly injections. This arises for different reasons, such as: 1) denosumab may be outside the local ICB formulary (hospital drug), 2) the need for availability of appointment with a trained clinician (usually practice nurse) to administer the injection (in which case the 'Enhanced services' mentioned below are relevant), 3) lack of clarity / communication with secondary care about length of treatment, or other barriers, all of which would need to be addressed, to avoid gaps in treatment leading to fractures.	The committee will consider equalities issues during the appraisal.

Section	Consultee/ Commentator	Comments [sic]	Action
		Please consider in the modeling the economic case for denosumab, that primary care refusal to provide voluntary local enhanced (6 monthly injection) services places drug VAT and double hospital appointment costs per patient per year into overburdened secondary care clinics. If necessary, please be robust in advising, with statements such as *'denosumab is only cost-effective if administered according to product economic development in primary care. If GP practices are unwilling or unable to enact treatments by Local Enhanced Service, then an alternative treatment should be commenced'*. This concern regarding inequity is partly driven by experience of patients being left 'at risk' of denosumab cessation fractures (multiple vertebral fractures) arising due to lack of GP resource.	
	Northumbria NHSFCT	Currently men (and trans women) with osteoporosis, multiple VF and VHFR are significantly disadvantaged compared to women (and trans men) in that they only have access to one anabolic agent (teriparatide) and only as a second line agent, when it is less likely to be effective after prior antiresorptive use. This is predicated upon the lack of evidence that standard therapies work in men, rather than concrete evidence that they do not. Studies in men are necessarily smaller scale than in women (as osteoporosis is rarer in men than women, so they are harder to recruit) but what little data is available suggests therapy is as effective. To promote equality of opportunity, men with similar fracture risk to women should have access to similar drug therapies, after appropriate risk/ benefit discussion. There is a reasonable concern that men with VHFR may also be at higher cardiovascular risk and so romosozumab may be less suitable for	Thank you for your comment. The committee will consider equalities issues during the appraisal.

Section	Consultee/ Commentator	Comments [sic]	Action
		them; but debarring them simply on grounds of lack of eligibility discriminates against men with VHFR and low CV risk.	
	PAO UK	None	No action required.
	PrescQIPP	None	No action required.
	ROS	We would also highlight the position of people who have already experienced a fragility fracture. Any framework that could result in individuals with a clear clinical history of fracture being considered ineligible for treatment warrants careful scrutiny from an equity perspective. From a patient standpoint, it is difficult to understand why someone who has already sustained a fracture related to bone fragility might not qualify for preventive treatment. Guidance should avoid creating unintended barriers for people with established clinical need and should support timely intervention to prevent further harm.	Thank you for your comment. The committee will consider equalities issues during the appraisal.
	Theramex	Theramex agree with the current positioning of abaloparatide in the secondary care setting. This setting ensures the drug is used to treat the most severe patients where clinical benefit is largest, and where the 'anabolic window' (where bone formation significantly exceeds resorption) can be best utilised. To maximise these gains, treatment with antiresorptive therapy follows osteoanabolic therapy. Theramex would like to clarify the scope of Subpopulations 1 and 2 to ensure that no protected groups are inadvertently excluded. In particular, consideration should be given to explicitly include patients with primary and premature ovarian insufficiency (e.g. iatrogenic menopause, including drug-induced menopause, for example following oncologic treatments or gonadotropin-releasing hormone (GnRH) agonists/antagonists) where the risk of fragility fracture is associated with low levels of oestrogen in addition to age. Explicitly including this expanded group prevents an arbitrary gap in	Thank you for your comment. Clinically relevant populations were determined by clinical expert consensus as part of the update to clinical guideline osteoporosis risk assessment, treatment and prevention of fragility fractures. The rationale for a 10% risk threshold for DXA (except in those with hip, vertebral or multiple fractures

Section	Consultee/ Commentator	Comments [sic]	Action
		protection and ensures equitable access to early screening and preventive treatment based on comparable medical risk rather circumstances causing it. The Guideline recommends criteria for treatment based on a 10-year risk of major osteoporotic fragility fracture. Theramex support the simplicity of the fixed 10% threshold to facilitate earlier identification of high and very high-risk patients. However, Theramex would like to raise the potential risk of excluding lower risk patients that fall outside of the fixed 10% threshold, but who would equally benefit from treatment. Inequality concerns include: • Potential unequal care by age rather than biological severity given a 10-year risk model rises strongly with age. Roux et al., (2014) and Gourlay et al., (2017) support this, wherein FRAX was found to underestimate the fragility fracture risk in patients younger than 65 years and after a single fragility fracture. (Roux S, Cabana F, Carrier N, et al. The World Health Organization Fracture Risk Assessment Tool (FRAX) underestimates incident and recurrent fractures in consecutive patients with fragility fractures. *J Clin Endocrinol Metab*. 2014;99(7):2400-2408. doi:10.1210/jc.2013-4507) (Gourlay ML, Overman RA, Fine JP, et al. Time to Clinically Relevant Fracture Risk Scores in Postmenopausal Women. *Am J Med*. 2017;130(7):862.e15-862.e23. doi:10.1016/j.amjmed.2017.02.012) • Recent fragility fractures may still produce less than 10% predicted risk, yet the patient may already be at very high-risk of fractures; the threshold delays access to therapy. Furthermore, the impact of fracture recency is not captured by current fracture risk assessment tools, including FRAX, underestimating fracture risk (Javaid MK, Harvey NC, McCloskey EV, Kanis JA, Cooper C. Assessment and	who do not need to meet a risk criteria) was made largely on a clinical basis but was supported by the economic analysis that found that it would likely also be associated with lower DXA resource use.

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		management of imminent fracture risk in the setting of the fracture liaison service. *Osteoporos Int*. 2022;33(6):1185-1189. doi:10.1007/s00198-021-06284-9). Therefore Theramex recommend considering adding hip fracture risk in decision making and evaluating replacing the fixed risk threshold by age-dependent intervention thresholds that allows for better prioritisation of highest-risk patients, improves equity (especially for younger very high risk patients for whom meeting the 10% fixed threshold is more challenging even though they may be at risk), and enhances cost-effective treatment stratification. Age-dependent risk assessment allows intervention eligibility based on comparable 10-year fracture risk at any age, regardless of prior fracture status, which also aligns with the proposed primary prevention segmentation in the Multiple Technology Appraisal (MTA). Fracture risk rises with age and the individuals' biology, trajectory, and urgency of access to appropriate treatment, and varies from a 50-year-old to an 80-year-old presenting with the same risk factors. In alignment with National Osteoporosis Guideline Group (NOGG) guidelines and supporting equity and long-term value of appropriate management approaches, we suggest an age dependent risk consideration to allow greater individualised accuracy of fracture risk and risk categorisation to guide management. As noted earlier, hip fracture has a distinct epidemiological and age-related profile. The peak number of hip fractures occur at 75-79 years of age for both sexes, whereas for all other fractures, the peak number occurs at 50-59 years and decreases with age (International Osteoporosis Foundation. Epidemiology of osteoporosis and fragility fractures. Facts & Statistics. Accessed February 20, 2026. https://www.osteoporosis.foundation/facts-statistics/epidemiology-of-osteoporosis-and-fragility-fractures). Therefore, this carries the theoretical risk that in the very elderly, the 10-year risk of major osteoporotic fracture probability may be driven by lower-severity fractures	

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		occurring earlier in life, whilst the absolute hip fracture risk continues to escalate. This may lead to scenarios where an older patient may have a borderline MOF probability which fails to meet treatment threshold yet carry a clinically significant and independently actionable 10-year risk of hip fracture probability which does meet treatment threshold. Overall, a too-strict use of this threshold potentially undermines appropriate and timely access to treatment with effective sequencing of treatments, particularly in younger patients.	
	UCB	None	No action required.
Other considerations	Amgen	NICE should strongly consider incorporating real-world evidence sources to inform the appraisal, particularly from registry data, fracture liaison services, and long-term pharmacovigilance data sources to better inform the modelling assumptions.	Thank you for your comment. NICE will consider the appropriateness of using real-world evidence during the appraisal.
	ABPI	No comments	No action required.
	BCUHB	None	No action required.
	BHC	Additional issues that should be covered include: the limited generalisability of trial evidence to diverse NHS populations; the management of post-denosumab rebound fracture risk; real-world adherence and persistence; safety outcomes such as ONJ, AFF and hypocalcaemia; the performance of fracture-risk tools across ethnic groups; the impact on long-term independence and social care; integration with Fracture Liaison	Thank you for your comment. The committee will consider relevant additional factors during the appraisal.

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		Services; and subgroup-specific cost-effectiveness. These issues are central to clinical practice and necessary for an equitable and robust evaluation	
	BSR	Osteoporosis is a common disease and so the guidance should be able to implemented by a wide range of healthcare professionals in both secondary, primary and community care as well as across medical and non-medical disciplines (e.g. nurses, pharmacist and DXA radiographers). The guidance process should reflect this diversity.	Thank you for your comment. No action required.
	FFFAP RCP	None	No action required.
	NOGG	**Decentralisation of iv Zoledronate provision** Currently patients who are intolerant of oral bisphosphonates are frequently stuck waiting in long bottlenecks for hospital access to parenteral therapies. The reflex referral to 'secondary care' for e.g zoledronate infusion, ibandronate infusion is challenging. Ideally (as per Australia), first line parenteral therapies would be initiated and delivered in primary care, with patient choice technologies enacted at source. Community hospitals, primary care clinics, home iv services and hospital at home models of care delivery all have scope to deliver an infusion of Zoledronate. Neighbourhood Health Centres and Community Diagnostic Centres are also coming as part if the NHS 10-year plan. We also advise inclusion of specifc research questions that align with moving patients out of hospitals who don't need to be there, i.e., decentralizated models of care. This is one of the 'Big 3' shifts of the current government/DOH (NHS 10 year plan) drive to deliver care closer to home. The MTA should make clear that anabolic therapies for Very High Risk/	Thank you for your comment. Decentralisation of zoledronate infusion provision is beyond the scope of this MTA.

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		Imminent risk or the management of complex osteoporosis challenges are the mainstay of secondary care clinics.	
	Northumbria NHSFCT	Imminent fracture risk Need to mention vertebral fracture cascade Use of iv Zoledronic acid opportunistically in elderly frail inpatients at high risk of fracture or who have sustained a fracture, without necessarily committing to OPD f/u, rescan or retreatment – simply acknowledging that a single dose may produce a long period of benefit.	Thank you for your comment. Please see the responses above on imminent fracture risk.
	PAO UK	None	No action required.
	PrescQIPP	Re-evaluate teriparatide and denosumab for clinical and cost effectiveness given the significant reduction in prices on introduction of biosimilars to the market. Evaluate and make recommendations on sequential use of treatments.	Thank you for your comment. Teriparatide and denosumab will be appraised within their marketing authorisations and within the context of the update of NICE's guideline on osteoporosis..
	ROS	None	No action required.
	Theramex	No comment	No action required.

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	UCB	Please note the spelling for romosozumab is not consistent. Undertaking an MTA within a complex disease area such as osteoporosis presents many challanges. To ensure the populations outlined in the draft scope are robust, a scoping workshop must take place before the final scope is published.	Thank you for your comment. The spelling of romosozumab has been corrected throughout the scope. A scoping workshop took place on 9 April 2026.
Questions for consultation	Amgen	None	No action required.
	ABPI	No comments	No action required.
	BCUHB	None	No action required.
	BHC	None	No action required.
	BSR	**In practice are oral bisphosphonates considered before intravenous bisphosphonates?** Response: In lower risk individuals, usually yes. However, in practice, oral bisphosphonates are not always considered prior to intravenous therapy. For example, patient preference, difficulties with adherence to oral regimens, high medication burden, and gastrointestinal contraindications can make intravenous therapy the preferred option from the outset. Recognising these factors in guidance would help support patient-centred care and shared decision-making. **Population 1**	Thank you for your comment. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
		Would it be appropriate to assess the cost effectiveness of raloxifene, teriparatide and denosumab for the primary prevention group (no fracture) that meet the primary treatment eligibility criteria? YES, denosumab is renal neutral and so there are patients with primary prevention who are eligible for bisphosphonates but have contra-indications for taking them. Teriparatide and raloxifene are rarely used for primary prevention Would it be appropriate to consider women aged over 65 years with BMD <-1 who do not meet the primary treatment eligibility criteria? Is this group covered within the marketing authorisations of the drugs? YES, BMD is a continuous risk factor for fracture with no thresholds for step change in fracture risk and other risk factors increase fracture risk independently of BMD. Zoledronate studies have clearly demonstrated fracture reduction in patients with T score ≥-1.5. However, this is for secondary prevention, not primary. Primary prevention for people with BMD<-1 includes people receiving glucocorticoids, and in those with high fracture risk even if BMD is normal. It may be that the BMD readings are inaccurate or it may be that the patient has such a combination of risk factors that clearly puts them at high risk of fracture. The current NICE recommendation for denosumab specifies for those unable to take alendronate and risedronate. Would it be appropriate to amend this to 'oral bisphosphonates'? This same question applies as relevant to the other populations.	

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		YES, and also to intravenous bisphosphonates, e.g. patients with hip fractures with a CrCl < 30 ml/min **Population 2** Would it be appropriate to assess the cost effectiveness of raloxifene, teriparatide and romosuzumab for the primary prevention group (no fracture) that meet the definition for being at very high risk of fragility fracture? YES, the benefit from osteoporosis therapies is based on baseline fracture risk, irrespective of whether the high fracture risk is in the primary or secondary fracture setting. **Population 3** In practice, which treatments are used for the secondary prevention group (previous fracture) who meet the primary treatment eligibility criteria? All approved osteoporosis therapies Is it appropriate to assess the cost effectiveness of abaloparatide and romosuzumab within this group? Yes Would it be appropriate to consider women aged over 65 years with BMD <-1 who do not meet the secondary prevention treatment eligibility criteria? Particularly those with non-hip, non-vertebral fractures. Is this group covered within the marketing authorisations of the drugs?	

Section	Consultee/ Commentator	Comments [sic]	Action
		YES, BMD is a continuous risk factor for fracture with no thresholds for step change in fracture risk and other risk factors increase fracture risk independently of BMD. **Population 4** In practice, which treatments are used for the secondary prevention group that meet the definition for being at very high risk of fragility fracture? Would it be appropriate to include oral bisphosphonates, IV bisphosphonates, denosumab, teriparatide, raloxifene, abaloparatide and romosuzumab here? Is it appropriate to consider HRT as a treatment option within this MTA? YES, all drugs should be included to demonstrate superiority between osteoporosis therapies. Is it appropriate to consider HRT as a treatment option within this MTA? Response: Yes, we consider it appropriate to include HRT as a treatment option within this MTA. HRT has received renewed attention in recent years, and its role in reducing fracture risk is a question of significant interest to patients. Including HRT in the appraisal would support evidence-informed shared decision-making, helping clinicians and patients weigh the benefits and risks of all relevant treatment options. For the following drugs, please select whether A, B, C or D applies: A. Prescribed in primary care with routine follow-up in primary care B. Prescribed in secondary care with routine follow-up in primary care C. Prescribed in secondary care with routine follow-up in secondary care D. Other (please give details): • Oral bisphosphonates – A (BC)	

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		• IV bisphosphonates – C D (some community administration models) • Denosumab – A B C • Teriparatide - C • Raloxifene – A B • Abaloparatide - C • Romosuzumab – C Do you consider that the use of any of these drugs can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? YES, the current methods of QALY calculation may not take into account a reduction imminent risk of fracture and competing risk of mortality. Given fracture risk is non-linear after an index fracture, applying a 3 or 5 year or longer horizon will miss up to 50% of fractures and so an early benefit for patients, especially for non-spine fractures maybe missed. Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits. Please indicate if any of the treatments in the scope are used in NHS practice differently than advised in their Summary of Product Characteristics. For example, if the dose or dosing schedule for a treatment is different in clinical practice. If so, please indicate the reasons for different usage of the treatment(s) in NHS practice. If stakeholders consider this a relevant issue, please provide references for data on the efficacy of any treatments in the pathway used differently than advised in the Summary of Product Characteristics.	

Section	Consultee/ Commentator	Comments [sic]	Action
		The FRAME trial for Romosozumab demonstrated an unexpected between country difference in non-vertebral fracture reduction. It is reasonable to use the subsequent published analyses for rest of world (Cosman JBMR 2018: https://pubmed.ncbi.nlm.nih.gov/29750828/) and European (Langdahl OI 2022: https://pubmed.ncbi.nlm.nih.gov/36173415/) data analyses demonstrate an early and significant efficacy in reduction in non-spine fractures, that is concordant with the ARCH study (Saag NEJM 2018: https://pubmed.ncbi.nlm.nih.gov/29320649/). NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope: • could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which the treatments are licensed; • could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology; • could have any adverse impact on people with a particular disability or disabilities.	

Section	Consultee/ Commentator	Comments [sic]	Action
		Patients with severe spinal and hip disability are unable to have a DXA and so would be excluded from access to effective medicines in this guide Consideration should be given to appropriate treatments for younger people.	
	FFFAP RCP	**Population 1** Would it be appropriate to assess the cost effectiveness of raloxifene, teriparatide and denosumab for the primary prevention group (no fracture) that meet the primary treatment eligibility criteria? FFFAP is targeted at secondary prevention so have no preference but would suggest they are included Would it be appropriate to consider women aged over 65 years with BMD <-1 who do not meet the primary treatment eligibility criteria? Is this group covered within the marketing authorisations of the drugs? BMD is a risk factor for fracture risk, so it is unreasonable to have a single threshold. Many older adults have degenerative changes at the spine from osteoarthritis or secondary to fractures and so will have a spine t score <-1 but still be at high fracture risk based on recency of fragility fractures etc. The current NICE recommendation for denosumab specifies for those unable to take alendronate and risedronate. Would it be appropriate to amend this to 'oral bisphosphonates'? This same question applies as relevant to the other populations. YES, and also to intravenous bisphosphonates, e.g. patients with hip fractures with a CrCl < 30 ml/min as per our 5 nations recommendation [https://academic.oup.com/ageing/article/52/9/afad172/7275533]	Thank you for your comment. See previous responses above regarding BMD thresholds.

Section	Consultee/ Commentator	Comments [sic]	Action
		Population 2 Would it be appropriate to assess the cost effectiveness of raloxifene, teriparatide and romosozumab for the primary prevention group (no fracture) that meet the definition for being at very high risk of fragility fracture? FFFAP is targeted at secondary prevention so have no preference but would suggest they are included **Population 3** In practice, which treatments are used for the secondary prevention group (previous fracture) who meet the primary treatment eligibility criteria? All approved osteoporosis therapies Is it appropriate to assess the cost effectiveness of abaloparatide and romosozumab within this group? Yes Would it be appropriate to consider women aged over 65 years with BMD <-1 who do not meet the secondary prevention treatment eligibility criteria? Particularly those with non-hip, non-vertebral fractures. Is this group covered within the marketing authorisations of the drugs? BMD is a risk factor for fracture risk, so it is unreasonable to have a single threshold. **Population 4**	

Section	Consultee/ Commentator	Comments [sic]	Action
		In practice, which treatments are used for the secondary prevention group that meet the definition for being at very high risk of fragility fracture? Would it be appropriate to include oral bisphosphonates, IV bisphosphonates, denosumab, teriparatide, raloxifene, abaloparatide and romosozumab here? Is it appropriate to consider HRT as a treatment option within this MTA? YES, all drugs should be included to demonstrate superiority between osteoporosis therapies. For the following drugs, please select whether A, B, C or D applies: A. Prescribed in primary care with routine follow-up in primary care B. Prescribed in secondary care with routine follow-up in primary care C. Prescribed in secondary care with routine follow-up in secondary care D. Other (please give details): • Oral bisphosphonates – A • IV bisphosphonates – C and B • Denosumab – A and B • Teriparatide - C • Raloxifene – A (recommended in secondary care) • Abaloparatide - C • Romosozumab – C Do you consider that the use of any of these drugs can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? YES, the current methods of QALY calculation may not take into account a reduction imminent risk of fracture and competing risk of mortality. Given fracture risk is non-linear after an index fracture, applying a 3 or 5 year or	

Section	Consultee/ Commentator	Comments [sic]	Action
		longer horizon will miss up to 50% of fractures and so an early benefit for patients, especially for non-spine fractures maybe missed. Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits. Please indicate if any of the treatments in the scope are used in NHS practice differently than advised in their Summary of Product Characteristics. For example, if the dose or dosing schedule for a treatment is different in clinical practice. If so, please indicate the reasons for different usage of the treatment(s) in NHS practice. If stakeholders consider this a relevant issue, please provide references for data on the efficacy of any treatments in the pathway used differently than advised in the Summary of Product Characteristics. The Lyles study clearly demonstrated a survival benefit in adults with a recent hip fracture [https://www.nejm.org/doi/full/10.1056/NEJMoa074941] The FRAME trial for Romosozumab demonstrated an unexpected between country difference in non-vertebral fracture reduction. It is reasonable to use the subsequent published analyses for rest of world (Cosman JBMR 2018: https://pubmed.ncbi.nlm.nih.gov/29750828/) and European (Langdahl OI 2022: https://pubmed.ncbi.nlm.nih.gov/36173415/) data analyses demonstrate an early and significant efficacy in reduction in non-spine fractures, that is concordant with the ARCH study (Saag NEJM 2018: https://pubmed.ncbi.nlm.nih.gov/29320649/). The Lyles study clearly demonstrated a survival benefit in adults with a recent hip fracture [https://www.nejm.org/doi/full/10.1056/NEJMoa074941} NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular	

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		protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope: • could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which the treatments are licensed; • could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology; • could have any adverse impact on people with a particular disability or disabilities. Patients with hip fracture often have mild to severe cognitive impairment and mobility restrictions that may make them unable to have a DXA but have the most to lose if they have another fracture. Hence, clinical appropriateness should be retained in the recommendations for adults who are likely very high fracture risk.	
	NOGG	In practice are oral bisphosphonates considered before intravenous bisphosphonates? Response: In lower risk individuals, yes. But for example, after hip fracture iv Zoledronate is used first line given the high risk of re-fracture, and the strong evidence of efficacy.	Thank you for your comment. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
		Population 1: **Primary prevention** for men aged 50 and over and women who have experienced menopause and meet the criteria for pharmacological treatment Would it be appropriate to assess the cost effectiveness of raloxifene, teriparatide and denosumab for the primary prevention group (no fracture) that meet the primary treatment eligibility criteria? Response: Yes. These cost effectiveness data would be welcomed across all the categories, since it has been a long time since previous TAs. In that time there have been biosimilar (generic) teriparatide products, biosimilar denosumab. In clinical practice use of any of these medications are very uncommon for primary prevention. Please also consider hormone replacement therapy in post-menopausal women. Population 1: **Primary prevention** for men aged 50 and over and women who have experienced menopause and meet the criteria for pharmacological treatment Would it be appropriate to consider women aged over 65 years with BMD <-1 who do not meet the primary treatment eligibility criteria? Is this group covered within the marketing authorisations of the drugs? Response: Yes, it would be appropriate given the evidence available. There have been a series of RCTs using iv Zoledronate which warrant evaluation. The first trial was in postmenopausal women with osteopenia and showed substantial fracture risk reduction over 6 years. Fracture Prevention with	

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		Zoledronate in Older Women with Osteopenia | New England Journal of Medicine Subsequent follow up showed benefits were maintained for 1.5-3.5 years Duration of fracture prevention after zoledronate treatment in women with osteopenia: observational follow-up of a 6-year randomised controlled trial to 10 years - The Lancet Diabetes & Endocrinology. More recently a trial of 5-yearly iv zoledronate in 50-60 year old women with normal or osteopenic BMD showed fracture risk reduction. Fracture Prevention with Infrequent Zoledronate in Women 50 to 60 Years of Age | New England Journal of Medicine. Given the low cost of Zoledronate, the clinical and cost effectiveness of infrequent Zoledronate dosing in non-osteoporotic post-menopausal women should be considered as a longer term strategy towards primary prevention in the UK. Population 1: **Primary prevention** for men aged 50 and over and women who have experienced menopause and meet the criteria for pharmacological treatment The current NICE recommendation for denosumab specifies for those unable to take alendronate and risedronate. Would it be appropriate to amend this to 'oral bisphosphonates'? This same question applies as relevant to the other populations. Response: Yes, this would make recommendations simpler. Population 2: **Primary prevention** for men aged 50 and over and women who have experienced menopause and meet the **very high risk** criteria	

Section	Consultee/ Commentator	Comments [sic]	Action
		Would it be appropriate to assess the cost effectiveness of raloxifene, teriparatide and romosuzumab for the primary prevention group (no fracture) that meet the definition for being at very high risk of fragility fracture? Response: Yes, certainly for Teriparatide and Romosozumab. We consider very high fracture risk to at times arise from a combination of clinical risk factors, accompanied by low BMD, where treatment first with an anabolic therapy can be justified. In reality Raloxifene is unlikely to be used for someone at very high risk, given there are more efficacious options available. Population 3: **Secondary prevention** for men aged 50 and over and women who have experienced menopause and meet the criteria for pharmacological treatment In practice, which treatments are used for the secondary prevention group (previous fracture) who meet the primary treatment eligibility criteria? Response: Hormone Replacement Therapy (female only), Alendronate, Risedronate, Zoledronate, Denosumab. Population 3: **Secondary prevention** for men aged 50 and over and women who have experienced menopause and meet the criteria for pharmacological treatment Is it appropriate to assess the cost effectiveness of abaloparatide and romosuzumab within this group?	

Section	Consultee/ Commentator	Comments [sic]	Action
		Response: Yes, and teriparatide. But comparison will need to be precise, given the differing sequential treatment requirements (1 yr romosozumab plus 2-year anti-resorptive) vs 18 months abaloparatide (followed by anti-resorptive) vs 24 months teriparatide (followed by anti-resorptive). It is important to bear in mind the secondary care clinical efficacy and safety criteria that are currently in place to recommend one treatment over another (e.g. hip fracture risk favouring romosozumab, CVS/CVA risk favouring teriparatide or abaloparatide). Population 3: **Secondary prevention** for men aged 50 and over and women who have experienced menopause and meet the criteria for pharmacological treatment Would it be appropriate to consider women aged over 65 years with BMD <-1 who do not meet the secondary prevention treatment eligibility criteria? Particularly those with non-hip, non-vertebral fractures. Is this group covered within the marketing authorisations of the drugs? Response: Yes absolutely essential. The majority of fragility fractures occur in people with a T-Score between –1 and –2.5. Humerus, wrist, pelvis etc fragility fractures identify a population at high imminent risk of future fractures, especially over the age of 65. They should all be offered treatment. This group should meet the 'secondary prevention treatment eligibility criteria', and we would urge NICE to revise these criteria accordingly. Population 4: **Secondary prevention** for men aged 50 and over and women who have experienced menopause and meet the **very high risk** criteria In practice, which treatments are used for the secondary prevention group that meet the definition for being at very high risk of fragility fracture?	

Section	Consultee/ Commentator	Comments [sic]	Action
		Response: An anabolic agent should first be considered, i.e. romosozumab (if CVD risk is low), or teriparatide or abaloparatide. If these are contraindicated or declined by the patient, then Zoledronate or Denosmuab would be alternatives. If patients decline a parenteral therapy, then an oral bisphosphonate is an alternative, occasionally HRT or Raloxifene if there are no other choices available. Population 4: **Secondary prevention** for men aged 50 and over and women who have experienced menopause and meet the **very high risk** criteria Would it be appropriate to include oral bisphosphonates, IV bisphosphonates, denosumab, teriparatide, raloxifene, abaloparatide and romosuzumab here? Response: Yes, but it is important to note that romosozumab and teriparatide were tested at the request of UK/European/US regulators vs. oral bisphosphonates (vs alendronate = ARCH Study, and vs risedronate VERO study) to provide specific clinical comparative data that informed both the licence for romosozumab and the first-line clinical usage scenario. The latter has led to reconfiguration of clinical services to accommodate their use. Abaloparatide also has lesser (but still worth considering) data from a network metanalysis vs other treatments. It would be unwise to compare treatments known to be considerably less efficacious in a cost per QALY scenario. Note earlier comment on medication duration and complexities of comparison between regimens and sequences of treatments given all anabolic therapies must be followed by an anti-resorptive. Is it appropriate to consider HRT as a treatment option within this MTA?	

Section	Consultee/ Commentator	Comments [sic]	Action
		Response: Yes. In some scenarios, such as osteoporosis just after menopause in women, or a wrist fracture and not ‘very high’ risk. HRT provides a good option in the early years of post-menopausal life, when considering the sequence of treatments that will be needed for a woman over potentially 35+ years. For the following drugs, please select whether A, B, C or D applies: A. Prescribed in primary care with routine follow-up in primary care B. Prescribed in secondary care with routine follow-up in primary care C. Prescribed in secondary care with routine follow-up in secondary care D. Other (please give details): Oral bisphosphonates: Mainly A, some B and rarely C IV bisphosphonates: Mainly currently C, but nationally our aim should be for B and then A Denosumab: Currently a mixture of B and A, with some C e.g. when Creatinine clearance between 15 and 35. It is important to note in scenario A, GPs need to be more aware that: Before starting denosumab, they should ensure there is a long-term treatment plan which considers the potential need to stop denosumab and how this would be managed (given the risk of multiple vertebral fractures on denosumab cessation). And hence that denosumab treatment must not be stopped without a plan for subsequent anti-resorptive therapy, where renal function permits. Often this does require consultation with secondary care. Teriparatide C	

Section	Consultee/ Commentator	Comments [sic]	Action
		Raloxifene B and C Abaloparatide C Romosuzumab C Do you consider that the use of any of these drugs can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? Response: Yes, for instance, the effects of anabolic-first strategies on preventing high grade clinical vertebral fractures - not all newly occurring vertebral fractures are equal in their effects on patients in terms of pain, disability and recovery. Note some trials focus on radiographic vertebral fractures only. A further consideration stems from the need to consider when starting denosumab it is very difficult to stop it – as indicated above. Unplanned cessation can lead to painful vertebral fractures that impact quality of life.	
	Northumbria NHSFCT	• Yes oral bisphosphonates are considered before IV bisphosphonates Population 1: 1. Yes 2. No 3. Yes appropriate to amend term to “oral bisphosphonates” Population 2 1. Yes. Patients with extremely low BMD who ahave very strong family history of fracture could benefit from these treatments	Thank you for your comment. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
		Population 3 1. Potentially all of them pending circumstance 2. Yes, alongside Teriparatide, as spinal bone density is often unreliable due to degenerative change. 3. No Population 4 1. All of the treatments mentioned in the MTA, pending patient preference (particularly relating to self-injection) and suitability 2. Yes 3. Yes but also in addition to other osteoporosis treatment, in young patients who are at very high fracture risk should not have HRT alone 4. i) Oral bisphosphonates A+B ii) IV bisphosphonates: C – but this should be changed to include primary care prescribing and administration and possibly follow-up. Community admin of IV zol should be a big priority iii) Denosumab: D Formal shared care agreement iV) Teriparatide: B or C (depending on what treatment is used after) v) Raloxifene B+C (Green+ on our formulary on specialist advice only) vi) Abaloparatide: B or C (depending on what treatment is used after) vii) Romosozumab: B or C (depending on what treatment is used after) 5. Big psychological benefits related to fear of future fractures, particularly hip or spontaneous vertebral fractures 6. Patient surveys relating to osteoporosis 7. Zoledronic acid we use every 18 months https://www.nejm.org/doi/full/10.1056/NEJMoa1808082	

Section	Consultee/ Commentator	Comments [sic]	Action
		https://www.sciencedirect.com/science/article/abs/pii/S2213858724000032 8. I think there needs to be more discussion on using potent anabolics in men with very high fracture risk	
	PAO UK	None	No action required.
	PrescQIPP	For the following drugs, please select whether A, B, C or D applies: A. Prescribed in primary care with routine follow-up in primary care B. Prescribed in secondary care with routine follow-up in primary care C. Prescribed in secondary care with routine follow-up in secondary care D. Other (please give details): Oral bisphosphonates: A (unless following romosozumab when we would expect the specialist to initiate and follow up) IV bisphosphonates: C Denosumab: D Current practice is secondary care specialist initiated then transfer to primary care for ongoing prescribing and monitoring Teriparatide: C Raloxifene: D Secondary care specialist advice or initiated then transfer to primary care for ongoing prescribing and monitoring Abaloparatide: C	Thank you for your comment. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
		Romosuzumab: C	
	PrescQIPP	None	No action required.
	ROS	In practice are oral bisphosphonates considered before intravenous bisphosphonates? Response: In lower risk individuals, yes. We would argue that, in practice, oral bisphosphonates are not always considered prior to intravenous therapy. For example, patient preference, difficulties with adherence to oral regimens, high medication burden, and gastrointestinal contraindications can make intravenous therapy the preferred option from the outset. Recognising these factors in guidance would help support patient-centred care and shared decision-making. Population 1: **Primary prevention** for men aged 50 and over and women who have experienced menopause and meet the criteria for pharmacological treatment Would it be appropriate to assess the cost effectiveness of raloxifene, teriparatide and denosumab for the primary prevention group (no fracture) that meet the primary treatment eligibility criteria? Response: The cost effectiveness data would be welcomed across all the categories. Updates are needed due to biosimilar (generic) teriparatide and denosumab products. In clinical practice use of raloxifene, teriparatide, and denosumab are very uncommon for primary prevention.	Thank you for your comment. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
		Population 1: **Primary prevention** for men aged 50 and over and women who have experienced menopause and meet the criteria for pharmacological treatment Would it be appropriate to consider women aged over 65 years with BMD <-1 who do not meet the primary treatment eligibility criteria? Is this group covered within the marketing authorisations of the drugs? Response: Primary prevention for people with BMD<-1 would in practice be restricted to people receiving glucocorticoids Population 1: **Primary prevention** for men aged 50 and over and women who have experienced menopause and meet the criteria for pharmacological treatment The current NICE recommendation for denosumab specifies for those unable to take alendronate and risedronate. Would it be appropriate to amend this to 'oral bisphosphonates'? This same question applies as relevant to the other populations. Response: Yes Population 2: **Primary prevention** for men aged 50 and over and women who have experienced menopause and meet the **very high risk** criteria Would it be appropriate to assess the cost effectiveness of raloxifene, teriparatide and romosuzumab for the primary prevention group (no fracture) that meet the definition for being at very high risk of fragility fracture?	

Section	Consultee/ Commentator	Comments [sic]	Action
		Response: Possibly for raloxifene but these drugs are rarely used in this context. Population 3: **Secondary prevention** for men aged 50 and over and women who have experienced menopause and meet the criteria for pharmacological treatment In practice, which treatments are used for the secondary prevention group (previous fracture) who meet the primary treatment eligibility criteria? Response: All approved treatments Population 3: **Secondary prevention** for men aged 50 and over and women who have experienced menopause and meet the criteria for pharmacological treatment Is it appropriate to assess the cost effectiveness of abaloparatide and romosuzumab within this group? Response: Yes, and teriparatide, including biosimilars. But comparing needs to consider different durations of treatment. It is important to bear in mind the clinical situations where one drug is preferable duie to efficacy (e.g. hip fracture risk favouring romosozumab, CVS/CVA risk favouring teriparatide or abaloparatide). Population 3: **Secondary prevention** for men aged 50 and over and women who have experienced menopause and meet the criteria for pharmacological treatment	

Section	Consultee/ Commentator	Comments [sic]	Action
		Would it be appropriate to consider women aged over 65 years with BMD <-1 who do not meet the secondary prevention treatment eligibility criteria? Particularly those with non-hip, non-vertebral fractures. Is this group covered within the marketing authorisations of the drugs? Response: Yes as treatment is considered based on fracture risk rather than BMD. Osteoporosis is diagnosed clinically in practice rather than by BMD thresholds. Population 4: **Secondary prevention** for men aged 50 and over and women who have experienced menopause and meet the **very high risk** criteria In practice, which treatments are used for the secondary prevention group that meet the definition for being at very high risk of fragility fracture? Response: All drugs – although anabolic are favoured other drugs may be considered due to patient situation or preferences Population 4: **Secondary prevention** for men aged 50 and over and women who have experienced menopause and meet the **very high risk** criteria Would it be appropriate to include oral bisphosphonates, IV bisphosphonates, denosumab, teriparatide, raloxifene, abaloparatide and romosuzumab here? Response: Yes Note earlier comment on medication duration and complexities of comparison between regimens and sequences of treatments.	

Section	Consultee/ Commentator	Comments [sic]	Action
		Is it appropriate to consider HRT as a treatment option within this MTA? Response: Yes For the following drugs, please select whether A, B, C or D applies: A. Prescribed in primary care with routine follow-up in primary care B. Prescribed in secondary care with routine follow-up in primary care C. Prescribed in secondary care with routine follow-up in secondary care D. Other (please give details): • Oral bisphosphonates A (BC) • IV bisphosphonates C D (community administration) • Denosumab A B and C • Teriparatide C • Raloxifene A and B • Abaloparatide C • Romosuzumab C Do you consider that the use of any of these drugs can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? Response: Yes, for instance, the effects of anabolic-first strategies on preventing vertebral fractures- vertebral fractures can be associated with significant pain and disability 1.3 Assessing fragility fracture risk 2 1.3.1 Offer a dual-energy X-ray absorptiometry (DXA) scan to measure bone 3 mineral density (BMD) when assessing fragility fracture risk (unless not 4 needed for treatment decisions or monitoring) in people aged between 50 5 and 90 who have had either: 6 • a previous hip or vertebral fragility fracture or 7 • 2 or more fragility fractures.	

Section	Consultee/ Commentator	Comments [sic]	Action
		8 1.3.2 When assessing fragility fracture risk with a risk prediction tool (FRAX or 9 QFracture) determine the 10-year risk of major osteoporotic fracture. 10 1.3.3 Use either FRAX or QFracture when assessing fragility fracture risk in 11 people aged between: 12 • 50 and 90 who do not meet the criteria in recommendation 1.3.1 Response: This guideline excludes patients aged 90 years or more with good functional and physiological baseline who have severe osteoporosis with major osteoporotic fractures and remain at very high imminent fracture risk from anabolic therapy which is superior in fracture risk reduction and bone density gains in the most immediate period following index fractures. With rising cost of hip fractures at an annual cost of £1.2Billion pounds and reported risk of the number of hip fractures doubling by 2060, withholding anabolic therapy by excluding this cohort from DEXA access is counter intuitive and inequitable. This cohort is also at higher mortality risk following fractures. A major incentive to develop fracture liaison services, include pelvic fractures into the national hip fracture database, is to facilitate early recognition of this most high-risk cohort and commence bone building medication when appropriate. Clinicians are best placed to assess appropriateness based on comprehensive geriatric assessments. Anabolic therapy reduces dependency on outpatient care as home based, followed sequentially with oral therapy. Current guideline for acute fractures recommends injectable therapy which are outpatient based with Denosumab lifelong and Zolendronate treatment for 5 years. Considering the time from onset of therapy to benefit of antiresorptive alone is statistically inferior to that of anabolic therapy, the overall benefit of excluding patients 90 years or more based on 10-year risk reduction rather than 2-year risk reduction is insufficient.	

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		Real-world evidence indicates that patients 90 years or more can successfully self-inject anabolic therapy and continue to live beyond expectation. We also know that people are living longer. Evidence also indicates that response to anabolic therapy is not negatively impacted by age, rather by severity of bone density. Patients aged 90 or more are then more likely to have more severe osteoporosis and better response to anabolic therapy. BMD measurement is an essential criterion for anabolic therapy consideration and ICB funding. This recommendation does not align with British Geriatric society Core20PLUS5 Framework: Reducing healthcare inequalities among older people. It guarantees inequality and an age-based exclusion.	
	Theramex	*Population 1:* *a. Would it be appropriate to assess the cost effectiveness of raloxifene, teriparatide and denosumab for the primary prevention group (no fracture) that meet the primary treatment eligibility criteria?* *b. Would it be appropriate to consider women aged over 65 years with BMD <-1 who do not meet the primary treatment eligibility criteria? Is this group covered within the marketing authorisations of the drugs?* *c. The current NICE recommendation for denosumab specifies for those unable to take alendronate and risedronate. Would it be appropriate to amend this to 'oral bisphosphonates'? This same question applies as relevant to the other populations.* a. No comment b. No comment	Thank you for your comment. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
		c. No comment *Population 2:* *a. Would it be appropriate to assess the cost effectiveness of raloxifene, teriparatide and romosuzumab for the primary prevention group (no fracture) that meet the definition for being at very high risk of fragility fracture?* a. No comment *Population 3:* *a. In practice, which treatments are used for the secondary prevention group (previous fracture) who meet the primary treatment eligibility criteria?* *b. Is it appropriate to assess the cost effectiveness of abaloparatide and romosuzumab within this group?* *c. Would it be appropriate to consider women aged over 65 years with BMD <-1 who do not meet the secondary prevention treatment eligibility criteria? Particularly those with non-hip, non-vertebral fractures. Is this group covered within the marketing authorisations of the drugs?* a. Theramex accept that medical practice and scientific literature demonstrate use of a wide range of treatments for the secondary prevention group outlined in Population 3. In this context, it is relevant to highlight the value of osteoanabolic treatments in building bone rather than preserving bone. This is supported by Cosman et al., 2017, wherein it is suggested that the common practice of switching to osteoanabolic agents only after patients	

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		have an inadequate response to antiresorptive agents (e.g., intercurrent fracture of inadequate bone mineral density (BMD) response) is sub-optimal and may instead result in transient loss in BMD and bone strength. (Cosman F, Nieves JW, Dempster DW. Treatment Sequence Matters: Anabolic and Antiresorptive Therapy for Osteoporosis. *J Bone Miner Res*. 2017;32(2):198-202. doi:10.1002/jbmr.3051) b. Theramex agree this is appropriate as per the single technology assessment (STA) for abaloparatide. c. Theramex agree with the committee's suggestion to consider the group of patients aged over 65 years with BMD <-1 who do not meet the secondary prevention treatment eligibility criteria. The marketing authorisation for abaloparatide covers this population if determined to be at an increased risk of fracture. *Population 4:* *a. In practice, which treatments are used for the secondary prevention group that meet the definition for being at very high risk of fragility fracture?* *b. Would it be appropriate to include oral bisphosphonates, IV bisphosphonates, denosumab, teriparatide, raloxifene, abaloparatide and romosuzumab here?* a. In UK practice for postmenopausal women at very high risk of fragility fracture in the secondary prevention setting, treatment typically involves first-line osteoanabolic therapy where available followed by potent antiresorptive therapy such as denosumab or intravenous zoledronic acid, with oral bisphosphonates used when appropriate. Moreover, the International	

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		Osteoporosis Foundation (IOF) and European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) recommend treatment initiation with an osteoanabolic (bone-forming) agent in patients at the highest risk of fracture, followed by an antiresorptive agent to maintain the gains in bone mineral density (BMD). This approach demonstrates a more rapid and greater fracture risk reduction (Curtis EM, Reginster JY, Al-Daghri N, et al. Management of patients at very high risk of osteoporotic fractures through sequential treatments. *Aging Clin Exp Res*. 2022;34(4):695-714. doi:10.1007/s40520-022-02100-4). b. Theramex agree it is appropriate to include abaloparatide in this population and would also like to raise the importance of considering its position in the treatment sequence. It is vital to also raise the importance of the value of osteoanabolics, such as abaloparatide, being used first, ahead of bisphosphonates, to preserve the 'anabolic window' and to maximise the value of the bone forming action as noted by the guidelines committee in Evidence Review E p46 ('The committee discussed that starting an antiresorptive treatment is not appropriate for people at high risk that may need to start osteoanabolic treatment as it would reduce effectiveness'). This is also supported by Cosman et al., 2017. (Cosman F, Nieves JW, Dempster DW. Treatment Sequence Matters: Anabolic and Antiresorptive Therapy for Osteoporosis. *J Bone Miner Res*. 2017;32(2):198-202. doi:10.1002/jbmr.3051). *Is it appropriate to consider HRT as a treatment option within this MTA?* Theramex also acknowledge that hormone replacement therapy (HRT) acts as a preventative anti-osteoporosis drug in women aged 50-60, but also younger postmenopausal women (early menopause) through the suppression of bone resorption and preservation of bone density. This preventative	

Section	Consultee/ Commentator	Comments [sic]	Action
		pathway may reduce the proportion of patients progressing to severe osteoporosis by early intervention. Theramex support the provision of HRT as an option in the treatment pathway for postmenopausal patients with osteoporosis aged ≤60 years where they can/will take HRT. Under the current license, HRT is indicated for the "prevention of osteoporosis in postmenopausal women at high risk of future fractures who are intolerant of, or contraindicated for, other medicinal products approved for the prevention of osteoporosis". (Source: Core SmPC for hormone replacement therapy products, December 2025, CMDh/131/2003, Rev. 11). We would like to specify that HRT is appropriate across the primary prevention populations and secondary prevention populations, according to products' label and following NICE recommendations, where patients are aged ≤60 years. Theramex believe that comparators will need to be defined considering the positioning of HRT early in the treatment pathway for all postmenopausal osteoporosis patients aged ≤60 years, and specifically in patients who are intolerant of, or contraindicated for, other medicinal osteoporosis products. *For the following drugs, please select whether A, B, C or D applies:* *A. Prescribed in primary care with routine follow-up in primary care* *B. Prescribed in secondary care with routine follow-up in primary care* *C. Prescribed in secondary care with routine follow-up in secondary care* *D. Other (please give details):* Abaloparatide: C Abaloparatide is an injectable osteoanabolic therapy requiring expert fracture-risk stratification, contraindication screening (e.g., hypercalcaemia risk), specialist-led initiation and ongoing monitoring within secondary care bone clinics, treatment duration control, and monitoring of bone response and safety that cannot be safely or consistently managed in primary care. Routine follow-up will be in the secondary care setting.	

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		Do you consider that the use of any of these drugs can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? Theramex consider that certain health-related benefits associated with these treatments may not be fully captured within the QALY framework as currently modelled. In particular, differential treatment persistence and adherence may translate into sustained fracture risk reduction, fewer subsequent fractures, and improved long-term patient outcomes, which may not be fully reflected if persistence assumptions are not explicitly incorporated. The External Assessment Group (EAG) previously noted that persistence is a key driver of the ICER (TA991); however, if the model does not transparently account for differential persistence across comparators, the associated health gains may be underestimated. Theramex, therefore, request that treatment persistence and adherence be specified as formal model inputs to ensure that the full extent of health benefits is appropriately captured and reflected in the QALY estimates. *Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.* Theramex would like to highlight the following data to address the benefit of abaloparatide with respect to treatment persistence and adherence: - Gold DT, Weiss R, Beckett T, et al. Abaloparatide Real-World Patient Experience Study. *JBMR Plus*. 2021;5(3):e10457. Published 2021 Feb 4. doi:10.1002/jbm4.10457 Gold DT, Beckett T, Deal C, et al. Treatment patterns in women with postmenopausal osteoporosis using abaloparatide: a real-world observational	

Section	Consultee/ Commentator	Comments [sic]	Action
		study. *Osteoporos Int*. 2024;35(8):1407-1415. doi:10.1007/s00198-024-07070-z *Please indicate if any of the treatments in the scope are used in NHS practice differently than advised in their Summary of Product Characteristics. For example, if the dose or dosing schedule for a treatment is different in clinical practice. If so, please indicate the reasons for different usage of the treatment(s) in NHS practice. If stakeholders consider this a relevant issue, please provide references for data on the efficacy of any treatments in the pathway used differently than advised in the Summary of Product Characteristics.* No comment *NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.* No comment	
	UCB	It is appropriate to assess the cost-effectiveness of romososumab in populations 2, 3 and 4. However, it is not appropriate to include oral bisphosphonates within population 4. Raloxifene is not commonly used as a treatment for osteoporosis in UK clinical practice and UCB questions it's inclusion in the MTA scope.	Thank you for your comment. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
		NICE previously explored assessing osteoporosis medicines via an MTA as part of the romosozumab appraisal. This approach proved challenging and was abandoned. UCB is unclear to what has changed in the interim and so is concerned that an MTA may not be the most appropriate methodology.	
Additional comments on the draft scope	Amgen	Amgen supports the proposed MTA and believes the draft remit and scope provide a sound basis for evaluation. We encourage NICE to further emphasise patient heterogeneity, treatment sequencing, and real-world use to ensure the appraisal fully reflects NHS practice. We thank NICE for the opportunity to comment and look forward to continued engagement during the appraisal process.	Thank you for your comment. No action required.
	ABPI	No comments	No action required.
	BHC	None	No action required.
	BSR	None	No action required.
	FFFAP RCP	None	No action required.
	NOGG	None	No action required.
	Northumbria NHSFCT	None	No action required.
	PAO UK	None	No action required.
	ROS	Clarity and consistency across national guidance are essential to reducing variation in access to osteoporosis care. The NOGG framework is widely	Thank you for your comment. The

Section	Consultee/ Commentator	Comments [sic]	Action
		embedded within UK clinical practice and commissioning pathways. Where recommendations diverge from established risk-based approaches currently in use, there is a risk of creating confusion for clinicians and commissioners, which may in turn delay decision making or lead to inconsistent application of treatment criteria. For patients, particularly those who have already experienced a fragility fracture, it can be difficult to understand why eligibility for treatment may differ depending on the framework applied. We would therefore encourage NICE to ensure that the final scope and recommendations are coherent with wider national standards and support clear, equitable, and practical implementation across the NHS, helping to close rather than widen the existing treatment gap. We would also encourage NICE to consider the broader policy context in which osteoporosis care sits. In other areas of long-term condition management, such as cardiovascular disease, treatment decisions are routinely guided by an individual's overall risk rather than a single test result. A similar approach in osteoporosis would support clearer shared decision-making conversations and greater consistency across disease areas. From a patient perspective, it is easier to understand decisions that are based on an assessment of overall fracture risk, rather than fixed thresholds tied to one measurement. Aligning osteoporosis policy with established risk-based approaches used elsewhere in the NHS would promote fairness, clarity and parity of esteem between conditions.	committee will consider current UK clinical practice and policy during the appraisal.
	Theramex	No comment	No action required.
	UCB	None	No action required.
	The Robert Jones and	**Section: Economic Analysis.** We strongly disagree with a "least expensive option" mandate. This fails to consider that drugs like **romosozumab** offer superior hip fracture reduction data (38% reduction in ARCH) compared to	Thank you for your comment. All

Section	Consultee/ Commentator	Comments [sic]	Action
	Agnes Hunt Orthopaedic Hospital	other anabolics. Clinicians must retain the autonomy to prescribe the most clinically appropriate agent based on the patient's specific fracture history and site-specific risk.	technologies will be appraised using a cost-utility analysis as set out in reference case set out in NICE health technology evaluations: the manual.