National Institute for Health and Care Excellence

Health Technology Evaluation

Abaloparatide for treating osteoporosis in postmenopausal women [ID882]
Response to stakeholder organisation comments on the draft remit and draft scope

Please note: Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Comment 1: the draft remit and proposed process

Section	Stakeholder	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	Theramex UK Limited	We welcome consideration of abaloparatide within its anticipated MHRA marketing authorisation: treatment of osteoporosis in post-menopausal women at increased risk of fracture.	Thank you. No action required.
	UCB Pharma	No comment	Thank you. No action required.
	British Society for Rheumatology	Appropriate to evaluate, as it is helpful to have a number of different treatment options available. A single technology appraisal seems appropriate given that the available comparator treatments have already been evaluated by NICE.	Thank you. No action required.
	Royal College of Physicians (RCP)	There are limited anabolic options at present compared with a range of anti-resorptives and we welcome addition anabolic options. It may be useul for positioning in clinical pathways to appraise Abaloparatide with teriparatide analogues as an MTA. On issue is duration of therapy, PTH analogues are	Thank you, your comments have been noted. There are no ongoing appraisals that are suitable to combine

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		recommended for 24 months while Abaloparatide is recommended for 18 months.	with this as an MTA. We have taken note of this suggestion and will consider for future planning. No action needed
	The Royal Osteoporosis Society	We are pleased to see that NICE plan to evaluate another osteoporosis drug treatment and agree that a single technology appraisal is appropriate	Thank you. No action required.
Wording	Theramex UK Limited	The remit adequately captures the decision problem. It may be appropriate to include “at increased risk of fracture” in accordance with the anticipated indication. Increased fracture risk is defined by prior fracture history and bone mineral density (BMD).	Thank you. The remit was kept intentionally broad. NICE will appraise abaloparatide within the terms of its marketing authorisation. No action needed.
	UCB Pharma	No comment	Thank you. No action required.
	Royal College of Physicians (RCP)	The clinical effectiveness should include patients at high and very high risk/ imminent risk of fracture	Thank you. The remit was kept intentionally broad. NICE will appraise abaloparatide within the terms of its marketing authorisation. No action needed.

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	The Royal Osteoporosis Society	Yes	Thank you. No action required.
Additional comments on the draft remit	Theramex UK Limited	None	Thank you. No action required.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Theramex UK Limited	No additional comments.	Thank you. No action required.
	UCB Pharma	No comment	Thank you. No action required.
	British Society for Rheumatology	Regarding the statement 'In the UK, it is estimated that around 3 million people have osteoporosis, which is defined as having a bone mineral density (BMD) that is 2.5 standard deviations or more below the average value for young healthy adults (usually referred to as a 'T-score' of -2.5 or lower): NICE itself (TA161, 2008) has previously stated that a diagnosis 'may be assumed in women aged 75 years or older if the responsible clinician considers a DXA scan to be clinically inappropriate or unfeasible'. and this is also quoted in the Quality and Outcomes framework. This is important as restricting this scope to people with BMD defined osteoporosis may restrict access as the majority of people with low trauma fragility fractures do not have BMD defined osteoporosis (Siris ES, Chen YT,	Thank you, your comments have been, noted. The background section is intended to provide a brief summary of the condition. Abaloparatide will be appraised within its marketing authorisation and the committee will consider any equalities issues during the

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		Abbott TA et al. Bone mineral density thresholds for pharmacological intervention to prevent fractures. Arch Intern Med 2004; 164: 1108–12.). The requirement for BMD definition excludes people who are unable to have a scan due to frailty or mobility, have unreliable scans and also causes delay where resources issues prevent easy access to scans. Much debate about the diagnosis of osteoporosis exists. Bringing osteoporosis up to date: time to address the identity crisis | Age and Ageing | Oxford Academic (oup.com)	appraisal. No action required.
	Royal College of Physicians (RCP)	From SCOPE 21, 3,775,000 individuals had osteoporosis in 2019.	Thank you. The background section has been amended.
Population	Theramex UK Limited	Yes	Thank you. No action required.
	UCB Pharma	This is in line with company's SmPC	Thank you. No action required.
	British Society for Rheumatology	It would be better to consider both men and women but we understand men are being considered in a separate TA.	Thank you. NICE can only appraise a technology within the terms of its marketing authorisation. If abaloparatide receives marketing authorisation in any other population it will be considered in a separate appraisal. No action required.

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	Royal College of Physicians (RCP)	Yes	Thank you. No action required.
	The Royal Osteoporosis Society	Yes. It is important there is clarity about the term 'osteoporosis'. There is a strict technical diagnosis of osteoporosis defined by bone density measurement (T score of -2.5 Standard Deviations below the average healthy adult range.) This is an important risk factor for fragility fractures. However, in the context of determining eligibility for osteoporosis treatments, ' 'high fracture risk' takes into account not only BMD, but also additional independent risk factors for fracture. Patients reaching this threshold for treatment as described in NOGG (referred to by NICE in CG 146) will usually, but not always have had 'osteoporosis' diagnosed on a bone density scan. Conversely some patients, with osteoporosis from a scan measurement, will not have a high enough fracture risk to need a treatment. People prescribed treatments have stressed to us that this confusion needs to be resolved in future guidance.	Thank you. No action required.
Subgroups	Theramex UK Limited	Subgroups were explored post-hoc on the ACTIVE Phase 3 population to investigate the impact of prior fracture, age and BMD values on outcomes with abaloparatide treatment	Thank you. The subgroups included in the scope are not exhaustive. The company can submit relevant subgroup analyses in their submission which will be considered by the Appraisal Committee. No action needed

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	UCB Pharma	Please ensure, appropriate comparators should be used for each sub-group to assess the cost-effectiveness of each sub-group population. Not all suggested comparators apply to all sub-groups based on NICE previous recommendations.	Thank you. The technology appraisal committee will consider all evidence when deciding on appropriate comparators for subgroups in the appraisal. No action required.
	British Society for Rheumatology	We agree with the suggestion to study effectiveness in different fracture groups, as evidence suggests people with vertebral fractures may be more likely to benefit. We agree with the suggestion to study effectiveness in those with recent (within 24 months) fracture in line with romosozumab guidance. In line with comments above we suggest studying effectiveness in those with osteoporotic and non-osteoporotic BMD if evidence is available.	Thank you. Abaloparatide will be appraised within its marketing authorisation. The subgroups included in the scope are not exhaustive. The company can submit relevant subgroup analyses in their submission which will be considered by the Appraisal Committee. No action needed
	Royal College of Physicians (RCP)	It is critical to include subgroups at high and very high fracture risk when assessing fracture risk over 10 years. Also the imminent risk of fracture after an index fracture should be modelled.	Thank you. No action required.

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	The Royal Osteoporosis Society	We suggest the addition of post menopausal women with multiple vertebral fractures (fragility fractures in the spine).	Thank you. No action required.
Comparators	Theramex UK Limited	Abaloparatide has been investigated for use in post-menopausal women at high risk of fracture. Like other anabolic treatments, it is used as part of a sequential regimen followed by ongoing bisphosphonate/anti-resorptive medication (including denosumab). Theramex suggest that the appropriate comparators for this appraisal are the alternative anabolic treatments which have been established in routine UK practice for use in such a sequential regimen in post-menopausal women at increased risk of fracture. Therefore the appropriate comparators for this intended position in therapy are teriparatide and romosozumab. No active treatment is also a reasonable comparator and the placebo arm of the ACTIVE study can be used to inform relative effects. Raloxifene is indicated for the prevention and treatment of post-menopausal osteoporosis but is not specially directed to women at increased risk of fracture. It is Theramex understanding that Strontium Ranelate is no longer used in routine UK practice and is reserved for those patients with severe osteoporosis where alternative treatment options are contra-indicated or not tolerated. Therefore Theramex do not believe it to be an appropriate comparator.	Thank you. The technology appraisal committee will consider all evidence when deciding on appropriate comparators. No action required.
	UCB Pharma	No comment	Thank you. No action required.

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	British Society for Rheumatology	Yes, the listed comparators are appropriate. However it is likely to be more appropriate to compare abaloparatide with other parenteral therapies (zoledronate / denosumab / teriparatide / romosozumab) rather than oral bisphosphonates (alendronate, risedronate), as it is likely to be most suitable for patients with more severe osteoporosis / higher fracture risk.	Thank you. The technology appraisal committee will consider all evidence when deciding on appropriate comparators. No action required.
	Royal College of Physicians (RCP)	Yes	Thank you. No action required.
	The Royal Osteoporosis Society	yes	Thank you. No action required.
Outcomes	Theramex UK Limited	Yes	Thank you. No action required.
	UCB Pharma	No comment	Thank you. No action required.
	British Society for Rheumatology	Yes – fragility fractures should be the primary outcome considered.	Thank you. No action required.
	Royal College of Physicians (RCP)	Osteoporotic fracture could be divided into a. All fragility fractures. b. Hip c. Spine	Thank you. The list of outcomes in the scope is not intended to be exhaustive, the

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		d. Major (Hip, spine, humerus, wrist) BMD should specify lumbar spine and hip as the effects are different	appraisal committee can consider other outcomes if appropriate. No action required.
	The Royal Osteoporosis Society	yes	Thank you. No action required.
Equality	Theramex UK Limited	Theramex highlight the importance of ensuring that transgender patients are afforded the full benefits as demonstrated by clinical trials for abaloparatide independent of gender assigned at birth.	Thank you. The committee will consider any equalities issues during the appraisal. No action required.
	UCB Pharma	No comment	Thank you. No action required.
	British Society for Rheumatology	Men and women should both be considered Relying on a BMD defined diagnosis risks excluding people who are unable to have a scan due to local availability, or mobility issues or have unreliable BMD readings due to surgery or osteoarthritis for example.	Thank you. NICE can only appraise a technology within the terms of it marketing authorisation. The committee will consider any equalities issues during the appraisal. No action required

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	The Royal Osteoporosis Society	People with cognitive or physical disability who have problems with administration or those with an aversion to injections, will need consideration and support if this treatment is recommended and prescribed.	Thank you. The committee will consider any equalities issues during the appraisal. No action required
Other considerations	Theramex UK Limited	None	Thank you. No action required.
	UCB Pharma	No comment	Thank you. No action required.
	Royal College of Physicians (RCP)	All PTH analogues are recommended as part of a sequence of treatment the ACTIVE extend studies permit assessment beyond the 18-month anabolic use.	Thank you. Your comment has been noted. No action required.
Questions for consultation	Theramex UK Limited	How is increased risk of fracture defined in routine clinical practice? The country-specific FRAX® tool, with or without bone mineral density (BMD) measurement, should be used for the assessment of fracture risk in postmenopausal women who have one or more clinical risk factors for fracture. Women with a prior fragility fracture might be considered for treatment without the need for further risk assessment, although BMD measurement may sometimes be appropriate. In women without a prior fragility fracture, the 10-year probabilities of a major osteoporotic fracture (clinical spine, hip, forearm or humerus) and hip fracture should be determined using FRAX without BMD (Kanis J, et al. Osteoporos Int (2019) 30:3–44),	Thank you. Your comments will be considered by the committee during the appraisal process. No action needed.

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		Where do you consider abaloparatide will fit into the existing care pathway for osteoporosis? Theramex suggest that abaloparatide will be positioned for use in post-menopausal women at increased risk of fracture. This may include women with past documented significant fracture, multiple present vertebral fractures and those unresponsive to other agents. Abaloparatide will form part of a sequential regimen, administered for 18months followed by a suitable anti-resorptive medication. Abaloparatide may be used as an alternative to teriparatide or romosozumab therapy. Do you consider that the use of abaloparatide can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? The burden of disease associated with osteoporosis is well characterised in the literature and HRQoL impact has been consistently demonstrated in clinical studies. The potential sequelae of osteoporotic fracture – including morbidity and mortality, increased caregiver needs (formal and informal) will, we believe, be captured in the QALY calculation. Theramex do not anticipate any specific issues with regard to equality or equity considerations.	
	UCB Pharma	No comment	Thank you. No action required.

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	British Society for Rheumatology	How is increased risk of fracture defined in routine clinical practice? • Using FRAX and clinical judgement o NOGG outlines patients considered at very high risk including o The presence of single but important clinical risk factors, such as, • A 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) o The presence of multiple clinical risk factors, particularly with a recent fragility fracture indicating high imminent risk of re-fracture, o Or other indicators of very high fracture risk. Where do you consider abaloparatide will fit into the existing care pathway for osteoporosis? • In secondary care, as an alternative second-line option to existing parenterals • Ideally as a first line option in patients at particularly high risk (given evidence that anabolic drugs given before antiresorptive have better results than when antiresorptive are started first), and given safety issues with romosuzumab which preclude use in a number of patents. Do you consider that the use of abaloparatide can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? Possibly, depending on the extent to which the impact of vertebral fracture on quality of life (as opposed to the impact of hip fracture, which is well	Thank you. Your comments will be considered by the committee during the appraisal process. No action needed.

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		documented from a health economic perspective) is taken into account A focus on hip fracture as an outcome may have led to previous under-valuation of osteoporosis prevention and treatment interventions.	
	The Royal Osteoporosis Society	*How do you define an increased risk of fracture defined in routine clinical practice* Identification and assessment of people with risk factors for fragility fracture using risk calculators, bone density measurement [NICE CG 146 NOGG guideline 2022] *Where do you consider abaloparatide will fit into the existing care pathway for osteoporosis?* We strongly advise consideration of abaloparatide as a first line "anabolic" therapy for post-menopausal women defined as 'very high risk' of fractures and especially those who have had vertebral fractures. We also anticipate its use as a second line or third line therapy for post-menopausal women defined as 'high risk' (as opposed to 'very high risk') who cannot tolerate or have had a poor response to oral bisphosphonates. This would mean continued loss of bone density or further fractures. ***Would it be a candidate for managed access*** **No** Are there other health reated benefits not included in the QALY calculations? **No**	Thank you. Your comments will be considered by the committee during the appraisal process. No action needed.
	Theramex UK Limited	None	Thank you. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
Additional comments on the draft scope	The Royal Osteoporosis Society	None	Thank you. No action required.

The following stakeholders indicated that they had no comments on the draft remit and/or the draft scope

Society for Endocrinology