abaloparatide solution for injection in pre-filled pen (Eladynos®)

Theramex

06 June 2025

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and, following review by the SMC executive, advises NHS Boards and Area Drug and Therapeutics Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

ADVICE: following a full submission

abaloparatide (Eladynos®) is accepted for restricted use within NHSScotland.

Indication under review: treatment of osteoporosis in postmenopausal women at increased risk of fracture.

SMC restriction: postmenopausal people with osteoporosis at very high risk of fracture, assessed using a validated fracture risk assessment tool.

In a randomised double-blind phase III study, abaloparatide was associated with a statistically significant reduction in the incidence of new vertebral fractures versus placebo.

This advice applies only in the context of approved NHSScotland Patient Access Scheme (PAS) arrangements delivering the cost-effectiveness results upon which the decision was based, or PAS/ list prices that are equivalent or lower.

Chair
Scottish Medicines Consortium

1. Clinical Context

1.1. Medicine background

Abaloparatide activates the parathyroid hormone 1 receptor signalling pathway, stimulating osteoblastic activity and subsequently stimulating new bone formation. It causes transient and limited increases in bone resorption and increases bone density. The recommended dose of abaloparatide is 80 micrograms subcutaneously once daily for a maximum duration of 18 months.[1] See Summary of Product Characteristics (SPC) for further information.

1.2. Disease background

Osteoporosis is a common disease of the skeleton that becomes more prevalent with advancing age. Low bone density leads to an increased risk of fracture. There are typically no symptoms, with fracture usually being the first presenting complaint. The most common osteoporotic fracture locations include spine, wrist and hip. Fractures can cause chronic pain and mobility issues. Hip fractures, and the subsequent surgeries, are associated with increased serious risks, permanent disability, and increased mortality. Osteoporosis is a major public health concern and is predicted to become more prevalent as life expectancy increases.[2, 3]

Clinically, osteoporosis is diagnosed using bone mineral density (BMD) values which are assessed using dual-energy X-ray absorptiometry (DXA) scans. Osteoporosis is defined as a BMD value less than or equal to 2.5 standard deviations (SD) below the mean value for young adults, referred to as T-score ≤–2.5 SD. Severe osteoporosis is defined as a T-score ≤–2.5 SD in the presence of one or more documented fragility fractures. Various techniques have been developed to quantify the risk of fracture in individuals; Fracture Risk Assessment Tool (FRAX) and QFracture are two common examples. These tools account for various risk factors for fractures and can identify patients at low, intermediate, high, or very high risk of fracture.[2, 4]

1.3. Company proposed position

Postmenopausal people with osteoporosis at very high risk of fracture, assessed using a validated fracture risk assessment tool.

1.4. Treatment pathway and relevant comparators

Pharmacological treatments for osteoporosis aim to reduce the risk of osteoporotic fractures. In broad terms, treatments either decrease bone loss (collectively known as antiresorptive treatments) or increase new bone formation and BMD (such as teriparatide, romosozumab and the medicine under review, abaloparatide). Scottish guidelines recommend bisphosphonate (antiresorptive) treatment for patients with postmenopausal osteoporosis without severe osteoporosis of the spine, and romosozumab or teriparatide for those that do. Furthermore, if patients have a high risk of hip or non-vertebral fracture, romosozumab is recommended, and in patients who are not at high risk of hip or non-vertebral fracture teriparatide is recommended. Romosozumab is contraindicated in patients with history of myocardial infarction or stroke and in such cases teriparatide could be offered as an alternative. Clinical experts consulted by SMC considered that teriparatide is the most relevant comparator for this submission, however romosozumab is used in similar scenarios.[4-6]

2. Summary of Clinical Evidence

2.1. Evidence for the licensed indication under review

Evidence to support the efficacy and safety of abaloparatide for the treatment of osteoporosis in patients at increased risk of fracture comes from the ACTIVE study. Details are summarised in Table 2.1.

Table 2.1. Overview of relevant studies[2, 7]

Criteria	ACTIVE
Study design	International, randomised, double-blind/open-label (teriparatide treatment group), phase III study.

Eligible patients	• Healthy ambulatory postmenopausal women from 50 to 85 years of age with osteoporosis with:
	  ○ BMD T-score ≤2.5 and >-5.0 at the lumbar spine or hip by DXA and radiological evidence of 2 or more mild or one or more moderate vertebral fractures, or history of low trauma fracture of the forearm, humerus, sacrum, pelvic, hip, femur, or tibia fracture within the past 5 years.
	  ○ Postmenopausal women ≥65 years who met the above fracture criteria but had a T-score ≤2.0 and >-5.0 could be enrolled; those who did not meet the fracture criteria could be enrolled if their T-score was ≤3.0 and >-5.0.
	• Normal levels of albumin-adjusted serum calcium, parathyroid hormone, serum phosphorus and alkaline phosphatase during the screening period. Serum 25-hydroxyvitamin D values above 15 ng/mL and within 3 times the upper normal range.
	• Resting 12-lead electrocardiogram obtained during screening showing no clinically significant abnormality and a QTc ≤470 msec.
	• Systolic blood pressure: ≥100 and ≤155 mmHg, diastolic blood pressure: ≥40 and ≤ 95 mmHg, and heartrate: ≥45 and ≤100 beats per minute (sitting or supine).
	• No clinically significant abnormality of serum haemoglobin, haematocrit, white blood cells and platelets, or usual serum biochemistry: electrolytes, renal function, liver function and serum proteins.

Treatments	Abaloparatide 80 micrograms SC once daily, teriparatide 20 micrograms SC once daily or placebo for 18 months.
Randomisation	Patients were randomised equally. Randomisation was not stratified.
Primary outcome	Percentage of patients with one or more incidents of new vertebral fracture from the baseline spine X-rays until post-baseline spine X-rays (over the study treatment period up to 18 months) in abaloparatide treated patients when compared with placebo.
Secondary outcomes	Change from baseline in BMD for total hip, femoral neck, lumbar spine at 18 months. Time to non-vertebral fracture.
Statistical analysis	A hierarchical statistical testing strategy was applied with no formal testing of outcomes after the first non-significant outcome in the hierarchy. Therefore, the results reported for these outcomes are descriptive only and not inferential (no p-

	values reported). The primary efficacy outcome was performed using a mITT population, defined as all ITT patients who had both a pre-treatment and a post-baseline evaluable radiologic assessment (spine X-ray). All other efficacy outcomes were assessed in the ITT population which included all randomised patients.

Abbreviations: BMD = bone mineral density; DXA = dual energy x-ray absorptiometry; SC = subcutaneous; ITT = intention-to-treat; mITT = modified intention-to-treat.

The ACTIVE study met its primary outcome; abaloparatide was associated with a statistically significant reduction in the incidence of new vertebral fractures versus placebo. See Table 2.2 for details.

Table 2.2. Key efficacy results from ACTIVE.[2]

	Abaloparatide	Teriparatide	Placebo
Primary outcome: new vertebral fractures at 18 months (mITT population)			
Number of patients	583	600	600
At least one new vertebral fracture, n	3	4	25
Risk reduction versus placebo (95% CI)	-3.65 (-5.59 to -2.00)	-3.50 (-5.45 to -1.82)	-
Relative risk reduction versus placebo (95% CI)	-0.88 (-0.96 to -0.59)	-0.84 (-0.94 to -0.54)	-
p-value versus placebo	<0.001	-	-
Secondary outcome: time to non-vertebral fracture (ITT population)			
Number of patients	696	686	688
Events, n	15	12	21
Hazard ratio versus placebo (95% CI)	0.74 (0.38 to 1.43) p = 0.37	0.56 (0.28 to 1.15)	-
Hazard ratio versus teriparatide (95% CI)	1.30 (0.61 to 2.79)	-	-
KM estimated event rate at 19 months	2.7%	2.0%	3.6%
Secondary outcomes: bone mineral density at 18 months (ITT population)			
Number of patients	694	686	687
Total hip mean % change from baseline	3.3%	3.0%	-0.03%
- p-value versus placebo	p<0.001	-	-
Femoral neck mean % change from baseline	2.7%	2.3%	-0.4%
- p-value versus placebo	p<0.001	-	-
Lumbar spine mean % change from baseline	9.1%	9.2%	0.5%
- p-value versus placebo	p<0.001	-	-

Abbreviations: CI = confidence interval; ITT = intention-to-treat population, defined as all randomised patients; KM = Kaplan Meier; mITT = modified intention-to-treat population, defined as all randomised patients who had both the pre-treatment and the post-baseline evaluable radiologic assessment (lumbar and thoracic spine X-rays).

ACTIVExtend was a 24-month extension study that enrolled patients from ACTIVE who were randomised to abaloparatide or placebo and had completed 18 months of treatment; patients in the teriparatide treatment group were not included. Patients enrolled in ACTIVExtend (from month 19 onwards) received alendronate for 24 months. To comply with regulators, treatment remained blinded for 6 months to provide data at 24 months (18 months from ACTIVE and 6 months from ACTIVExtend); ACTIVExtend was open-label thereafter. During the 24-month study period, 2 and 10 new vertebral fractures occurred in the former abaloparatide and former placebo groups respectively. The risk reduction for new vertebral fractures remained statistically significant in ACTIVExtend; risk reduction versus former placebo was -2.83 at 18 months, -3.86 at 25 months, -4.44 at 43 months. There were no statistically significant reductions in the risk of non-vertebral

fractures in the former abaloparatide group versus the former placebo group at 18 months, 25 months, or 43 months. There were continued increases in BMD; statistically significant results favouring abaloparatide/alendronate over placebo/alendronate were reported for BMD at the total hip, femoral neck, and lumbar spine for all timepoints.[2]

2.2. Evidence to support the positioning proposed by the submitting company

The submitting company maintained that their proposed positioning is in line with the population of the ACTIVE study and therefore subgroup analysis was not prominent in their submission.

Pre-planned subgroup analyses were performed for the primary outcome of ACTIVE in the following subgroups: age, years since menopause, race, region, any prior fracture, any prior vertebral fracture, any prior non-vertebral fracture, any prior major osteoporotic fracture, prevalence of vertebral fracture at baseline, severity of fracture (SQ score) at baseline, severe disease at baseline, lumbar spine BMD T-score at baseline, total hip BMD T-score at baseline, femoral neck BMD T-score at baseline. Generally, results were consistent with the primary findings and abaloparatide was favoured over placebo.[2]

2.3. Health-related quality of life outcomes

Health-related quality of life outcomes were not assessed in ACTIVE or ACTIVExtend.

2.4. Supportive studies

The submitting company presented a retrospective, observational study that used anonymised insurance claims data from the United States to compare abaloparatide and teriparatide [8]. The study included women aged 50 years old or above with at least one prescription fill for abaloparatide or teriparatide during the identification period, at least 1 claim for a medical or hospital visit, and a pharmacy claim in the 12 months prior to the index date. Propensity score matching was used to match the two cohorts based on 73 baseline parameters, which reduced the sample size from 120,581 to 43,352 patients. The primary outcome was time to the first incidence of hip fracture. After 18 months, 245 (1.1%) and 296 (1.4%) patients in the abaloparatide and teriparatide cohorts respectively had a hip fracture; hazard ratio = 0.83 (95% CI: 0.70 to 0.98).[8]

ITM-058-301 was a randomised, double-blind, placebo-controlled phase III study in Japanese patients (male and postmenopausal female patients aged 55 to 85 years) with osteoporosis at high risk of fracture. Patients were randomised in a 2:1 ratio to receive abaloparatide or placebo, and the primary outcome was percent change in BMD in lumbar spine at the last visit. The least squares mean of the percent change in lumbar spine BMD at the last visit from the baseline test was 16% in the abaloparatide group (n=136) and 3.8% in the placebo group (n=70) in the entire population ($p<0.001$).[2]

2.5. Indirect evidence to support clinical and cost-effectiveness comparisons

In the absence of direct evidence comparing abaloparatide with relevant comparators, the submitting company presented indirect treatment comparisons. These have been used to inform the economic base case.

Table 2.3. Summary of indirect treatment comparison.

Criteria	Overview
Design	Bayesian NMA using binomial likelihood and cloglog link models.
Population	Postmenopausal people with osteoporosis at increased risk of fracture.
Comparators	Teriparatide 20 micrograms subcutaneously once daily. Romosozumab 210 mg subcutaneously once monthly. Other less relevant comparators (alendronate, denosumab, raloxifene, etc) were included in the NMA however these will not be discussed further.
Studies included	Twenty-five studies were included in the global network of evidence. The studies with key comparators are described below: ACTIVE study[2, 7]: abaloparatide, teriparatide, placebo. Neer et al. (2001)[9]: teriparatide 20 micrograms, teriparatide 40 micrograms, placebo. Cosman et al. (2016)[10]: romosozumab, placebo. Saag et al. (2017)[11]: romosozumab. Langdahl et al. (2017)[12]: teriparatide, romosozumab.
Outcomes	New vertebral fracture Hip fracture Non-vertebral fracture
Results	Overall, there was no evidence of a difference between abaloparatide, teriparatide, and romosozumab; central estimates were in favour of abaloparatide versus teriparatide and romosozumab for new vertebral fractures and hip fractures but not for non-vertebral fracture. However, 95% credible intervals were very wide suggesting high uncertainty in the results.

Abbreviations: CrI = credible intervals; HR = hazard ratio; NMA = network meta-analysis.

*Other data were also assessed but remain confidential.**

3. Summary of Safety Evidence

Key evidence to support the safety of abaloparatide came from ACTIVE. The mean duration of exposure in the abaloparatide (n=694), teriparatide (n=686), and placebo (n=687) groups was 15.0 months, 15.6 months, and 15.8 months respectively. The incidence of adverse events was higher in patients on abaloparatide compared with teriparatide and placebo for cardiac disorders (12%, 6.3%, 5.4%), gastrointestinal disorders (27%, 23%, 24%) and nervous system disorders (25%, 20%, 20%). The most common cardiac disorder was palpitations (5.6%, 1.7%, 0.4%); the most common gastrointestinal disorder was nausea (8.5%, 5.4%, 3.1%); the most common nervous system disorders were dizziness (11%, 8.2%, 7.1%) and headache (8.5%, 7.1%, 5.8%). Hypercalciuria and hypercalcaemia occurred slightly less frequently in patients receiving abaloparatide (16% and 2.2%) than those on teriparatide (18% and 4.8%) but more often than those on placebo (13% and 0.6%). The incidence of AEs leading to study discontinuation was higher with abaloparatide (9.8%) than with teriparatide (6.7%) or placebo (6.0%). Approximately 80% of AEs were mild to moderate in severity; severe AEs occurred too infrequently to be reliably compared between treatment groups. There were no notable differences in serious AEs between treatment groups and no deaths in ACTIVE were considered related to study treatment. Orthostatic hypotension and transient episodes of increased heart rate may occur with abaloparatide, typically within 4 hours of administration; blood pressure, cardiac status and ECG should be assessed prior to beginning treatment with abaloparatide; patients with cardiac disease should be monitored for worsening of their disease. However, a strict contraindication has not been imposed.[1, 2]

4. Summary of Clinical Effectiveness Considerations

4.1. Key strengths

- Key evidence to support the efficacy and safety of abaloparatide came from ACTIVE, a large phase III study.
- Abaloparatide was associated with a statistically significant and clinically relevant reduction in the incidence of new vertebral fractures versus placebo; at 18 months, 3 (0.5%) patients in the abaloparatide group and 25 (4.2%) patients in the placebo group had a new vertebral fracture, representing a relative reduction in risk of new vertebral fracture of 88%.[2]
- The statistically significant improvements in BMD at total hip, femoral neck, and lumbar spine versus placebo at month 18 can also be considered clinically relevant. These were supported by further observed increases in BMD at all timepoints (up to month 43) in the ACTIVExtend study (where patients were switched to alendronate) and the randomised, phase 3 study, ITM-058-301.[2]

4.2. Key uncertainties

- Although ACTIVE included a treatment group with a relevant comparator, there were limitations with the study design that limits the comparison between abaloparatide and teriparatide. ACTIVE was not powered to detect statistical differences between these treatments and furthermore, the teriparatide treatment group was open-label in an otherwise double-blinded study. Comparisons of abaloparatide and teriparatide from ACTIVE are also limited to 18 months; patients randomised to teriparatide in ACTIVE were not included in the extension study. The recommended total duration of treatment with teriparatide is 24 months.[2, 6]
- The ITC conducted by the submitting company to compare abaloparatide with teriparatide and romosozumab had several limitations and the company's conclusion that abaloparatide has comparable efficacy to teriparatide and romosozumab, based on the ITCs, is associated with some uncertainty. However, given the similarities in class of medicine and mechanism of action between teriparatide and abaloparatide, the real-world evidence presented[8], and the direct but flawed evidence from ACTIVE, it would seem reasonable to conclude that abaloparatide and teriparatide have comparable efficacy.
- The assessment of fractures at 18 months in ACTIVE is suboptimal; guidelines recommend 24 months of fracture data. This was addressed with the extension study ACTIVExtend, where patients in the abaloparatide and placebo treatment groups continued blinded treatment (with alendronate) for a further 6 months. However, this study was not considered to be truly randomised because approximately 30% of patients in the abaloparatide and placebo groups who were randomised in ACTIVE were not included in ACTIVExtend.[2, 13]
- The exclusion criteria were strict, excluding many patients with concomitant chronic conditions, which may affect the generalisability of results to the relevant population in

practice. Several inclusion and exclusion criteria from ACTIVE were considered of clinical importance to the known safety profile of abaloparatide.[2]

- The submitting company have proposed that abaloparatide be positioned for use in postmenopausal women with osteoporosis at very high risk of fracture; it is not clear how many patients in ACTIVE were at very high risk of fracture. In ACTIVE, the median FRAX 10-year probability for major osteoporotic fracture calculated with BMD suggested that many patients had an intermediate or low risk of fracture. However, pre-specified exploratory analysis of FRAX in ACTIVE suggest consistent treatment effect of abaloparatide irrespective of baseline fracture probability.[2, 3, 14]
- Abaloparatide did not statistically significantly delay time to non-vertebral fracture compared with placebo. There were no statistically significant reductions in the risk of nonvertebral fractures with abaloparatide versus placebo at 18 months (ACTIVE) or at 25 months and 43 months (ACTIVExtend). In the time to non-vertebral fracture analysis, there were few overall events, and there was a high level of censored data; discontinuations were more frequent and occurred earlier in the abaloparatide group. Considering data from the ACTIVE study in addition to supportive studies, and that teriparatide has the same mechanism of action and belongs to the same class as abaloparatide, regulators concluded that there does not appear to be a scientific reason to presume efficacy for vertebral but not for non-vertebral fractures.[2]

4.3. Clinical expert input

Clinical experts consulted by SMC on balance do not consider abaloparatide to fill an unmet need and were mixed in their views that it is a therapeutic advancement. However, they stated that there are limited treatment options available at present, and that abaloparatide would be a useful option in some scenarios. Compared with teriparatide, they noted the reduced rates of hypercalcaemia, the shorter treatment duration of 18 months versus 24 months, and that it does not need to be stored in a fridge after first use, which would be useful for patients who travel. Abaloparatide is likely to be used as an alternative to teriparatide and in patients who have contraindications to romosozumab.

4.4. Service implications

No service implications are anticipated with introduction of abaloparatide.

5. Summary of Patient and Carer Involvement

No patient group submission was received.

6. Summary of Comparative Health Economic Evidence

6.1. Economic case

Table 6.1 below provides a summary of the economic analysis.

Table 6.1 Description of economic analysis

Criteria	Overview
Analysis type	Cost-utility analysis
Time horizon	Lifetime horizon
Population	The target population considered in this submission is postmenopausal women with osteoporosis at *very high risk* of fracture.
Comparators	Teriparatide and romosozumab were included as relevant comparators. All treatments were followed by a sequential course of alendronate.
Model description	A patient-level Markov micro-simulation model was developed to track individual patients over time, which captured their risk of experiencing fractures by transitioning between 5 health states (at-risk, hip, vertebral, non-hip/non-vertebral, death). Cycle length was 6 months, and the model allowed for treatment sequencing and discontinuation. No adverse events were included in the model.
Clinical data	Baseline characteristics were taken from the abaloparatide arm of the ACTIVE study. The risk of having a fracture was based on a combination of 4 components: - General population fracture incidence rates were sourced from Singer et al (1998)[15] and Kanis et al (2000).[16] - FRAX algorithm was used to determine additional baseline fracture risk for each simulated patient over and above that of the general population. - Imminent fracture risk following a recent fracture was incorporated using estimates from Söreskog et al. (2021).[17] - Treatment efficacy for each treatment was informed by the network meta analysis (NMA). The NMA produced hazard ratios for hip, vertebral, and non-hip/non-vertebral fractures for each treatment versus placebo.
Extrapolation	Treatment effects were extrapolated using constant hazard ratios over the duration of treatment. A dynamic offset approach was used, where treatment effects waned linearly over a period equal to treatment durations. Persistent rates were based on real-world data; treatment discontinuation was modelled, but re-initiation was not permitted. All-cause mortality was applied using UK age-and sex-specific life tables, Additional mortality risk following a hip or vertebral fracture was incorporated based on van Staa et al (2007) and applied for 6 months post-fracture.[18]
Quality of life	EQ-5D utility multipliers were taken from the International Costs and Utilities Related to Osteoporotic Fractures Study (ICUROS) and applied to general UK population utility values (Hernandez et al, 2022)[19, 20]. Utility multipliers were assigned by fracture type and year (initial year and subsequent years after fracture). If a patient experienced multiple fractures of different types, a multiplicative approach was used. If a patient experienced more than one fracture of the same type, the maximum disutility approach was taken.
Costs and resource use	Medicines acquisition, administration, health state unit and resource use costs were included in the model. Fracture related costs were applied by type and differed between first year costs and subsequent year costs.
PAS	A Patient Access Scheme (PAS) was submitted by the company and assessed by the Patient Access Scheme Assessment Group (PASAG) as acceptable for implementation in NHSScotland. Under the PAS, a discount was offered on the list price. A PAS discount is in place for romosozumab and this was included in the results used for decision-making by using estimates of the comparator PAS price.

6.2. Results

SMC considered results for decision-making that took into account all relevant PAS. SMC is unable to present these results due to competition law issues.

Table 6.2 Base case results (abaloparatide PAS price)

Technologies	Incremental QALYs (abaloparatide vs comparators)	ICER (£/QALY)
abaloparatide/alendronate	-	-
romosozumab/alendronate	0.03	CIC
teriparatide/alendronate	0.01	CIC

Abbreviations: CIC = commercial in confidence; ICER = incremental cost-effectiveness ratio; PAS = patient access scheme; QALYs = quality-adjusted life years.

6.3. Sensitivity analyses

The company conducted probabilistic, deterministic and scenario analysis. Descriptions of key scenarios are provided in table 6.3 below.

Table 6.3 Sensitivity and Scenario Analysis Results (PAS price)

	Parameter	Base case	Scenario	abaloparatide vs teriparatide			abaloparatide vs romosozumab		
				Incr. costs	Incr. QALYs	ICER (£/QALY)	Incr. costs	Incr. QALYs	ICER (£/QALY)
	Base case			CIC	0.0128	CIC	CIC	0.03	CIC
1	FRAX based estimation for mortality risk	Included	Excluded	CIC	-0.0005	CIC	CIC	0.0034	CIC
2	Imminent risk of fracture	Included	Excluded	CIC	0.0119	CIC	CIC	0.0256	CIC
3	Persistence	Included	Excluded	CIC	0.0872	CIC	CIC	0.1065	CIC
4	Offset method (residual effect)	Dynamic	Fixed method	CIC	0.0097	CIC	CIC	0.0297	CIC
5			Fixed offset 3 years	CIC	-0.0141	CIC	CIC	0.0067	CIC
6	Drug administration cost	Included	Excluded	CIC	0.0128	CIC	CIC	0.0312	CIC
7	Excess mortality applied on	Both hip and vertebral	Hip fracture only	CIC	0.0128	CIC	CIC	0.0312	CIC
8	Maximum treatment duration for all treatment sequences	No uniform cap (duration differs by strategy)	5 years	CIC	0.0128	CIC	CIC	0.0312	CIC
9	Source of persistence rates	Various RWE studies	Clinical trial data	CIC	0.0692	CIC	CIC	0.0734	CIC
10	For different treatment strategies persistence rates sample from	Common random numbers	Different random numbers	CIC	0.0125	CIC	CIC	0.0218	CIC
11	Sequential treatment efficacy modelling	No sequential treatment	Sequential treatment efficacy from NMA	CIC	-0.0034	CIC	CIC	0.0019	CIC

	Parameter	Base case	Scenario	abaloparatide vs teriparatide			abaloparatide vs romosozumab		
				Incr. costs	Incr. QALYs	ICER (£/QALY)	Incr. costs	Incr. QALYs	ICER (£/QALY)
		efficacy modelled							
12	Source of clinical data (for the HR)	NMA	ACTIVE study	CIC	-0.0034	CIC	CIC	0.0116	CIC
13	Model Type	CUA	CMA (HR = 1)	CIC	-	-	CIC	-	-

Abbreviations: CIC = commercial in confidence; ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life year; HR = hazard ratio; NMA= network meta-analysis; RWE = real world evidence; incr.= incremental; CUA = cost-utility analysis; CMA = cost-minimisation analysis.

6.4. Key strengths

- The comparators included in the model, teriparatide and romosozumab, align with SMC clinical expert feedback and reflect the most relevant treatment options for patients in this proposed indication.
- The model structure was well justified. Osteoporosis is a chronic, recurrent condition with patient-specific histories affecting fracture risk. The use of a micro-simulation allowed for tracking of individual fracture events, treatment persistence and fracture risk over time.
- The model incorporates both imminent fracture risk and sequential treatment pathway with alendronate. These features reflect clinical practice.

6.5. Key uncertainties

- In practice, the cost of teriparatide is lower than the price assumed in the economic model due to the existence of a national framework agreement. Incorporating the national framework contract price has a substantial upward impact of the cost-effectiveness results.
- There is no direct clinical evidence comparing abaloparatide with romosozumab. The ACTIVE study only compared abaloparatide with teriparatide, and even within this study, the number of fracture events was low which limited statistical power to detect differences. Also, it is unclear whether the ACTIVE study population fully reflects the proposed positioning. These limitations introduce uncertainty around the clinical evidence used in the economic model.
- Despite applying distinct hazard ratios for each treatment based on the NMA, the model only produces very small differences in total fractures, time to first fracture, and QALYs across treatment arms. Most patients spend majority of their time in the 'at-risk of fracture' health state, and there were relatively few transitions into the fracture health states. As a result, the incremental QALY gains between treatments were minimal. This introduced uncertainty around whether the model was sufficiently sensitive to differences in treatment effect, particularly when these were expected to drive the primary cost-effectiveness outcomes. The small differences in the base case results contributed to the instability seen in the scenario analysis. These scenarios did not reflect substantially large differences in clinical outcomes or costs between treatments, but rather highlighted that the model was operating within a narrow margin of difference between treatment arms,

thereby introducing uncertainty about the reliability and robustness of the model's outputs.

- The company concludes from the NMA that abaloparatide has comparable efficacy to teriparatide and romosozumab. Given the clinical uncertainties underpinning the NMA (including few events, wide credible intervals, and inconsistencies with real world evidence data) and the minimal QALY differences between treatments, the Committee considered a cost-minimisation analysis (CMA) to be a more appropriate approach. A CMA scenario is therefore presented in Table 6.3 (Scenario 13).
- The model did not apply a separate reduction in quality of life for patients who may enter long-term care following a hip fracture. In addition, there was no scenario analysis provided to explore alternative utility values or test the impact of the multipliers used. However, given that the fracture rates produced by the model were similar across treatment groups, changes to these utility assumptions are unlikely to affect the overall conclusions.

7. Conclusion

After considering all the available evidence, the Committee accepted abaloparatide for restricted use in NHSScotland.

8. Guidelines and Protocols

The National Osteoporosis Guideline Group (NOGG) published a clinical guideline for the prevention and treatment of osteoporosis, last updated in December 2024.[3]

The Scottish Intercollegiate Guidelines Network published SIGN 142, a clinical guideline for management of osteoporosis and the prevention of fragility fractures, revised in January 2021.[4]

9. Additional Information

9.1 Product availability date

27 March 2023

Table 9.1 List price of medicine under review

Medicine	Dose regimen	Cost per 30 days (£)
abaloparatide	**80 micrograms subcutaneously once daily for a maximum duration of 18 months.**	**295**

Costs from BNF online on 03 April 2025. Costs do not take any patient access schemes into consideration.

10. Company Estimate of Eligible Population and Estimated Budget Impact

The submitting company estimated there would be 1,268 patients eligible for treatment with abaloparatide in year 1 and 1,376 year 5, to which confidential uptake rates were applied.

SMC is unable to publish the with PAS budget impact due to commercial in confidence issues. A budget impact template is provided in confidence to NHS health boards to enable them to estimate the predicted budget with the PAS. This template does not incorporate any PAS discounts associated with comparator medicines.

*Other data were also assessed but remain confidential.**

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This assessment is based on data submitted by the applicant company up to and including 14 May 2025.

**Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal:*https://www.scottishmedicines.org.uk/about-us/policies-publications/

Medicine prices are those available at the time the papers were issued to SMC for consideration. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document. Area Drug and Therapeutics Committees and NHS Boards are therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

Patient access schemes: A patient access scheme is a scheme proposed by a pharmaceutical company in order to improve the cost-effectiveness of a medicine and enable patients to receive access to cost-effective innovative medicines. A Patient Access Scheme Assessment Group (PASAG), established under the auspices of NHS National Services Scotland reviews and advises NHSScotland on the feasibility of proposed schemes for implementation. The PASAG operates separately from SMC in order to maintain the integrity and independence of the assessment process of the SMC. When SMC accepts a medicine for use in NHSScotland on the basis of a patient access scheme that has been considered feasible by PASAG, a set of guidance notes on the operation of the scheme will be circulated to Area Drug and Therapeutics Committees and NHS Boards prior to publication of SMC advice.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.