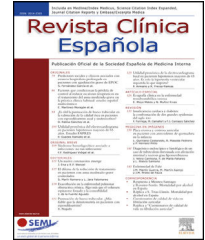




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## SPECIAL ARTICLE

# Update of the SEIOMM clinical guideline of osteoporosis: abaloparatide<sup>☆</sup>



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Received 4 February 2025; accepted 4 May 2025

### KEYWORDS

Osteoporosis;  
Fractures;  
Abaloparatide;  
Clinical guidelines

### Abstract

**Introduction:** Osteoporosis is a highly prevalent condition. SEIOMM has published guidelines for managing these patients in 2022. The recent introduction of a new drug in Europe, abaloparatide, makes it advisable to consider its role among therapeutic options.

**Objective and results:** This article summarizes the existing information on the efficacy and safety of abaloparatide and it updates the therapeutic algorithms proposed in the guidelines.

**Conclusion:** Abaloparatide is an osteoanabolic drug with efficacy and safety similar to teriparatide. It represents a new option for treating patients with severe osteoporosis and a very high risk of fracture.

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### PALABRAS CLAVE

Osteoporosis;  
Fracturas;  
Abaloparatida;  
Guías clínicas

### Actualización de las guías de manejo de la osteoporosis de la SEIOMM: abaloparatida

### Resumen

**Introducción:** La osteoporosis es un trastorno de elevada prevalencia. La SEIOMM publicó en 2022 unas guías de manejo de estos pacientes. La reciente comercialización en Europa de un nuevo fármaco, la abaloparatida, hace aconsejable considerar su papel dentro de las opciones terapéuticas.

<sup>☆</sup> This paper was jointly developed by Revista Clínica Española, Revista de Osteoporosis y Metabolismo Mineral, Revista Clínica Española (English Edition) and jointly published by Elsevier España S.L.U. and ARÁN EDICIONES, S.L.. The articles are identical except for minor stylistic and spelling differences in keeping with each journal's style. Either citation can be used when citing this article.

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<https://doi.org/10.1016/j.rceng.2025.502338>

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**Objetivo y resultados:** En este artículo se resume la información existente sobre la eficacia y la seguridad de la abaloparatida y se actualizan los algoritmos terapéuticos propuestos en la guía.

**Conclusión:** La abaloparatida es un fármaco osteoformador con eficacia y seguridad similares a la teriparatida. Representa una nueva opción en el tratamiento de la osteoporosis grave con muy alto riesgo de fractura.

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## Introduction

Following the publication of the SEIOMM (Spanish Society of Bone and Mineral Metabolism Research) osteoporosis management guidelines in 2022,<sup>1</sup> abaloparatide has been approved for marketing in Spain and other European countries. This increases the number of bone-forming drugs available for the treatment of osteoporosis and makes updating these guidelines appropriate. To this end, the committee appointed by SEIOMM (see authors) reviewed the existing literature on abaloparatide and prepared a draft, which was then submitted for discussion by the rest of the Guidelines Drafting Committee (see Appendix A). Their conclusions are summarized here.

Abaloparatide is a synthetic peptide analogue of the first 34 amino acids of human parathyroid hormone-related peptide (PTHrP) that belongs to the group of osteoanabolic agents. It acts through activation of the PTH receptor 1 (PTH1R), promoting the differentiation of osteoblast precursors and inhibiting osteocyte apoptosis. Activation of PTH1R in these cells also induces the expression of the receptor activator of nuclear factor kappa-B ligand (RANKL), thereby indirectly stimulating osteoclastogenesis. Mechanistically, abaloparatide differs from teriparatide in its greater affinity for binding to the R<sup>G</sup> conformation of PTH1R, resulting in a shorter-lasting intracellular response than when activation is mediated through the R<sup>0</sup> conformation, which is the one utilized by teriparatide. It has been suggested that this would result in a lower induction of RANKL production and bone resorption by abaloparatide.<sup>2</sup> This drug is administered subcutaneously at a dose of 80 µg/day for up to 18 months.

## Effect on bone mineral density (BMD) and fractures

The efficacy of abaloparatide in postmenopausal women with osteoporosis was evaluated in the ACTIVE trial, which compared abaloparatide treatment with placebo.<sup>3</sup> It was also compared with an open-label arm of women treated with teriparatide. After 18 months of follow-up, compared with placebo, abaloparatide reduced the risk of vertebral fractures (relative risk, RR: 0.14; 95% CI 0.05–0.39). It also reduced the risk of major osteoporotic fractures (hazard ratio, HR: 0.30; CI 0.15–0.60), clinical fractures (HR: 0.57; CI 0.35–0.91), and nonvertebral fractures (HR: 0.57;

CI 0.32–1.0; p=0.049). Therefore, it is considered indicated for the treatment of osteoporosis in postmenopausal women who have a high risk of fracture (Fig. 1).

Abaloparatide also increased BMD at all sites, by approximately 8–11% in the spine and 3–4% in the hip, compared with placebo. The ATOM study also showed BMD gains in men,<sup>4</sup> but it is not currently approved for male osteoporosis in Europe. As with other bone-forming agents, after completing treatment with abaloparatide, it is recommended to administer an antiresorptive (usually a bisphosphonate), which maintains the reduction in fracture risk<sup>5</sup> (Fig. 2).

## Adverse effects

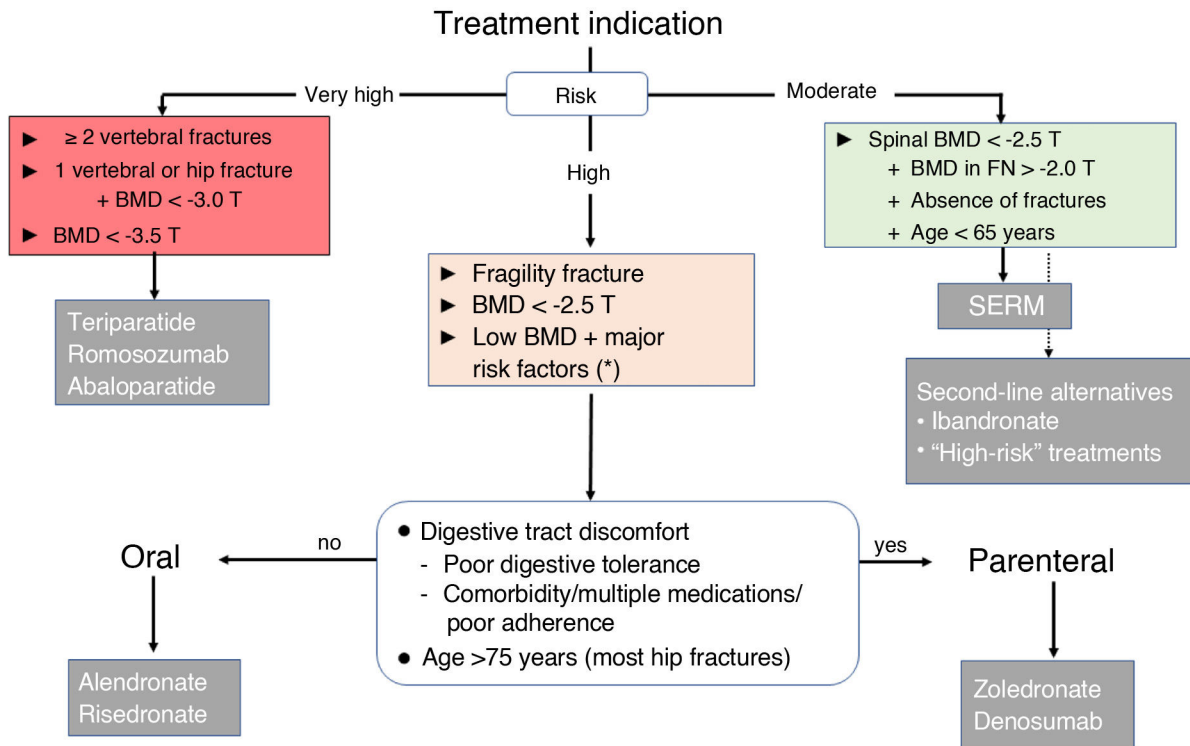
Abaloparatide is generally well-tolerated. The most frequently reported adverse effects are nausea, headache, arthralgia, changes in blood pressure (hypertension and, especially, orthostatic hypotension), tachycardia, palpitations, hyperuricemia, hypercalcemia, and hypercalciuria. They do not usually require discontinuation of treatment.<sup>6</sup> However, given the possibility of orthostatic hypotension, the summary of product characteristics recommends that the first doses be administered under the supervision of a healthcare professional. Finally, this drug is considered contraindicated in patients with a known risk of osteosarcoma, such as those who have received radiation therapy, and in those with malignancies with skeletal involvement.

## Comparison of abaloparatide with other anabolic agents

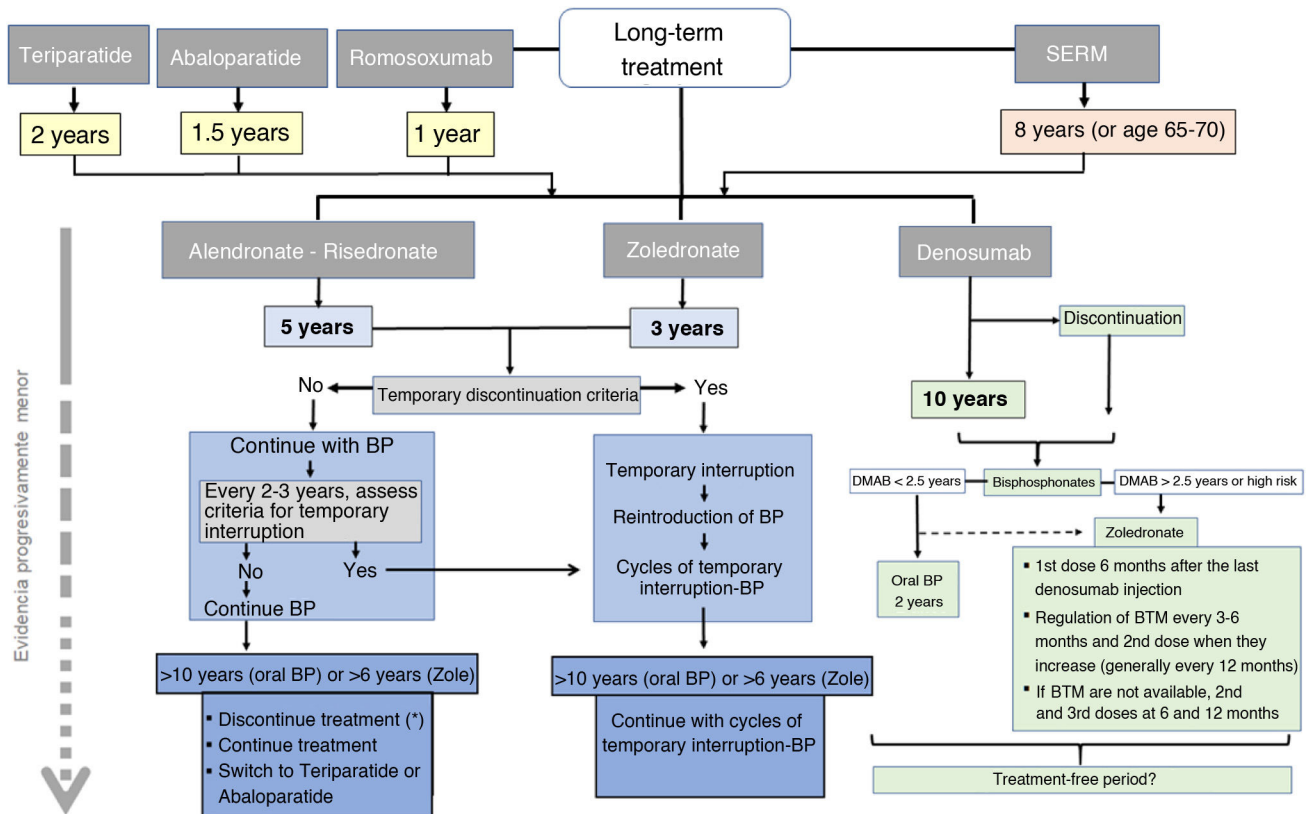
Regarding BMD, in the ACTIVE study, abaloparatide and teriparatide had a similar effect on the lumbar spine, but at the hip the increase was somewhat greater with abaloparatide (0.8% difference at 6 months, p<0.001), apparently at the expense of a greater effect on cortical bone.<sup>3</sup>

Like teriparatide, abaloparatide induces an increase in bone formation markers. After 2–3 months, an increase in resorption markers is also observed. The increase in both types of markers is smaller with abaloparatide than with teriparatide.

Only in the ACTIVE study was a direct comparison of abaloparatide with another bone-forming agent performed. When the antifracture effects of abaloparatide were compared with teriparatide, the two treatments were generally



**Figure 1** Initial therapeutic management. FN, femoral neck; BMD, bone mineral density; SERM, selective estrogen receptor modulators; T, T-score.



**Figure 2** Long-term management. BP, bisphosphonates; DMAB, denosumab; BTM, bone turnover markers; SERM, selective estrogen receptor modulators.

comparable in reducing the incidence of vertebral fractures, nonvertebral fractures, and clinical fractures, but abaloparatide was superior in reducing major osteoporotic fractures (1.5% vs. 3.1%,  $p=0.03$ ).<sup>3</sup> Similarly, two real-life studies from the same American database have suggested that abaloparatide reduces the risk of peripheral fractures somewhat more than teriparatide. Although adjustments were made for various clinical characteristics (propensity score), its retrospective and nonrandomized nature is a major limitation.<sup>7,8</sup>

Since data from direct comparisons are very limited, several network meta-analyses have attempted to compare the effects of various bone-forming agents. The results do not consistently reveal differences between the effects of teriparatide, abaloparatide, and romosozumab on fracture risk.<sup>9–13</sup>

Regarding side effects, in the ACTIVE study, abaloparatide and teriparatide showed a similar profile. Although the frequency of hypercalcemia was slightly higher with teriparatide (6.4% vs. 3.4%), the frequency of adverse events leading to treatment discontinuation was slightly higher in the abaloparatide group (9.9% vs. 6.8%).

Therefore, abaloparatide and teriparatide are drugs with similar antifracture efficacy and safety profiles. Although they may cause changes in blood pressure in some patients, they are not associated with serious effects, and both are considered safe from a cardiovascular perspective.<sup>14</sup> In addition to specific contraindications, its use should be carefully assessed in patients with a history of tumors (such as breast, lung, or prostate tumors) with a high tendency to metastasize to bone.

## Funding

This work has not received funding from any public or private entity.

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### Declaration of competing interest

The authors declare that they have received conference fees, travel grants, or research grants from: Amgen, UCB, Lilly, Merck, Gedeon Richter, Theramex, Stada, and Angelini Pharma.

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