

**COST-MINIMIZATION ANALYSIS AND BUDGET
IMPACT OF ROMOSUZUMAB IN
POSTMENOPAUSAL WOMEN WITH SEVERE
OSTEOPOROSIS AND TREATMENT FAILURE IN
BRAZIL**

*ANÁLISE DE CUSTO-MINIMIZAÇÃO E IMPACTO
ORÇAMENTÁRIO DO ROMOSUZUMABE EM MULHERES NA PÓS-
MENOPAUSA GRAVE COM FALHA DE TRATAMENTO, NO
BRASIL*

*ANÁLISIS DE MINIMIZACIÓN DE COSTOS E IMPACTO
PRESUPUESTARIO DEL ROMOSUZUMAB EN MUJERES
POSMENOPÁUSICAS CON OSTEOPOROSIS GRAVE Y FRACASO
DEL TRATAMIENTO EN BRASIL*

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ABSTRACT:

Osteoporosis is characterized by low bone mass and decline of bone quality, resulting in a heightened risk of fracture. It affects 10 million Brazilians, predominantly postmenopausal women. The present study aims to assess the economic impact of romosozumab versus teriparatide in postmenopausal women with severe osteoporosis and treatment failure in the Brazilian Unified Health System (SUS). A cost-minimization assessment was carried out between romosozumab 210 mg and teriparatide 250 mg x 2.4 ml. The model used only drug-related costs for the full course of both romosozumab and teriparatide. The cost-minimization assessment demonstrated the superiority of romosozumab to teriparatide. The total cost of treatment per patient produced a reduction in expenses of 13 thousand reais/year, according to the current purchase price of teriparatide. In all scenarios, romosozumab proved to be cost-effective when compared to teriparatide. The result of the budgetary impact indicates the possibility of a reduction in the amounts spent on purchasing medicines. At current prices, the use of romosozumab instead of teriparatide has the potential to save resources of 143 million reais in five years. In all scenarios analyzed, the use of romosozumab produces resource savings compared to teriparatide.

PALAVRAS-CHAVE: Osteoporosis, Postmenopausal; Very high fracture risk; romosozumab; Analysis, Cost-Minimization

RESUMO:

A osteoporose é uma doença caracterizada por baixa massa óssea e deterioração da qualidade óssea, resultando em aumento do risco de fratura. Afeta 10 milhões de brasileiros, predominantemente mulheres na pós-menopausa. O objetivo deste estudo é avaliar o impacto econômico do romosozumabe versus teriparatida em mulheres na pós-menopausa com osteoporose grave e falha terapêutica, na perspectiva do Sistema Único de Saúde (SUS). Foi realizada uma análise de custo-minimização (ACM) entre o romosozumabe 210 mg e teriparatida 250 mg x 2,4 ml. O modelo utilizou apenas os custos relacionados com o medicamento para o ciclo completo do uso de ambos. A ACM demonstrou a superioridade do romosozumabe em relação à teriparatida. O custo total do tratamento por paciente produziu uma redução de gastos de 13 mil reais/ano, de acordo com o preço atual de compra da teriparatida. Em todos os cenários, o romosozumabe mostrou-se custo-efetivo quando comparado à teriparatida. O resultado do impacto orçamentário indica a possibilidade de redução nos valores gastos com aquisição de medicamentos. A preços atuais, o uso do romosozumabe tem potencial para economizar recursos de 143 milhões de reais em cinco anos. Em todos os cenários analisados, o uso do romosozumabe produz economia de recursos em comparação à teriparatida.

KEYWORDS: Osteoporose, Pós-menopausa; Alto risco de fraturas; Romosozumabe; Análise de custo-minimização

RESUMEN:

La osteoporosis es una enfermedad caracterizada por una baja masa ósea y un deterioro de la calidad ósea, lo que resulta en un mayor riesgo de fractura. Afecta a 10 millones de brasileños, predominantemente mujeres posmenopáusicas. El objetivo de este estudio es evaluar el impacto económico de romosozumab versus teriparatida en mujeres posmenopáusicas con osteoporosis grave y fracaso del tratamiento, desde la perspectiva del Sistema Único de Salud (SUS). Se realizó un análisis de minimización de costos (AMC) entre romosozumab 210 mg y teriparatida 250 mg x 2,4 ml. El modelo utilizó únicamente los costos relacionados con el medicamento para el ciclo completo de uso de ambos. La AMC demostró la superioridad de romosozumab sobre teriparatida. El costo total del tratamiento por paciente produjo una reducción de 13 mil reales/año, según el precio de compra actual de la teriparatida. En todos los escenarios, romosozumab demostró ser rentable en comparación con teriparatida. El resultado del impacto presupuestario indica la posibilidad de una reducción de los importes gastados en la compra de medicamentos. A los precios actuales, el uso de romosozumab tiene el potencial de ahorrar recursos por 143 millones de reales en cinco años. En todos los escenarios analizados, el uso de romosozumab produce un ahorro de recursos respecto a teriparatida.

Palabras clave: Osteoporosis, posmenopausia; Alto riesgo de fracturas; Romosozumab; Análisis de minimización de costos

INTRODUCTION

Osteoporosis increases bone fragility and susceptibility to fracture, playing an important role in the etiopathogenesis of fractures in the elderly, given that its prevalence increases with age (BEAUDART *et al.*, 2023). Worldwide, it affects approximately 200 million people (CONITEC, 2022a). The geographic variability in the prevalence of vertebral and hip fractures is accentuated (KANIS *et al.*, 2012). It's reduced in emerging countries, given the obstacles in accessing the health system, lack of diagnosis, variations in age distribution among population groups, and lack of studies (BRASIL, 2022a; CONITEC, 2022a; ROCHA *et al.*, 2018). In Brazil, this prevalence varies from 6 to 33% and the average costs of hospitalizations and medications, potentially underestimated, were R\$70 million in 2006, with 35,490 deaths/year in patients over 60 years of age (ROCHA *et al.*, 2018).

As fractures are the main complication associated with the disease, treatment aims to prevent them. Different classes of drugs are indicated for the prevention of osteoporosis-related fractures. Among the possibilities are calcium carbonate and vitamin D as part of all therapeutic regimens; anti-resorptive agents (bisphosphonates - alendronate, risedronate, pamidronate, and zoledronic acid); the selective estrogen receptor modulator (raloxifene); conjugated estrogens; calcitonin and the anabolic agent (teriparatide). These are options available in the Clinical Protocol of Therapeutic Guidelines (PCDT) for Osteoporosis of the Ministry of Health (MH) (CONITEC, 2022a).

The currently treatment of osteoporosis in postmenopausal women at high risk for fracture (history of fracture, or multiple risk factors for fracture) are oral bisphosphonates (NHS, 2023; CADTH, 2021, 2022). However, they are related with significant adverse events (AEs) and are possibly associated with serious adverse events (SAEs), including osteonecrosis of the jaw (ONJ), and atypical femoral fractures (CADTH, 2021, 2022). For therapeutic failure (presenting two or more fractures), which can occur in 25% of patients, guidelines from medical societies recommend the use of denosumab or teriparatide (CONITEC, 2022a; DAVIS *et al.*, 2020). In SCTIE/MH ordinance No. 166, dated December 5, 2022 (BRASIL, 2022a, BRASIL, 2022b), it was decided to incorporate romosozumab, a humanized monoclonal antibody, a regulatory factor in bone metabolism (CONITEC, 2022b), for women with postmenopausal

osteoporosis, aged 70 and over, who are at very high risk of fragility fractures and who have failed.

Some studies have equated the efficacy in reducing the risk of fractures of romosozumab therapy to teriparatide (DAVIS *et al.*, 2020; DING *et al.*, 2020), but romosozumab dosage is more spaced compared to teriparatide (monthly treatment for 12 months versus daily for 24 months, respectively), bringing the possibility of dosing comfort to the patient. Considering osteoporosis's economic burden, availability of new anti-osteoporosis drugs, and the limits of healthcare resources, economic evaluation studies of osteoporosis management strategies are important. This study aims to assess the cost-minimization analysis (CMA) and budget impact analysis (BIA) of implementing the expansion of romosozumab use in postmenopausal women with severe osteoporosis and treatment failure, compared to teriparatide, current practice available in SUS.

METHODS

As the medications have the same efficacy (DAVIS *et al.*, 2020; DING *et al.*, 2020), the economic evaluation was carried out based on a cost-minimization study from the perspective of the SUS. The population chosen was postmenopausal women with severe osteoporosis and treatment failure available on SUS. The treatment time for romosozumab was 12 months and for teriparatide 24 months (EVENTY, 2021; DAVIS *et al.*, 2020; DING *et al.*, 2020; FORTÉO, 2021). Only the costs of medications were calculated, disregarding the costs that apply equally to both alternatives, in addition to the possibility of discontinuing treatment. A discount rate of 5% (BRASIL, 2014) was applied to teriparatide only. The analysis was based on the dosage regimens contained in each manufacturer's information documents (EVENTY, 2021; FORTÉO, 2021). A deterministic sensitivity analysis was performed with the parameters of drug costs and teriparatide treatment time.

A 2-year horizon was considered for teriparatide according to the dosage described in the guidelines (CADTH, 2021; BRASIL, 2014). It was assumed that teriparatide would be marketed in a pen for subcutaneous application of 28 doses, where for 1 recommended dose per day, 730 doses or 26.07 pens (Table 1).

Table 1 - Costs per dose used for the alternatives compared in the model

Drug	Dosage	Unit cost (R\$)
Romosozumab	210mg 1x per month (12 months)	1.646,76
Teripatide	20mcg 1x per day (24 months)	1.286,06

Source: BRASIL, 2024

For BIA calculation, the eligible population was women over 50 years old selected based on the parameters included in the recommendation report 742 for the incorporation of teriparatide estimated using the National Database of Pharmaceutical Assistance Actions and Services in the SUS (BNAFAR) and the Basic Component of Pharmaceutical Assistance (CBAF)(BRASIL, 2024) (Table 2).

Table 2- Population eligible to use the medication.

Parameters	2024	2025	2026	2027	2028	Source
Population of eligible menopausal women	32.714.712	33.582.988	34.475.002	35.389.523	36.322.777	IBGE, 2024
Absolute incidence		868.276	892.014	914.521	933.254	Calculation
% treatment of severe osteoporosis	2,4%	2,4%	2,4%	2,4%	2,4%	Measured demand) CONITEC, 2024
Patients with severe osteoporosis	785.153	20.839	21.408	21.949	22.398	Calculation
% therapeutic failure	7%	7%	7%	7%	7%	Measured demand) CONITEC, 2024
Population with severe osteoporosis and therapeutic failure	54.961	1.459	1.499	1.536	1.568	Calculation
Teriparatide diffusion rate	20%	40%	60%	60%	60%	Assumption
Eligible population	10.992	583	899	922	941	Calculation

Source: BRASIL, 2024; CONITEC, 2024; IBGE, 2024

To estimate the budgetary impact, considering that the entire eligible population uses teriparatide, we started from an adoption of 30% in the first year until reaching 80% of the market share in the fifth year, since there are patients in which teriparatide is the only therapeutic alternative (Table 3).

Table 3 - Market Share of Technology Use

Market Share	(Base Scenario)				
	2024	2025	2026	2027	2028
Romosozumab diffusion	30%	50%	70%	80%	80%
Teriparatide diffusion	70%	50%	30%	20%	20%
Romosozumab population	3.298	292	629	737	753
Teriparatide population	7.695	292	270	184	188

Source: Own authorship

This study did not require institutional review board approval or informed consent, as it was based on public data and did not involve patient records.

RESULTS AND DISCUSSION

The result of the cost minimization assessment presented shows that 210 mg romosozumab has an average saving per patient of R\$ 12,868.18 (twelve thousand, eight hundred and sixty-eight reais and eighteen cents). to the use of teriparatide 250mcg/ml x 2.4 ml.

Table 4 - Results of the economic assessment

Drug	Cost 1ºyear	Cost 2ºyear	Number of doses during treatment	Total cost of treatment *	Incremental cost
Romosozumab	R\$19.761,12	R\$-	12	R\$19.761,12	-R\$12.868,18
Teriparatide	R\$16.712,57	R\$15.916,73	730	R\$32.629,30	

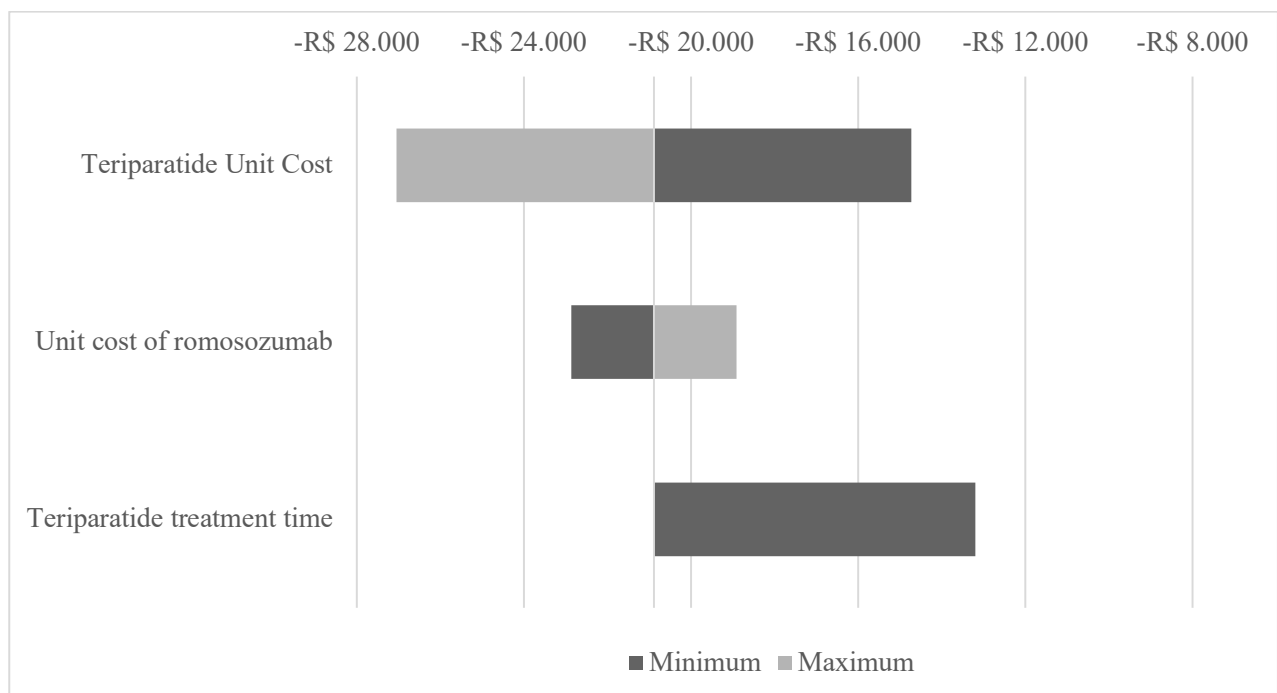
Source: Own authorship

Sensitivity analysis

A deterministic sensitivity analysis was carried out, varying the price of the two drugs by 20% and the treatment period with teriparatide to 18 months. The impact of prices

on the cost minimization assessment did not change the result and romosozumab appears to be more cost effective.

Figure 1- Tornado diagram of price variation and duration of use of teriparatide



Source: Own authorship

As the teriparatide showed to be a dominated strategy with changes in the absolute response rate, the BIA was estimated in these situations. The expansion of the use of romosozumab has a negative budgetary impact, with savings in resources when replacing teriparatide, this saving was in the order of R\$51.1 million and R\$143.4 million in a total exchange scenario.

Table 5 - Incremental budgetary impact

Standard Scenario.			
Year	Current scenario (R\$)	Proposed Scenario (R\$)	Budget Impact (R\$)
2024	169.111.045,82	183.542.850,52	14.431.804,69
2025	178.087.744,90	128.631.205,31	49.456.539,59
2026	22.809.871,78	21.076.050,63	1.733.821,15
2027	28.015.379,43	21.559.621,07	6.455.758,35
2028	28.654.921,01	20.602.729,35	8.052.191,65
Total	426.678.962,94	375.412.456,88	51.266.506,05
Total exchange scenario			
Year	Current scenario (R\$)	Proposed Scenario (R\$)	Budget Impact (R\$)
2024	169.111.045,82	217.217.061,46	48.106.015,64
2025	178.087.744,90	11.530.247,39	166.557.497,51
2026	22.809.871,78	17.768.213,26	5.041.658,52
2027	28.015.379,43	18.216.534,90	9.798.844,53
2028	28.654.921,01	18.589.681,44	10.065.239,57
Total	426.678.962,94	283.321.738,45	143.357.224,49

Source: Own authorship

For a scenario of total exchange of teriparatide for romosozumab, the resource savings would be in the order of 82 million reais.

Sensitivity Analysis

A deterministic sensitivity analysis was carried out with a 20% variation in the prices of romosozumab and teriparatide, as well as the population treated (measured demand) and the probability of therapeutic failure. For the standard scenario, only if the price of teriparatide is equal to R\$ 878,81 will there be a greater expense for the use of romosozumab. In all other hypotheses, there is a lower use of resources due to the use of romosozumabe.

Different pharmacoeconomic analyses for these diseases and their pharmacotherapy were performed in the international context (GOEREE *et al.*, 2022; HAGINO *et al.*, 2021; LUO *et al.*, 2023; SÖRESKOG *et al.*, 2021). In the Brazilian scenario, they are non-existent, even though a public consultation on the incorporation of romosozumab for the treatment of postmenopausal women in Brazil with osteoporosis and history of osteoporotic fracture and very high risk for future fracture is in progress. This economic evaluation assessed the cost-minimization of 1 year of romosozumab versus teriparatide (2 years). Treatment with romosozumab was associated with the lowest costs, relative to the comparator. Romosozumab has a higher treatment management cost, but it produces an overall cost reduction versus teriparatide from SUS perspective. Evaluation of the conclusion's robustness after accounting for structural and parameter uncertainty was made by deterministic and scenario analyses. The parameters that had the largest impact on CMA were teriparatide and romosozumab unit costs.

The cost-effectiveness of romosozumab has been calculated in different countries (GOEREE *et al.*, 2022; HAGINO *et al.*, 2021; SÖRESKOG *et al.*, 2021). Hagino *et al.* (2021) evaluated the cost-effectiveness of romosozumab *versus* teriparatide for the treatment of severe postmenopausal osteoporosis in Japanese women treated previously with bisphosphonates. A Markov model was adopted for the analysis, conducted from the Japanese healthcare system perspective. Base case results showed that compared to teriparatide/alendronate, romosozumab/alendronate reduced costs by US\$5,134/patient and conceded 0,045 additional QALYs. Probabilistic sensitivity analyses and scenario analyses confirmed robustness in model assumptions and data. For Sweden, Söreskog *et al.* (2021), investigated the cost-effectiveness of romosozumab/alendronate compared with alendronate from a societal perspective, using a microsimulation model with a Markov. The sequential romosozumab-to-alendronate treatment was related with an additional cost of €3.002 compared to alendronate alone and 0,089 additional QALYs, following in an €33,732 ICER. The results were sensitive to persistence assumptions, treatment efficacy, time horizon and patient age.

This analysis has several limitations that deserve to be discussed. Some of them are inherent to the assumptions of cost-minimization analysis, as interventions with identical health outcomes. It can oversimplify the model. Unit costs were derived from SIGTAP and may have been underestimated. The BIA was development based on the product of the previous economic assessment. Subsequently, limitations listed there also apply to this study.

FINAL CONSIDERATIONS

Teriparatide and romosozumab are indicated for the treatment of postmenopausal women with severe osteoporosis and treatment failure. As there are no significant differences in the effectiveness of the two drugs, the economic analysis was based on a cost-minimization model. The result, considering the real need for 13 pens per patient, was a favorable economy for romosozumab, with a reduction in the total cost of treatment per patient of 13 thousand reais, confirmed by sensitivity analysis.

The estimated budget impact assuming a market share of 80% in 2026 and 100% from the first year of implementation. For the current conditions for acquiring teriparatide, expenses would decrease by R\$51 million, for the first possibility, and R\$143 million for the second.

Declarations

Ethics approval and consent to participate: Not applicable

Consent for publication: Not applicable

Availability of data and materials: All data generated or analyzed during this study are included in this published article.

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