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El *American College of Physicians* (*ACP*) de EE.UU. ha elaborado dos documentos dedicados a la prevención de fracturas en pacientes con osteoporosis primaria o disminución de masa ósea: una revisión sistemática con metanálisis sobre la eficacia y seguridad de los tratamientos y una guía sobre el tratamiento farmacológico.

La **revisión sistemática**, incluyó un total de 34 ensayos clínicos aleatorios y 36 estudios observacionales, siendo sus principales conclusiones:

• Los bifosfonatos y el denosumab redujeron las fracturas de cadera, vertebrales clínicas y radiográficas y otras fracturas clínicas en mujeres posmenopáusicas con osteoporosis (grado de evidencia: moderado a alto).
• Aunque fueron eventos raros, el tratamiento de larga duración con bisfosfonatos mostraron un aumento en el riesgo de fracturas femorales atípicas y osteonecrosis de la mandíbula.
• La abaloparatida y la teriparatida redujeron las fracturas vertebrales clínicas y radiográficas, pero aumentaron el riesgo de retirada debida a eventos adversos (grado de evidencia: moderado a alto).
• A largo plazo, los tratamientos con raloxifeno y bazedoxifeno redujeron las fracturas vertebrales radiográficas, pero no clínicas (grado de evidencia: bajo a moderado).
• La abaloparatida, la teriparatida y el romosozumab secuencial (seguido de alendronato), muestran más eficacia que los bisfosfonatos en la reducción de las fracturas clínicas en mujeres posmenopáusicas mayores con muy alto riesgo de fractura (grado de evidencia: bajo a moderado).
• Los bisfosfonatos pueden reducir las fracturas clínicas en mujeres mayores con masa ósea baja (grado de evidencia: bajo) y las fracturas vertebrales radiográficas en hombres con osteoporosis (grado de evidencia: bajo a moderado).

A partir de la revisión sistemática anterior, la **guía de 2023** (que actualiza la de 2017) establece como recomendaciones principales:

Recomendación 1a: se recomienda utilizar bisfosfonatos como tratamiento farmacológico inicial para reducir el riesgo de fracturas en mujeres posmenopáusicas con diagnóstico de osteoporosis primaria (recomendación fuerte; grado de evidencia alto)

Recomendación 1b: se sugiere el uso de bifosfonatos para el tratamiento farmacológico inicial para reducir el riesgo de fracturas

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en hombres con diagnóstico de osteoporosis primaria (recomendación condicional; grado de evidencia bajo).

Recomendación 2a: se sugiere utilizar denosumab como tratamiento de segunda línea para reducir el riesgo de fracturas en mujeres posmenopáusicas con diagnóstico de osteoporosis primaria que tienen contraindicaciones o experimentan efectos adversos a los bisfosfonatos (recomendación condicional; grado de evidencia moderado).

Recomendación 2b: se sugiere utilizar denosumab como tratamiento de segunda línea para reducir el riesgo de fracturas en hombres diagnosticados con osteoporosis primaria que tienen contraindicaciones o experimentan efectos adversos de los bisfosfonatos (recomendación condicional; grado de evidencia bajo).

Recomendación 3: se sugiere utilizar romosozumab (grado de evidencia moderado) o teriparatida (grado de evidencia bajo), seguido de un bisfosfonato, para reducir el riesgo de fracturas sólo en mujeres con osteoporosis primaria y riesgo muy alto de fractura (recomendación condicional).

Recomendación 4: se sugiere un enfoque individualizado sobre el inicio del tratamiento farmacológico con bisfosfonatos en mujeres mayores de 65 años con baja masa ósea (osteopenia) para reducir el riesgo de fracturas (recomendación condicional; grado de evidencia bajo).

Al final se reproduce la figura 1 que muestra los tratamientos para reducir las fracturas en mujeres posmenopáusicas con osteoporosis primaria.

En relación con el tratamiento de la osteoporosis, se puede consultar el BTA de 2022 sobre osteoporosis: actualización, y el documento del SSPA de Recomendaciones para el uso racional del medicamento en el el tratamiento farmacológico de las enfermedades reumáticas y musculoesqueléticas. Osteoporosis.

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CLINICAL GUIDELINE — Pharmacologic Treatment of Primary Osteoporosis or Low Bone Mass in Adults

Figure 1. Treatments to reduce fractures in postmenopausal females with primary osteoporosis.

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Treatments to Reduce Fractures in Postmenopausal Females With Primary Osteoporosis

Recommendations

RECOMMENDATION: ACP recommends that clinicians use bisphosphonates for initial pharmacologic treatment to reduce the risk of fractures in postmenopausal females diagnosed with primary osteoporosis (strong recommendation; high-certainty evidence).

RECOMMENDATION: ACP suggests that clinicians use the RANK ligand inhibitor (denosumab) as a second-line pharmacologic treatment to reduce the risk of fractures in postmenopausal females diagnosed with primary osteoporosis who have contraindications to or experience adverse effects of bisphosphonates (conditional recommendation; moderate-certainty evidence).

RECOMMENDATION: ACP suggests that clinicians use the sclerostin inhibitor (romosozumab, moderate-certainty evidence) or recombinant PTH (teriparatide; low-certainty evidence), followed by a bisphosphonate, to reduce the risk of fractures only in females with primary osteoporosis with very high risk of fracture (conditional recommendation).

RATIONALE: Bisphosphonates had the most favorable balance among benefits, harms, patient values and preferences, and cost among the examined drugs in postmenopausal females with primary osteoporosis and should be used as first-line treatment. Denosumab also had a favorable long-term net benefit, but bisphosphonates are much cheaper than other pharmacologic treatments and available in generic formulations. Evidence showed that the benefits of recombinant PTH (teriparatide) or the sclerostin inhibitor (romosozumab) may have outweighed harms compared with placebo in a select population of postmenopausal females (mean age >74 years) with osteoporosis and very high risk for fracture. Bisphosphonates and denosumab were associated with higher risk for osteonecrosis of the jaw and atypical femoral fractures, and romosozumab was associated with adverse cardiovascular events. The long-term safety of teriparatide in humans is unknown.

Patient Population
Postmenopausal females diagnosed with primary osteoporosis

Interventions Compared With Placebo
Bisphosphonates (alendronate, risedronate, zoledronate), denosumab, teriparatide, abaloparatide, romosozumab, raloxifene

Key Outcomes Assessed at 12–36 and ≥36 Months
Hip fracture, any clinical and clinical vertebral fractures, radiographic vertebral fractures, harms (serious adverse effects and treatment withdrawal due to adverse effects)

Key Outcomes

Hip Fractures, ≥36 Months

	−50 per 1000 treated patients 0	CERTAINTY OF THE EVIDENCE
BISPHOSPHONATES VS. PLACEBO	6 fewer	HIGH
DENOSUMAB VS. PLACEBO	4 fewer	MODERATE

Raloxifene may not differ from placebo (low-certainty evidence). Evidence is not available for other treatments.

Clinical Vertebral Fracture, ≥36 Months

	−50 per 1000 treated patients 0	CERTAINTY OF THE EVIDENCE
BISPHOSPHONATES VS. PLACEBO	18 fewer	HIGH
DENOSUMAB VS. PLACEBO	16 fewer	HIGH

Raloxifene may not differ from placebo (low-certainty evidence). Evidence is not available for other treatments.

Hip Fractures, 12–36 Months

	−50 per 1000 treated patients 0	CERTAINTY OF THE EVIDENCE
BISPHOSPHONATES VS. PLACEBO	8 fewer	HIGH
SEQUENTIAL THERAPY OF ROMOSOZUMAB TO ALENDRONATE VS. ALENDRONATE ALONE	12 fewer	MODERATE

Teriparatide may not differ from placebo (low-certainty evidence). Evidence is not available for other treatments.

Clinical Vertebral Fracture, 12–36 Months

	−100 per 1000 treated patients 0	CERTAINTY OF THE EVIDENCE
BISPHOSPHONATES VS. PLACEBO	21 fewer	HIGH
ROMOSOZUMAB VS. PLACEBO	4 fewer	MODERATE
TERIPARATIDE VS. PLACEBO	45 fewer	LOW
RALOXIFENE VS. PLACEBO	35 fewer	LOW
SEQUENTIAL THERAPY OF ROMOSOZUMAB TO ALENDRONATE VS. ALENDRONATE ALONE	13 fewer	MODERATE

Evidence is very uncertain (insufficient) about the effect of denosumab. Evidence is not available for other treatments.

Withdrawal Due to Adverse Events, ≥36 Months

	0 per 1000 treated patients 150	CERTAINTY OF THE EVIDENCE
TERIPARATIDE VS. PLACEBO	127 more	MODERATE

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Serious Adverse Events, ≥36 Months

	CERTAINTY OF THE EVIDENCE
Bisphosphonates and denosumab resulted in no differences in serious adverse events and withdrawals due to adverse events in RCTs.	HIGH
Bisphosphonates and denosumab were associated with higher risk for osteonecrosis of the jaw and atypical femoral or subtrochanteric fractures in observational studies, with higher risk after longer treatment duration.	LOW
Romosozumab followed by alendronate probably did not increase risk for serious harms or withdrawal due to adverse effects compared with bisphosphonate alone at 12- to 36-month outcome assessment in an RCT.	MODERATE
Romosozumab was associated with higher risk for adverse cardiovascular events and raloxifene was associated with thromboembolism in observational studies.	LOW
Long-term safety of teriparatide in humans is unknown.	INSUFFICIENT

Clinical Considerations

- Clinicians should prescribe generic medications if possible rather than more expensive brand-name medications.
- Clinicians treating postmenopausal females with osteoporosis should encourage adherence to recommended drug treatments and healthy lifestyle modifications, including exercise, and counseling for evaluation and prevention of falls.
- Adequate calcium and vitamin D intake should be part of fracture prevention in all postmenopausal females with low bone mass or osteoporosis.
- Clinicians should assess baseline risk for fracture based on individualized assessment of bone density, history of fractures, response to prior treatments for osteoporosis, and multiple risk factors for fractures in postmenopausal females with primary osteoporosis.
- Current evidence suggests that increasing the duration of bisphosphonate therapy to longer than 5 years probably reduced risk for new vertebral fractures but not risk for other fractures at the expense of increased risk for long-term harms. Therefore, clinicians should consider stopping bisphosphonate treatment after 5 years unless the patient has a strong indication for treatment continuation.
- The decision of a temporary treatment discontinuation (holidays) should be individualized and based on baseline risk for fractures, type of medication and its half-life in bone, duration of discontinuation, benefits and harms of discontinuation, and higher risk for fracture due to drug discontinuation.
- Females initially treated with an anabolic agent should be offered an antiresorptive agent after discontinuation to preserve gains and because of serious risk for rebound and multiple vertebral fractures.
- Older postmenopausal females with primary osteoporosis who are at increased risk for falls and other adverse events due to polypharmacy or drug interactions need individualized treatment selection based on comorbidities and concomitant medications associated with higher risk for falls/fractures.tt

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