Bisphosphonates for postmenopausal osteoporosis: length of treatment, length of "holiday," and whether to restart

By Judy Lee, MD, Endocrinology

Clinical questions

- What is the recommended duration of bisphosphonate therapy in postmenopausal women?
- When is it appropriate to restart bisphosphonate therapy after a "drug holiday"?
- When should I refer my patient to Endocrinology?

Recommendations

Bisphosphonates continue to be the first-line therapy for osteoporosis.

There is insufficient evidence to guide decisions about the duration of bisphosphonate therapy in postmenopausal women. Decisions on therapy should be individualized based on the patient’s DEXA (dual energy X-ray absorptiometry) scores and clinical risk factors. It is helpful to stratify patients according to their level of risk for osteoporotic fractures during their initial evaluation.

Patients at **low to moderate risk** for osteoporotic fractures (also known as fragility or low-trauma fractures) are those with:

- No previous fragility fractures
- Mild to moderate osteoporosis (T-score above -3.5)
- Low risk of falls

Patients at **high risk** are those with:

- Previous fragility fracture
- T-score below -3.5 in the absence of fracture
- Loss of vertebral height
- High risk of falls
Initial bisphosphonate therapy

<table>
<thead>
<tr>
<th>Osteoporotic fracture risk</th>
<th>Duration of initial treatment</th>
<th>Monitoring during initial treatment</th>
<th>Duration of drug holiday</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low to moderate</td>
<td>5 years alendronate * or 3 years zoledronic acid **</td>
<td>For all risk levels: • DEXA every 2 years. • Measure vertebral height annually. If patient loses more than 2 cm (0.8 in) in height, suggest vertebral imaging.</td>
<td>3–5 years</td>
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<tr>
<td>High</td>
<td>Up to 10 years alendronate * or Up to 6 years zoledronic acid **</td>
<td></td>
<td>1–2 years</td>
</tr>
</tbody>
</table>

* Risedronate may be used if patient is intolerant to alendronate. The safety and efficacy of risedronate beyond 7 years has not been established in clinical trials.

** If patient is intolerant to oral bisphosphonates.

Restarting bisphosphonate therapy
The decision to resume therapy after a drug holiday should be based on a combination of factors, including length of holiday, subsequent DEXAs, clinical risk assessment, and interval fracture history. Patients at all risk levels should receive comprehensive clinical risk assessment and DEXA every 2 years from the time they start their drug holiday.

Resumption of therapy is recommended when the patient has:
- Experienced persistent bone loss of 5% or more at the femoral neck on two DEXAs taken at least 2 years apart.
- Sustained a fragility fracture while off therapy.
- Been re-stratified from the low-to-moderate-risk group to the high-risk group for osteoporotic fracture.

When to refer to Endocrinology
Consider referring your patient to Endocrinology if:
- She can’t tolerate bisphosphonates after a "good trial" of the medication. Nonspecific symptoms may not be related to bisphosphonates.
- She has recurrent fractures or continued bone loss while on therapy, in the absence of treatable causes of bone loss (failure of therapy).
- Her osteoporosis is unexpectedly severe or has unusual features.
- She has or develops a condition that complicates management, such as renal failure.

How could this change my practice?
Decisions about the duration of bisphosphonate therapy need to be individualized to each patient. Because the benefits of bisphosphonate therapy for fracture prevention and bone mineral density (BMD) last beyond discontinuation of the medication, a drug holiday is recommended for all patients after a certain period of therapy.

Why did we choose this topic?
The question of what to do beyond 5 years of oral bisphosphonate therapy in postmenopausal osteoporosis comes up frequently in the primary care setting.
Evidence summary
In the Fracture Intervention Trial Long-term Extension (FLEX) (Black 2006), 1,099 postmenopausal women who had previously received alendronate for 5 years in the Fracture Intervention Trial (FIT) were randomly assigned to either an additional 5 years of alendronate or placebo. Women at highest risk were excluded from FLEX. The authors concluded that stopping alendronate after 5 years resulted in gradual decreases in bone mineral density and increases in bone turnover markers, but did not lead to significantly higher risk of fractures. Based on the FLEX findings, discontinuation of bisphosphonates after 5 years is reasonable in lower-risk patients when accompanied by close monitoring of BMD and clinical risk factors. For patients who are at the highest risk for fracture, suggest continuing therapy for up to 10 years.

References


Resource
Group Health [Osteoporosis Screening, Diagnosis, and Treatment Guideline]