For Fosamax+D: the patient cannot take alendronate and vitamin D separately.

Contraindication

Intolerable adverse effects

MTF Formulary Management for Oral Bisphosphonates
Defense Health Agency Pharmacy Operations Division
September 2014

Bottom-line

- Alendronate (generic Fosamax) is the preferred oral bisphosphonate and remains BCF.
- Prior Authorization (Step Therapy) applies in this class – see below.
- Ibandronate (Boniva) is no longer BCF, but remains Uniform Formulary. Current users of ibandronate may continue therapy. New users of ibandronate must try alendronate first.
- New AND current users of risedronate (Actonel) must try alendronate first. Risedronate users are not grandfathered.
- Fosamax Plus D is no longer BCF, it moves to Non-Formulary.
- All the oral bisphosphonates have similar efficacy with regard to increasing bone density.
- The FDA released new oral bisphosphonates safety information suggesting patients at low to moderate fracture risk may benefit from a drug holiday after 3-5 years of therapy.

Uniform Formulary Decision: The Director, DHA approved the recommendations from the May 2014 DoD P&T Committee meeting in September 2014, with an implementation date of December 17, 2014.

<table>
<thead>
<tr>
<th>Uniform Formulary (UF) drugs</th>
<th>Non-Formulary (NF) drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCF drugs - MTFs must have on formulary</td>
<td>MTFs may have on formulary</td>
</tr>
<tr>
<td>Step-preferred:</td>
<td>Non step-preferred*:</td>
</tr>
<tr>
<td>- Alendronate (generic Fosamax)</td>
<td>- Ibandronate (Boniva)</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Step therapy applies to all new patients–must try alendronate first
**Step therapy applies to all new and current patients – must try alendronate first

Prior Authorization and Step Therapy information

- Prior authorization (step therapy) criteria apply to all new users ibandronate ("grandfathered") and to all new and current users of risedronate, Atelvia, Binosto, or Fosamax+D (not "grandfathered").
- Generic alendronate is the step-preferred bisphosphonate.
- A new user is a patient who has been prescribed a non step-preferred product (ibandronate, risedronate, Atelvia, Binosto, or Fosamax+D) and does not have a prescription for the non step-preferred medication in their drug profile in the past 180 days.
- All new users of ibandronate and all new and current users of risedronate, Atelvia, Binosto and Fosamax+D must try alendronate first, unless the following issues with alendronate, which is not expected to occur with the non step-preferred oral bisphosphonate:
  - Intolerable adverse effects
    - The patient requires monthly ibandronate or Actonel 150 mg due to GI adverse effects from alendronate weekly dosing.
    - The patient has experience significant adverse events from alendronate, which is not expected to occur with the non preferred products.
    - For Binosto: the patient has swallowing difficulties and cannot consume 8 ounces of water and has no sodium restrictions.
    - For Fosamax+D: the patient cannot take alendronate and vitamin D separately.
  - Contraindication
Clinical Summary

- Relative superiority of one oral bisphosphonate vs. another cannot be determined by bone mineral density (BMD) data alone. Available data from placebo-controlled trials is not sufficient to clearly establish superiority of one oral bisphosphonate vs. another for fracture prevention. No sufficient head-to-head studies exist to establish superiority.

- Clinical guidelines list ibandronate as 2nd line therapy due to the lack of data for hip fracture prevention and the lack of long-term data. However, ibandronate has the convenience of once monthly dosing, and an MHS study showed improved persistence with the once monthly ibandronate formulation over the other once-weekly bisphosphonates.

- Risedronate formulations: Atelvia offers a once weekly risedronate regimen. Binosto allows for less consumption of water; however the formulation contains an additional sodium load. Atelvia and Binosto offer no clinically compelling advantages over existing UF agents.

  - Risk of osteonecrosis of the jaw is low but is most often observed after invasive dental procedures during oncology therapy.
  - The FDA concluded that concerns about atrial fibrillation need not be considered in decisions about osteoporosis therapy.
  - With regard to esophageal cancer, the FDA determined there is not enough information to make definitive conclusions about a possible connection between oral bisphosphonates and esophageal cancer.
  - Risk of atypical femur fractures rises with increased duration of bisphosphonate exposure and decreases rapidly after discontinuation.
  - Use of glucocorticoids and PPIs increase the risk of atypical femur fractures.
  - Data suggests that patients at low to moderate fracture risk may benefit from a drug holiday after 3-5 years of exposure.
  - BMD should be monitored every 2-3 years to reassess risk.

References

- Current/future drug classes under review by the DOD P&T Committee: http://pec.ha.osd.mil/PT_Committee.php?submenuheader=4
- Prior Authorization/Medical Necessity forms: http://pec.ha.osd.mil/forms_criteria.php?submenuheader=1
- Point of contact for additional information: usarmy.jbsa.medcom-ameddcs.list.pecul2@mail.mil

Additional References

- National Osteoporosis Foundation guidelines: http://nof.org/hcp/clinicians-guide

<table>
<thead>
<tr>
<th>Oral Bisphosphonate Price Comparison at MTF</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Drug &amp; Dosage Form</strong></td>
</tr>
<tr>
<td><strong>Basic Core Formulary</strong></td>
</tr>
<tr>
<td>Alendronate generics</td>
</tr>
<tr>
<td><strong>Uniform Formulary</strong></td>
</tr>
<tr>
<td>Ibandronate (Boniva and generics)</td>
</tr>
<tr>
<td><strong>Non-Formulary</strong></td>
</tr>
<tr>
<td>Alendronate/Vitamin D (Fosamax+D)</td>
</tr>
<tr>
<td>Risedronate (Actonel)</td>
</tr>
<tr>
<td>Risedronate delayed-release (Atelvia)</td>
</tr>
<tr>
<td>Alendronate effervescent tablet (Binosto)</td>
</tr>
</tbody>
</table>