Clinical Policy: Etidronate (Didronel)
Reference Number: CP.PMN.94
Effective Date: 03.01.18
Last Review Date: 02.19
Line of Business: Medicaid

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Etidronate (Didronel®) is an oral bisphosphonate.

FDA Approved Indication(s)
Didronel is indicated for:
- Treatment of symptomatic Paget’s disease of bone
- Prevention and treatment of heterotopic ossification following total hip replacement or due to spinal cord injury.

Limitation(s) of use: Etidronate is not approved for the treatment of osteoporosis.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Didronel is medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Paget’s Disease (must meet all):
      1. Diagnosis of Paget’s disease;
      2. Failure of ≥ 6 month trial of alendronate at maximum indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
      3. Dose does not exceed 20 mg/kg per day.
      Approval duration:
      Doses up to 10 mg/kg/day – 6 months
      Doses greater than 10 mg/kg/day – 3 months

   B. Heterotopic Ossification or Hypercalcemia of Malignancy (must meet all):
      1. Diagnosis of one of the following (a or b):
         a. Hypercalcemia associated with malignancy (off-label);
         b. Heterotopic ossification resulting from spinal cord injury or following total hip arthroplasty;
      2. Dose does not exceed 20 mg/kg per day.
      Approval duration:
      Hypercalcemia/spinal cord injury – 3 months
      Total hip arthroplasty – 4 months
C. Other diagnoses/indications
   1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

II. Continued Therapy
   A. Paget’s Disease (must meet all):
      1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
      2. Three months have elapsed since the completion of previous therapy with Didronel;
      3. Disease has relapsed or progressed (e.g., increases in or failure to achieve normalization of serum ALP, radiographic progression of disease);
      4. If request is for a dose increase, new dose does not exceed 20 mg/kg/day.
      Approval duration:
      Doses up to 10 mg/kg/day – 6 months
      Doses greater than 10 mg/kg/day – 3 months

   B. Heterotopic Ossification (must meet all):
      1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
      2. Member has NOT received ≥ 3 months of treatment for heterotopic ossification from spinal cord injury or ≥ 4 months treatment following total hip arthroplasty;
      3. Member is responding positively to therapy;
      4. If request is for a dose increase, dose does not exceed 20 mg/kg per day.
      Approval duration:
      Allow for no more than 4 months of treatment TOTAL for total hip arthroplasty
      Allow for no more than 3 months of treatment TOTAL for spinal cord injury

   C. Hypercalcemia of Malignancy (off-label) (must meet all):
      1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria.
      2. Member has not received ≥ 90 days of therapy;
      3. Member is responding positively to therapy;
      4. If request is for a dose increase, dose does not exceed 20 mg/kg per day.
      Approval duration:
      Allow for no more than 3 months of treatment TOTAL

   D. Other diagnoses/indications (must meet 1 or 2):
      1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
      Approval duration: Duration of request or 6 months (whichever is less); or
      2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.
III. Diagnoses/Indications for which coverage is NOT authorized:
   A. Non-FDA approved indications, which are not addressed in this policy, unless there is 
sufficient documentation of efficacy and safety according to the off label use policy - 
CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information
   Appendix A: Abbreviation Key
   FDA: Food and Drug Administration

   Appendix B: Therapeutic Alternatives
   This table provides a listing of preferred alternative therapy recommended in the approval 
criteria. The drugs listed here may not be a formulary agent for all relevant lines of business 
and may require prior authorization.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>alendronate</td>
<td>PMO/MO treatment: 10 mg PO QD or 70 mg PO once weekly</td>
<td></td>
</tr>
<tr>
<td></td>
<td>PMO Prevention: 5 mg PO QD or 35 mg PO once weekly</td>
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</tr>
<tr>
<td></td>
<td>Paget’s disease: 40 mg PO QD for 6 months</td>
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<tr>
<td></td>
<td></td>
<td>40 mg/day 70 mg/week</td>
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</tbody>
</table>

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only 
and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings
   • Contraindication(s): abnormalities of the esophagus which delay esophageal emtiping 
such as stricture or achalasia; hypersensitivity
   • Boxed warning(s): none reported

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paget’s disease</td>
<td>5 to 10 mg/kg/day, not to exceed 6 months or 11 to 20 mg/kg/day, not to exceed 3 months</td>
<td>20 mg/kg/day</td>
</tr>
<tr>
<td>Heterotopic ossification</td>
<td>Total hip replacement patients: 20 mg/kg/day for 1 month before and 3 months after surgery (4 months total)</td>
<td>20 mg/kg/day</td>
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<tr>
<td></td>
<td>Spinal cord-injured patients: 20 mg/kg/day for 2 weeks followed by 10 mg/kg/day for 10 weeks (12 weeks total)</td>
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</tr>
</tbody>
</table>

VI. Product Availability
   Tablets: 200 mg, 400 mg
VII. References


<table>
<thead>
<tr>
<th>Reviews, Revisions, and Approvals</th>
<th>Date</th>
<th>P &amp; T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>-New policy created</td>
<td>12.01.17</td>
<td>02.18</td>
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<tr>
<td>-Split from CP.PMN.43 – oral bisphosphonates.</td>
<td></td>
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<tr>
<td>-No significant changes from previous corporate approved policy.</td>
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<tr>
<td>-References reviewed and updated.</td>
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<tr>
<td>1Q 2019 annual review: for Paget’s disease – removed alkaline phosphate requirement, revised initial approval duration to 3 or 6 months based on requested dose, modified response criteria to “Disease has relapsed or progressed (e.g., increases in or failure to achieve normalization of serum ALP, radiographic progression of disease)”; for hypercalcemia of malignancy modified approval duration to 3 months, clarified in continued approval for maximum 3 months of total treatment; references reviewed and updated.</td>
<td>11.01.18</td>
<td>02.19</td>
</tr>
</tbody>
</table>

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

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Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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