Clinical Policy: Conjugated Estrogens/Bazedoxifene (Duavee)
Reference Number: HIM.PA.140
Effective Date: 10.24.17
Last Review Date: 02.18
Line of Business: Health Insurance Marketplace

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

Description
Conjugated estrogens/bazedoxifene (Duavee®) is a combination of conjugated equine estrogens and an estrogen agonist/antagonist. The pairing of conjugated estrogens with bazedoxifene produces a composite effect that is specific to each target tissue. The bazedoxifene component reduces the risk of endometrial hyperplasia that can occur with the conjugated estrogens component.

FDA Approved Indication(s)
Duavee is indicated for the treatment of the following conditions in women with a uterus:
• Treatment of moderate-to-severe vasomotor symptoms associated with menopause
• Prevention of postmenopausal osteoporosis

Limitation(s) of use:
• Duavee should be used for the shortest duration consistent with treatment goals and risks for the individual woman. Postmenopausal women should be re-evaluated periodically as clinically appropriate to determine if treatment is still necessary.
• When prescribing solely for the prevention of postmenopausal osteoporosis, therapy should only be considered for women at significant risk of osteoporosis and non-estrogen medication should be carefully considered.

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria

I. Initial Approval Criteria
   A. Vasomotor Symptoms (must meet all):
      1. Diagnosis of vasomotor symptoms associated with menopause;
      2. Member has not undergone a hysterectomy;
      3. Failure of 2 formulary estrogen products (not contraceptives) unless contraindicated or clinically significant adverse effects are experienced;
      4. Dose does not exceed 0.45 mg conjugated estrogens/20 mg bazedoxifene per day (1 tablet per day).

   Approval duration: 6 months

   B. Osteoporosis (must meet all):
      1. Prescribed for the prevention of postmenopausal osteoporosis;
2. Member has not undergone hysterectomy;
3. Failure of an oral bisphosphonate (alendronate is preferred) as evidenced by one of the following (a or b), unless contraindicated or clinically significant adverse effects are experienced:
   a. Documented history of fracture at any time while on therapy;
   b. Lack of improvement in bone mineral density from baseline after ≥ 12 months;
4. Failure of raloxifene as evidenced by one of the following (a or b), unless contraindicated or clinically significant adverse effects are experienced:
   a. Documented history of fracture at any time while on therapy;
   b. Lack of improvement in bone mineral density from baseline after ≥ 12 months;
5. Dose does not exceed 0.45 mg conjugated estrogens/20 mg bazedoxifene per day (1 tablet per day).

Approval duration: 6 months

C. Other diagnoses/indications
   1. Refer to HIM.PHAR.21 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy
   A. All Indications in Section 1 (must meet all):
      1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
      2. Member is responding positively to therapy;
      3. If request is for a dose increase, new dose does not exceed 0.45 mg conjugated estrogens/20 mg bazedoxifene per day (1 tablet per day).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2):
   1. Currently receiving medication via health plan benefit and documentation supports positive response to therapy. 
   Approval duration: Duration of request or 12 months (whichever is less); or
   2. Refer to HIM.PHAR.21 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 – HIM.PHAR.21 or evidence of coverage documents.

IV. Appendices/General Information
   Appendix A: Abbreviation/Acronym 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 and may require prior authorization.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
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<tbody>
<tr>
<td>estradiol (Alora®, Climara®, Divigel®, Elestrin®, Estrace®, EstroGel®, Evamist®, Menostar®, Minivelle®, Vivelle Dot®)</td>
<td>Varies by formulation</td>
<td>Varies</td>
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<tr>
<td>Premphase®, Prempro® (conjugated estrogens/medroxyprogesterone)</td>
<td>1 tablet PO QD</td>
<td>1 tablet/day</td>
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<tr>
<td>Premarin® (conjugated estrogens)</td>
<td>0.3 mg PO QD; may titrate if needed</td>
<td>1.25 mg/day</td>
</tr>
<tr>
<td>Menest® (esterified estrogens)</td>
<td>0.3 to 1.25 mg PO QD</td>
<td>1.25 mg/day</td>
</tr>
<tr>
<td>estropipate</td>
<td>0.75 mg PO QD; may titrate if needed (range: 0.75 to 6 mg/day)</td>
<td>6 mg/day</td>
</tr>
<tr>
<td>alendronate (Fosamax®)</td>
<td>5 mg PO QD or 35 mg PO q week</td>
<td>5 mg/day or 35 mg/week</td>
</tr>
<tr>
<td>ibandronate (Boniva®)</td>
<td>2.5 mg PO QD or 150 mg PO q month</td>
<td>2.5 mg/day or 150 mg/month</td>
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<tr>
<td>risedronate (Actonel®, Atelvia®)</td>
<td>5 mg PO QD or 35 mg PO q week for 2 consecutive days for 2 doses/month or 150 mg PO q month</td>
<td>5 mg/day or 35 mg/week or 75 mg/day for 2 days per month or 150 mg/month</td>
</tr>
<tr>
<td>raloxifene (Evista®)</td>
<td>60 mg PO QD</td>
<td>60 mg/day</td>
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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: General Information

- Duavee is not recommended for use in women greater than 75 years of age. An increased risk of probable dementia in women over 65 years of age was reported in the Women's Health Initiative Memory ancillary studies of the Women's Health Initiative using daily conjugated estrogens (0.625 mg).
- Women taking Duavee should not take additional estrogens.
- There is an increased risk of endometrial cancer in a woman with a uterus who uses unopposed estrogens. Duavee has been shown to reduce the risk of endometrial hyperplasia, which may be a precursor to endometrial cancer.
- Estrogen therapy should not be used for the prevention of cardiovascular disease or dementia.
- The Women's Health Initiative (WHI) estrogen-alone substudy reported increased risks of stroke and deep vein thrombosis (DVT) in postmenopausal women (50 to 79 years of age).
V. References

<table>
<thead>
<tr>
<th>Reviews, Revisions, and Approvals</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
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<td>Policy created</td>
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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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