# Clinical Policy: Conjugated Estrogens/Bazedoxifene (Duavee)

Reference Number: HIM.PA.140
Effective Date: 10.24.17
Last Review Date: 02.20
Line of Business: HIM

Revision Log

**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 in women with a uterus for:

- 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 (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 Duavee is **medically necessary** when the following criteria are met:

**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 (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 a hysterectomy;
3. Failure of a 12-month trial of an oral bisphosphonate (*alendronate is preferred*) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
4. Failure of a 12-month trial of raloxifene, unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed 0.45 mg conjugated estrogens/20 mg bazedoxifene (1 tablet) per day.

**Approval duration: 6 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): HIM.PHAR.21 for health insurance marketplace.

## 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 (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 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): HIM.PHAR.21 for health insurance marketplace.

## 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 for health insurance marketplace or evidence of coverage documents.

## IV. Appendices/General Information

*Appendix A: Abbreviation/Acronym Key*
FDA: Food and Drug Administration
WHI: Women's Health Initiative

*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.*

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|---|---|---|
| **Estrogen Products** | | |
| estradiol (Alora®, Climara®, Divigel®, Elestrin®, Estrace®, EstroGel®, Evamist®, Menostar®, Minivelle™, Vivelle Dot™) | Varies by formulation | Varies |
| estropipate | 0.75 mg PO QD; may titrate if needed (range: 0.75 to 6 mg/day) | 6 mg/day |
| Menest® (esterified estrogens) | 0.3 to 1.25 mg PO QD | 1.25 mg/day |
| Premarin® (conjugated estrogens) | 0.3 mg PO QD; may titrate if needed | 1.25 mg/day |
| Premphase®, Prempro® (conjugated estrogens/ medroxyprogesterone) | 1 tablet PO QD | 1 tablet/day |
| **Oral Bisphosphonates** | | |
| alendronate (Fosamax®) | 5 mg PO QD or 35 mg PO q week | 5 mg/day or 35 mg/week |
| ibandronate (Boniva®) | 2.5 mg PO QD or 150 mg PO q month | 2.5 mg/day or 150 mg/month |
| risedronate (Actonel®, Atelvia®) | 5 mg PO QD or 35 mg PO q week or 75 mg PO QD for 2 consecutive days for 2 doses/month or 150 mg PO q month | 5 mg/day or 35 mg/week or 75 mg/day for 2 days per month or 150 mg/month |
| **Selective Estrogen Receptor Modulator (SERM)** | | |
| raloxifene (Evista®) | 60 mg PO QD | 60 mg/day |

*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): undiagnosed abnormal uterine bleeding; known suspected or past history of breast cancer; known or suspected estrogen-dependent neoplasia; active or past history of venous thromboembolism; active or past history of arterial thromboembolism; hypersensitivity (angioedema, anaphylaxis) to estrogens, bazedoxifene, or any ingredients; known hepatic impairment or disease; known protein C, protein S, or antithrombin deficiency or other known thrombophilic disorders; pregnancy, women who may become pregnant, and nursing mothers
- Boxed warning(s): endometrial cancer, cardiovascular disorders, and probable dementia

*Appendix D: 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 (WHI) Memory ancillary studies of the WHI 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 WHI estrogen-alone substudy reported increased risks of stroke and deep vein thrombosis (DVT) in postmenopausal women (50 to 79 years of age) during 7.1 years of treatment with daily oral conjugated estrogens (0.625 mg)-alone, relative to placebo.

## V. Dosage and Administration

| Indication | Dosing Regimen | Maximum Dose |
|---|---|---|
| Vasomotor symptoms, osteoporosis | 1 tablet PO QD | 1 tablet/day |

## VI. Product Availability

Tablet: 0.45 mg/20 mg

## VII. References

1. Duavee Prescribing Information. Philadelphia, PA: Wyeth Pharmaceuticals Inc.; December 2018. Available at: www.duavee.com. Accessed November 4, 2019.
2. Goodman NF, Cobin RH, Ginzburg SB, et al. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the diagnosis and treatment of menopause. Endocr Pract. 2011; 17(Suppl 6): 1-24.
3. Stuenkel CA, Davis SR, Gompel A, et al. Treatment of the symptoms of the menopause: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2015; 100(11): 3975-4011.
4. Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists and American College of Endocrinology clinical practice guidelines for the diagnosis and treatment of postmenopausal osteoporosis - 2016. Endocr Pract. 2016; 22(Suppl 4): 1-42.
5. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2017. Available at: http://www.clinicalpharmacology-ip.com/.

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| Policy created | 10.24.17 | 02.18 |
| 1Q 2019 annual review: no significant changes; osteoporosis – removed definition of treatment failure to align with other osteoporosis agent policies; references reviewed and updated. | 12.06.18 | 02.19 |
| 1Q 2020 annual review: no significant changes; references reviewed and updated. | 11.04.19 | 02.20 |

**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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This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

**Note:**
**For Health Insurance Marketplace members**, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the non-formulary policy; HIM.PA.103.

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