Clinical Policy: Bupropion/Naltrexone (Contrave)
Reference Number: ERX.NPA.96
Effective Date: 12.01.18
Last Review Date: 11.18

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

Description
Bupropion/naltrexone (Contrave®) is a combination of naltrexone, an opioid antagonist, and bupropion, an aminoketone antidepressant.

FDA Approved Indication(s)
Contrave is indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adults with an initial body mass index (BMI) of:
- 30 kg/m² or greater (obese), or
- 27 kg/m² or greater (overweight) the presence of at least one weight-related comorbidity such as hypertension, type 2 diabetes mellitus, or dyslipidemia.

Limitation(s) of use:
- The effect of Contrave on cardiovascular morbidity and mortality has not been established.
- The safety and effectiveness of Contrave in combination with other products intended for weight loss, including prescription drugs, over-the-counter drugs, and herbal preparations, have not been established.

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 Envolve Pharmacy Solutions™ that Contrave is medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Weight Management (must meet all):
      1. Member meets one of the following (a or b):
         a. BMI ≥ 30 kg/m²;
         b. BMI ≥ 27 kg/m² with at least one indicator of increased cardiovascular risk (e.g., coronary artery/heart disease, hypertension, dyslipidemia, diabetes, elevated waist circumference) or other obesity-related medical condition (e.g., sleep apnea);
      2. Age ≥ 18 years;
      3. Dose does not exceed 32/360 mg per day (4 tablets per day).
      Approval duration: 16 weeks
   
   B. Other diagnoses/indications
      1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy
   A. Weight Management (must meet all):
      1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
      2. BMI ≥ 25 kg/m²;
      3. Member meets one of the following (a or b):
         a. If this is the first renewal request, member has lost ≥ 5% of baseline body weight;
         b. If this is a second or subsequent renewal request, member has lost weight and/or maintained weight loss on therapy;
4. If request is for a dose increase, new dose does not exceed 32/360 mg per day (4 tablets per day).

Approval duration:
First reauthorization – 12 weeks
Second or subsequent reauthorizations – 6 months

B. Other diagnoses/indications (must meet 1 or 2):
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 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 – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information
Appendix A: Abbreviation/Acronym Key
BMI: body mass index
FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications/Boxed Warnings
- Contraindication(s): uncontrolled hypertension; seizure disorders; anorexia nervosa or bulimia; undergoing abrupt discontinuation of alcohol, benzodiazepines, barbiturates, and antiepileptic drugs; use of other bupropion-containing products; chronic opioid use; during or within 14 days of taking monoamine oxidase inhibitors; known allergy to any of the ingredients in Contrave; pregnancy
- Boxed warning(s): suicidal thoughts and behaviors

Appendix D: General Information
- BMI = 703 x [weight (lbs)/height (inches)^2]
- Examples of coronary artery/heart disease include: coronary artery bypass graft, angina, history of myocardial infarction or stroke.
- Per Contrave’s prescribing information, response to therapy should be evaluated after 12 weeks at the maintenance dosage. If a patient has not lost at least 5% of baseline body weight, Contrave should be discontinued, as it is unlikely that the patient will achieve and sustain clinically meaningful weight loss with continued treatment. This is in line with the Endocrine Society’s definition of an effective response to a weight loss medication (2015).

V. Dosage and Administration

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<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
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<tbody>
<tr>
<td>Weight management</td>
<td>Week 1: One tablet PO QAM   &lt;br&gt;Week 2: One tablet PO BID  &lt;br&gt;Week 3: Two tablets PO QAM and 1 tablet PO QPM  &lt;br&gt;Week 4 and onward: 2 tablets PO QPM</td>
<td>32/360 mg per day</td>
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VI. Product Availability
Extended-release tablet: 8 mg naltrexone/90 mg bupropion

VII. 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: adapted from previously approved policy ERX.NPA.18; added coronary artery/heart disease as an example of cardiovascular risk indicator; modified re-auth approval duration to 6 months for second/subsequent requests (first re-auth request remains at 12 weeks); references reviewed and updated.</td>
<td>08.07.18</td>
<td>11.18</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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.

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