Clinical Policy: Celecoxib (Celebrex, Elyxyb)
Reference Number: CP.PMN.122
Effective Date: 01.01.07
Last Review Date: 05.20
Line of Business: Commercial, HIM, Medicaid

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

Description
Celecoxib (Celebrex®, Elyxyb™) is a nonsteroidal anti-inflammatory drug (NSAID).

FDA Approved Indication(s)
Celebrex is indicated for the treatment of:
- Osteoarthritis
- Rheumatoid arthritis
- Juvenile rheumatoid arthritis in patients 2 years and older
- Ankylosing spondylitis
- Acute pain
- Primary dysmenorrhea

Elyxyb is indicated for the acute treatment of migraine with or without aura in adults.

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 Celebrex and Elyxyb are medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. All Indications (must meet all):
      1. For Celebrex requests, age ≥ 2 years;
      2. For Elyxyb requests, age ≥ 18 years;
      3. Member meets one of the following (a, b, c, d, or e):
         a. Age > 65 years;
         b. Current use of a corticosteroid;
         c. Current use of an anticoagulant (e.g., aspirin, warfarin, low molecular weight heparin, direct thrombin inhibitors, factor Xa inhibitors, clopidogrel);
         d. Prior gastrointestinal bleed or active peptic ulcer disease (not gastroesophageal reflux disease [GERD]);
         e. Both of the following (i and ii):
            i. Failure of a ≥ 4 week trial of meloxicam at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
ii. Failure of a ≥ 4 week trial of one additional generic NSAID at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated;

4. Dose does not exceed one of the following (a or b):
   a. Celebrex: 800 mg (2 capsules) per day;
   b. Elyxyb: 120 mg (4.8 mL) per day.

Approval duration:
Medicaid/HIM – 12 months
Commercial – Length of Benefit

B. 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.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy
A. All Indications (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 one of the following (a or b):
      a. Celebrex: 800 mg (2 capsules) per day;
      b. Elyxyb: 120 mg (4.8 mL) per day.

Approval duration:
Medicaid/HIM – 12 months
Commercial – Length of Benefit

B. 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 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): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and 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 policies – CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.
IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
GERD: gastroesophageal reflux disease
NSAID: nonsteroidal anti-inflammatory drug

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>naproxen sodium (Anaprox®, Anaprox DS®)</td>
<td>275 - 550 mg PO BID</td>
<td>1,650 mg/day</td>
</tr>
<tr>
<td>sulindac (Clinoril®)</td>
<td>150 mg - 200 mg PO BID</td>
<td>400 mg/day</td>
</tr>
<tr>
<td>salsalate (Disalcid®)</td>
<td>500 - 750 mg PO TID, titrated up to 3,000 mg/day</td>
<td>3,000 mg/day</td>
</tr>
<tr>
<td>piroxicam (Feldene®, Indocin®)</td>
<td>10 - 20 mg PO QD</td>
<td>20 mg/day</td>
</tr>
<tr>
<td>indomethacin (Indocin®)</td>
<td>25 - 50 mg PO BID -TID</td>
<td>200 mg/day</td>
</tr>
<tr>
<td>indomethacin SR (Indocin® SR)</td>
<td>75 mg PO QD - BID</td>
<td>150 mg/day</td>
</tr>
<tr>
<td>meclofenamate (Meclomen®)</td>
<td>50 - 100 mg PO Q4-6hr</td>
<td>400 mg/day</td>
</tr>
<tr>
<td>meloxicam (Mobic®)</td>
<td>7.5 – 15 mg PO QD</td>
<td>15 mg/day</td>
</tr>
<tr>
<td>ibuprofen (Motrin®)</td>
<td>400 - 800 mg PO Q6-8hr</td>
<td>3,200 mg/day</td>
</tr>
<tr>
<td>fenoprofen (Nalfon®)</td>
<td>200 mg PO Q4-6hr</td>
<td>3,200 mg/day</td>
</tr>
<tr>
<td>naproxen (Naprosyn®)</td>
<td>250 – 500 mg PO BID</td>
<td>1,500 mg/day</td>
</tr>
<tr>
<td>ketoprofen (Orudis®)</td>
<td>25 - 75 mg PO Q6-8hr</td>
<td>300 mg/day</td>
</tr>
<tr>
<td>nabumetone (Relafen®)</td>
<td>1000 mg PO QD or 500 mg PO BID</td>
<td>2,000 mg/day</td>
</tr>
<tr>
<td>tolmetin (Tolmetin® DS)</td>
<td>400 mg PO TID, titrated up to 1800 mg/day</td>
<td>1,800 mg/day</td>
</tr>
<tr>
<td>diclofenac sodium (Voltaren®)</td>
<td>50 mg PO Q6-8hr</td>
<td>200 mg/day</td>
</tr>
<tr>
<td>oxaprozin (Daypro®)</td>
<td>600 – 1,200 mg PO BID</td>
<td>1,800 mg/day</td>
</tr>
<tr>
<td>etodolac (Lodine®)</td>
<td>400 - 500 mg PO BID</td>
<td>1,200 mg/day</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): hypersensitivity to celecoxib or any components of the drug product; history of asthma, urticaria, or other allergic-type reactions to aspirin or other NSAIDs; in the setting of coronary artery bypass graft (CABG) surgery; allergic-type reactions to sulfonamides.
Boxed warning(s): increased risk of serious cardiovascular thrombotic events, including myocardial infarction, and stroke; increased risk of serious gastrointestinal (GI) adverse events including bleeding, ulceration, and perforation of the stomach or intestines; celebrex is contraindicated in the setting of coronary artery bypass graft (CABG) surgery.

Appendix D: General Information
- The risk vs. benefit of COX-II therapy should be individualized based on patient's previous GI history, other co-morbid conditions (e.g., angina, ischemic heart disease, myocardial infarction (MI), coronary artery disease, stroke), age, concurrent medications (e.g., warfarin, oral corticosteroids), duration and dose.
- Celebrex has been associated with an increased risk of serious adverse cardiovascular (CV) events in a long-term placebo controlled trial. Based on the currently available data, FDA has concluded that an increased risk of serious adverse CV events appears to be a class effect of NSAIDs. FDA has requested that the package insert for all NSAIDs, including Celebrex, be revised to include a boxed warning to highlight the potential increased risk of CV events and the well described risk of serious, and potentially life-threatening, gastrointestinal bleeding.

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Celecoxib (Celebrex)</td>
<td>Osteoarthritis</td>
<td>200 mg PO QD or 100 mg PO BID</td>
<td>800 mg/day</td>
</tr>
<tr>
<td>Celecoxib (Celebrex)</td>
<td>Rheumatoid arthritis</td>
<td>100 to 200 mg PO BID</td>
<td>800 mg/day</td>
</tr>
<tr>
<td>Celecoxib (Celebrex)</td>
<td>Juvenile rheumatoid arthritis</td>
<td>10-25 kg: 50 mg PO BID &gt; 25 kg: 100 mg PO BID</td>
<td>200 mg/day</td>
</tr>
<tr>
<td>Celecoxib (Celebrex)</td>
<td>Ankylosing spondylitis</td>
<td>200 mg PO QD or 100 mg PO BID. If no effect is observed after 6 weeks, a trial of 400 mg (single or divided doses) may be of benefit.</td>
<td>800 mg/day</td>
</tr>
<tr>
<td>Celecoxib (Celebrex)</td>
<td>Acute pain or Primary dysmenorrhea</td>
<td>400 mg PO initially, followed by a 200 mg dose if needed on the first day. On subsequent days, 200 mg PO BID as needed</td>
<td>800 mg/day</td>
</tr>
<tr>
<td>Celecoxib (Elyxyb)</td>
<td>Migraine</td>
<td>120 mg PO PRN. Use the fewest number of days per month, as needed.</td>
<td>120 mg/day</td>
</tr>
</tbody>
</table>

VI. Product Availability

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Availability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Celecoxib (Celebrex)</td>
<td>Capsules: 50 mg, 100 mg, 200 mg, and 400 mg</td>
</tr>
<tr>
<td>Celecoxib (Elyxyb)</td>
<td>Oral solution: 120 mg/4.8 mL</td>
</tr>
</tbody>
</table>
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>Converted to new template</td>
<td>08.15</td>
<td>08.15</td>
</tr>
<tr>
<td>Removed criteria C: No reported allergy to sulfonamides, or ASA or other NSAIDs (e.g., asthma, urticaria or other allergic reaction)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Removed Criteria D: Patient does not have severe renal insufficiency – an eGFR (estimated glomerular filtration rate) below 30 OR severe hepatic impairment (Child-Pugh Class C) as safety criteria will be programmed as a safety edit</td>
<td></td>
<td></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.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy,
contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

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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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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