Clinical Policy: Aspirin/Dipyridamole (Aggrenox)
Reference Number: CP.PMN.20
Effective Date: 09.01.06
Last Review Date: 02.21
Line of Business: HIM, Medicaid

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

Description
Aspirin/dipyridamole (Aggrenox®) is a combination antiplatelet agent.

FDA Approved Indication(s)
Aggrenox is indicated to reduce the risk of stroke in patients who have had transient ischemia of the brain or completed ischemic stroke due to thrombosis.

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 Aggrenox is medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Secondary Prevention of Stroke (must meet all):
      1. Age ≥ 18 years;
      2. Medical history includes ischemic stroke or transient ischemic attack (TIA);
      3. Failure of aspirin used as a single agent (e.g., stroke or TIA while on aspirin therapy);
      4. Member is not a candidate for clopidogrel therapy due to contraindications or clinically significant adverse effects/drug interactions;
      5. If request is for Aggrenox, medical justification supports inability to use generic aspirin/dipyridamole (e.g., contraindications to excipients in aspirin/dipyridamole);
      6. Dose does not exceed 50 mg aspirin/400 mg extended-release dipyridamole (2 capsules) per day.

   Approval duration: 12 months

   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): HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid.

II. Continued Therapy
   A. Secondary Prevention of Stroke (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 Aggrenox, medical justification supports inability to use generic aspirin/dipyridamole (e.g., contraindications to excipients in aspirin/dipyridamole);
4. If request is for a dose increase, new dose does not exceed 50 mg aspirin/400 mg extended-release dipyridamole (2 capsules) per day.

Approval duration: 12 months

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): HIM.PA.154 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 – HIM.PA.154 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
TIA: transient ischemic attack

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>aspirin</td>
<td>50-325 mg PO QD</td>
<td>325 mg/day</td>
</tr>
<tr>
<td>clopidogrel (Plavix®)</td>
<td>75 mg PO QD</td>
<td>75 mg/day</td>
</tr>
</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 any product ingredients
  - Patients with known allergy to NSAIDs
  - Patients with the syndrome of asthma, rhinitis, and nasal polyps
- Boxed warning(s): none reported
Appendix D: General Information

- Aggrenox is not interchangeable with the individual components of aspirin and dipyridamole tablets.

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Secondary prevention of stroke</td>
<td>1 capsule PO BID (morning and evening)</td>
<td>2 capsules/day</td>
</tr>
<tr>
<td></td>
<td>If there are intolerable headaches during initial treatment, switch to 1 capsule at bedtime and low-dose aspirin in the morning; resume twice daily dosing within 1 week</td>
<td></td>
</tr>
</tbody>
</table>

VI. Product Availability

Capsules: 25 mg aspirin/200 mg extended-release dipyridamole

VII. References


Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Description</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Converted to new integrated template. Modified stroke diagnosis criteria to exclude the word “recent” as 1) there is no defined time frame for recent and 2) antiplatelet therapy is indicated for secondary prevention in all stroke patients regardless of when the stroke occurred. Removed requirement for diagnosis of stroke to have been made by a neurology specialist or in consult with a neurologist or vascular specialist as other specialties can diagnose stroke (plus, documentation to support diagnosis is now required per new template). Added workflow document. Updated references.</td>
<td>11.16</td>
<td>02.17</td>
</tr>
</tbody>
</table>
CLINICAL POLICY
Aspirin/Dipyridamole

<table>
<thead>
<tr>
<th>Reviews, Revisions, and Approvals</th>
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</tr>
</thead>
<tbody>
<tr>
<td>1Q18 annual review: Policies combined for Centene Medicaid and Marketplace lines of business; no significant changes from previous corporate approved policy; HIM: Removed criterion directing requests for the branded product to the generic product since the branded product is not on formulary; references reviewed and updated.</td>
<td>10.30.17</td>
<td>02.18</td>
</tr>
<tr>
<td>1Q 2019 annual review: no significant changes; references reviewed and updated.</td>
<td>10.30.18</td>
<td>02.19</td>
</tr>
<tr>
<td>1Q 2020 annual review: no significant changes; references reviewed and updated.</td>
<td>11.09.19</td>
<td>02.20</td>
</tr>
<tr>
<td>1Q 2021 annual review: added generic redirection language to initial and continuation criteria; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.</td>
<td>11.09.20</td>
<td>02.21</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.

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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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