Clinical Policy: Aspirin/Dipyridamole (Aggrenox)

Reference Number: CP.PMN.20
Effective Date: 09.01.06
Last Review Date: 02.24
Line of Business: HIM, Medicaid

Revision Log

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 (*generic preferred)* 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, member must use generic aspirin/dipyridamole, unless contraindicated or clinically significant adverse effects are experienced;
6. Dose does not exceed both of the following (a and b):
   a. 50 mg aspirin/400 mg extended-release dipyridamole per day;
   b. 2 capsules per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: HIM.PA.33 for health insurance marketplace and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: HIM.PA.103 for health insurance marketplace and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: 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. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy;
3. If request is for Aggrenox, member must use generic aspirin/dipyridamole, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, new dose does not exceed both of the following (a and b):
   a. 50 mg aspirin/400 mg extended-release dipyridamole per day;
   b. 2 capsules per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: HIM.PA.33 for health insurance marketplace and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: HIM.PA.103 for health insurance marketplace and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: 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.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
aspirin	50-325 mg PO QD	325 mg/day
clopidogrel (Plavix®)	75 mg PO QD	75 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):
  - Hypersensitivity to any product ingredients
  - Patients with known allergy to nonsteroidal anti-inflammatory drugs (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

Indication	Dosing Regimen	Maximum Dose
Secondary prevention of stroke	1 capsule PO BID (morning and evening) 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	2 capsules/day

VI. Product Availability

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

VII. References

1. Aggrenox Prescribing Information. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals Inc.; May 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/020884s040lbl.pdf. Accessed November 15, 2023.
2. Kleindorfer DO, Towfighi A, Chaturvedi S, et al. 2021 Guideline for the prevention of stroke in patients With stroke and transient ischemic attack: a guideline from the American Heart Association/American Stroke Association. *Stroke*. 2021 Jul;52(7):e364-e467. doi: 10.1161/STR.0000000000000375.
3. Lansberg MG, O'Donnell MJ, Khatri P et al. Antithrombotic and thrombolytic therapy for ischemic stroke: antithrombotic therapy and prevention of thrombosis, 9th ed.: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2012; 141(2 Suppl): e601S-636S.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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.	11.09.20	02.21
1Q 2022 annual review: no significant changes; revised "Medical justification…" to "Member must use…"; references reviewed and updated.	11.23.21	02.22
Template changes applied to other diagnoses/indications and continued therapy section.	09.20.22	
1Q 2023 annual review: no significant changes; references reviewed and updated.	10.07.22	02.23
1Q 2024 annual review: no significant changes; clarified generic aspirin is preferred; references reviewed and updated.	11.15.23	02.24

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.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members 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 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.