Clinical Policy: Edoxaban (Savaysa)
Reference Number: CP.PMN.227
Effective Date: 01.01.20
Last Review Date: 02.20
Line of Business: Medicaid

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

Description
Edoxaban (Savaysa®) is a factor Xa inhibitor.

FDA Approved Indication(s)
Savaysa is indicated:
- To reduce the risk of stroke and systemic embolism in patients with non-valvular atrial fibrillation (NVAF)
- For the treatment of deep venous thrombosis (DVT) and pulmonary embolism (PE) following 5 to 10 days of initial therapy with a parenteral anticoagulant

Limitation(s) of use: For NVAF, Savaysa should not be used in patients with creatinine clearance (CrCL) > 95 mL/min because of increased risk of ischemic stroke compared to warfarin at the highest dose studied (60 mg).

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 Savaysa is medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Non-Valvular Atrial Fibrillation, Deep Venous Thrombosis, Pulmonary Embolism (must meet all):
      1. Prescribed for one of the following conditions (a or b):
         a. Reduction of the risk of stroke and systemic embolism in member with NVAF;
         b. Treatment of DVT or PE;
      2. Failure of Eliquis® and Xarelto®, each used for ≥ 30 days at up to maximally indicated doses, unless both are contraindicated or clinically significant adverse effects are experienced;
      3. If member has NVAF, recent (within the past 90 days) creatinine clearance (CrCl) is ≤ 95 mL/min;
      4. Dose does not exceed 60 mg (1 tablet) 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): CP.PMN.53 for Medicaid

II. Continued Therapy
A. Non-Valvular Atrial Fibrillation, Deep Venous Thrombosis, Pulmonary Embolism (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 60 mg (1 tablet) 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): CP.PMN.53 for Medicaid or evidence of coverage documents.

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.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information
Appendix A: Abbreviation/Acronym Key
CrCl: creatinine clearance
DVT: deep vein thrombosis
FDA: Food and Drug Administration
NAVF: non-valvular atrial fibrillation
PE: pulmonary embolism

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>Eliquis®</td>
<td>NVAF</td>
<td>20 mg/day</td>
</tr>
<tr>
<td>(apixaban)</td>
<td>5 mg PO BID</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Treatment of DVT/PE</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10 mg PO BID for 7 days, then 5 mg PO BID</td>
<td></td>
</tr>
<tr>
<td>Xarelto®</td>
<td>NVAF</td>
<td>30 mg/day</td>
</tr>
<tr>
<td>(rivaroxaban)</td>
<td>20 mg/day</td>
<td></td>
</tr>
<tr>
<td>Drug Name</td>
<td>Dosing Regimen</td>
<td>Dose Limit/Maximum Dose</td>
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<tr>
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</tr>
<tr>
<td>Treatment of DVT/PE</td>
<td>15 mg PO BID for 21 days, then 20 mg/day PO</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):
  - Active pathological bleeding
- Boxed warning(s):
  - Reduced efficacy in nonvalvular atrial fibrillation patients with CrCL > 95 mL/min
  - Premature discontinuation of Savaysa
  - Spinal/epidural hematoma may occur in patients treated with Savaysa who are receiving neuraxial anesthesia or undergoing spinal puncture

Appendix D: General Information
- Savaysa should not be used in NVAF patients with CrCL > 95 mL/min due to reduced efficacy. In the ENGAGE AF-TIMI 48 study, NVAF patients with CrCL > 95 mL/min had an increased rate of ischemic stroke with Savaysa 60 mg once daily compared to patients treated with warfarin. In these patients, another anticoagulant should be used.

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>NVAF</td>
<td>If CrCl &gt; 50 to ≤ 95 mL/min: 60 mg PO QD</td>
<td>60 mg/day</td>
</tr>
<tr>
<td></td>
<td>If CrCl 15-50 mL/min: 30 mg PO QD</td>
<td></td>
</tr>
<tr>
<td>Treatment of DVT and PE</td>
<td>If CrCl &gt; 50 mL/min: 60 mg PO QD</td>
<td>60 mg/day</td>
</tr>
<tr>
<td></td>
<td>If CrCl 15-50 mL/min or body weight ≤ 60 kg: 30 mg PO QD</td>
<td></td>
</tr>
</tbody>
</table>

VI. Product Availability
- Tablets: 60 mg, 30 mg, 15 mg

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>Policy created based on SDC decision and prior clinical guidance.</td>
<td>01.01.20</td>
<td>02.20</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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