Clinical Policy: Enoxaparin (Lovenox)

Reference Number: CP.PHAR.224
Effective Date: 05.01.16
Last Review Date: 02.22
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

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

Description

Enoxaparin (Lovenox®) is a low molecular weight heparin (LMWH).

FDA Approved Indication(s)

Lovenox is indicated:

- For prophylaxis of deep vein thrombosis (DVT), which may lead to pulmonary embolism pulmonary embolism (PE):
  - In patients undergoing
    - Abdominal surgery who are at risk for thromboembolic complications;
    - Hip replacement surgery, during and following hospitalization;
    - Knee replacement surgery;
  - In medical patients who are at risk for thromboembolic complications due to severely restricted mobility during acute illness.
- For treatment of acute DVT:
  - Inpatient treatment of acute DVT with or without PE, when administered in conjunction with warfarin sodium.
  - Outpatient treatment of acute DVT without pulmonary embolism when administered in conjunction with warfarin sodium.
- For prophylaxis of ischemic complications of unstable angina and non-Q-wave myocardial infarction, when concurrently administered with aspirin.
- For treatment of acute ST-elevation myocardial infarction (STEMI).

Policy/Criteria

Provider must submit documentation (including 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 Lovenox is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Thrombosis/Thromboembolism* (must meet all)**:**

1. Any of the following indications (a, b, or c):
   a. Thrombosis or thromboembolism prevention associated with any of the following conditions:
      i. Cancer (s*ee Appendix D*);
      ii. Unstable angina or myocardial infarction;
      iii. Atrial fibrillation or prosthetic heart valve;

iv. Major surgery - orthopedic or non-orthopedic;
v. Critical illness related to ICU admissions or events;
vi. Restricted mobility associated with acute illnesses or conditions;
vii. Implanted devices-vascular (e.g., central venous access device, umbilical venous catheter, devices/fistulas related to hemodialysis, ventricular assist devices);

b. Thrombosis or thromboembolism treatment;
c. Short-term prophylaxis for transition to or from oral anticoagulation;

2. If request is for Lovenox, member must use generic enoxaparin, unless contraindicated or clinically significant adverse effects are experienced.

Approval duration:
Medicaid/HIM – 6 months
Commercial – 6 months or to the member's renewal date, whichever is longer

**Includes off-label use for adults and pediatrics.*

B. Anticoagulation in Pregnancy: Ante- and Postpartum (off-label) (must meet all)**:**

1. Any of the following indications:
   a. Acute venous thrombosis during current pregnancy;
   b. Prior venous thrombosis;
   c. Receiving long-term therapy with a vitamin K antagonist (e.g., warfarin);
   d. Prosthetic heart valve;
   e. Inherited thrombophilia;
   f. Antiphospholipid antibody syndrome;
   g. Development of severe ovarian hyperstimulation syndrome post assisted reproduction;
   h. Cesarean section – current pregnancy and request is for the postpartum period;
   i. Any other indication not listed here that is listed in section I.A.
2. Member is pregnant or < 6 months postpartum;
3. If request is for Lovenox, member must use generic enoxaparin, unless contraindicated or clinically significant adverse effects are experienced.

Approval duration: Antepartum (to estimated delivery date); postpartum (6 months)

C. 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: CP.CPA.190 for commercial, 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:

CP.CPA.190 for commercial, 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: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Thrombosis/Thromboembolism (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. Continued use is limited to any of the following indications (a, b, or c):
   a. Venous thrombosis prophylaxis or treatment in the presence of cancer;
   b. Past history of failed anticoagulation therapy (clot development) on a non-LMWH* (e.g., failed therapy on heparin, fondaparinux, warfarin, apixaban, dabigatran, edoxaban, rivaroxaban);
   **LMWHs include enoxaparin and dalteparin*
   c. Any other indication in section I.A where bridging to warfarin is inappropriate or member has a contraindication to warfarin and extended (indefinite duration) anticoagulation therapy is required;
4. If request is for Lovenox, member must use generic enoxaparin, unless contraindicated or clinically significant adverse effects are experienced.

Approval duration:
Medicaid/HIM – 6 months
Commercial – 6 months or to the member's renewal date, whichever is longer

B. Anticoagulation in Pregnancy: Ante- and Postpartum (off-label) (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. See Section II.A for continued anticoagulation therapy beyond 6 months postpartum;
4. If request is for Lovenox, member must use generic enoxaparin, unless contraindicated or clinically significant adverse effects are experienced.

Approval duration: Antepartum (to estimated delivery date); postpartum (6 months)

C. 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: CP.CPA.190 for commercial, 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: CP.CPA.190 for commercial, 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: CP.CPA.09 for commercial, 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 – CP.CPA.09 for commercial, 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

DVT: deep vein thrombosis
LMWH: low molecular weight heparin
NCCN: National Comprehensive Cancer Network
PE: pulmonary embolism
STEMI: ST-elevation myocardial infarction

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Active major bleeding
  - History of immune-mediated heparin-induced thrombocytopenia (HIT) within the past 100 days or in the presence of circulating antibodies
  - Known hypersensitivity to enoxaparin sodium (e.g., pruritus, urticaria, anaphylactic/anaphylactoid reactions)
  - Known hypersensitivity to heparin or pork products
  - Known hypersensitivity to benzyl alcohol (which is in only the multidose formulation of Lovenox)

- Boxed warning(s): spinal/epidural hematomas

Appendix D: General information

- Per National Comprehensive Cancer Network (NCCN) guidelines for cancer-associated venous thromboembolic disease, enoxaparin is recommended for:
  - Anticoagulation for acute and chronic management of acute superficial vein thrombosis, consider for management of chronic splanchnic vein thrombosis in cancer patients, management of acute splanchnic vein thrombosis, anticoagulation for acute DVT, acute catheter-related DVT, and/or acute pulmonary embolism in cancer patients with no contraindication to anticoagulation (preferred for patients with gastric or gastroesophageal lesions):
    - as monotherapy
    - for 5 - 10 days given concurrently with warfarin until transition to warfarin monotherapy, prior to switching to edoxaban, prior to switching to dabigatran for patients who refuse or have compelling reasons to avoid long-term low-molecular weight heparin
  - Anticoagulation for cancer patients following therapeutic anticoagulation failure with: heparin sodium, fondaparinux, warfarin sodium, apixaban, dabigatran, edoxaban, or rivaroxaban
  - Venous thromboembolism prophylaxis for adult patients with no contraindication to anticoagulation
    - for inpatient medical and/or surgical patients with cancer or those for whom a clinical suspicion of cancer exists
    - for inpatient surgical patients with cancer or those for whom a clinical suspicion of cancer exists as preoperative dosing for high-risk surgery (e.g., abdominal/pelvic)
    - for outpatient surgical patients with cancer for up to 4 weeks following high-risk surgery (e.g., abdominal/pelvic)

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Adults		
DVT prophylaxis in abdominal surgery	40 mg SC once daily	Dose as specified; duration may vary.
DVT prophylaxis in knee replacement surgery	30 mg SC every 12 hours	
DVT prophylaxis in hip replacement surgery	30 mg SC every 12 hours or 40 mg SC once daily	
DVT prophylaxis in medical patients	40 mg SC once daily	
Inpatient treatment or acute DVT with or without PE	1 mg/kg SC every 12 hours or 1.5 mg/kg SC once daily	
Outpatient treatment of acute DVT without PI	1 mg/kg SC every 12 hours	

Indication	Dosing Regimen	Maximum Dose
Adults		
Unstable angina and non-Q wave MI	1 mg/kg SC every 12 hours (with aspirin)	
Cancer-associated venous thromboembolic disease	1 mg/kg SC every 12 hours or 1.5 mg/kg SC once daily after first month	
Acute STEMI in patient < 75 years of age	30 mg single IV bolus plus a 1 mg/kg SC dose followed by 1 mg/kg SC every 12 hours (with aspirin)	
Acute STEMI in patient ≥ 75 years of age	0.75 mg/kg SC every 12 hours (no bolus) (with aspirin)	

VI. Product Availability

- Prefilled syringes: 30 mg/0.3 mL, 40 mg/0.4 mL
- Graduated prefilled syringes: 60 mg/0.6 mL, 80 mg/0.8 mL,100 mg/1 mL, 120 mg/0.8 mL, 150 mg/1 mL
- Multiple-dose vial: 300 mg/3 mL

VII. References

1. Lovenox Prescribing Information. Bridgewater, NJ: Sanofi-Aventis U.S., LLC; May 2020. Available at http://products.sanofi.us/Lovenox/Lovenox.pdf. Accessed November 23, 2021.
2. Executive summary: Antithrombotic therapy and prevention of thrombosis: CHEST guidelines and expert panel reports. Available at http://www.chestnet.org/Guidelines-and-Resources/CHEST-Guideline-Topic-Areas/Pulmonary-Vascular. Accessed November 6, 2020. *The CHEST guideline series presents recommendations for the prevention, diagnosis, and treatment of thrombosis, addressing a comprehensive list of clinical conditions, including medical, surgery, orthopedic surgery, atrial fibrillation, stroke, cardiovascular disease, pregnancy, and neonates and children*.
3. Thromboembolism in pregnancy. Practice Bulletin No. 196. American College of Obstetrics and Gynecologists. *Obstet Gynecol.* July 2018; 132: e1-17.
4. Enoxaparin. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at nccn.org. Accessed November 23, 2021.
5. National Comprehensive Cancer Network. Cancer-Associated Venous Thromboembolic Disease Version 3.2021. Available at: http://www.nccn.org. Accessed November 23, 2021.
6. Kearon C, Akl EA, Omelas J, et al. Antithrombotic Therapy for VTE Disease: CHEST Guideline and Expert Panel Report. *Chest* 2016;149:315-352.
7. Ortel TL, Neumann I, Ageno W, et al. American Society of Hematology 2020 guidelines for management of venous thromboembolism: treatment of deep vein thrombosis and pulmonary embolism. Blood Adv. 2020 Oct 13;4(19):4693-38.

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J1650	Injection, enoxaparin sodium, 10 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q18 annual review: - Combined policies for Medicaid and commercial lines of business - Section I.A., Venous Thrombosis, is changed to "Thrombosis and Thromboembolism" so as not to restrict to venous thrombi. Section I.A criteria are edited to encompass CHEST guidelines for neonates and children (seen primarily under implantable devices), and the criteria is collapsed to maximize consistency across the Lovenox, Fragmin and Arixtra policies. - Per specialist recommendation an additional indication is added for short-term prophylaxis to or from oral anticoagulation. Continuation criteria added for pregnancy. - References reviewed and updated.	12.01.17	02.18
1Q 2019 annual review; no significant changes; references reviewed and updated.	11.13.18	02.19
1Q 2020 annual review: no significant changes; references reviewed and updated.	11.01.19	02.20
1Q 2021 annual review: added HIM line of business; added generic redirection language to initial and continuation criteria; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	11.01.20	02.21
1Q 2022 annual review: no significant changes; changed "Medical justification" language to "Member must use"; references reviewed and updated.	11.23.21	02.22
Template changes applied to other diagnoses/indications and continued therapy section.	10.05.22	

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.