TEXAS Health and Human Services

Medicaid Drug Use Criteria

Low-Molecular-Weight Heparins

- Developed August 1999.
- Revised March 2020; March 2018; May 2017; April 2015; February 2015; May 2013; June 2011; January 2009; August 2003; July 2002; July 2001; August 2000.

Information on indications for use or diagnosis is assumed to be unavailable. All criteria may be applied retrospectively; prospective application is indicated with an asterisk [*]. The information contained is for the convenience of the public. The Texas Health and Human Services Commission is not responsible for any errors in transmission or any errors or omissions in the document.

Medications listed in the tables and non-FDA approved indications included in these retrospective criteria are not indicative of Vendor Drug Program formulary coverage.

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1 Dosage

1.1 Adults

Low-molecular-weight heparins (LMWH) are FDA-approved in adults to prevent deep vein thrombosis (DVT) in patients undergoing abdominal surgery, hip replacement surgery, as well as those medical patients with acute illness and severely limited mobility, and prevent ischemic complications of unstable angina

and non-Q-wave myocardial infarction.[1-5] Enoxaparin is also indicated to prevent DVT in patients requiring knee replacement surgery, treat inpatient DVT with or without pulmonary embolism (PE), treat outpatient acute DVT without PE, and treat acute ST-segment elevation myocardial infarction (STEMI) in patients managed medically,[1, 3-5] while dalteparin is FDA-approved to treat venous thromboembolism (VTE) to reduce recurrence in cancer patients.[2-5] However, dalteparin is not FDA-approved to treat acute venous thromboembolism.[2-5] Adult dosages are dependent upon therapeutic diagnosis, body weight, and renal function and are summarized in Table 1. In some circumstances (e.g., weight-based dosages), maximum daily dosages are not readily identifiable.

Table 1. Adult LMWH Recommended Dosages[1-5]

Treatment Indication	Drug Name	Maximum Recommended Dosage - Standard	Maximum Recommended Dosage - Severe Renal Impairment (CrCl Less Than 30 ml/min)
Deep vein thrombosis (DVT)/pulmonary embolus (PE) prophylaxis for hip replacement surgery	Enoxaparin (Lovenox®)	30 mg SC every 12 hours or 40 mg subcutaneously (SC) once daily	30 mg SC once daily
Deep vein thrombosis (DVT)/pulmonary embolus (PE) prophylaxis for hip replacement surgery	Dalteparin (Fragmin®)	5000 IU SC once daily	---
DVT/PE prophylaxis for knee replacement surgery	Enoxaparin	30 mg SC every 12 hours	30 mg SC once daily
DVT/PE prophylaxis for abdominal surgery	Enoxaparin	40 mg SC once daily	30 mg SC once daily
DVT/PE prophylaxis for abdominal surgery	Dalteparin	moderate risk: 2500 IU SC once daily high risk: 5000 IU SC once daily	---
DVT prophylaxis for acute illness and significantly limited mobility	Enoxaparin	40 mg SC once daily	30 mg SC once daily
DVT prophylaxis for acute illness and significantly limited mobility	Dalteparin	5000 IU SC once daily	---

Treatment Indication	Drug Name	Maximum Recommended Dosage - Standard	Maximum Recommended Dosage - Severe Renal Impairment (CrCl Less Than 30 ml/min)
Outpatient DVT treatment without PE, co-administered with warfarin	Enoxaparin	1 mg/kg SC every 12 hours	1 mg/kg SC once daily
DVT/PE treatment in cancer patients	Dalteparin	• month 1: 200 IU/kg SC once daily • month 2-6: 150 IU/kg SC once daily (maximum total daily dose = 18,000 IU)	---*
Inpatient DVT treatment with or without PE, co-administered with warfarin	Enoxaparin	1 mg/kg SC every 12 hours or 1.5 mg/kg SC daily	1 mg/kg SC once daily
Unstable angina/non-Q-wave myocardial infarction (MI), when co-administered with aspirin	Enoxaparin	1 mg/kg SC every 12 hours	1 mg/kg SC once daily
Unstable angina/non-Q-wave myocardial infarction (MI), when co-administered with aspirin	Dalteparin	120 IU/kg SC every 12 hours (maximum single dose = 10,000 units)	---
Acute STEMI	Enoxaparin	Less than 75 years: 30 mg IV bolus x 1 + 1 mg/kg SC, followed by 1 mg/kg SC every 12 hours with aspirin	30 mg IV bolus x1 + 1 mg/kg SC, followed by 1 mg/kg SC once daily with aspirin
Acute STEMI	Enoxaparin	Greater than or equal to 75 years: 0.75 mg/kg SC every 12 hours with aspirin (no bolus)	1 mg/kg SC once daily with aspirin (no bolus)

- * = In severe renal impairment in cancer patients, monitor anti-Xa levels to determine dalteparin dose necessary to achieve anti-Xa levels in the range of 0.5 to 1.5 IU/ml.

1.2 Pediatrics

Safety and efficacy of enoxaparin for use in children younger than 18 years of age have not been established. Dalteparin has recently gained approval for use to treat VTE to reduce VTE recurrence in pediatric patients greater than or equal to 1 month of age. Dalteparin pediatric dosages are summarized in Table 2. Dosages exceeding these recommendations will be reviewed. [1-5]

Table 2. Pediatric LMWH Recommended Dosages[2-5]

Treatment Indication	Drug Name	Maximum Recommended Dosage
Venous thromboembolism treatment	Dalteparin	4 weeks to less than 2 years: 150 IU/kg twice daily as starting dose; adjust to maintain anti-Xa level between 0.5-1 IU/mL 2 years to less than 8 years: 125 IU/kg twice daily as starting dose; adjust to maintain anti-Xa level between 0.5-1 IU/mL 8 years to less than 17 years: 100 IU/kg twice daily as starting dose; adjust to maintain anti-Xa level between 0.5-1 IU/mL

2 Duration of Therapy

2.1 Adults [1-19]

When prescribed as preventive therapy, LMWH should be administered until the risk of deep venous thrombosis has diminished. When utilized in the management of DVT and pulmonary embolism, warfarin therapy is typically initiated within 72 hours of enoxaparin therapy. Enoxaparin is continued until a therapeutic anticoagulant effect with warfarin has been achieved. Recent studies suggest that LMWH are as effective as oral monotherapy in preventing VTE when utilized for certain postsurgical conditions (e.g., total knee replacement) or in patients requiring continued anticoagulant therapy for management of venous thromboembolism on an outpatient basis in place of warfarin. Advantages include shortened hospital stays and reduced need for laboratory monitoring. Long-term treatment of VTE in cancer patients is managed with dalteparin rather than warfarin for three to six months.

Enoxaparin has been determined to be more effective than heparin in limiting coronary ischemic complications associated with unstable angina or non-Q-wave myocardial infarction (MI). Dalteparin has been shown to be more effective than placebo and comparable to heparin therapy in reducing mortality and MI in patients with unstable angina or non-Q-wave MI. Dalteparin or enoxaparin treatment is administered in conjunction with aspirin therapy and should be continued until clinical stabilization is achieved in these patients (a minimum of 2 days for enoxaparin therapy). Compared to unfractionated heparin, enoxaparin has been shown to significantly reduce MI recurrence in patients with acute STEMI receiving concurrent aspirin therapy when administered for a maximum of 8 days or hospital discharge, whichever came first. LMWH treatment duration varies with respect to therapeutic indication and is summarized in **Table 3**.

Table 3. LMWH Recommended Treatment Duration (Adults)[1-19]

Treatment Indication	Drug Name	Treatment Duration Range	Maximum Treatment Duration
DVT/PE prophylaxis for hip replacement surgery	Enoxaparin	7 to 10 days	14 days
DVT/PE prophylaxis for hip replacement surgery	Dalteparin	5 to 10 days	14 days
DVT/PE prophylaxis for knee replacement surgery	Enoxaparin	7 to 10 days	14 days
DVT/PE prophylaxis for abdominal surgery	Enoxaparin	7 to 10 days	12 days
DVT/PE prophylaxis for abdominal surgery	Dalteparin	5 to 10 days	10 days
DVT/PE prophylaxis for acute illness and significantly limited mobility	Enoxaparin	6 to 11 days	14 days
DVT/PE prophylaxis for acute illness and significantly limited mobility	Dalteparin	12 to 14 days	14 days
DVT/PE treatment in cancer patients	Dalteparin	6 months	6 months
Outpatient DVT treatment without pulmonary embolus (PE)	Enoxaparin	7 days^	17 days
Inpatient DVT treatment with or without PE	Enoxaparin	7 days^	17 days
Unstable angina/non-Q-wave myocardial infarction (MI)	Enoxaparin	2 to 8 days	12.5 days

Treatment Indication	Drug Name	Treatment Duration Range	Maximum Treatment Duration
Unstable angina/non-Q-wave myocardial infarction (MI)	Dalteparin	5 to 8 days	8 days
Acute STEMI	Enoxaparin	up to 8 days or hospital discharge, whichever is first	not determined

- * = Although not FDA-approved, LMWH are also recommended for prevention of VTE in hip fracture surgery.[6]
- ^ = Enoxaparin may be continued for up to 21 days[1];In hip replacement surgery patients with high thromboembolic risk, dalteparin and enoxaparin may be continued for 28 to 35 days.[6]

2.2 Pediatrics [2-5, 20]

Although treatment durations have not been solidified, experts recommend that dalteparin therapy should be continued for less than or equal to 3 months in pediatric patients with provoked DVT or PE and up to 12 months (range, 6 to 12 months) in pediatric patients with unprovoked DVT or PE. Dalteparin treatment recommendations for pediatric patients are summarized in Table 4.

Table 4. LMWH Recommended Treatment Duration (Pediatric Patients)[2-5, 20]

Treatment Indication	Drug Name	Treatment Duration Range	Maximum Treatment Duration
Venous thromboembolism treatment	Dalteparin	3 to 12 months	12 months

3 Duplicative Therapy

Concurrent administration of multiple LMWH products does not provide additional therapeutic benefit and is not recommended. Patient profiles containing concomitant prescriptions for two or more LMWH products will be reviewed.

4 Drug-Drug Interactions

Patient profiles will be assessed to identify those drug regimens which may result in clinically significant drug-drug interactions. Drug-drug interactions considered clinically relevant for LMWHs are summarized in Table 5. Only those drug-drug interactions classified as clinical significance level 1 or those considered life-threatening which have not yet been classified will be reviewed.

Table 5. LMWH Drug-Drug Interactions[1-5]

Target Drug	Interacting Drug	Interaction	Recommendation	Clinical Significance Level
LMWHs	defibrotide	enhances LMWH pharmacologic effects, increasing bleeding risk	avoid concurrent use	contraindicated (DrugReax); 1-severe (CP)
LMWHs	drugs affecting hemostasis (e.g., anticoagulants, NSAIDs)	combined use may produce additive prolongation of bleeding time and increased bleeding risk, including gastrointestinal bleeding; prolonged bleeding risk may persist for several days following LMWH discontinuation; spinal, epidural hematomas reported with enoxaparin use in patients receiving spinal or epidural anesthesia (many also receiving drugs that affect hemostasis like NSAIDs)	avoid combination, if possible; discontinue drugs that affect hemostasis prior to initiating LMWH therapy; non-acetylated salicylate may be administered in conjunction with LMWH to avoid antiplatelet activity; acetaminophen, narcotic analgesics additional alternative analgesics for use in patients without inflammatory pain requiring LMWH therapy; if coadministration necessary, monitor closely for clinical, laboratory bleeding complications	major (DrugReax) apixaban: 1-severe (CP); other DOACs: 2- major (CP)
LMWHs	SSRIs, SNRIs	combined use may increase bleeding event risk (e.g., ecchymosis, epistaxis, hematoma, petechiae, life-threatening hemorrhages) as SSRIs and SNRIs may mechanistically interfere with platelet function since serotonin contributes to hemostasis	patients requiring adjunctive therapy should be closely monitored for bleeding, with treatment adjustments as necessary, when doses are modified or therapy is initiated/ discontinued	major (DrugReax); 2-major (CP)

- + CP = Clinical Pharmacology

- DOACs = direct oral anticoagulants
- LMWHs = low-molecular-weight heparins
- NSAIDs = nonsteroidal anti-inflammatory drugs
- SNRIs = serotonin-norepinephrine reuptake inhibitors
- SSRIs = selective serotonin reuptake inhibitors

5 References

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