



# CIGNA PHARMACY COVERAGE POLICY

This Coverage Policy should NOT be used for Great-West benefit plans.

**Subject Low Molecular Weight Heparin  
Therapy: dalteparin  
(Fragmin®), enoxaparin  
(Lovenox®), fondaparinux  
(Arixtra®), tinzaparin  
(Innohep®)**

**Effective Date .....4/15/2009  
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Coverage Policy Number ..... 4032**

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## Hyperlink to Related Coverage Policies

### INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans as well as benefit plans formerly administered by Great-West Healthcare. Please note, the terms of a participant's particular benefit plan document [Group Service Agreement (GSA), Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a participant's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a participant's benefit plan document **always supercedes** the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable group benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. Proprietary information of CIGNA. Copyright ©2009 CIGNA

## Coverage Policy

**Low Molecular Weight Heparin (LMWH) therapy includes the following preferred brand (PB) drugs:**

- Dalteparin (Fragmin®.)
- Enoxaparin (Lovenox®.)
- Fondaparinux (Arixtra®.)
- Tinzaparin (Innohep®)

**Note: Prior-authorization is required for quantities exceeding a 30-day supply.**

**CIGNA covers Low Molecular Weight Heparin (LMWH) as medically necessary for any of the following:**

- pregnancy when anticoagulation is required **OR**
- failure, contraindication, or intolerance to oral anticoagulation for **ANY** of the following indications:
  - prophylaxis of deep vein thrombosis (DVT) for **ANY** of the following:
    - abdominal surgery
    - hip replacement surgery
    - knee replacement surgery
    - other high-risk medical patients
    - recurrent DVT
    - treatment of acute DVT with or without PE in conjunction with warfarin sodium

- prophylaxis or treatment of pulmonary embolism (PE)
  - prophylaxis and/or treatment of thromboembolic complications associated with atrial fibrillation and/or mechanical cardiac valve replacement
  - prophylaxis of ischemic complications of unstable angina and non-Q-wave myocardial infarction [MI]
  - treatment of acute ST-segment elevation myocardial infarction [STEMI] managed medically or with subsequent percutaneous coronary intervention [PCI]
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## General Background

### FDA Approved Indications

#### Fragmin

Fragmin injection is indicated for the prophylaxis of ischemic complications in unstable angina and non-Q-wave myocardial infarction, when concurrently administered with aspirin. Fragmin is also indicated for the prophylaxis of deep vein thrombosis (DVT), which may lead to pulmonary embolism (PE): In patients undergoing hip replacement surgery; In patients undergoing abdominal surgery who are at risk for thromboembolic complications; In medical patients who are at risk for thromboembolic complications due to severely restricted mobility during acute illness. Fragmin is also indicated for the extended treatment of symptomatic venous thromboembolism (VTE) (proximal DVT and/or PE), to reduce the recurrence of VTE in patients with cancer.

#### Lovenox

Lovenox is a low molecular weight heparin [LMWH] indicated for: Prophylaxis of deep vein thrombosis (DVT) in abdominal surgery, hip replacement surgery, knee replacement surgery, or medical patients with severely restricted mobility during acute illness; Inpatient treatment of acute DVT with or without pulmonary embolism; Outpatient treatment of acute DVT without pulmonary embolism; Prophylaxis of ischemic complications of unstable angina and non-Q-wave myocardial infarction [MI]; Treatment of acute ST-segment elevation myocardial infarction [STEMI] managed medically or with subsequent percutaneous coronary intervention [PCI]

#### Arixtra

Arixtra Injection is indicated for the prophylaxis of deep vein thrombosis, which may lead to pulmonary embolism: in patients undergoing hip fracture surgery, including extended prophylaxis; in patients undergoing hip replacement surgery; in patients undergoing knee replacement surgery; in patients undergoing abdominal surgery who are at risk for thromboembolic complications. Arixtra Injection is indicated for: the treatment of acute deep vein thrombosis when administered in conjunction with warfarin sodium, and the treatment of acute pulmonary embolism when administered in conjunction with warfarin sodium when initial therapy is administered in the hospital.

#### Innohep

Innohep is indicated for the treatment of acute symptomatic deep vein thrombosis with or without pulmonary embolism when administered in conjunction with warfarin sodium. The safety and effectiveness of Innohep were established in hospitalized patients.

### FDA Recommended Dosing

#### Fragmin

In patients with unstable angina or non-Q-wave myocardial infarction, the recommended dose of Fragmin Injection is 120 IU/kg of body weight, but not more than 10,000 IU, subcutaneously (s.c.) every 12 hours with concurrent oral aspirin (75 to 165 mg once daily) therapy. Treatment should be continued until the patient is clinically stabilized. The usual duration of administration is 5 to 8 days. Concurrent aspirin therapy is recommended except when contraindicated. In patients undergoing abdominal surgery with a risk of thromboembolic complications, the recommended dose of Fragmin is 2500 IU administered by s.c. injection once daily, starting 1 to 2 hours prior to surgery and repeated once daily postoperatively. The usual duration of administration is 5 to 10 days. In patients undergoing abdominal surgery associated with a high risk of thromboembolic complications, such as malignant disorder, the recommended dose of Fragmin is 5000 IU s.c. the evening before surgery, then once daily postoperatively. The usual duration of administration is 5 to 10 days. Alternatively, in patients with malignancy, 2500 IU of Fragmin can be administered s.c. 1 to 2 hours before surgery followed by 2500 IU s.c. 12 hours later, and then 5000 IU once daily postoperatively. The usual duration

of administration is 5 to 10 days. Dosage adjustment and routine monitoring of coagulation parameters are not required if the dosage and administration recommendations specified above are followed. Medical Patients with Severely Restricted Mobility During Acute Illness - In medical patients with severely restricted mobility during acute illness, the recommended dose of Fragmin is 5000 IU administered by s.c. injection once daily.

### **Lovenox**

Dosing as follows: DVT prophylaxis in abdominal surgery - 40 mg SC once daily standard regimen, 30 mg SC once daily for those with severe renal impairment; DVT prophylaxis in knee replacement surgery - 30 mg SC every 12 hours standard regimen, 30 mg SC once daily for those with severe renal impairment; DVT prophylaxis in hip replacement surgery - 30 mg SC every 12 hours or 40 mg SC once daily standard regimen, 30 mg SC once daily for those with severe renal impairment; DVT prophylaxis in medical patients 40 mg SC once daily standard regimen, 30 mg SC once daily for those with severe renal impairment; Inpatient treatment of acute DVT with or without pulmonary embolism - 1 mg/kg SC every 12 hours or 1.5 mg/kg SC once daily (with warfarin) standard regimen, 1 mg/kg SC once daily for those with severe renal impairment; Outpatient treatment of acute DVT without pulmonary embolism - 1 mg/kg SC every 12 hours (with warfarin) standard regimen, 1 mg/kg SC once daily for those with severe renal impairment; Unstable angina and non-Q-wave MI - 1 mg/kg SC every 12 hours (with aspirin) standard regimen, 1 mg/kg SC once daily for those with severe renal impairment; Acute STEMI in patients <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) standard regimen, 30-mg single IV bolus plus a 1 mg/kg SC dose followed by 1 mg/kg SC once daily for those with severe renal impairment; Acute STEMI in patients ≥75 years of age 0.75 mg/kg SC every 12 hours (no bolus) standard regimen, 1 mg/kg SC once daily (no bolus) for those with severe renal impairment. Do not use as intramuscular injection. For subcutaneous use, do not mix with other injections or infusions.

### **Arixtra**

Arixtra Injection is administered by subcutaneous injection once daily. Deep Vein Thrombosis Prophylaxis Following Hip Fracture, or Hip or Knee Replacement Surgeries: In patients undergoing hip fracture, hip replacement, or knee replacement surgery, the recommended dose of Arixtra is 2.5 mg administered by subcutaneous injection once daily. After hemostasis has been established, the initial dose should be given 6 to 8 hours after surgery. Administration before 6 hours after surgery has been associated with an increased risk of major bleeding. The usual duration of administration is 5 to 9 days, and up to 11 days administration has been tolerated. In patients undergoing hip fracture surgery, an extended prophylaxis course of up to 24 additional days is recommended. In patients undergoing hip fracture surgery, a total of 32 days (peri-operative and extended prophylaxis) has been tolerated. Deep Vein Thrombosis Prophylaxis Following Abdominal Surgery: In patients undergoing abdominal surgery, the recommended dose of Arixtra is 2.5 mg administered by subcutaneous injection once daily after hemostasis has been established. The initial dose should be given 6 to 8 hours after surgery. Administration before 6 hours after surgery has been associated with an increased risk of major bleeding. The usual duration of administration is 5 to 9 days, and up to 10 days of Arixtra injection has been administered. Deep Vein Thrombosis and Pulmonary Embolism Treatment: In patients with acute symptomatic DVT and in patients with acute symptomatic PE the recommended dose of Arixtra is 5 mg (body weight <50 kg), 7.5 mg (body weight 50-100 kg), or 10 mg (body weight >100 kg) by subcutaneous injection once daily (Arixtra treatment regimen). Treatment with Arixtra should be continued for at least 5 days and until a therapeutic oral anticoagulant effect is established (INR 2.0 to 3.0). Concomitant treatment with warfarin sodium should be initiated as soon as possible, usually within 72 hours. The usual duration of administration of Arixtra is 5 to 9 days; up to 26 days of Arixtra injection has been administered.

### **Innohep**

The recommended dose of Innohep for the treatment of DVT with or without PE is 175 anti-Xa IU/kg of body weight, administered SC once daily for at least 6 days and until the patient is adequately anticoagulated with warfarin (INR at least 2.0 for two consecutive days). Warfarin sodium therapy should be initiated when appropriate (usually within 1-3 days of Innohep initiation). Pregnancy has little or no influence on the pharmacokinetics of Innohep and no dosing adjustment is needed for pregnancy. As Innohep may theoretically affect the PT/INR, patients receiving both Innohep and warfarin should have blood for PT/INR determination drawn just prior to the next scheduled dose of Innohep. Innohep doses for the treatment of DVT with or without PE is 175 IU/kg SC Once Daily (20,000 IU per mL). An appropriately calibrated syringe should be used to assure withdrawal of the correct volume of drug from Innohep vials.

Thrombosis is the formation of clots in the circulatory system caused by endothelial injury, static or turbulent blood flow, and blood hypercoagulability. Three types of agents used in the prevention and treatment of deep

venous thrombosis are anticoagulants, antiplatelet agents, and thrombolytic drugs. Unfractionated heparin (UFH) and low molecular-weight heparins (LMWHs) are the anticoagulants of choice when a rapid anticoagulant effect is desired. Dalteparin, enoxaparin, tinzaparin, and fondaparinux are LMWHs available in the United States.

UFH is a chain of glycosaminoglycans. Its major mechanism of anticoagulant effect is by binding to antithrombin (AT) and inactivating clotting factors IIa (thrombin), Xa, IXa, and XIIa. UFH also binds to platelets and inhibits their function. LMWHs, derivatives of UFH, are less than 18 saccharide units and range from 2000 to 9000 daltons. These smaller fragments inhibit factor Xa, but inhibit factor IIa to a lesser extent than UFH. Therefore, LMWHs result in minimal inhibition of clotting time compared to UFH. LMWHs provide antithrombotic activity without influencing bleeding time, platelet function, prothrombin time, or aPTT.

Numerous studies evaluate the use of LMWHs in outpatients for many different indications, including deep venous thrombosis (DVT) and pulmonary embolism (PE) treatment in general populations and in pregnancy, and prophylaxis in general and orthopedic surgery patients, trauma patients, spinal-cord injury patients, and in pregnancy. No studies directly compare any two LMWHs for any of these indications. Most studies conclude that there are no significant differences between LMWHs and traditional inpatient treatments for any clinical efficacy outcomes. Dalteparin, enoxaparin and fondaparinux are approved for use in outpatient therapy.

The most common side effects associated with LMWHs are pain and hematomas at the site of injection. LMWH exhibits cross-reactivity with heparin in 70-80% of patients with heparin antibodies, causing heparin-induced thrombocytopenia (HIT); but the risk is lower than with UFH. LMWH should be used with extreme caution in patients with history of HIT. The main drug interactions with LMWHs are medications predisposing patients to bleeding. These include non-steroidal anti-inflammatory drugs, warfarin, salicylates, and dipyridamole.

LMWH's are contraindicated in patients with known hypersensitivity to the drug, active major bleeding, or thrombocytopenia associated with positive in vitro tests for antiplatelet antibody in the presence of LMWHs. LMWH is not intended for intramuscular administration and cannot be used interchangeably with UFH or other LMWHs. LMWHs should be used with extreme caution in patients who have an increased risk of hemorrhage, such as those with severe uncontrolled hypertension, bacterial endocarditis, congenital or acquired bleeding disorders, active ulceration and angiodysplastic gastrointestinal disease, hemorrhagic stroke, or shortly after brain, spinal or ophthalmological surgery. Spinal or epidural hematomas can occur with the associated use of LMWHs or heparinoids and neuraxial (spinal/epidural) anesthesia or spinal puncture, which can result in long-term or permanent paralysis. The risk of these events is higher with the use of indwelling epidural catheters or concomitant use of additional drugs affecting hemostasis such as NSAIDs.

The main drug interactions with LMWHs are medications predisposing patients to bleeding. These include non-steroidal anti-inflammatory drugs, warfarin, salicylates, and dipyridamole. These medications should be discontinued far enough in advance that they do not interfere with LMWH therapy. LMWHs are not metabolized through the cytochrome P450 system so no drug interactions should be expected with other medications metabolized by these enzymes.

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## Coding/Billing Information

**Note:** This section is not in use

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