

DALTEPARIN SODIUM

Class: Low Molecular Weight Heparin

Indications: Prevention of deep vein thrombosis (DVT) which may lead to pulmonary embolism, in patients requiring abdominal surgery who are at risk for thromboembolism complications (eg, patients >40 years of age, obesity, patients with malignancy, history of DVT or pulmonary embolism, and surgical procedures requiring general anesthesia and lasting >30 minutes); prevention of DVT in patients undergoing hip-replacement surgery; patients immobile during an acute illness; prevention of ischemic complications in patients with unstable angina or non-Q-wave myocardial infarction on concurrent aspirin therapy; in patients with cancer, extended treatment (6 months) of acute symptomatic venous thromboembolism (DVT and/or PE) to reduce the recurrence of venous thromboembolism

Unlabeled : Active treatment of deep vein thrombosis (noncancer patients)

Dosage:

Note: Each 2500 units of anti-Xa activity is equal to 16 mg of dalteparin.

-Anticoagulant for hemodialysis and hemofiltration: I.V.: Canadian labeling (not in U.S. labeling):

-Chronic renal failure with no other bleeding risks:

-Hemodialysis/filtration ≤ 4 hours: I.V. bolus: 5,000 units

-Hemodialysis/filtration > 4 hours: I.V. bolus: 30-40 units/kg, followed by an infusion of 10-15 units/kg/hour (typically produces plasma concentrations of 0.5-1 units anti-Xa/mL)

-Acute renal failure and high bleeding risk: I.V. bolus: 5-10 units/kg, followed by an infusion of 4-5 units/kg/hour (typically produces plasma concentrations of 0.2-0.4 units anti-Xa/mL)

-DVT prophylaxis: Note: In morbidly obese patients (BMI ≥ 40 kg/m²), increasing the prophylactic dose by 30% may be appropriate

-Abdominal surgery:

-Low-to-moderate DVT risk: SubQ: 2500 units 1-2 hours prior to surgery, then once daily for 5-10 days postoperatively

-High DVT risk: SubQ: 5000 units the evening prior to surgery and then once daily for 5-10 days postoperatively. Alternatively in patients with malignancy: 2500 units 1-2 hours prior to surgery, 2500 units 12 hours later, then 5000 units once daily for 5-10 days postoperatively.

-General surgery with risk factors for VTE: Canadian labeling (not in U.S. labeling): 2500 units 1-2 hours preoperatively followed by 2500-5000 int.units every morning (may administer 2500 units no sooner than 4 hours after surgery and 8 hours after previous dose provided hemostasis has been achieved) or if other risk factors are present (eg, malignancy, heart failure), then may administer 5000 units the evening prior to surgery followed by 5000 units every evening postoperatively; continue treatment until patient is mobilized (approximately $\geq 5-7$ days)

-Total hip replacement surgery: SubQ: Note: Three treatment options are currently available. Dose is given for 5-10 days, although up to 14 days of treatment have been tolerated in clinical trials. The American College of Chest Physicians (ACCP) recommends a minimum duration of at least 10-14 days; extended duration of up to 35 days is suggested.

-Postoperative regimen:

-Initial: 2500 units 4-8 hours after surgery (or later if hemostasis not achieved). The ACCP recommends initiation ≥ 12 hours after surgery if postoperative regimen chosen

-Maintenance: 5000 int. units once daily; allow at least 6 hours to elapse after initial postsurgical dose (adjust administration time accordingly)

-Preoperative regimen (starting day of surgery):

-Initial: 2500 int. units within 2 hours before surgery. The ACCP recommends initiation ≥ 12 hours before surgery if preoperative regimen chosen. At 4-8 hours after surgery (or later if hemostasis not achieved), administer 2500 int. units.

-Maintenance: 5000 units once daily; allow at least 6 hours to elapse after initial postsurgical dose (adjust administration time accordingly.)

-Preoperative regimen (starting evening prior to surgery):

-Initial: 5000 int. units 10-14 hours before surgery. The ACCP recommends initiation ≥ 12 hours before surgery if preoperative regimen chosen. At 4-8 hours after surgery (or later if hemostasis not achieved), administer 5000 int. units.

-Maintenance: 5000 int. units once daily, allowing 24 hours between doses

-Immobility during acute illness: 5000 units once daily

-Unstable angina or non-Q-wave myocardial infarction: SubQ: 120 units/kg body weight (maximum dose: 10,000 units) every 12 hours for up to 5-8 days with concurrent aspirin therapy. Discontinue dalteparin once patient is clinically stable.

*Obesity: Use actual body weight to calculate dose; dose capping at 10,000 units recommended

-Venous thromboembolism, extended treatment in cancer patients: SubQ:

-Initial (month 1): 200 units/kg (maximum dose: 18,000 units) once daily for 30 days

-Maintenance (months 2-6): ~ 150 units/kg (maximum dose: 18,000 units) once daily. If platelet count between 50,000-100,000/ mm^3 , reduce dose by 2,500 units until platelet count recovers to $\geq 100,000/\text{mm}^3$. If platelet count $< 50,000/\text{mm}^3$, discontinue dalteparin until platelet count recovers to $> 50,000/\text{mm}^3$.

-Obesity: Use actual body weight to calculate dose; dose capping is not recommended (Nutescu, 2009). However, the manufacturer recommends a maximum dose of 18,000 units per day for the treatment of VTE in cancer patients.

-DVT (with or without PE) treatment in noncancer patients (unlabeled use in U.S.): SubQ: 200 units/kg once daily or 100 units/kg twice daily. Use of once daily administration is suggested.

-Canadian labeling: SubQ: 200 units/kg once daily (maximum dose: 18,000 units/day) or alternatively, may adapt dose as follows (SubQ):

- 46-56 kg: 10,000 units once daily
- 57-68 kg: 12,500 units once daily
- 69-82 kg: 15,000 units once daily
- ≥ 83 kg: 18,000 units once daily

Note: If increased bleeding risk, may give 100 units/kg SubQ twice daily. Concomitant treatment with a vitamin-K antagonist is usually initiated immediately.

-Obesity: Use actual body weight to calculate dose; dose capping is not recommended (Nutescu, 2009). One study demonstrated similar anti-Xa levels after 3 days of therapy in obese patients ($>40\%$ above IBW; range: 82-190 kg) compared to those $\leq 20\%$ above IBW or between 20% to 40% above IBW .

-Pregnant women: 200 units/kg/dose once daily or 100 units/kg/dose every 12 hours. Discontinue ≥ 24 hours prior to the induction of labor or cesarean section. Dalteparin therapy may be substituted with heparin near term. Continue anticoagulation therapy for ≥ 6 weeks postpartum (minimum duration of therapy: 3 months). LMWH or heparin therapy is preferred over warfarin during pregnancy .

-Prevention of recurrent venous thromboembolism in pregnancy (unlabeled use): SubQ: 5000 units once daily. Therapy should continue for 6 weeks postpartum in high-risk women .

Renal Impairment :

Half-life is increased in patients with chronic renal failure, use with caution, accumulation can be expected; specific dosage adjustments have not been recommended. Accumulation was not observed in critically ill patients with severe renal insufficiency ($Cl_{cr} < 30$ mL/minute) receiving prophylactic doses (5000 units) for a median of 7 days . In cancer patients, receiving treatment for venous thromboembolism, if $Cl_{cr} < 30$ mL/minute, manufacturer recommends monitoring anti-Xa levels to determine appropriate dose.

Hepatic Impairment:

No dosage adjustment provided in manufacturer's labeling; use with caution.

Available dosage form in the hospital: 2500IU/0.2ML PREFILLED SYRINGE, 5000IU/0.2ML PREFILLED SYRINGE

Common side effect: As with all anticoagulants, bleeding is the major adverse effect of dalteparin. Hemorrhage may occur at virtually any site. Risk is dependent on multiple variables.

$>10\%$: Hematologic: Bleeding (3% to 14%), thrombocytopenia (including heparin-induced thrombocytopenia, $<1\%$; cancer clinical trials: $\sim 11\%$)

1% to 10%:

Hematologic: Major bleeding (up to 6%), wound hematoma (up to 3%)

Hepatic: AST >3 times upper limit of normal (5% to 9%), ALT >3 times upper limit of normal (4% to 10%)

Local: Pain at injection site (up to 12%), injection site hematoma (up to 7%)

Pregnancy Risk Factor: B