Prescribing Information: Clexane® (Enoxaparin sodium)
Please refer to the Summary of Product Characteristics (SmPC) before prescribing.

Presentations: ***Clexane®*** ***Syringes:*** single dose, pre-filled syringes containing: enoxaparin sodium (IU) in water (ml) in the quantities; 2,000IU (20mg) in 0.2ml, 4,000IU (40mg) in 0.4ml, 6,000IU (60mg) in 0.6ml, 8,000IU (80mg) in 0.8ml or 10,000IU (100mg) in 1ml. ***Clexane®*** ***Forte Syringes:*** single dose, pre-filled syringes containing either: 12,000IU (120mg) enoxaparin sodium in 0.8ml or 15,000IU (150mg) enoxaparin sodium in 1ml. ***Clexane®*** ***Multidose vial:*** containing 30,000IU (300mg) enoxaparin sodium in 3ml solution for injection for single patient use.

Indications: In adults for: prophylaxis of venous thromboembolic disease in moderate and high risk surgical patients, in particular those undergoing orthopaedic or general surgery including cancer surgery; prophylaxis of venous thromboembolic disease in medical patients with an acute illness and reduced mobility at increased risk of venous thromboembolism (VTE); treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), excluding PE likely to require thrombolytic therapy or surgery; extended treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE) and prevention of its recurrence in patients with active cancer; prevention of thrombus formation in extra corporeal circulation during haemodialysis; treatment of unstable angina and non ST-segment elevation myocardial infarction (NSTEMI), in combination with oral acetylsalicylic acid; treatment of acute ST-segment elevation myocardial infarction (STEMI) including patients to be managed medically or with subsequent percutaneous coronary intervention (PCI).

Dosage & Administration: Clexane® should not be administered by the intramuscular route. ***Prophylaxis in Surgical Patients:*** With moderate risk of thromboembolism, recommended dose is 2,000IU (20mg) once daily by subcutaneous (SC) injection. Initiation 2 hours before surgery was proven effective and safe in moderate risk surgery. Treatment should be maintained for at least 7–10 days and until the patient no longer has significantly reduced mobility. In patients at high risk of thromboembolism, the recommended dose of is 4,000IU (40mg) once daily by SC injection preferably started 12 hours before surgery. If there is a need for preoperative prophylactic initiation earlier than 12 hours (e.g. high risk patient waiting for a deferred orthopaedic surgery), the last injection should be administered no later than 12 hours prior to surgery and resumed 12 hours after surgery. For patients undergoing major orthopaedic surgery, an extended thromboprophylaxis up to 5 weeks is recommended. For patients with high risk of VTE undergoing abdominal or pelvic surgery for cancer, extended thromboprophylaxis up to 4 weeks is recommended. ***Prophylaxis in Medical Patients:*** Recommended dose is 4,000IU (40mg) once daily by SC injection. Treatment with enoxaparin sodium is prescribed for at least 6–14 days. Benefit is not established for treatment longer than 14 days. ***Treatment of DVT and PE:*** 150IU/kg (1.5mg/kg) administered SC once-daily should be used in uncomplicated patients with low risk of VTE recurrence. 100IU/kg (1mg/kg) twice-daily should be used in all other patients such as those with obesity, symptomatic PE, cancer, recurrent VTE or proximal (vena iliaca) thrombosis. The regimen should be selected based on individual assessment including evaluation of the thromboembolic risk and risk of bleeding. Enoxaparin sodium treatment is prescribed for an average period of 10 days. Oral anticoagulant therapy should be initiated when appropriate. In the extended treatment of DVT and PE and prevention of its recurrence in patients with active cancer, physicians should carefully assess the individual thromboembolic and bleeding risks of the patient. The recommended dose is 100IU/kg (1mg/kg) administered twice daily by SC injections for 5–10 days, followed by a 150IU/kg (1.5mg/kg) once daily SC injection up to 6 months. The benefit of continuous anticoagulant therapy should be reassessed after 6 months of treatment. ***During haemodialysis:*** 100IU/kg (1mg/kg) Clexane® introduced into arterial line of the circuit at beginning of dialysis. This dose is usually sufficient for a 4 hour session. If fibrin rings are found, e.g. after a longer session, a further 50–100IU/kg (0.5–1mg/kg) may be given. In patients with high risk of haemorrhage reduce the dose to 50IU/kg (0.5mg/kg) (double vascular access) or 75IU/kg (0.75mg/kg) (single vascular access).***Treatment of Acute Coronary Syndromes:*** For treatment of unstable angina and NSTEMI, the recommended dose is 100IU/kg (1mg/kg) every 12 hours by SC injection administered in combination with antiplatelet therapy. Treatment should be for a minimum of 2 days and until clinical stabilization (usual duration 2–8 days). Acetylsalicylic acid recommended for all patients without contraindications at an initial oral loading dose of 150–300mg (in acetylsalicylic acid-naive patients) and a maintenance dose of 75–325mg/day long-term. For treatment of acute STEMI, recommended dose of enoxaparin sodium is a single intravenous (IV) bolus of 3,000IU (30mg) plus a 100IU/kg (1mg/kg) SC dose followed by 100IU/kg (1mg/kg) administered SC every 12 hours (maximum 10,000IU (100mg) for each of the first 2 SC doses). Appropriate antiplatelet therapy such as oral acetylsalicylic acid (75–325mg once daily) should be administered concomitantly unless contraindicated. Recommended duration of treatment is 8 days or until hospital discharge. When administered in conjunction with a thrombolytic (fibrin specific or non-fibrin specific), enoxaparin sodium should be given between 15 minutes before and 30 minutes after the start of fibrinolytic therapy. For patients managed with PCI, if the last dose of enoxaparin sodium SC was given less than 8 hours before balloon inflation, no additional dosing needed. If the last SC administration was given more than 8 hours before balloon inflation, an IV bolus of 30IU/kg (0.3mg/kg) enoxaparin sodium should be administered.

Special populations: ***Elderly:*** For treatment of acute STEMI in elderly ≥75 years of age, an initial IV bolus must not be used. Initiate dosing with 75IU/kg (0.75mg/kg) SC every 12 hours (maximum 7,500IU (75mg) for each of the first two SC doses only, followed by 75IU/kg (0.75mg/kg) SC dosing for the remaining doses). ***Children:*** Safety and efficacy not established. ***Renal impairment:*** Not recommended for patients with end stage renal disease Dosage adjustment required for patients with severe renal impairment. See SmPC for full details. ***Hepatic Impairment***: Limited data. Caution should be used.

Contraindications: Hypersensitivity to enoxaparin sodium, heparin or its derivatives, including low molecular weight heparins (LMWH) or any of the excipients. Recent (<100 days) history of immune mediated heparin-induced thrombocytopenia (HIT) or in the presence of circulating antibodies. Active clinically significant bleeding and conditions with a high risk of haemorrhage, including recent haemorrhagic stroke, gastrointestinal ulcer, presence of malignant neoplasm at high risk of bleeding, recent brain, spinal or ophthalmic surgery, known or suspected oesophageal varices, arteriovenous malformations, vascular aneurysms or major intraspinal or intracerebral vascular abnormalities. ***Multiple dose vials contain benzyl alcohol*** therefore contraindicated in: those with hypersensitivity to benzyl alcohol and newborns or premature neonates.

Warnings and Precautions: Do not use interchangeably (unit for unit) with other LMWHs. In order to improve the LMWH traceability, healthcare professionals should record the trade name and batch number administered. ***Heparin-induced Thrombocytopenia:*** Use with extreme caution in patients with a history (>100 days) of HIT without circulating antibodies, only after careful benefit-risk assessment and after non-heparin

alternative treatments are considered; platelet counts should be measured before and regularly thereafter during the treatment and patients should be warned of symptoms. In patients with cancer with a platelet count below 80 g/L, anticoagulation treatment can only be considered on a case-by-case basis and careful monitoring is recommended. ***Haemorrhage:*** Use with caution in conditions with increased potential for bleeding (e.g. impaired haemostasis, history of peptic ulcer, recent ischemic stroke, severe arterial hypertension, recent diabetic retinopathy, neuro- or ophthalmologic surgery). *Laboratory tests:* Increases in activated partial thromboplastin time (aPTT), and activated clotting time (ACT) may occur at higher doses but not linearly correlated with dose. Spinal/epidural anaesthesia or lumbar puncture must not be performed within 24 hours of administration of therapeutic doses of enoxaparin sodium; placement or removal of an epidural catheter or lumbar puncture is best performed when the anticoagulant effect of enoxaparin sodium is low. ***Severe skin reactions:*** Skin necrosis, cutaneous vasculitis and acute generalised exanthematous pustulosis have been reported with LMWHs. At the time of prescription, patients should be advised of the symptoms and monitored closely, and any signs should lead to prompt treatment discontinuation. ***Cardiac precautions:*** Following vascular instrumentation during the treatment of unstable angina, NSTEMI and acute STEMI: adhere precisely to the recommended dosing intervals; in case a closure device is used, the sheath can be removed immediately; If a manual compression method is used, sheath should be removed 6 hours after the last IV/SC enoxaparin sodium injection; The site should be observed for signs of bleeding or hematoma. Use of heparin is usually not recommended in patients with acute infective endocarditis. Enoxaparin sodium has not been adequately studied for thromboprophylaxis in patients (including in pregnancy) with mechanical prosthetic heart valves. ***Special populations:*** Elderly patients, and those with renal or hepatic impairment may be at increased risk of bleeding at treatment doses. ***Weight:*** Low body weight patients are at increased risk of bleeding at prophylactic and treatment dose ranges. Obese patients are at higher risk for thromboembolism however there is no consensus for dose adjustment; these patients should be observed carefully. ***Hyperkalaemia:*** Heparins can suppress adrenal secretion of aldosterone leading to hyperkalaemia, particularly in patients such as those with diabetes mellitus, chronic renal failure, pre-existing metabolic acidosis, taking medicinal products known to increase potassium; plasma potassium should be monitored regularly especially in patients at risk. ***Sodium:*** For patients receiving doses higher than 210mg/day, this medicine contains more than 24mg sodium, equivalent to 1.2% of WHO recommended maximum daily intake.

Pregnancy: Enoxaparin sodium should be used during pregnancy only if the physician has established a clear need. As benzyl alcohol may cross the placenta, it is recommended to use a formulation that does not contain benzyl alcohol.

Interactions: ***Not Recommended:*** Systemic salicylates, acetylsalicylic acid at anti-inflammatory doses, and NSAIDs including ketorolac. Other thrombolytics (e.g. alteplase, reteplase, streptokinase, tenecteplase, urokinase) and anticoagulants. ***Caution:*** Platelet aggregation inhibitors including acetylsalicylic acid used at anti-aggregant dose (cardioprotection), clopidogrel, ticlopidine, and glycoprotein IIb/IIIa antagonists indicated in acute coronary syndrome due to the risk of bleeding. Dextran 40. Systemic glucocorticoids. Medicinal products increasing potassium levels.

Adverse Reactions: For all indications, ***Very Common:*** Hepatic enzyme increases (mainly transaminases >3x the upper limit of normal), ***Common:*** Haemorrhage, haemorrhagic anaemia, thrombocytopenia, thrombocytosis, allergic reaction, headache, urticaria, pruritus, erythema, injection site-haematoma, pain, other reaction (such as oedema, haemorrhage, hypersensitivity, inflammation, mass, pain, or reaction). ***Uncommon:*** Hepatocellular liver injury, bullous dermatitis, local irritation, skin necrosis at injection site. ***Rare:*** Eosinophilia, cases of immune-allergic thrombocytopenia with thrombosis (in some, thrombosis was complicated by organ infarction or limb ischaemia), anaphylactoid reactions including shock, spinal/neuraxial haematoma resulting in varying degrees of neurologic injuries including long-term or permanent paralysis, cholestatic liver injury, alopecia, cutaneous vasculitis, skin necrosis usually occurring at the injection site (these phenomena have been usually preceded by purpura or erythematous plaques, infiltrated and painful). Osteoporosis (following therapy >3 months), hyperkalaemia. ***Frequency not known:*** Acute generalised exanthematous pustulosis. *Prescribers should consult the SmPC in relation to other adverse reactions.*

Legal Category: POM.

Marketing Authorisation (MA) Holder: Sanofi, 410 Thames Valley Park Drive, Reading, Berkshire, RG6 1PT, UK.

MA numbers: *Clexane® Forte Syringes:* PL 04425/0185, *Clexane® Multidose Vials:* PL 04425/0186, *Clexane® Syringes:* PL 04425/0187.

UK list prices: *10x prefilled syringes: 2,000IU:* £20.86, *4,000IU:* £30.27, *6,000IU:* £39.26, *8,000IU:* £55.13, *10,000IU:* £72.30, *12,000IU:* £87.93, *15,000IU:* £99.91. *1x Multidose Vial:* £21.33.

For more information please contact: Sanofi Medical Information, 410 Thames Valley Park Drive, Reading, Berkshire, RG6 1PT, UK. uk-medicalinformation@sanofi.com

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Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.
Adverse events should also be reported to Sanofi Tel: 0800 0902314. Alternatively, send via email to UK-drugsafety@sanofi.com