CUSTOMER ANNOUNCEMENT

CLEXANE 4,000 IU (40mg)/0.4ml SYRINGES ALTERNATIVE DEVICE

Sanofi UK is experiencing a temporary shortage in supply of Clexane 4,000 IU (40mg)/0.4ml syringes in January 2019 due to a global increase in demand for enoxaparin sodium. This applies to the 4,000IU (40mg) syringes only.

In order to minimise the impact of the shortage of Clexane 4,000 IU (40mg)/0.4ml syringes on your trust Sanofi UK will be introducing, on a temporary basis, the Italian pack with the PREVENTIS (user activation) safety system.

For a short period of time, we will be supplying **imported LICENSED Italian Clexane 4,000 IU (40mg)/0.4ml syringes** with the PREVENTIS safety system in the UK. It is still the **same** Clexane from Sanofi but it comes and with a different safety system. Although in the original Italian packaging, the box will contain an English (rather than Italian) patient information leaflet.
Please find additional information about the device below .

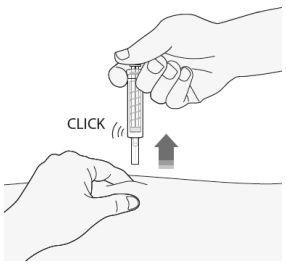
Comparative table of PREVENTIS and ERIS systems features	CLEXANE ITALY PREVENTIS	CLEXANE UK ERIS
4,000 IU (40 mg)/0.4 ml solution for injection in pre-filled syringes	✓	✓
Blistered pre-filled syringes	✓	✓
Auto-Activated ERIS needle protective sleeve	✗	✓
User-activated PREVENTIS needle protective sleeve	✓	✗
Audible click when activating the safety device	✓	✓
Plunger colour	Yellow	White
Number of Syringes per pack	6	10
Pack dimensions (mm)	63 x 86 x 169	138 x 84 x 162

Italian Clexane pack with PREVENTIS system

UK Clexane pack with ERIS system

Introducing the PREVENTIS system

Where the most widely used ERIS system in the UK has an auto-activation of the protective sleeve mechanism, please be aware that the PREVENTIS system works differently.



After injecting, users will need to **firmly push the plunger to activate the safety system**. The protective sleeve will automatically cover the needle. You will hear an audible “click” to confirm the activation of the protective sleeve.

For additional information on the safety system and how to inject Clexane, please refer to the translated Patient Information Leaflet available on the eMC website under the “Risk Materials” section of the Clexane syringes page.

Should you require any further information on Clexane or the alternative PREVENTIS system, please refer to **Customer Services at 0800 854 430** or **Sanofi Medical Information at 0845 372 7101**

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CLEXANE PRESCRIBING INFORMATION

Presentations: Clexane® Syringes: single dose pre-filled syringes containing either: 2,000 IU (20mg) enoxaparin sodium in 0.2ml, 4,000 IU (40mg) enoxaparin sodium in 0.4ml, 6,000 IU (60mg) enoxaparin sodium in 0.6ml, 8,000 IU (80mg) enoxaparin sodium in 0.8ml or 10,000 IU (100mg) enoxaparin sodium in 1ml. Clexane® Forte Syringes: single dose pre-filled syringes containing either: 12,000 IU (120mg) enoxaparin sodium in 0.8ml or 15,000 IU (150mg) enoxaparin sodium in 1ml. Clexane® Multidose vial: Vial containing 30,000 IU (300mg) enoxaparin sodium in 3.0ml 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; 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: ***Prophylaxis in Surgical Patients:*** With moderate risk of thromboembolism, recommended dose of enoxaparin sodium is 2,000 IU (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 enoxaparin sodium is 4,000 IU (40 mg) once daily by SC injection preferably started 12 hours before surgery. If there is a need for earlier than 12 hours enoxaparin sodium preoperative prophylactic initiation (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 of enoxaparin sodium is 4,000 IU (40 mg) once daily by SC injection. Treatment with enoxaparin sodium is prescribed for at least 6 to 14 days. Benefit is not established for treatment longer than 14 days. ***Treatment of VTE:*** 150 IU/kg (1.5 mg/kg) administered SC once-daily should be used in uncomplicated patients with low risk of VTE recurrence. 100 IU/kg (1 mg/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. ***Treatment of Acute Coronary Syndromes:*** For treatment of unstable angina and NSTEMI, the recommended dose of enoxaparin sodium is 100 IU/kg (1 mg/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 to 8 days). Acetylsalicylic acid recommended for all patients without contraindications at an initial oral loading dose of 150–300 mg (in acetylsalicylic acid-naive patients) and a maintenance dose of 75–325 mg/day long-term. For treatment of acute STEMI, recommended dose of enoxaparin sodium is a single intravenous (IV) bolus of 3,000 IU (30 mg) plus a 100 IU/kg (1 mg/kg) SC dose followed by 100 IU/kg (1 mg/kg) administered SC every 12 hours (maximum 10,000 IU (100 mg) for each of the first two SC doses). Appropriate antiplatelet therapy such as oral acetylsalicylic acid (75 mg to 325 mg 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 30 IU/kg (0.3 mg/kg) enoxaparin sodium should be administered. ***During haemodialysis:*** 1mg/kg (100 IU/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 0.5 to 1mg/kg (50 to 100 IU/kg) may be given. In patients with high risk of haemorrhage reduce the dose to 0.5mg/kg (50 IU/kg) (double vascular access) or 0.75mg/kg (75IU/kg) (single vascular access). ***Elderly:*** For treatment of acute STEMI in elderly patients ≥75 years of age, an initial IV bolus must not be used. Initiate dosing with 75 IU/kg (0.75 mg/kg) SC every 12 hours (maximum 7,500 IU (75 mg) for each of the first two SC doses only, followed by 75 IU/kg (0.75 mg/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. ***Hepatic Impairment:*** Limited data in this population therefore 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 containing benzyl alcohol:*** Hypersensitivity to benzyl alcohol. Newborns or premature neonates.
Warnings and Precautions. Do not use interchangeably (unit for unit) with other LMWHs. 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. 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). 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. Skin necrosis and cutaneous vasculitis have been reported with LMWHs and should lead to prompt treatment discontinuation. 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. Elderly patients may be at increased risk of bleeding at treatment doses. 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. 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. ***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: *Very Common:* Hepatic enzyme increases (mainly transaminases > 3 times the upper limit of normality), haemorrhage, thrombocytosis (platelet increase >400 G/L). *Common:* haemorrhagic anaemia, thrombocytopenia, allergic reaction, headache, urticarial, pruritus, erythema, injection site haematoma / pain / other reaction (such as oedema, haemorrhage, hypersensitivity, inflammation, mass, pain, or reaction). Uncommon: hepatocellular liver injury, skin necrosis at injection site, intracranial haemorrhage. Rare: Retroperitoneal haemorrhage, eosinophilia, cases of immuno-allergic thrombocytopenia with thrombosis (in some cases thrombosis was complicated by organ infarction or limb ischaemia), anaphylactic/anaphylactoid reactions including shock, spinal/neuraxial haematoma resulting in varying degrees of neurologic injuries including long-term or permanent paralysis, cholestatic liver injury, Osteoporosis following therapy > 3 months, hyperkalaemia. *For a full list of undesirable effects please refer to the Summaries of Product Characteristics.* **Pharmaceutical Precautions:** Do not mix with other products. Do not store above 25°C. Do not refrigerate or freeze. The contents of the multidose vial should be used within 28 days of opening. **Legal Category:** POM; PL04425/0187: Clexane® Syringes; PL04425/0185: Clexane® Forte Syringes; PL 04425/0186: Clexane® Multidose Vials **Basic NHS cost for 10 pre-filled syringes:** 2,000 IU - £20.86, 4,000 IU - £30.27, 6,000 IU - £39.26, 8,000 IU - £55.13, 10,000 IU - £72.30, 12,000 IU - £87.93, 15,000 IU - £99.91. **Basic NHS cost for 6 pre-filled syringes:** 4,000 IU - £18.16**. NHS cost for one Multidose Vial** - £21.33**. Date of Revision: December 2018** ® denotes a Registered Trade Mark. Further information is available on request **from Sanofi, One Onslow St, Guildford, Surrey, GU1 4SY 0845 372 7101.**

Adverse events should be reported.
Reporting forms and information can be found at www.mhra.gov.uk/yellowcard
Adverse events should also be reported to Sanofi Tel: 0800 090 2314.
Alternatively, send via email to UK-drugsafety@sanofi.com

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