29th January 2020

# Introducing the new Clexane® (enoxaparin) compact packaging

Sanofi has introduced a new compact packaging for the following Clexane presentations:

- 2,000 IU (20mg) /0.2ml Clexane Syringe
- 4,000 IU (40mg) /0.4 ml Clexane Syringe
- 6,000 IU (60mg) /0.6 ml Clexane Syringe
- 8,000 IU (80mg) / 0.8ml Clexane Syringe
- 10,000 IU (100mg) / 1.0ml Clexane Syringe

The 12,000 IU (120mg) / 0.8ml Clexane Syringe and 15,000 IU (150mg) / 1.0ml Clexane Syringe will continue in the existing packaging.


The new Clexane compact packs are significantly smaller than the current packaging, providing a reduction in occupied space on the shelves (see table in the Q&A below). The transition to the new packaging is in response to feedback from Healthcare professionals and will improve the continuity of supply to the UK.

This change in packaging is also part of Sanofi's engagement in reducing its environmental impact by lowering the amount of cardboard and plastics needed to produce the compact packaging.

Apart from the dimensions and the way syringes are arranged in the box, nothing else changes. The PIP codes stays the same, and the packs will still contain 10 pre-filled syringes with the safety system remains the ERIS Auto-activated protective needle guard.

The new compact packs also come with a QR code on them that can be easily scanned with a smartphone to access online content and patient resources in more than 15 languages.

We are committed to making this transition with minimal disturbance. Our distribution partners (Phoenix and McKesson) will supply you with the new packaging when it is available. You do not need to order a different product. Please continue to order Clexane as normal.

Please find on the next page a detailed Q&A document to respond to all your questions.

# Questions & Answers – Clexane compact packs

**Q1. Why has Sanofi changed the packaging?**

A1. The new packaging is part of Sanofi's on-going commitment to improve the long term sustainability of Clexane. Initially, the new packaging was investigated due to feedback from healthcare professionals that the current packaging is too bulky. Sanofi's manufacturing team have been exploring options to tackle this and improve manufacturing capacity. The result is the new compact packaging that has been introduced in the UK throughout the 2019.

**Q2. What strengths are impacted?**

A2. Below is a table listing all the Clexane strengths that have transitioned to the compact packaging

| Product | PIP CODE |
|---|---|
| Clexane 150Mg Pfs (S/Lock) | 3578341 |
| Clexane 120Mg Pfs (S/Lock) | 3578358 |
| Clexane 60Mg X 10 Pfs Sl Compact | 2369353 |
| Clexane 40Mg X 10 Pfs Sl Compact | 179309 |
| Clexane 100Mg X 10 Pfs Sl Compact | 2369387 |
| Clexane 20Mg X 10 Pfs Sl Compact | 179259 |
| Clexane Mdv 1 X 3Ml | 3284304 |
| Clexane 80Mg X 10 Pfs Sl Compact | 2369361 |

A1. Clexane (enoxaparin) compact packs introduction schedule

**Q3. What about the two higher strengths the 12,000 IU (120mg) / 0.8ml Clexane Syringe and 15,000 IU (150mg)/ 1.0ml Clexane Syringe, will they be transition to the new packaging?**

A3. No, there are no immediate plans to transition these two presentations to the new packaging. The 12,000 IU (120mg) / 0.8ml Clexane Syringe and 15,000 IU (150mg)/ 1.0ml Clexane Syringe will continue to be available in the existing packaging.

**Q4. What are the main differences between the compact packaging and the current packaging?**

A4. The most important difference between the compact packaging and the existing packaging is the reduction in occupied space of 57.6% (1081.7 $cm^3$ box volume reduction) of the compact packaging

The second important change is that the syringes are not individually blistered. The sterility of the syringes is maintained.

There are no differences in devices and safety mechanism between the 2 pack types.

Below is a table that highlights the differences and similarities between the two packs

| A2. Comparative table of the Clexane compact pack and regular pack | COMPACT PACK | REGULAR PACK |
|---|---|---|
| Single use doses with ERIS auto activated safety device | ✓ | ✓ |
| Individually packed syringes in plastic blisters | ✗ | ✓ |
| Maintained sterility of the syringes | ✓ | ✓ |
| QR code for online patient resources in 15 languages | ✓ | ✗ |
| Number of Syringes per pack | 10 | |
| Pack dimensions (mm) | 203 x 148 x 26.5 | 138 x 84 x 162 |
| Pack volume (cc, $cm^3$) | 796.2 | 1877.9 |
| PIP Code | Identical | |

**Q5. What are the advantages of changing to the new pack?**

A5. **- Stock management**:
The compact packs provide a volume reduction of 57.6% (1081.7 $cm^3$ box volume reduction). These will help supply the same quantity of syringes to the healthcare professionals whilst reducing the burden of the bulky packs on the storage shelves.

**- Supply continuity:**
The simplification of the production line and reduction of steps needed for the compact packs is expected to improve the long term continuity of the supply of the product for the UK.

**- Environmental impact:**
The new compact packs have been designed to minimise Sanofi's environmental impact : the boxes require less cardboard, less plastics to be produced and the QR code with digital resources is here to avoid unnecessary prints.

**- Easy patient resources access:**
By scanning the QR code on the compact pack with a compatible device, you will be redirected to the website www.clexanepatientsupport.co.uk. By going there, patients and healthcare professionals will be able to access online patient resources translated in more than 15 languages.

**Q6. How am I going to be transitioned to the new packs?**

A6. There is no action to be taken from the healthcare professional's standpoint. Across 2019, the compact packs have progressively replaced the regular packs as the stocks deplete. **Continue to order Clexane in the same way**.

**Q7. What support is available for me?**

A7. Sanofi are providing the following:
1. Communication letter to all trusts and pharmacies
2. Ward posters introducing the improved compact packs
   All these items above are available in print and electronically.

3. Sanofi Sales representatives to support individual trusts

| Region | Name | Contact number | Email |
|---|---|---|---|
| Clexane National Account Lead | Joanne Graham | 07841 051959 | Joanne.Graham@sanofi.com |
| London | Melissa Tindall | 07803 412892 | Melissa.Tindall@sanofi.com |
| Midlands and East of England, Wales | Rajni Begum | 07740 935162 | Rajni.Begum@sanofi.com |
| South of England | Jacinta Stellema | 07545 513815 | Jacinta.Stellema@sanofi.com |
| Northern Ireland and Scotland | Richard Kyle | 07753 832112 | Richard.Kyle@sanofi.com |
| North of England | Peter Peterson | 07730 896803 | Peter.Peterson@sanofi.com |

4. Sanofi Key Account Managers to support individual pharmacy groups

| Pharmacy Group | Name | Contact number | Email |
|---|---|---|---|
| Lloyds | Jenny Hoban<br>Yvonne Wick | 07801 979 042<br>07801 378 795 | Jennyfer.Hoban@sanofi.com<br>Yvonne.Wick@sanofi.com |
| Boots<br>Well<br>Rowlands<br>Superdrug | Nick Bellinger | 07841 033754 | Nick.Bellinger@sanofi.com |
| Day Lewis<br>Cohens Chemist | James Bessell | 07718 475 611 | James.Bessell@sanofi.com |
| PCT Healthcare<br>Knights Pharmacy<br>Other Pharmacy Groups | Yvonne Wick | 07801 378 795 | Yvonne.Wick@sanofi.com |

**Q8. Who do I contact for further information?**

A8.

- Contact your local representative or key account manager from the table above.
- For questions relating to supply of stock please contact our customer service team on email: GB-CustomerServices@sanofi.com or telephone 0800 854 430
- For medical enquiries, please contact our medical information team on email uk-medicalinformation@sanofi.com or telephone 0845 372 7101

**Prescribing Information: Clexane® Syringes, Clexane® Forte Syringes, and Clexane® Multidose Vial**
**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; 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 VTE 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. ***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 SPC 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. 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:** ***Pooled 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. *For more information please refer to the SPC.*

**Legal Category:** POM. **Clexane® Forte Syringes:** PL04425/0185, **Clexane® Multidose Vials:** PL04425/0186, **Clexane® Syringes:** PL04425/0187. **Marketing Authorisation Address:** Sanofi, 410 Thames Valley Park Drive, Reading, Berkshire, RG6 1PT, UK. **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:** Medical Information, Sanofi, 410 Thames Valley Park Drive, Reading, Berkshire, RG6 1PT, UK. Tel: 0845 372 7101. uk-medicalinformation@sanofi.com **Date of Revision.** January 2020. ® denotes a Registered Trade Mark.

Adverse events should be reported. Reporting forms and information can be found at yellowcard.mhra.gov.uk
Adverse events should also be reported to Sanofi Tel: 0800 0902314.
Alternatively, send via email to UK-drugsafety@sanofi.com