

**PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986**

The medicine is dispensed with a doctor's prescription only

## **XEPLION®**

### **Extended-release suspension for intramuscular injection**

#### **The active ingredient and its quantity:**

Xeplion 50 mg contains Paliperidone (as palmitate) 50 mg

Xeplion 75 mg contains Paliperidone (as palmitate) 75 mg

Xeplion 100 mg contains Paliperidone (as palmitate) 100 mg

Xeplion 150 mg contains Paliperidone (as palmitate) 150 mg

#### **Inactive ingredients and allergens in the preparation – see section 6 – “Further Information”.**

**Read the leaflet carefully in its entirety before using the medicine.** This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.

This medicine has been prescribed for the treatment of your ailment. Do not pass it on to others. It may harm them even if it seems to you that their ailment is similar.

The medicine is not intended to treat children and adolescents below 18 years of age.

The medicine is not intended for use in patients with dementia-related psychosis. Clinical studies have shown that elderly patients who used antipsychotics similar to Xeplion had a higher risk of stroke and death.

#### **1. WHAT IS THE MEDICINE INTENDED FOR?**

This medicine is intended for:

- treatment of schizophrenia, in adults.
- treatment of schizoaffective disorder as monotherapy or as an adjunct therapy to mood stabilizers or antidepressants.

**Therapeutic group:** atypical antipsychotic

#### **2. BEFORE USING THE MEDICINE**

##### **Do not use the medicine if**

- You are allergic to paliperidone or to any of the additional ingredients contained in the medicine.
- You are allergic to other antipsychotic medicines including risperidone-containing medicine.

### **Special warnings regarding use of the medicine**

#### **Before treatment with Xeplion, tell the doctor if you suffer from any of the following conditions:**

All medicines have side effects and some of the side effects of this medicine can worsen the symptoms of other medical conditions. For that reason, it is important to tell your doctor if you suffer from any of the following conditions, which can worsen during treatment with Xeplion:

- if you have Parkinson's disease.
- if you have previously suffered from neuroleptic malignant syndrome whose signs are high temperature and muscle stiffness.
- if you have previously experienced abnormal movements of the face or the tongue, tardive dyskinesia.
- if you know that you have had a low count of white blood cells in the past (which may have been caused by use of other medicines or a different reason).
- if you are diabetic or at risk of developing diabetes.
- if you have had breast cancer or a tumour in the pituitary gland.
- if you have heart disease or are taking medicines to treat heart diseases that may cause low blood pressure.
- if you have low blood pressure when you stand up or sit up suddenly.
- if you have epilepsy.
- if you have kidney function problems.
- if you have liver function problems.
- if you have a prolonged and/or painful erection.
- if you have a problem with body temperature regulation or overheating.
- if you have abnormally high levels of prolactin in your blood or if you possibly have a prolactin-dependent tumour.
- if you, or your family, have a history of development of blood clots, as antipsychotics may be associated with formation of blood clots.

If you have any of these conditions, talk to your doctor. The doctor may adjust your dose of Xeplion or monitor your condition for a while.

Talk to your doctor, pharmacist or nurse before using Xeplion.

This medicine has not been studied in elderly patients with dementia. However, in elderly patients who suffered from dementia and were treated with similar medicines, there was an increased risk of stroke and death.

Because in rare cases of use of Xeplion, dangerous decrease in certain white blood cell counts, which are designed to fight infections in your blood, has been observed, your doctor may want to check your white blood cell count.

Even if you have previously taken oral paliperidone or risperidone and did not develop an allergic reaction, rarely, allergic effects

occur after receiving an injection of Xeplion. Refer to your doctor immediately if you experience a rash, swelling of the throat, itching, or breathing problems, as these may be signs of a severe allergy.

This medicine may cause weight gain. Significant weight gain may adversely affect your health. Your doctor should regularly measure your body weight.

As diabetes mellitus or worsening of pre-existing diabetes mellitus have been observed in patients taking Xeplion, the doctor should check for signs of high sugar levels. The doctor should monitor blood sugar levels regularly in every diabetic patient receiving Xeplion.

The medicine may weaken your gag reflex, thereby masking the natural responses of your body to ingestion of toxic substances or to other medical conditions.

During cataract surgery, the pupil (the black circle in the middle of the eye) may not grow to the required size. In addition, the iris (the coloured part of the eye) may become floppy during surgery, which may lead to eye damage.

If you are planning to have eye surgery, tell your doctor that you are being treated with this medicine.

### **Children and adolescents**

The medicine is not intended for treatment in children and adolescents under 18 years of age.

**If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist. It is especially important to inform the doctor or pharmacist if you are taking:**

- Carbamazepine (an antiepileptic medicine and mood stabiliser). Concomitant use may require a dose adjustment of Xeplion.
- Since this medicine works primarily in the brain, a combination with other medicines that affect the brain, such as other antipsychotic medicines, opioids, antihistamines and sleep-inducing medicines may exacerbate side effects such as sleepiness or other effects on the brain.
- Since Xeplion can cause a decrease in blood pressure, care should be taken when administering with other medicines that lower blood pressure.
- This medicine can reduce the effect of medicines that treat Parkinson's disease and restless legs syndrome (e.g., levodopa).
- Xeplion may abnormally affect an ECG (electrical tracing of the heart activity) and demonstrate a prolonged QT interval. Other medicines that affect the ECG include medicines to treat heart rhythm disorders, or to treat infections, and other antipsychotics.
- If you may suffer from convulsions, Xeplion may increase your chance of getting a seizure attack. Other medicines that cause the same effect include some medicines to treat depression or medicines to treat infection, and other antipsychotics.
- Xeplion should be used with caution together with medicines that increase the activity of the central nervous system (psychostimulants such as methylphenidate).

### **Use of the medicine and consumption of alcohol**

Do not drink alcohol during the course of treatment with Xeplion.

### **Pregnancy and breastfeeding**

- Talk to your doctor before using the medicine if you are pregnant or breastfeeding, think you may be pregnant or are planning to become pregnant. Do not use Xeplion during pregnancy, unless under a doctor's orders.  
The following side effects may occur in babies born to women who were treated with Xeplion during the last trimester of their pregnancy (the last three months of pregnancy): shaking, muscle stiffness and/or weakness, sleepiness, nervousness, breathing difficulties and feeding difficulties. If any of these effects occur in your baby, contact the doctor.
- Xeplion can pass from the mother to the baby through the breast milk and can harm the baby. Do not breastfeed during the course of treatment with Xeplion.

### **Driving and use of machines**

Dizziness, extreme tiredness and vision problems may occur during treatment with this medicine (see section 4 – Side effects). Be careful when driving a car, operating machines and performing activities requiring alertness.

### **Important information about some of the ingredients of the medicine**

#### **Xeplion contains sodium**

Sodium – This medicine contains less than 1 mmol (23 mg) sodium per dose, that is to say, it is considered essentially “sodium-free”.

### **3. HOW SHOULD THE MEDICINE BE USED?**

- Always use according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain.
- The dosage and the treatment regimen will be determined by the doctor only.
- Xeplion is a medicine with prolonged activity, administered by injection by a medical staff member. Your doctor will tell you when you need to receive your next injection.
- It is important to be sure to come to the appointments that have been set for you, in order to get each injection on time. If you think you may miss an appointment, it is important that you call the doctor or nurse at the clinic in which you are being treated right away, to set up a new appointment as soon as possible.
- The first and second dose of the medicine will be injected into the shoulder muscle. The second dose will be given one week after the first dose. The following doses will be given a month apart between doses, to the shoulder muscle or buttock muscle.
- Your doctor may increase or decrease the dose of the medicine by one dose level during your monthly injection.
- Patients with kidney problems  
Your doctor may adjust the dose of the medicine according to your kidney function.

If you have mild kidney disease, your doctor may reduce the dosage of the medicine.

If you have moderate or severe kidney disease, do not use this medicine.

- **Elderly patients**

Your doctor may reduce your dose of the medicine if your kidney function is reduced.

- Do not exceed the recommended dose.
- Adhere to the treatment regimen as recommended by the doctor.
- If you forget to take this medicine at the scheduled time, consult the doctor or the nurse at the clinic in which you are being treated.

**If you accidentally received a higher dosage**

The medicine is administered by a member of the medical staff; therefore, it is unlikely that you will be given a double dose.

Patients who have been given too much paliperidone may experience the following symptoms: drowsiness or reduced consciousness, fast heart rate, low blood pressure, an abnormal electrocardiogram (electrical tracing of the heart), or slow or abnormal movements of the face, body, arms or legs.

**If you stop treatment with Xeplion**

If you stop getting the injection, the effect of the medicine will wear off. Even if your health improves, do not stop treatment with the medicine without consulting your doctor, as the symptoms of the disease may return.

Adhere to the treatment regimen as recommended by the doctor.

**Do not take medicines in the dark! Check the label and the dose each time you take medicine. Wear glasses if you need them. If you have any further questions regarding use of this medicine, consult with your doctor or pharmacist.**

**4. SIDE EFFECTS**

**As with any medicine, use of Xeplion may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.**

**Refer to your doctor immediately if:**

- you develop blood clots in the veins, especially in the legs (symptoms include swelling, pain and redness in the leg), which may travel through blood vessels to the lungs, causing chest pain and difficulty breathing. If you notice any of these symptoms, seek medical assistance immediately.
- you have dementia and experience a sudden change in your mental state or sudden weakness or numbness of your face, arms or legs, especially on one side of your body, or speech disturbances, even for a short time. These effects may indicate a stroke.
- you develop fever, muscle stiffness, sweating or a decreased level of consciousness (a disorder called “neuroleptic malignant

syndrome"). Seek medical assistance immediately.

- you are a man and are suffering from a prolonged or painful erection. This condition is called priapism. Seek medical assistance immediately.
- you develop uncontrollable spasmodic or jittery movements of the tongue, mouth and face. Discontinuation of paliperidone treatment may be required.
- you develop a severe allergic reaction characterised by fever, swelling in the mouth, face, lips or tongue, shortness of breath, itching, skin rash and sometimes drop in blood pressure (amounting to an 'anaphylactic reaction'). Even if you have previously taken oral risperidone or oral paliperidone and did not have an allergic reaction, rarely, allergic reactions occur after receiving an injection of paliperidone.
- If you are planning to undergo an eye operation, tell your eye doctor that you are taking Xeplion. During a cataract operation, the iris (the coloured part of the eye) may become floppy (floppy iris syndrome), which may cause damage to the eye.
- you know that the levels of certain white blood cells in your blood is dangerously low. These cells are needed to fight infections in the blood.

#### **Very common side effects (occur in more than 1 in 10 users)**

- difficulty falling asleep or sleep difficulties

#### **Common side effects (occur in 1 to 10 users, out of 100)**

- common cold symptoms, urinary tract infections, flu-like sensation
- Xeplion may increase the level of the prolactin hormone, which can be seen in blood tests (which may or may not be manifested in symptoms). If symptoms of high prolactin appear, they can include: In men – swelling of the breasts, difficulties in getting or maintaining an erection and other problems with sexual function. In women, a high prolactin level can lead to breast discomfort, leakage of milk from the breasts, irregularities or other menstrual disorders.
- high blood sugar level, weight gain, weight loss, decreased appetite
- irritability, depression, anxiety
- parkinsonism, a condition manifested by disturbed and slowed movement, sensation of stiffness and tightness of the muscles (causing spastic movements), and sometimes even a sensation of movement "freezing up" and then restarting. Other signs of Parkinsonism include a slow shuffling walk, a tremor while at rest, increased salivation and a loss of expression on the face.
- restlessness, sleepiness or impaired alertness
- dystonia – a condition involving slow or sustained involuntary contraction of muscles. While dystonia can involve any part of the body (and may manifest in abnormal posture), dystonia usually affects the muscles of the face and includes abnormal movements of the eyes, mouth, tongue or jaw.

- dizziness
- dyskinesia – this is a condition involving involuntary muscle movements, and can include repetitive, spastic or writhing movements or twitching.
- tremor
- headache
- rapid heart rate
- high blood pressure
- cough, stuffy nose
- abdominal pain, vomiting, nausea, constipation, diarrhoea, indigestion, toothache
- increased liver transaminase levels in the blood
- bone or muscle pain, back pain, joint pain
- loss of menstrual periods
- leakage of milk from the breasts
- fever, weakness, fatigue (tiredness)
- a reaction at the injection site, including itching, pain or swelling

**Uncommon side effects (occurs in 1 to 10 users, out of 1,000)**

- pneumonia, inflammation of the bronchi (bronchitis), infection of the breathing passages, sinus infection, bladder infection, ear infection, fungal infection of the nails, tonsillitis, infection of the skin
- decreased white blood cell count, decrease in a certain type of white blood cells that are intended to help protect you against infection, decrease in platelet count (blood cells that help you stop bleeding), anaemia
- allergic reaction
- occurrence of diabetes or worsening of pre-existing diabetes, increased insulin levels (a hormone that controls blood sugar levels) in your blood
- increased appetite
- loss of appetite resulting in malnutrition and weight loss
- high blood triglyceride levels (fats), increased cholesterol level in your blood
- sleep disorders, elated mood (mania), decreased sexual drive, nervousness, nightmares
- tardive dyskinesia, a condition manifested by uncontrollable muscle spasms in your face, tongue, or other parts of your body. Tell your doctor immediately if you experience involuntary muscle spasms of the face, tongue or mouth. It may be necessary to discontinue

treatment with the medicine.

- fainting, an uncontrollable urge to move parts of your body, dizziness upon standing, concentration disorders, problems with speech, loss or impaired sense of taste, reduced ability of the skin to sense touch and pain, a sensation of tingling, a feeling of pricking in the skin or loss of sensation in the skin
- blurry vision, eye infection or red eyes, dry eyes
- sensation of spinning (vertigo), ringing in the ears, ear pain
- disturbance in conduction between the upper and lower parts of the heart, impaired electrical conduction of the heart, prolongation of the QT interval, rapid heartbeat upon standing, slow heart rate, abnormal ECG (electrical tracing of the heart), palpitations
- low blood pressure, low blood pressure upon standing (consequently, some Xeplion patients may experience a feeling of faintness, dizziness, or may pass out when transitioning suddenly to sitting/standing)
- shortness of breath, congestion of breathing passages, wheezing, sore throat, nosebleed
- abdominal discomfort, stomach or intestinal infection, difficulty swallowing, dry mouth
- wind in digestive system
- increased GGT (a liver enzyme called gamma-glutamyltransferase) in your blood, increased liver enzyme levels in your blood
- hives (urticaria), itching, rash, hair loss, eczema, dry skin, skin redness, acne
- an increase in the CPK enzyme level (creatine phosphokinase) in your blood, an enzyme which is sometimes released during muscle injury
- muscle spasms, joint stiffness, muscle weakness, neck pain
- incontinence of urine, increased frequency of passing urine, pain when passing urine
- erectile disorders, ejaculation disorders, delay or other disorders in the monthly menstrual cycle, development of breasts in men, sexual dysfunction, breast pain
- swelling of the face, mouth, eyes, or lips, swelling of the body, hands or legs
- an increase in body temperature
- a change in the way you walk
- chest pain, chest discomfort, generally feeling unwell
- hardening of the skin
- fall



**Rare side effects (occurs in 1 to 10 users, out of 10,000)**

- eye infection
- skin inflammation caused by mites, abscess under the skin
- increase in eosinophils (a type of white blood cell) in your blood
- inappropriate secretion of a hormone that controls urine volume
- sugar in the urine
- life-threatening complications of uncontrolled diabetes
- low blood sugar levels
- excessive drinking of water
- catatonia – lack of movement and response while awake
- confusion
- sleepwalking
- lack of emotion
- inability to reach orgasm
- neuroleptic malignant syndrome (confusion, reduced level or loss of consciousness, high fever and severe muscle stiffness), blood vessel problems in the brain, including sudden impairment in blood supply to brain (stroke or transient stroke), loss of response to stimuli, loss of consciousness, low level of consciousness, convulsions, balance impairment
- abnormal coordination
- glaucoma (increased intraocular pressure)
- eye movement disturbances, eye rolling, oversensitivity of the eyes to light, excessive tearing, red eyes
- abnormal heart rate, irregular heart rate
- blood clots in the veins, especially in the legs (symptoms include swelling, pain and redness of the leg), that can travel through the blood vessels to the lungs and cause chest pain and breathing difficulties. If you notice any of these symptoms, seek medical assistance immediately.
- flushing
- breathing difficulties during sleep
- lung congestion
- crackly lung sounds
- inflammation of the pancreas, swollen tongue, stool incontinence, very hard stool

- chapped lips
- rash on skin related to use of the medicine, thickening of skin, dandruff
- breakdown of muscle fibers and pain in muscles (rhabdomyolysis)
- joint swelling
- urinary retention
- breast discomfort, enlargement of the glands in your breasts, breast enlargement
- vaginal discharge
- very low body temperature, chills, feeling thirsty
- withdrawal symptoms
- accumulation of pus caused by infection at injection site, deep skin infection, cysts at injection site, bruising at injection site

#### **Side effects of unknown frequency**

- dangerously low level of certain types of white blood cells. These cells are necessary to fight infections in your blood.
- severe allergic reaction manifested by fever, swelling of the mouth, face, lips or tongue, shortness of breath, itching, skin rash and sometimes drop in blood pressure
- excessive drinking of water, to a dangerous degree
- sleep-related eating disorder
- coma due to uncontrolled diabetes
- shaking of the head
- blood clot in the lungs causing chest pain and breathing difficulties. If you notice any of these symptoms, seek medical assistance immediately.
- decreased oxygen in different parts of your body (because of decreased blood flow)
- fast and shallow breathing, pneumonia caused by inhalation of food, voice disorders
- a blockage in the bowels, lack of muscle movement in the digestive system causing blockage
- yellowing of the skin and the eyes (jaundice)
- severe or life-threatening rash with blisters and peeling skin that may start in and around the mouth, nose, eyes and genitals and spread to other areas of the body (Stevens-Johnson syndrome or toxic epidermal necrolysis)
- serious allergic reaction with swelling that may involve the throat and lead to breathing difficulties
- skin discolouration, flaky and itchy skin or scalp
- abnormal posture

- babies born to mothers who were treated with Xeplion during pregnancy may suffer from side effects of the medicine or withdrawal symptoms of the medicine, such as: irritability, slow, or sustained muscle contraction, shaking, sleepiness, breathing or feeding problems.
- priapism (a prolonged erection that may require surgery)
- a decrease in body temperature
- dead skin cells at the injection site and an ulcer at the injection site.

In any event where you experience side effects not mentioned in this leaflet, or if there is a change in your general feeling, consult the doctor immediately.

If one of the side effects occurs, if one of the side effects worsens, or if you are suffering from a side effect not mentioned in the leaflet, consult the doctor.

Side effects can be reported to the Ministry of Health by clicking on the link “Report side effects of drug treatment” found on the Ministry of Health homepage ([www.health.gov.il](http://www.health.gov.il)) that directs you to the online form for reporting side effects, or by entering the link: <https://sideeffects.health.gov.il>.

## **5. HOW SHOULD THE MEDICINE BE STORED?**

Avoid poisoning! This medicine and any other medicine must be kept in a safe place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.

Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month. Store at a temperature below 30°C.

Store in the original package.

## **6. FURTHER INFORMATION**

In addition to the active ingredient, the medicine also contains:

Polyethylene glycol 4000, Polysorbate 20, Citric acid monohydrate, Disodium hydrogen phosphate anhydrous, Sodium hydroxide, Sodium dihydrogen phosphate monohydrate, Water for injection

- What the medicine looks like and the contents of the package: Xeplion is a white to off-white suspension, provided in a pre-filled syringe for intramuscular (IM) injection by a medical staff member only. The package contains one pre-filled syringe and two needles.
- Registration Holder and Importer: J-C Health Care Ltd., Kibbutz Shefayim 6099000, Israel.

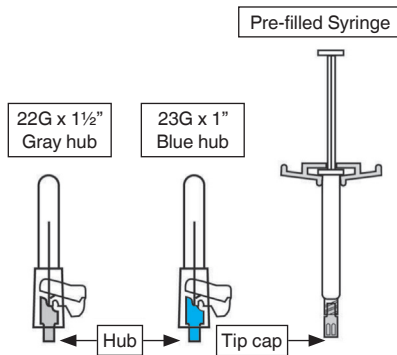
Revised in August 2021 according to MOH guidelines.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 144893305500

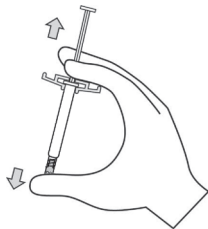
**The following information is intended for medical or healthcare professionals only and should be read by the medical or healthcare professional in conjunction with the full prescribing information (Summary of Product Characteristics).**

The suspension for injection is for single use only. It should be inspected visually for foreign matter before administration. Do not use if the syringe is not visually free of foreign matter.

The pack contains a pre-filled syringe and 2 safety needles (a 1½-inch 22 gauge needle [38.1 mm x 0.72 mm] and a 1-inch 23 gauge needle [25.4 mm x 0.64 mm]) for intramuscular injection. Xeplion is also available in a treatment initiation pack which contains two pre-filled syringes (150 mg + 100 mg) and 2 additional safety needles.



1. Shake the syringe vigorously for a minimum of 10 seconds to ensure a homogeneous suspension.



2. Select the appropriate needle.

The first initiation dose of Xeplion (150 mg) is to be administered on Day 1 in the DELTOID muscle using the needle for DELTOID injection. The second initiation dose of Xeplion (100 mg) is to also be administered in the DELTOID muscle one week later (Day 8) using the needle for DELTOID injection.

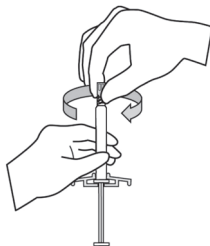
If the patient is being switched from risperidone long-acting injection to Xeplion, the first injection of Xeplion (ranging from 50 mg to 150 mg) can be administered in either the DELTOID or GLUTEAL muscle using the appropriate needle for the injection site at the time of the next scheduled injection.

Thereafter, the monthly maintenance injections can be administered in either the DELTOID or GLUTEAL muscle using the appropriate needle for the injection site.

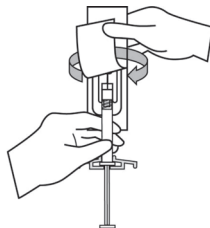
For DELTOID injection, if the patient weighs < 90 kg, use the 1-inch, **23** gauge needle (25.4 mm x 0.64 mm) (needle with **blue** coloured hub); if the patient weighs ≥ 90 kg, use the 1½-inch, **22** gauge needle (38.1 mm x 0.72 mm) (needle with **grey** coloured hub).

For GLUTEAL injection, use the 1½-inch, **22** gauge needle (38.1 mm x 0.72 mm) (needle with **grey** coloured hub).

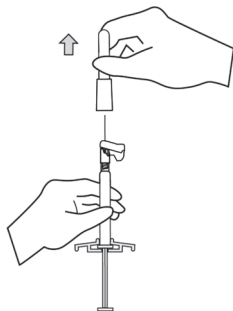
3. While holding the syringe upright, remove the rubber tip cap with a twisting motion.



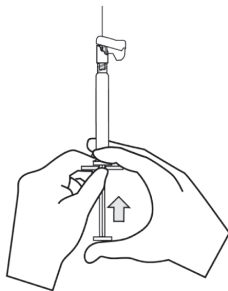
4. Peel the safety needle blister pouch half way open. Grasp the needle sheath using the plastic peel pouch. Attach the safety needle to the luer connection of the syringe with an easy clockwise twisting motion.



5. Pull the needle sheath away from the needle with a straight pull. Do not twist the sheath as the needle may be loosened from the syringe.



6. Bring the syringe with the attached needle in upright position to de-aerate. De-aerate the syringe by moving the plunger rod carefully forward.

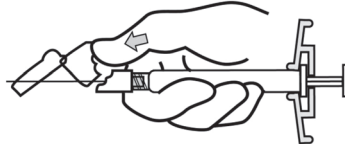




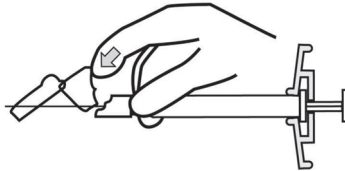
7. Inject the entire contents intramuscularly slowly, deep into the selected deltoid or gluteal muscle of the patient. **Do not administer intravascularly or subcutaneously.**

8. After the injection is complete, use either thumb or finger of one hand (8a, 8b) or a flat surface (8c) to activate the needle protection system. The system is fully activated when a 'click' is heard. Discard the syringe with needle appropriately.

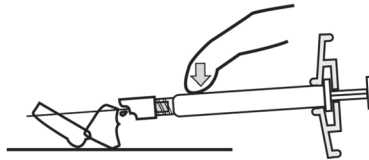
8a



8b



8c



Any unused product or waste material should be disposed of in accordance with local requirements.