

Package leaflet: Information for the user

EXPAREL liposomal 133 mg/10 mL prolonged-release dispersion for injection EXPAREL liposomal 266 mg/20 mL prolonged-release dispersion for injection bupivacaine

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or nurse.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What EXPAREL liposomal is and what it is used for
2. What you need to know before you are given EXPAREL liposomal
3. How you will be given EXPAREL liposomal
4. Possible side effects
5. How to store EXPAREL liposomal
6. Contents of the pack and other information

1. What EXPAREL liposomal is and what it is used for

EXPAREL liposomal is a local anaesthetic which contains the active ingredient bupivacaine.

EXPAREL liposomal is used in adults to reduce pain in a specific part of the body following surgery (such as knee or shoulder joint surgery).

EXPAREL liposomal is also used in adults and children aged 6 years or older to reduce pain in small- to medium-sized wounds following surgery.

2. What you need to know before you are given EXPAREL liposomal

You must **NOT** be given this medicine:

- if you are allergic to bupivacaine (or other similar local anaesthetics) or any of the other ingredients of this medicine (listed in section 6 of this leaflet).
- if you are pregnant and need a local anaesthetic to be injected at the top of the vagina by the cervix. Bupivacaine may seriously harm the unborn baby if it is used for this purpose.
- into a blood vessel or into your joints.

Warnings and precautions

EXPAREL liposomal should not be used in large abdominal, blood vessel and chest surgeries.

Talk to your doctor or nurse before being given EXPAREL liposomal:

- if you have a heart problem;
- if you have liver or kidney problems.

EXPAREL liposomal use may cause temporary loss of sensation or movement. You may notice a difference in your ability to feel things or move normally for up to 5 days after being given the medicine.

The following conditions have sometimes been reported with use of other local anaesthetics:

- Allergic reactions

Allergic reactions may rarely occur after being given any local anaesthetic. Signs of allergic reactions to look out for include: hives or skin rash, swelling around the eyes, face, lips, mouth or throat, shortness of breath or difficulty breathing, feeling dizzy or fainting, or fever. **Seek urgent medical attention** if you notice any of these symptoms after being given EXPAREL liposomal as in rare cases these reactions can become life-threatening (see also section 4 of this leaflet).

- Neurological conditions

Toxicity of the central nervous system can also sometimes occur. Early signs of this can include: restlessness, anxiety, difficulty speaking, lightheadedness, feeling sick (nausea) or being sick (vomiting), numbness and tingling of the mouth and lips, metallic taste, tinnitus (i.e. ringing in the ears), dizziness, blurred vision, tremors or twitching, depression, drowsiness. **Seek urgent medical attention** if you notice any of these symptoms after being given EXPAREL liposomal. More serious side effects from being given too much bupivacaine include fits (convulsions), loss of consciousness and heart attack (see also section 4 of this leaflet).

- Cardiovascular conditions

Cardiovascular conditions can also sometimes occur after use of local anaesthetics. Signs to look out for include: abnormal/irregular heartbeat, low blood pressure, fainting, dizziness or lightheadedness, fatigue (tiredness), shortness of breath, or chest pain. Heart attack can also sometimes occur. **Seek urgent medical attention** if you notice any of these symptoms after being given EXPAREL liposomal (see also section 4 of this leaflet).

- Methaemoglobinemia

Methaemoglobinemia is a blood disorder affecting the red blood cells. This condition can occur immediately or a few hours after use of local anaesthetics. Signs and symptoms to look out for include: pale or grey/blue skin, shortness of breath, feeling lightheaded or fainting, confusion, palpitations, or chest pain. **Seek urgent medical attention** if you notice any of these symptoms after being given EXPAREL liposomal. Sometimes methaemoglobinemia can cause more serious symptoms such as irregular heartbeat, seizures, coma and even death (see also section 4 of this leaflet).

- Chondrolysis

Chondrolysis (breakdown of cartilage in bone joints) has been noticed in patients receiving intra-articular infusion of local anaesthetics. Exparel liposomal must not be used for intra-articular infusion.

Children and adolescents

EXPAREL liposomal is not for use in children under 6 years of age to reduce pain in small- to medium-sized wounds following surgery . This medicine has not been studied in this age group. EXPAREL liposomal is not for use in children and adolescents under 18 years of age to reduce pain in a specific part of the body following surgery (such as knee or shoulder joint surgery) . This medicine has not been studied in this age group.

Other medicines and EXPAREL liposomal

Tell your doctor if you are taking or have recently taken any other medicines.

Taking some medicines together can be harmful. In particular, tell your doctor if you are taking any of the following:

- Nitrates/Nitrites - nitroglycerin, nitroprusside, nitric oxide, nitrous oxide;
- Local anaesthetics - benzocaine, lidocaine, bupivacaine, mepivacaine, tetracaine, prilocaine, procaine, articaine, ropivacaine;
- Anti-arrhythmic - medicines used to treat an uneven heart beat (arrhythmia), such as lidocaine and mexiletine;
- Anti-cancer medicines - cyclophosphamide, flutamide, rasburicase, isofamide, hydroxyurea;
- Antibiotics - dapsone, sulfonamides, nitrofurantoin, para-aminosalicylic acid;
- Antimalarials - chloroquine, primaquine, quinine;
- Anticonvulsants - phenytoin, sodium valproate, phenobarbital;
- Other medicines – acetaminophen (paracetamol), metoclopramide (for stomach problems and anti-sickness), sulfasalazine (for inflammatory conditions), povidone iodine (topical antiseptic).

If you are in doubt about any of these medicines, ask your doctor.

Pregnancy and breast-feeding

EXPAREL liposomal is **NOT** recommended for pregnant women and women of childbearing-age who are not using contraception. If you are pregnant, think you may be pregnant or are planning to have a baby, tell your doctor or nurse before being given this medicine.

EXPAREL liposomal passes into breast milk at very low levels and could cause serious adverse reactions in your baby. Ask your doctor for advice before breastfeeding your baby. They will decide if you should stop breastfeeding your baby or if you should not be given this medicine.

Driving and using machines

EXPAREL liposomal may affect your ability to feel things or move normally for up to 5 days after being given the medicine. You should not drive or use tools or machines if you have any of these side effects.

EXPAREL liposomal contains sodium

This medicine contains 21 mg sodium (main component of cooking/table salt) in each 10 mL vial, and 42 mg in each 20 mL vial. This is equivalent to 1.1% and 2.1%, respectively, of the recommended maximum daily dietary intake of sodium for an adult.

3. How you will be given EXPAREL liposomal

EXPAREL liposomal will be given to you by your doctor during your surgery.

The recommended dose that you will be given will be decided by your doctor. It will depend on the type of pain relief that you need and the part of your body that the medicine will be injected into. It will also depend on the size of the surgical site and your physical condition.

EXPAREL liposomal will be given to you as an injection. Your doctor will inject EXPAREL liposomal in one of the following places:

- the site of surgery;
- close to the nerves that supply the area of the body that has had surgery.

If you are given more EXPAREL liposomal than you should

EXPAREL liposomal is intended for use by trained doctors that will check your blood pressure, heart rate, breathing rate, state of consciousness and monitor for any signs that indicate that you have received too much bupivacaine after giving EXPAREL liposomal.

Seek urgent medical attention if you notice any of the below side effects after being given EXPAREL liposomal (see also section 4 of this leaflet). These are signs of having received too much bupivacaine.

- fits (convulsions);
- loss of consciousness;
- feeling restless or anxious;
- difficulty speaking;
- feeling dizzy or lightheaded;
- feeling or being sick;
- numbness and tingling of the mouth and lips;
- changes in vision, hearing, or taste;
- tremors or twitching;
- feeling drowsy, confused or not fully alert;
- increased or decreased blood pressure;
- increased or decreased heart rate.

If you miss a dose of EXPAREL liposomal

It is unlikely you will miss a dose. EXPAREL liposomal will be given to you by your doctor only once (during your surgery).

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Seek urgent medical attention if you experience any of the following serious side effects that have been reported with use of other local anaesthetics (see section 2):

- abnormal/irregular heartbeat, low blood pressure, fainting, dizziness or lightheadedness, fatigue, shortness of breath, chest pain, cardiac arrest (symptoms of cardiovascular reaction).
- restlessness, anxiety, difficulty speaking, lightheadedness, feeling sick (nausea) or being sick (vomiting), numbness and tingling of the mouth and lips, metallic taste, tinnitus (i.e. ringing in the ears), dizziness, blurred vision, tremors or twitching, depression, drowsiness, fits (symptoms of central nervous system reaction).
- hives or skin rash, swelling around the eyes, face, lips, mouth or throat, shortness of breath or difficulty breathing, fast heart beat, feeling sick, being sick, feeling dizzy or fainting, or fever (symptoms of allergic reaction).

- pale or grey/blue skin, shortness of breath, feeling lightheaded or fainting, confusion, palpitations, chest pain, irregular heartbeat, seizures, or coma (symptoms of methaemoglobinemia).

Other side effects may include:

Common (may affect up to 1 in 10 people):

- distortion of the sense of taste;
- constipation;
- feeling sick or being sick;
- oral loss of sensation.

Uncommon (may affect up to 1 in 100 people):

- feeling hot;
- general bruising or falls;
- abnormal blood test results;
- pain in the joints;
- decreased mobility or involuntary/uncontrolled body movements;
- injury, pain, spasms, twitching or weakness in the muscles;
- burning sensation;
- headache;
- loss of sensation;
- itchy skin or skin irritation.

Rare (may affect up to 1 in 1,000 people):

- abdominal discomfort, bloating or indigestion;
- diarrhoea;
- dry mouth, difficulty or pain with swallowing;
- itching inside the mouth;
- excess saliva in the mouth;
- chills;
- pain (in the abdomen, wound site, muscles, groin, hands or feet);
- swelling in ankles, feet, legs or joints;
- stiffness in the joints;
- abnormal ECG;
- fresh blood passing from anus, usually with stools;
- feeling tired;
- partial paralysis;
- difficulty breathing;
- reddening of the skin or around the wound site;
- complications (e.g., redness, swelling, pain) with the wound site;
- excessive sweating;
- nail discolouration.

Not known (frequency cannot be estimated from the available data):

- inability to urinate (i.e. completely or partially empty the bladder);
- Exparel liposomal does not work.

Some of the above side effects may be seen more frequently in children and adolescents aged 6 years or older.

Additional side effects seen in children and adolescents aged 6 years or older

Very common (may affect more than 1 in 10 people)

- anaemia

Common (may affect up to 1 in 10 people):

- tingling sensation ('pins and needles');
- hearing loss;
- rapid breathing;
- delayed recovery from anaesthesia.

Reporting of side effects

If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via Yellow Card Scheme at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store EXPAREL liposomal

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the vial label after EXP. The expiry date refers to the last day of that month.

Store in a refrigerator (2°C - 8°C). Do not freeze.

EXPAREL liposomal may also be stored at room temperature (below 25°C) for up to 30 days in sealed, unopened vials. Vials should not be re-refrigerated.

After first opening

Chemical and physical in-use stability of EXPAREL liposomal withdrawn from vials and transferred into polypropylene syringes has been demonstrated for 48 hours when stored in a refrigerator (2°C to 8°C), or 6 hours when stored at room temperature (below 25°C). From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and should not be longer than 24 hours at 2°C to 8°C unless opening has taken place in controlled and validated aseptic conditions.

After dilution

Chemical and physical in-use stability of EXPAREL liposomal when admixed with other formulations of bupivacaine has been demonstrated for 24 hours at room temperature (below 25°C). When admixed with 9 mg/mL (0.9%) sodium chloride or lactated Ringer's solution, chemical and physical in-use stability has been demonstrated for 4 hours when stored in a refrigerator (2°C to 8°C) and at room temperature (below 25°C). From a microbiological point of view, unless the method of dilution precludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

6. Contents of the pack and other information

What EXPAREL liposomal contains

The active substance is bupivacaine. Each mL contains liposomal 13.3 mg of bupivacaine in a prolonged-release dispersion for injection.

Each vial of 10 mL prolonged-release dispersion for injection contains 133 mg bupivacaine free base.

Each vial of 20 mL prolonged-release dispersion for injection contains 266 mg bupivacaine free base.

The other ingredients are dierucoylphosphatidylcholine (DEPC), dipalmitoylphosphatidylglycerol (DPPG), cholesterol for parenteral use, tricaprilyn, sodium chloride, phosphoric acid and water for injection.

What EXPAREL liposomal looks like and contents of the pack

EXPAREL liposomal is a white to off-white, prolonged-release dispersion for injection.

It is available in 10 mL or 20 mL, single-use glass vials with an ethylenetetrafluoroethylene-faced grey butyl rubber stopper, and an aluminium/polypropylene flip-tear-up seal.

Each pack contains 4 or 10 vials.

Not all pack sizes may be marketed.

Marketing Authorisation Holder

Pacira Limited
c/o Hillier Hopkins LLP
Radius House, First Floor
51 Clarendon Road
Watford, WD17 1HP
United Kingdom

Manufacturer

Millmount Healthcare Limited
Block-7, City North Business Campus
Stamullen, Co. Meath
K32 YD60
Ireland

For any information about this medicine, please contact the Marketing Authorisation Holder.

This leaflet was last revised in: October 2023

The following information is intended for healthcare professionals only:

Important: Please refer to the Summary of Product Characteristics (SmPC) before using.

Each EXPAREL liposomal vial is for single use only.

Unopened EXPAREL liposomal vials should be refrigerated between 2°C to 8°C. EXPAREL liposomal should not be frozen.

Sealed, unopened EXPAREL liposomal vials may also be stored at room temperature (below 25°C) for up to 30 days. Vials should not be re-refrigerated.

After first opening

Chemical and physical in-use stability of EXPAREL liposomal withdrawn from vials and transferred into polypropylene syringes has been demonstrated for 48 hours when stored in a refrigerator (2°C to 8°C), or 6 hours when stored at room temperature (below 25°C). From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and should not be longer than 24 hours at 2°C to 8°C unless opening has taken place in controlled and validated aseptic conditions.

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EXPAREL liposomal vials should be visually inspected prior to administration. The vials should be gently inverted to re-suspend the particles in the dispersion immediately prior to withdrawal from the vial. Multiple inversions may be necessary if the contents of the vial have settled.

EXPAREL liposomal is intended for single-dose administration only. The maximum dose should not exceed 266 mg (20 mL). The recommended dose for local infiltration is based on size of the surgical site, volume required to cover the area and individual patient factors that may impact the safety of an amide local anesthetic (see SmPC section 4.2).

EXPAREL liposomal can be administered in the ready to use dispersion or diluted to a concentration of up to 0.89 mg/mL (i.e. 1:14 dilution by volume) with 9 mg/mL (0.9%) sodium chloride or lactated Ringer's solution. EXPAREL liposomal should not be mixed with any other medicinal products, nor diluted with water or other hypotonic agents as it will result in disruption of the liposomal particles.

EXPAREL liposomal is a liposomal preparation and should not be used interchangeably with any other formulations of bupivacaine. Bupivacaine hydrochloride (immediate release formulations) and EXPAREL liposomal may be administered simultaneously in the same syringe as long as the ratio of the milligram dose of bupivacaine solution to EXPAREL liposomal does not exceed 1:2. The total amount of bupivacaine HCl and EXPAREL liposomal being co-administered should not exceed 400 mg equivalents of bupivacaine HCl in adults. Bupivacaine amount in EXPAREL liposomal is expressed as the free base of bupivacaine, thus, when calculating the total dose of bupivacaine for coadministration, the amount of bupivacaine from EXPAREL liposomal should be converted to the equivalent of bupivacaine HCl by multiplying EXPAREL liposomal dose with a factor of 1.128.

Caution is advised when co-administering EXPAREL liposomal and bupivacaine HCl, particularly when administering to highly vascular areas where higher systemic absorption is expected (see SmPC section 4.4).

The administration of EXPAREL liposomal may follow the administration of lidocaine after a delay of 20 minutes or more.

When a topical antiseptic such as povidone iodine is applied, the site should be allowed to dry before EXPAREL liposomal is administered into the site. EXPAREL liposomal should not be allowed to come into contact with antiseptics such as povidone iodine in solution.

EXPAREL liposomal should be injected slowly (generally 1 to 2 mL per injection) using a 25 gauge or larger bore needle. The surgical site should be aspirated frequently, when clinically appropriate, during administration to check for blood and minimize the risk of inadvertent intravascular injection.

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