Package leaflet:
Information for the user
Parecoxib 40 mg Powder for solution for injection
parecoxib

Read all of this leaflet carefully before you are given 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 Parecoxib is and what it is used for
2. What you need to know before you are given Parecoxib
3. How Parecoxib is given
4. Possible side effects
5. How to store Parecoxib
6. Contents of the pack and other information

1. What Parecoxib is and what it is used for

Parecoxib contains the active substance parecoxib.
Parecoxib is used for the short-term treatment of pain in adults after an operation. It belongs to the group of medicines called COX-2 inhibitors (this is short for cyclo-oxygenase-2 inhibitors). Pain and swelling are sometimes caused by substances in the body called prostaglandins. Parecoxib works by lowering the amount of these prostaglandins.

2. What you need to know before you are given Parecoxib

Parecoxib must not be given:
- if you are allergic to parecoxib or any of the other ingredients of this medicine (listed in section 6)
- if you have had a serious allergic reaction (especially a serious skin reaction) to any medicines
- if you have had an allergic reaction to a group of medicines called “sulfonamides” (e.g.some antibiotics used to treat infections)
- if you currently have a gastric or intestinal ulcer or bleeding in the stomach or gut
- if you have had an allergic reaction to acetylsalicylic acid or to other NSAIDs (e.g.ibuprofen) or to COX-2 inhibitors. Reactions might include wheezing (bronchospasm), badly blocked nose, itchy skin, rash or swelling of the face, lips or tongue, other allergic reactions or nasal polyps after taking these medicines.
- if you are more than 6 months pregnant
- if you are breast-feeding
- if you have severe liver disease
- if you have inflammation of the intestines (ulcerative colitis or Crohn’s disease)
- if you have heart failure
- if you are about to have heart surgery or surgery on your arteries (including any coronary artery procedure)
- if you have established heart disease and /or cerebrovascular disease e.g. if you have had a heart attack, stroke, mini-stroke (TIA) or blockages to blood vessels to the heart or brain or an operation to clear or bypass blockages
- if you have or have had problems with your blood circulation (peripheral arterial disease).

If any of these applies to you, you will not be given the injection. **Tell your doctor or nurse immediately.**

Warnings and precautions
Talk to your doctor or nurse before Parecoxib is given:
- If you have previously had an ulcer, bleeding or perforation of the gastrointestinal tract
- If you are taking acetylsalicylic acid or other NSAIDs (e.g. ibuprofen)
- If you smoke or drink alcohol
- If you have diabetes
- If you have angina, blood clots, high blood pressure or raised cholesterol
- If you are taking anti-platelet therapies
- If you have fluid retention (oedema)
- If you have liver or kidney disease
- If you are dehydrated - this may happen if you have had diarrhoea or have been vomiting (being sick) or unable to drink fluids
- If you have an infection as it may hide a fever (which is a sign of infection)
- If you use medicines to reduce blood clotting (e.g. warfarin/ warfarin like anticoagulants or novel oral anti-clotting medicines, e.g. apixaban, dabigatran, and rivaroxaban)
- If you use medicines called corticosteroids (e.g prednisone)
- If you use a class of medicines used to treat depression called selective serotonin re-uptake inhibitors (e.g. sertraline).

Parecoxib can lead to an increase in blood pressure or worsening of existing high blood pressure which may result in an increase in side-effects associated with heart conditions. Your doctor may want to monitor your blood pressure during treatment with this medicine.

Children and adolescents
Parecoxib should not be used in children and adolescents under the age of 18.

Other medicines and Parecoxib
Tell your doctor or nurse if you are taking, have recently taken or might take any other medicines. Medicines can sometimes interfere with each other. Your doctor may reduce the dose of Parecoxib or other medicines, or you may need to take a different medicine. It’s especially important to mention:
- Acetylsalicylic acid or other anti-inflammatory medicines
- Fluconazole - used for fungal infections
- ACE inhibitors, Angiotensin-II inhibitors, beta blockers and diuretics - used for high blood pressure and heart conditions
- Ciclosporin or Tacrolimus - used after transplants
- Warfarin - or other warfarin e.g. medicines used to prevent blood clots including newer medicines e.g. apixaban, dabigatran, and rivaroxaban
- Lithium - used to treat depression
- Rifampicin - used for bacterial infections
- Antiarrhythmics - used to treat an irregular heartbeat
- Phenytoin or Carbamazepine - used for epilepsy
- Methotrexate - used for rheumatoid arthritis and cancer
- Diazepam - used for sedation and anxiety
- Omeprazole - used for treating ulcers

Pregnancy, breast-feeding and fertility
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before you are given this medicine.
- **If you are pregnant or trying to become pregnant,** tell your doctor. Parecoxib is not recommended in the first 6 months of pregnancy and you must not receive Parecoxib in the last three months of pregnancy
- **If you are breast-feeding,** you must not receive Parecoxib, as a small amount of the active substance will pass into your breast milk
- NSAIDs, including Parecoxib, may make it more difficult to become pregnant. Tell your doctor if you are planning to become pregnant or if you have problems becoming pregnant.

Driving and using machines
If this medicine makes you feel dizzy or tired, do not drive or use machines until you feel better again.

Parecoxib contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per vial that is to say essentially ‘sodium-free’.

3. How Parecoxib is given

Parecoxib will be given to you by a doctor or nurse.

The usual dose to start with is 40 mg.

You may be given another dose - either 20 mg or 40 mg - 6 to 12 hours after the first one.

You will not be given more than 80 mg in 24 hours.

Some people may be given lower doses:
- People with liver problems
- People with severe kidney problems
- Patients over 65 who weigh less than 50 kg
- People taking fluconazole.

If Parecoxib is used with strong pain killers (called opioid analgesics) such as morphine the dose of Parecoxib will be the same as explained above.

Your doctor or nurse will dissolve the powder before giving you the injection, and will inject the solution into a vein or a muscle (intravenous or intramuscular use). The injection may be given rapidly and directly into a vein or into an existing intravenous line (a thin tube running into a vein), or it can be given slowly and deeply into a muscle.

You will only be given this medicine for short periods.

If you are given more Parecoxib than you should
You may experience side-effects that have been reported with recommended doses.

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

4. Possible side effects

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

The following information is intended for healthcare professionals only

Dosing. The recommended dose is 40 mg administered intravenously (IV) or intramuscularly (IM), followed every 6 to 12 hours by 20 mg or 40 mg as required, not to exceed 80 mg / day. The IV bolus injection may be given rapidly and directly into a vein or into an existing IV line. The IM injection should be given slowly and deeply into the muscle. There is limited clinical experience with parecoxib treatment beyond three days.
As the cardiovascular risk of cyclooxygenase-2 (COX-2) specific inhibitors may increase with dose and duration of exposure, the shortest duration possible and the lowest effective daily dose should be used.
Cases of severe hypotension shortly following parecoxib administration have been reported in postmarketing experience with parecoxib. Some of these cases have occurred without other signs of anaphylaxis. The physician should be prepared to treat severe hypotension.

Administration is by intramuscular (IM) or intravenous (IV) injection. The IM injection is to be given slowly and deeply into the muscle and the IV bolus injection may be given rapidly and directly into a vein or into an existing IV line.

Administration other than IV or IM
Methods of administration other than IV or IM (e.g. intra-articular, intrathecal) have not been studied and should not be used.

Reconstitution solvents
- **This medicinal product must not be mixed** with other medicinal products. The **only** acceptable solvents for reconstitution are:
- sodium chloride 9 mg / mL (0.9 %) solution for injection/ infusion
- glucose 50 mg / mL (5 %) solution for infusion or
- sodium chloride 4.5 mg / mL (0.45 %) and glucose 50 mg / mL (5 %) solution for injection/infusion

The following solutions **cannot** be used for reconstitution:
- Use of Ringer-Lactate solution for injection or glucose 50 mg / mL (5 %) in Ringer-Lactate solution for injection for reconstitution will cause the parecoxib to precipitate from solution and therefore is **not** recommended.
- Use of Sterile Water for Injection for reconstitution is not recommended, as the resulting solution is **not** isotonic.

Reconstitution process
Use aseptic technique to reconstitute the powder.

Stop using Parecoxib and tell your doctor immediately:
- if you develop a rash or ulceration in any part of your body (e.g. skin, mouth, eyes, face, lips or tongue), or develop any other signs of an allergic reaction such as skin rash, swelling of the face, lips or tongue which may cause wheezing, difficulty breathing, or swallowing - this occurs rarely
- if you have blistering or peeling of the skin - this occurs rarely
- the onset of skin reactions can occur at any time but most often occur in the first month of treatment; the reported rate of these events appears to be greater for valdecoxib, a medicine related to parecoxib, as compared to other COX-2 inhibitors
- if you have jaundice (your skin or the whites of your eyes appear yellow)
- if you have any signs of bleeding in the stomach or intestine, such as passing a black or blood-stained bowel movement or vomiting blood

Very common: may affect more than 1 in 10 people
- nausea (feeling sick)

Common: may affect up to 1 in 10 people
- change in your blood pressure (up or down)
- back pain
- swelling of the ankles, legs and feet (fluid retention)
- feeling numb - your skin may lose sensitivity to pain and touch
- vomiting, stomach ache, indigestion, constipation, bloating and wind
- tests may show abnormal kidney function
- feeling agitated or find it hard to sleep
- dizziness
- there is a risk of anaemia - changes in red blood cells after an operation that may cause fatigue and breathlessness
- sore throat or difficulty breathing (shortness of breath)
- itchy skin
- passing less urine than usual
- dry socket (inflammation and pain after a tooth extraction)
- increased sweating
- low levels of potassium in blood test results

Uncommon: may affect up to 1 in 100 people
- heart attack
- there is a risk of cerebrovascular disease e.g. stroke, or transient ischaemic attack (transient reduced blood flow to the brain)/mini-stroke or angina, or blockages to blood vessels to the heart or brain
- blood clot in the lungs
- worsening of high blood pressure
- ulcers in the digestive system, chronic stomach acid reflux
- the heart may beat more slowly
- low blood pressure on standing
- blood tests may show abnormal liver function
- bruising easily due to a low blood platelet count
- abnormal discharge from surgical wounds, surgical wounds may become infected
- skin discolouration or bruising
- complications with skin healing after operations
- high sugar levels in blood tests
- injection site pain or injection site reaction
- rash, or raised itchy rash (hives)
- anorexia (loss of appetite)
- joint pain
- high levels of blood enzymes in blood tests that indicate injury or stress to the heart, the brain, or muscle tissue dry mouth
- muscle weakness
- ear ache
- unusual abdominal sounds

Rare: may affect up to 1 in 1,000 people
- rash or ulceration in any part of your body (such as skin, mouth, eyes, face, lips or tongue), or any other signs of allergic reactions such as skin rash, swelling of the face, lips and tongue, wheezing, difficulty breathing or swallowing (potentially fatal)
- swelling, blistering or peeling of the skin
- acute kidney failure
- hepatitis (inflamed liver)
- inflammation of the gullet (oesophagus)
- inflammation of the pancreas (can lead to stomach pain)

Not known: frequency cannot be estimated from the available data
- collapse due to severe low blood pressure
- heart failure
- kidney failure
- racing or irregularity of the heartbeat
- breathlessness

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
For UK: Yellow Card Scheme
Website:
www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.
For IE: HPRA Pharmacovigilance,
Website: www.hpra.ie.
By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Parecoxib

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 carton and on the vial label after "EXP". The expiry date refers to the last day of that month.
This medicine does not require any special storage conditions.
It is recommended that Parecoxib is used as soon as possible after it is mixed with solvent, although it may be stored if the instructions at the end of the leaflet are strictly followed.

The injection solution should be a clear and colourless to almost colourless solution. **If there are particles** in the injection solution or if either the powder or solution is discoloured, the solution will not be used.

Do not throw away any medicines via wastewater. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Parecoxib contains
- The active substance is parecoxib.

Each vial contains 40 mg parecoxib (as 42.36 mg parecoxib sodium). After reconstitution with 2 mL solvent, each mL contains 20 mg of parecoxib.
- The other ingredients are: Disodium hydrogen phosphate anhydrous, phosphoric acid, sodium hydroxide.

What Parecoxib looks like and contents of the pack
Parecoxib is a powder for solution for injection.
White to off white powder contained in type I clear glass vials with 20 mm bromobutyl rubber stopper & aluminum flip off cap.

Pack sizes of 10 vials.

Marketing Authorisation Holder:
Noridem Enterprises Limited, Evagorou & Makariou, Mitsi Building 3, Office 115, 1065 Nicosia, Cyprus
Manufacturer:
DEMO S.A. PHARMACEUTICAL INDUSTRY, 21st Km National Road Athens-Lamia, 14568 Krioneri, Attiki, Greece

This medicine is authorised in the Member States of the European Economic Area and in the United Kingdom (Northern Ireland) under the following names:

Germany:	Parecoxib Noridem 40 mg Pulver zur Herstellung einer Injektionslösung
Greece:	COXIDEM 40 mg Κόνις για ενέσιμο διάλυμα
Ireland:	Parecoxib 40 mg Powder for solution for injection
Portugal:	Parecoxib Noridem 40 mg Pó para solução injetável
Sweden:	Parecoxib Noridem 40 mg Pulver till injektionsvätska, lösning
United Kingdom (Northern Ireland):	Parecoxib 40 mg Powder for solution for injection

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Remove the flip-off cap to expose the central portion of the rubber stopper of the powder vial. Withdraw with a sterile needle and syringe, 2 mL of an acceptable solvent and insert the needle through the central portion of the rubber stopper transferring the solvent into the powder vial.

Dissolve the powder completely using a gentle swirling motion. The reconstitution time is not more than 30 seconds. Inspect the reconstituted product before use.

The reconstituted solution should be a clear and colourless to almost colourless solution.

The reconstituted solution must not be used if discoloured or cloudy or if particulate matter is observed.

The entire contents of the vial should be withdrawn for a single administration. If a dose lower than 40 mg is required, excess medicine should be discarded.

IV line solution compatibility
Precipitation may occur when Parecoxib is combined in solution with other medicines and therefore Parecoxib must not be mixed with any other medicine, either during reconstitution or injection. In those patients where the same IV line is to be used to inject another medicine, the line must be adequately flushed prior to and after Parecoxib injection with a solution of known compatibility.

After reconstitution with acceptable solvents, Parecoxib may only be injected IV or IM, or into IV lines delivering the following:
- sodium chloride 9 mg / mL (0.9 %) solution for injection/ infusion
- glucose 50 mg / mL (5 %) solution for infusion
- sodium chloride 4.5 mg / mL (0.45 %) and glucose 50 mg / mL (5 %) solution for injection/infusion or
- Ringer-Lactate solution for injection

It is not recommended to inject into an IV line delivering glucose 50 mg / mL (5 %) in Ringer-Lactate solution for injection, or other IV fluids not listed in this section, as this may cause precipitation from solution.

The solution is for single use only. Chemical and physical in-use stability has been demonstrated for 12 hours at 5±3ºC or -20ºC and for 24 hours at 25±2°C, if diluted in 2 ml of sodium chloride 9 mg / mL (0.9 %), glucose 50 mg / mL (5 %) and sodium chloride 4.5 mg / mL (0.45 %) and glucose 50 mg / mL (5 %). From a microbiological point of you, the reconstituted solution should be used immediately. If not used immediately, in use storage times and conditions prior to use are in the responsibility of the user and would normally not be longer than 24 hours at 2-8°C, unless reconstitution has taken place in controlled and validated aseptic conditions.