Package leaflet: Information for the user

Dynastat 40 mg powder for solution for injection
parecoxib

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 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 Dynastat is and what it is used for

Dynastat contains the active substance parecoxib. Dynastat is used for the short-term treatment of pain in adults after an operation. It is one of a family 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*. Dynastat works by lowering the amount of these prostaglandins.

2. What you need to know before you use Dynastat

Do not use Dynastat:
- 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 (aspirin) 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

Do not use Dynastat if you currently have a gastric or intestinal ulcer or gastrointestinal bleeding

Do not use Dynastat if you have severe liver disease

Talk to your doctor or nurse before using Dynastat:

- If you have previously had an ulcer, bleeding or perforation of the gastrointestinal tract
- If you are taking acetylsalicylic acid (aspirin) 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 (e.g. acetylsalicylic acid)
- 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)

Dynastat 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 Dynastat.

Children and adolescents
Children and adolescents under the age of 18 should not be given Dynastat.

Other medicines and Dynastat
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 Dynastat or other medicines, or you may need to take a different medicine. It's especially important to mention:

- Acetylsalicylic acid (aspirin) 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 like medicines used to prevent blood clots including newer medicines like 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

Pregnancy, breast-feeding and fertility
- **If you are pregnant or trying to become pregnant**, tell your doctor. Dynastat is not recommended in the first 6 months of pregnancy and you must not receive Dynastat in the last three months of pregnancy.

- **If you are breast-feeding**, you must not receive Dynastat, as a small amount of Dynastat will be transferred to your breast milk.
- NSAIDs, including Dynastat, may make it more difficult to become pregnant. You should tell your doctor if you are planning to become pregnant or if you have problems becoming pregnant.

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or nurse for advice before taking this medicine.

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

Dynastat contains
This medicinal product contains less than 23 mg of sodium in each dose and therefore is essentially sodium-free.

3. How to use Dynastat

Dynastat will be given to you by a doctor or nurse. They will dissolve the powder before giving you the injection, and will inject the solution into a vein or a muscle. 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 Dynastat for short periods, and only for pain relief.

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

If you are given more Dynastat 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.

Stop taking Dynastat 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)
- You may get back pain
- Ankles, legs and feet may swell (fluid retention)
- You may feel numb - your skin may lose sensitivity to pain and touch
- You may get vomiting, stomach ache, indigestion, constipation, bloating and wind
- Tests may show abnormal kidney function
- You may feel 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
- You may get a sore throat or difficulty breathing (shortness of breath)
- Your skin may be itchy
- You may pass 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
- You may bruise easily due to a low blood platelet count
- Surgical wounds may become infected, abnormal discharge from surgical wounds
- 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 (e.g. 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 (see details below). By reporting side effects you can help provide more information on the safety of this medicine.

United Kingdom
Yellow Card Scheme at: www.mhra.gov.uk/yellowcard

Ireland
HPRA Pharmacovigilance
Earlsfort Terrace
IRL - Dublin 2
Tel: +353 1 6764971
Fax: +353 1 6762517
Website: www.hpra.ie
E-mail: medsafety@hpra.ie

Malta
ADR Reporting

www.medicinesauthority.gov.mt/adrportal

5. How to store Dynastat

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 prior to reconstitution.

It is recommended that Dynastat 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 colourless liquid. **If there are particles** in the injection solution or if either the powder or solution is discoloured, the solution will not be used.

6. Contents of the pack and other information

What Dynastat contains

- The active substance is parecoxib (as parecoxib sodium). Each vial contains 40 mg parecoxib, as 42.36 mg parecoxib sodium. When reconstituted with 2 ml solvent, provides 20 mg/ml of parecoxib. When reconstituted in sodium chloride 9 mg/ml (0.9%) solution, Dynastat contains approximately 0.44 mEq of sodium per vial.

- The other ingredients are:
  Disodium hydrogen phosphate
  Phosphoric acid and/or sodium hydroxide (for pH adjustment).

What Dynastat looks like and contents of the pack

Dynastat is available as a white to off-white powder.
The powder is contained in colourless glass vials (5 ml) with a stopper, sealed with a purple flip-off cap on the aluminium overseal.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder: Pfizer Limited, Sandwich, Kent CT13 9NJ United Kingdom

Manufacturer: Pfizer Manufacturing Belgium NV, Rijksweg 12, 2870 Puurs, Belgium

For any information about this medicinal product, please contact the local representative of the Marketing Authorisation Holder.

Malta
V.J. Salomone Pharma Ltd.
Tel: +356 21 22 01 74

Ireland
Pfizer Healthcare Ireland
Tel: 1800 633 363 (toll free)
+44 (0)1304 616161

United Kingdom
Pfizer Limited
Tel: +44 (0)1304 616161

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Detailed information on this medicine is available on the European Medicines Agency website: http://www.ema.europa.eu

Ref: DY 24_1

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 Dynastat 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 post-marketing 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
Modes 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. It is to be reconstituted only with one of the following:

- 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 lyophilised parecoxib (as parecoxib sodium).
40 mg vial: Remove the purple flip-off cap to expose the central portion of the rubber stopper of the parecoxib 40 mg 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 parecoxib 40 mg vial.

Dissolve the powder completely using a gentle swirling motion and inspect the reconstituted product before use.

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 Dynastat is combined in solution with other medicinal products and therefore Dynastat must not be mixed with any other drug, either during reconstitution or injection. In those patients where the same IV line is to be used to inject another medicinal product, the line must be adequately flushed prior to and after Dynastat injection with a solution of known compatibility.

After reconstitution with acceptable solvents, Dynastat 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 and must not be stored in a refrigerator or freezer.
Chemical and physical in-use stability of the reconstituted solution have been demonstrated for up to 24 hours at 25°C. Thus, 24 hours should be considered the maximum shelf life of the reconstituted product. However, due to the importance of microbiological infection risk for injectable products, the reconstituted solution should be used immediately unless reconstitution has taken place in controlled and validated aseptic conditions. Unless such requirements are met, in-storage times and conditions prior to use are the responsibility of the user, and would not normally be longer than 12 hours at 25°C.