

Package leaflet: Information for the user
Difene 75 mg Dual Release Capsules
(diclofenac sodium)

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 pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Difene is and what it is used for
2. What you need to know before you take Difene
3. How to take Difene
4. Possible side effects
5. How to store Difene
6. Contents of the pack and other information

1. What Difene is and what is it used for

Difene contains diclofenac sodium as the active ingredient which is a non-steroidal anti-inflammatory drug (NSAID). This means that it is a “painkilling” medicine which reduces inflammation and swelling, but it does not contain any steroid medicine. Difene is used to relieve pain and inflammation. It is used to relieve painful conditions associated with your bones and joints and to reduce swelling and inflammation (e.g. arthritis) and for sprains, strains and bruising of tendons and ligaments, acute gout and for period pain. It can also be used to reduce pain or inflammation after surgery.

2. What you need to know before you take Difene

Do not take Difene if you:

- are allergic (hypersensitive) to diclofenac or to any of the other ingredients of Difene, (listed in section 6).
- have ever had an allergic reaction (difficulty in breathing, skin rash and runny nose) to aspirin (acetylsalicylic acid) or any other NSAID such as ibuprofen.
- have or have ever suffered from a stomach ulcer or bleeding from the stomach.
- if you have been told that you have bleeding in the brain or other bleeding elsewhere.
- have had any gastrointestinal problems after taking any other NSAID e.g. vomiting blood or passing black, tarry stools.
- have severe heart failure.
- 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
- have or have had problems with your blood circulation (peripheral arterial disease)
- have severe kidney failure or liver failure.
- Difene should not be used in the last three months of pregnancy -please see section on ‘Pregnancy and breastfeeding.

Warnings and Precautions

Speak to your doctor before taking Difene if you:

- think you may be allergic to diclofenac sodium, aspirin, ibuprofen or any other NSAID, or to any of the other ingredients of Difene. (These are listed at the end of the leaflet.) Signs of a hypersensitivity reaction include swelling of the face and mouth (angioedema), breathing problems, chest pain, runny nose, skin rash or any other allergic type reaction
- if you have experienced asthma, allergic inflammation of the nasal airways
- if any skin rash develops such as hives or itchy skin
- if you have experienced symptoms of chronic obstructive pulmonary diseases (COPD), shortness of breath, persistent cough
- have high blood pressure
- have heart problems
- have mild to moderate heart failure
- have liver or kidney problems
- have severe liver or kidney disease
- suffer from porphyria
- suffer from any bowel problems such as ulcerative colitis or Crohn's disease
- suffer from an upset stomach or irritation of the gut
- have suffered from any blood or bleeding disorder such as haemophilia
- are pregnant or think you may become pregnant
- are breast feeding
- are elderly
- have peripheral arterial disease(signs and symptoms of this may be pain and numbness in the arms and legs)
- have cerebrovascular disease, this is a condition that develops as a result of problems with blood vessels in the brain. If you have a history of strokes or mini-strokes please speak to your doctor
- are taking Difene long-term or if you are a patient with severe liver impairment as you will need to undergo monitoring while taking Difene.
- if you have heart problems, previous strokes or think that you might be at risk of these conditions (for example if you have high blood pressure, diabetes, or high cholesterol or are a smoker) you should discuss your treatment with your doctor or pharmacist.
- have recently had major surgery

If any of these apply to you, tell your doctor or pharmacist. Your doctor will decide whether this medicine is suitable for you.

Make sure your doctor knows, before you are given diclofenac

- If you smoke
- If you have diabetes
- If you have angina, blood clots, high blood pressure, raised cholesterol or raised Triglycerides
- If you recently had or you are going to have a surgery of the stomach or intestinal tract, as Difene can sometimes worsen wound healing in your gut after surgery.

Any risk is more likely with high doses and prolonged treatment. Do not exceed the recommended dose or duration of treatment.

You may also be prescribed a medicine to protect the lining of stomach while taking diclofenac. Non-steroidal anti-inflammatory drug (NSAIDs) can cover the signs and symptoms of an infection. If you experience the onset or worsening of signs of infection, contact your doctor as you may require antibiotic therapy.

If you have asthma, hayfever (seasonal allergic rhinitis), swelling of the nasal mucosa (nasal polyps), narrowing of the airways (due to a condition known as chronic obstructive pulmonary disease) or

chronic infections of the respiratory tract (e.g. chest infections and especially allergic symptoms affecting the nose) you are more likely to experience reactions to NSAIDs (e.g. diclofenac). These reactions could include worsening of asthma (often referred to as intolerance to analgesics/analgesics asthma), development of hives on the skin and swelling of the eyes and lips and mucous membranes. You may be at greater risk of developing these reactions to NSAIDs if you are already allergic to, and have had reactions to, other substances. A doctor's supervision and extreme precaution is advised with the use of NSAIDs if you have any allergic condition as described here that could predispose you to an allergic reaction.

Side effects may be minimised by using the lowest effective dose for the shortest duration necessary.

Medicines such as diclofenac may be associated with a small increased risk of heart attack (“myocardial infarction”) or stroke.

Other medicines and Difene

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

If you are taking other medicines make sure your doctor is aware of them before you take Difene, particularly if they are any of the following:

- other anti-inflammatory or “painkilling” medicines (NSAIDs)
- water tablets (diuretics)
- steroids which are used as the main treatment for certain inflammatory conditions (corticosteroids)
- medicines used to thin blood, such as warfarin (anticoagulants)
- aspirin (anti-platelet agents)
- mood stabilising drugs such as lithium
- immunosuppressive agents, which are drugs that inhibit or prevent activity of the immune system (ciclosporine)
- medicines which may be used to treat cancer (methotrexate)
- medicines for heart conditions or high blood pressure (beta blockers, ACE inhibitors, digoxin)
- quinolone antibiotics (ciprofloxacin, ofloxacin)
- aminoglycosides antibiotics used in serious infections (streptomycin)
- tablets to treat diabetes
- medicines for the treatment of gout (probenecid)
- medicines for the treatment of depression (selective serotonin re-uptake inhibitors.)
- an anticoagulant such as heparin
- treatment of hypertension and congestive heart failure (angiotensin-receptor blockers)
- if taking tablets to relieve the symptoms of inflammation and pain (COX inhibitors)
- medicine for epilepsy (phenytoin)
- cholesterol medication (colestipol)
- medicine used to reduce bile acid (cholestyramine)
- medicine used for gout (sulfipyrazone)
- antifungal medication (voriconazole)

If you are presently taking any of these medicines and are unsure talk to your doctor or pharmacist.

Difene with food, drink and alcohol

As with other anti-inflammatory medicines, Difene may cause stomach upset. To reduce this effect swallow your Difene capsules whole with a glass of water or milk, either with or after a meal.

Taking Difene at the same time as alcohol can increase the risk and severity of side effects, especially those relating to the gut.

Pregnancy, breastfeeding and fertility

Difene may make it more difficult to become pregnant. You should inform your doctor if you are planning to become pregnant or if you have problems becoming pregnant.

Do not take Difene if you are in the last 3 months of pregnancy as it could harm your unborn child or cause problems at delivery. It can cause kidney and heart problems in your unborn baby. It may affect your and your baby's tendency to bleed and cause labour to be later or longer than expected. You should not take Difene during the first 6 months of pregnancy unless absolutely necessary and advised by your doctor. If you need treatment during this period or while you are trying to get pregnant, the lowest dose for the shortest time possible should be used. If taken for more than a few days from 20 weeks of pregnancy onward, Difene can cause kidney problems in your unborn baby, that may lead to low levels of amniotic fluid that surrounds the baby (oligohydramnios) or narrowing of a blood vessel (ductus arteriosus) in the heart of the baby. If you need treatment for longer than a few days, your doctor may recommend additional monitoring.

Do not use Difene if you are breast-feeding. This is because small amounts may pass into the mother's milk.

Ask your doctor for advice before taking any medicine.

Driving and using machines

Taking Difene should not affect your ability to drive or operate machinery. If in the unlikely event that you have dizziness or blurred vision do not drive or operate machinery.

Contains Sodium

This medicine contains less than 1 mmol sodium (23 mg) per capsule, that is to say essentially 'sodium-free'.

3. How to take Difene

Always take Difene exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

- Difene should be swallowed whole not chewed or crushed
- Take Difene capsules with or after food with a glass of water or milk
- It is important that you use the lowest dose that controls your pain and you should not use Difene for longer than necessary
- If two capsules are taken in one day, the dose should be divided (e.g., one in the morning and one in the evening). Never take two Difene 75mg capsules in a single dose.

Adults:

The usual dose is one to two capsules daily. The dose should not exceed 150mg daily.

Elderly:

The dosage should be kept as low as possible.

Children:

Use in children and adolescents is not recommended

If you take more than you should

If you take too many Difene capsules, tell your doctor or hospital emergency department at once. Take your medicine with you.

If you forget to take Difene

If you forget to take a dose, take one as soon as you remember. Do not double up on the next dose to make up for the one missed. Do not take more than 150 mg in 24 hours.

If you stop taking Difene

Your doctor will decide how long you will take this medicine. Your doctor has carefully chosen the correct dosage for you taking into account the severity of your condition, your age and any other reasons special to you, therefore you should always take the dose prescribed. If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, Difene can cause side effects, although not everybody gets them, these may occur in the initial stages of treatment and may be more serious if they occur in the elderly.

If the following happens at any time during your treatment, stop taking the capsules and tell your doctor immediately or go to the casualty department at your nearest hospital:

- an allergic reaction (swelling of the lips, face or neck leading to severe difficulty in breathing, skin rash or hives)
- passing blood in your faeces (stools/motions)
- passing black tarry stools
- vomiting any blood or dark particles that look like coffee grounds
- a serious illness with blistering of the skin, mouth, eyes and genitals (Stevens-Johnson syndrome)
- indigestion or heartburn
- abdominal pain (pains in your stomach) or other abnormal stomach symptoms.
- mild cramping and tenderness of the abdomen, starting shortly after the start of treatment with Difene and followed by rectal bleeding or bloody diarrhoea usually within 24 hours of the onset of the abdominal pain (frequency not known, cannot be estimated from the available data)
- chest pain, which can be a sign of a potentially serious allergic reaction called Kounis syndrome

Very common ($\geq 1/10$);

Common ($\geq 1/100$ to $< 1/10$)

Uncommon ($\geq 1/1,000$ to $< 1/100$)

Rare ($\geq 1/10,000$ to $< 1/1,000$)

Very Rare ($< 1/10,000$)

Not Known (cannot be estimated from available data).

Common:

- Headache, dizziness, agitation
- Vertigo
- Nausea, vomiting, diarrhoea, indigestion, flatulence, abdominal pain, loss of appetite
- Skin rash
- Increased levels of serum glutamic oxaloacetic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGTP), enzymes that are normally present in liver and heart cells, SGOT and SGTP are released into blood when the liver or heart are damaged.

Rare:

- Allergic reactions (e.g. difficulties in breathing, wheezing or low blood pressure)
- Drowsiness, tiredness
- Asthma, shortness of breath
- Inflammation of the lining of the stomach
- Any sign of bleeding in the stomach or intestine, for example, when emptying your bowels
- Gastro-intestinal ulcers with or without bleeding
- Yellowing of your skin or the whites of your eyes (hepatitis or liver function disorders)
- Hives
- Fluid retention

Very Rare:

- Blood disorders such as low red blood cell count (anaemia), low white blood cell count or low platelet count. Signs of a blood disorder could include fever, sore throat, blisters in the mouth, flu-like symptoms, severe exhaustion, nosebleeds or bleeding into the skin
- Rapid swelling, including swelling of the face
- Disorientation, depression, insomnia, nightmares, irritability, psychotic disorder
- Sensation of tingling, pricking, or numbness of skin
- Impaired memory
- Convulsions, tremors
- Anxiety
- Symptoms of aseptic meningitis with neck stiffness, headaches, nausea, vomiting or clouding of consciousness
- Impaired sense of taste
- Loss of appetite
- Lesions in the food pipe
- Stroke
- Visual disturbances (blurred and double vision)
- Hearing loss, tinnitus (ringing in the ears)
- Palpitations, chest pain
- Cardiac failure
- Heart attack
- High blood pressure
- Inflammatory destruction of blood vessels, symptoms of which can be fever and weight loss
- Inflammation of lung tissue
- Swelling of the large intestine
- Crohn's disease
- Inflammation of the pancreas
- Constipation
- Inflammation of the mucous lining in the mouth
- Swollen tongue and colour change of the tongue
- Reflux, heartburn
- Fulminant hepatitis
- Liver failure
- Eczema
- Reddening of the skin
- Skin diseases known as Steven Johnson syndrome and Lyell's, which are the detachment of top layers of skin from bottom layers.
- Inflammation of scaling of skin
- Loss of hair
- Photosensitivity reactions, abnormal responses to sunlight or artificial light
- Purpura, the appearance of red or purple discolouration on the skin
- Allergic reaction of unknown origin causing red patches on the skin

- Kidney failure, signs and symptoms of this are bloody stools, fatigue, bruising easily and fluid retention
- Blood in the urine
- Excess protein in your urine which can cause your urine to become foamy
- Nephrotic syndrome, which is a disorder in which the kidneys can become damaged the most common signs of this are weight gain due to excess fluid retention, swelling and foamy urine
- Interstitial nephritis, which is a kidney disorder in which the spaces between the kidney tubules become swollen (inflamed). Some symptoms of this condition may be blood in urine, fever, nausea and vomiting
- Renal papillary necrosis, which is a disorder of the kidneys, symptoms of this may be back pain blood in urine, cloudy urine

Gastrointestinal bleeding associated with this product can be fatal.

If you have a rare disease called systemic lupus erythematosus, you might be at increased risk of some of the side effects of Difene, such as skin reactions, allergic reactions, damage to the liver and aseptic meningitis.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly to:

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

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

Do not store above 25°C. Do not use Difene after the expiry date which is stated on the label and carton.

The expiry date refers to the last day of the month. Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What Difene contains

The active substance is diclofenac sodium 75 mg (25 mg as gastro-resistant pellets and 50 mg as prolonged-release pellets). The other ingredients are microcrystalline cellulose, gelatin, povidone, talc, methacrylic acid ethylacrylate copolymer, ammonio methacrylate copolymer, colloidal anhydrous silica, propyleneglycol, triethylcitrate, sodium hydroxide, titanium dioxide E171, indigo carmine E132 and shellac.

What Difene looks like and contents of the pack

Difene capsules are modified release hard gelatin capsules with a light blue opaque cap and a colourless transparent body printed with "D75M" in white, containing white to cream pellets. Difene capsules are available in packs of 4 and 56 capsules on prescription from your doctor.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:

Glenwood GmbH
Pharmazeutische Erzeugnisse
Arabellastraße 17
81925 Munich
Germany

Manufacturer:

Swiss Caps GmbH, Grassingerstraße 9, 83043 Bad Aibling, Germany

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

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