

PATIENT INFORMATION LEAFLET

FLEXO® 1g/2ml I.M Solution for Injection

Given as an injection into the muscle.

- **Active substance:** Each 2 ml ampoule contains 1 g of etofenamate.
- **Excipients:** Medium-chain triglycerides.

Read all of this PATIENT INFORMATION LEAFLET carefully before you start taking this medicine, because it contains useful information for you.

- *Keep this leaflet. You may need to read it again.*
- *If you have further questions, please ask your doctor or pharmacist.*
- *This medicine has been prescribed for you personally and you should not pass it on to others.*
- *When you see a doctor or go to hospital while you are on the drug, tell your doctor that you are using this medicine.*
- *Precisely follow the instructions included in this leaflet. Do not use any dose **higher or lower** than what was prescribed for you.*

In This Leaflet:

1. *What FLEXO® is and what it is used for*
2. *What you need to know before you take FLEXO®*
3. *How to take FLEXO®*
4. *Possible side effects*
5. *How to store FLEXO®*

1. What FLEXO® is and what it is used for

FLEXO® is presented as colorless glass ampoules containing 2 ml of clear and viscous solution for administration into a muscle. It is available in packs of 1 ampoule or 3 ampoules.

FLEXO® contains etofenamate as the active substance.

Etofenamate is an active substance belonging to the group of nonsteroidal analgesic/anti-rheumatic agents and has inflammation relieving (anti-inflammatory), pain relieving (analgesic) properties.

It is used in the treatment of the following conditions:

- Degenerative joint disease, joint arthritis (osteoarthritis)
- Rheumatic disease associated with inflammation of the joints (rheumatoid arthritis)
- A rheumatic disease associated with fusion of the spine and loss of motion in the joints of the spine (ankylosing spondylitis)
- An inflammation of the joints manifesting itself with sudden onset of severe pain in an inflamed joint, usually starting in the big toe, causing severe pain, tenderness, redness and swelling in the joints (acute gouty arthritis)
- Acute musculoskeletal system pains
- Inflammation, swelling and soft tissue injury seen after surgery (postoperative pain)
- Menstrual pain (dysmenorrhea)

Note: The solution for injection is used only for conditions where local application of etofenamate is not useful or suitable. As a rule, treatment should be limited to a single injection.

Due to slow release of its active ingredient, FLEXO[®] is not suitable for initiation of treatment in conditions requiring a rapid onset of action.

Due to slow release of the active ingredient from the oily formulation, the duration of action may be extended up to 24 hours after FLEXO[®] administration.

2. What you need to know before you take FLEXO[®]

Consult your doctor or pharmacist before taking any medicine.

Do NOT take FLEXO[®] in case of the following conditions

Heart-Vascular System Risk:

NSAIDs or pain relievers may cause an increased risk of serious thrombotic events related to heart-vascular system, heart attack, and stroke, which can be fatal. This risk may increase with duration of use. Patients with heart-vascular disease or risk factors for heart-vascular disease may be at greater risk

FLEXO[®] should not be used for treatment of pain in the preparation of coronary artery bypass graft surgery.

Stomach-Intestinal System Risk:

NSAIDs or pain relievers cause an increased risk of serious stomach or intestinal adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients are at greater risk for serious stomach-intestinal events

- If you have hypersensitivity to etofenamate or to any of the ingredients of FLEXO[®].
- If you previously experienced asthma, wheezing, runny nose, urticaria, or allergic-type reactions associated with the use of aspirin or other non-steroidal anti-inflammatory drug.
- If you have or have ever had ulcers or bleeding in the stomach or intestines.
- If you are going to have an operation for vessels supplying the heart (coronary arteries)
- If you taking medicines that prevent blood clotting or blood thinners (anticoagulant or antithrombotic)
- If you have serious heart insufficiency
- If you have liver or kidney insufficiency
- If you are in the late stages of pregnancy (after sixth month)
- If you are breast feeding
- If you are under 18 years of age

Take SPECIAL CARE with FLEXO[®] in case of the following conditions

Conditions where FLEXO[®] should be used only after careful assessment of risk-benefit ratio:

- If you are suffering from porphyria can be triggered (congenital or acquired disorder of the substance that gives blood its color; acute attacks of this disease can be triggered by certain substances)

Conditions where FLEXO[®] should be used only under careful medical monitoring:

- If you have had stomach-intestinal bleeding or perforation associated with NSAIDs or pain relievers
- If you have active or previous history of stomach or duodenal ulcer or bleeding (one or two episodes of proven ulceration or bleeding)
- If you have or have had inflammatory bowel disease (ulcerative colitis, Crohn's disease)

- If you have heart or vascular disorder
- If you suffer from high blood pressure (hypertension)
- If you have heart disease or edema problems
- If you have had stroke
- If you have had recent surgery
- If you are over 65 years of age or have a debilitating disorder

Please consult your doctor if any of the above applies to you, even at any time period in the past.

Taking FLEXO® with food and drink

There is no interaction with food and drink regarding method of administration.

Pregnancy

Consult your doctor or pharmacist before taking this medicine.

FLEXO® is not used after the sixth month of pregnancy. Before this period also, do not take FLEXO® unless your doctor tells that you must take it.

Consult your doctor or pharmacist immediately if you find out you are pregnant during your treatment.

Breastfeeding

Consult your doctor or pharmacist before taking this medicine.

Do not take FLEXO® during breastfeeding

Driving and using machines

FLEXO® may affect your attention especially during the beginning of your treatment or when your dose is increased.

Do not drive and use machines if you are taking FLEXO®.

Concomitant use with other medicines

Do not take FLEXO® with the following medicines.

- Aspirin and other NSAIDs

FLEXO® should be used with caution with the following medicines.

- Angiotensin converting enzyme (ACE) inhibitors (used to treat high blood pressure)
- Furosemide and diuretics (water pills)
- Antihypertensives (high blood pressure lowering drugs)
- Lithium (used for the treatment of mania and depression)
- Methotrexate (used in the treatment of rheumatoid arthritis, and some cancers)
- Medicines that prevent blood clotting or thin blood such as warfarin and similar drugs
- Digoxin (used for the treatment of heart failure)
- Phenytoin (used for the treatment of epilepsy)
- Corticosteroids (a group of drugs used in quite a wide range of conditions including inflammation, allergy, or organ transplantation)
- Potassium-sparing diuretics
- Selective serotonin reuptake inhibitors (SSRIs) (used to treat depression)
- Probenecid or sulfinpyrazone (used to reduce increased uric acid levels in the blood)

- Alcohol
- Cyclosporine (used to prevent tissue rejection)
- Antidiabetic drugs (used to lower blood sugar)

Please tell your doctor or pharmacist about any medicines, prescription or non-prescription, you are currently taking or have recently taken.

3. How to take FLEXO®

Instructions for proper use and dosage/frequency of administration:

Your doctor will determine the dose of FLEXO® depending on your illness and administer it to you. General usage dosage is one FLEXO® ampoule with deep injection into the muscle.

If it is considered to continue etofenamate treatment, your doctor may tell you that after the administration of FLEXO® ampoule you may continue treatment with FLEXO® gel or FLEXO® spray which you can apply topically.

Route and method of administration:

FLEXO® ampoule is for administration into the muscle. After breaking the ampoule, the solution for injection is withdrawn into a syringe and is injected deeply into the muscle with a sufficiently long injection needle. Before injecting the solution, the plunger of the syringe is withdrawn slightly to ensure that a blood vessel has not been entered.

Due to the possibility of anaphylactic reactions (sudden onset of severe allergy) may need to be monitored for at least 1 hour after FLEXO® injection.

Different age groups

Use in children:

Since there is no experience with etofenamate in children and adolescents, FLEXO® should not be used in patients under 18 years of age.

Use in the elderly (65 years and older):

Because of the possible adverse effects, FLEXO® should be used with caution in elderly patients.

Special use conditions:

Kidney/Liver impairment:

Do not use FLEXO® if you have kidney and/or liver impairment.

Talk to your doctor or pharmacist if you have an impression that the effect of FLEXO® is too strong or too weak.

If you take more FLEXO® than you should

Contact a doctor or pharmacist if you take more FLEXO® than you should.

If you use more FLEXO® than required, the drug's adverse effects and their severity may increase. If an overdose of FLEXO® is administered, central nervous system effects including headache, dizziness, drowsiness, and confusion as well as symptoms such as nausea, vomiting, abdominal pain may occur. In addition, gastrointestinal bleeding, and liver and kidney dysfunction may occur. Your doctor or pharmacist will help you if you experience these symptoms.

If you forget to take FLEXO®

Do not take a double dose to make up for a forgotten dose.

The effects that may occur if treatment with FLEXO® is stopped.

Any effect is unlikely to occur.

4. Possible side effects

Like all medicines, side effects may occur in persons who are sensitive to the ingredients of FLEXO®.

Very common ($> 1/10$) May affect at least 1 in 10 patients.

Common ($\geq 1/100$ to $< 1/10$) May affect less than 1 in 10 patients, but more than 1 in 100 patients.

Uncommon ($\geq 1/1000$ to $< 1/100$) May affect less than 1 in 100 patients, but more than 1 in 1.000 patients.

Rare ($\geq 1/10.000$ to $< 1/1000$) May affect less than 1 in 1.000 patients, but more than 1 in 10.000 patients.

Very rare ($< 1/10.000$) May affect less than 1 in 10.000 patients.

Not known: Frequency cannot be estimated from the available data.

Stop taking FLEXO® and tell your doctor IMMEDIATELY or go to the emergency department at your nearest hospital if any of the following happens:

- Severe forms of skin reactions (Stevens-Johnson syndrome, Lyell syndrome)
- Severe hypersensitivity reactions are likely and the following can be seen:

When one of the serious allergic reaction-like symptoms associated with swelling of the face, tongue and throat, skin rash, wheezing, difficulty breathing, laryngeal edema narrowing the airway, difficulty in breathing which leads to asthma attack, increased heart rate, a drop in blood pressure leading to potentially fatal shock, fever or shock occur.

These reactions may be seen when the drug is used for the first time.

All of these are very serious side effects.

If you notice any side effects not mentioned in this leaflet, please tell your doctor or pharmacist.

It should be kept in mind that the following undesirable effects are dose-dependent and may vary from person to person.

The most commonly observed adverse events are digestive in nature. Stomach-intestinal ulcer (peptic ulcer), perforation or stomach-intestinal bleeding, some times fatal, particularly in the elderly, may occur. Nausea, vomiting, diarrhea, flatulence, constipation, digestive problems, abdominal pain, darkening of the stool, blood vomiting, mouth ulcers, exacerbation of colitis and Crohn's disease have been reported following administration. Less frequently, inflammation in the stomach has been observed. Generally the risk for gastrointestinal bleeding is dependent on the duration of treatment with NSAIDs and the dose range used.

Edema, high blood pressure and heart failure associated with NSAID treatment have been reported.

Medicines such as FLEXO® may be associated with a small increase in risk for heart attack (myocardial infarction or stroke).

Undesirable effects reported for intramuscular etofenamate:

Common side effects:

Gastrointestinal symptoms such as nausea, vomiting, diarrhea, and mild gastrointestinal blood loss which can lead to anemia in exceptional cases.

Uncommon side effects:

Headache, excitation, irritability, fatigue, drowsiness and dizziness

Digestive disturbances, flatulence, abdominal cramps, loss of appetite, stomach and duodenal ulcers (sometimes associated with bleeding and perforation)

Hypersensitivity reactions such as skin rash and itching

Elevations in blood liver enzymes (serum transaminases)

Rare side effects:

Blood production disorders Hematopoietic disorders (anemia, leucopenia, agranulocytosis, thrombocytopenia). The initial symptoms include fever, sore throat, superficial lesions in the mouth, flu-like symptoms, severe fatigue, nose bleeds and bleeding in the skin. Blood picture of patients receiving long-term therapy should be monitored at regular intervals.

Blood in the vomit, stool or diarrhea

Urticaria and/or hair loss

Liver damage (hepatitis with or without jaundice, in very rare cases fulminant, and without prodromal symptoms rarely) Therefore, liver values of the patient should be monitored periodically.

Edema (peripheral edema) may occur especially in patients with high blood pressure (hypertension) or in patients with impaired kidney function.

Very rare side effects:

Palpitations, chest pain, high blood pressure and circulatory collapse

Heart failure

Hemolytic anemia

Sensory disturbance, taste disturbances, ringing in the ears and temporary hearing impairment, memory loss, disorientation, convulsions, anxiety, nightmares, tremor, depression and other psychotic reactions.

Inflammations in oral mucosa, tongue, esophageal lesions, lower abdominal complaints (e.g. hemorrhagic colitis or exacerbation of Crohn's disease/ulcerative colitis) and constipation.

Visual disturbances (blurred vision and/or double vision)

Skin rash with fluid-filled blisters, eczema, redness, sensitivity to light, flares (also allergic purpura)

In sporadic cases: Renal tissue damage which may be accompanied by acute renal failure (interstitial nephritis, papillary necrosis), protein in urine (proteinuria) and/or blood in urine (hematuria).

Nephritic syndrome may develop in isolated cases. Therefore, kidney function should be checked regularly.

Inflammations of the pancreas have been reported in isolated cases.

In isolated cases, allergy-related inflammations of the lungs and blood vessels have been observed.

In isolated cases, infection-related inflammation may worsen upon administration of nonsteroidal anti-inflammatory drugs (development of necrotizing fasciitis). This is probably associated with the mechanism of action of nonsteroidal anti-inflammatory drugs. Therefore, consult your doctor immediately if you develop symptoms related to a new infection or if existing symptoms worsen when you use FLEXO®. Need for any antibiotic or anti-infectious therapy should be evaluated.

After intramuscular administration, uncommon local side effects at the injection site (burning sensation) or tissue injury (such as sterile abscess formation, fatty tissue or skin necrosis) may occur.

For the above-mentioned side effects, please consider the suggestions listed.

If you notice any side effects not mentioned in this leaflet, please tell your doctor or pharmacist.

5. How to store FLEXO®

Keep FLEXO® out of the reach and sight of children and in the original package.

Store at room temperature below 25°C. Protect from light.

Use in line with the expiry date.

Do not use FLEXO® after the expiry date which is stated on the package.

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