APPROVED
Order of the Ministry of Health of Ukraine
_____ No. _____
Marketing Authorization
No. _____

INSTRUCTION
for medical use of the drug product

ELIPROB

Composition:
active substance: meloxicam;
1.5 mL of solution contains meloxicam 15 mg;
excipients: meglumine, glycofurol, poloxamer 188, glycine, sodium chloride, 1M sodium hydroxide solution, water for injection.

Dosage form. Solution for injection.
Main physicochemical properties: transparent yellow greenish solution, practically free from particles

Pharmacotherapeutic group. Nonsteroidal anti-inflammatory and antirheumatic drugs. Oxicams.
ATC code M01A C06.

Pharmacological properties
Pharmacodynamics
ELIPROB is a nonsteroidal anti-inflammatory drug (NSAID) of the oxicam class, which has anti-inflammatory, analgesic and antipyretic effects.
Meloxicam has shown high anti-inflammatory activity in all standard models of inflammation. As with other NSAIDs, its exact mechanism of action remains unknown. However, there is a common mechanism of action for all NSAIDs (including meloxicam): inhibition of the biosynthesis of prostaglandins, which are inflammation mediators.

Pharmacokinetics
Absorption. Meloxicam is completely absorbed after intramuscular injection. The relative bioavailability compared to oral administration is almost 100%. Therefore, dose adjustment is not required when switching from the intramuscular to the oral method of administration. After an intramuscular injection of 15 mg, the maximum plasma concentration is about 1.6–1.8 μg/mL and is reached in 1–6 hours.
Distribution. Meloxicam is very strongly bound to plasma proteins, mainly albumin (99%). Meloxicam penetrates the synovial fluid, where its concentration is half that in plasma. The distribution volume is low, on average 11 L after intramuscular or intravenous administration, and shows individual deviations of 7–20%. The distribution volume after multiple oral doses of meloxicam (7.5 to 15 mg) is 16 L with a coefficient of variation ranging from 11% to 32%.
Biotransformation. Meloxicam undergoes extensive biotransformation in the liver.
Four different metabolites of meloxicam, which are pharmacodynamically inactive, have been identified in the urine. The main metabolite, 5'-carboxymeloxicam (60% of the dose), is formed by oxidation of the intermediate metabolite, 5’-hydroxymeloxicam, which is also excreted to a lesser extent (9% of the dose). *In vitro* studies suggest that CYP 2C9 plays an important role in

the metabolism process, while the CYP 3A4 isoenzyme is involved to a lesser extent. Peroxidase activity in patients is probably responsible for the other two metabolites, which account for 16% and 4% of the administered dose, respectively.
Elimination. Meloxicam is eliminated mainly in the form of metabolites in equal parts with urine and feces. Less than 5% of the daily dose is excreted unchanged in the feces; a small amount is excreted in the urine. The half-life is 13 to 25 hours depending on the method of administration (oral, intramuscular, or intravenous). Plasma clearance is about 7-12 mL/min after a single oral, intravenous or rectal administration.
Dose linearity. Meloxicam demonstrates linear pharmacokinetics within the therapeutic dose range of 7.5 mg to 15 mg after oral and intramuscular administration.
Special patient populations
Patients with hepatic/renal impairment. Mild to moderate hepatic and renal impairment do not significantly affect the pharmacokinetics of meloxicam. Patients with moderate renal impairment had a significantly higher total clearance. Reduced binding to plasma proteins was observed in patients with end-stage renal failure. In end-stage renal failure, an increase in the volume of distribution may lead to an increase in the concentration of free meloxicam (see sections "Posology and method of administration" and "Contraindications").
Elderly patients. In elderly male patients, the mean pharmacokinetic parameters are similar to those in young male volunteers. In elderly female patients, AUC values are higher and the half-life is longer compared to the corresponding values in young volunteers of both sexes. The mean steady-state plasma clearance in elderly patients was slightly lower than in young volunteers (see section "Posology and method of administration").

Clinical particulars
Therapeutic indications. ELIPROB, solution for injection, is indicated in adults for the short-term symptomatic treatment of acute attacks of rheumatoid arthritis and ankylosing spondylitis when other methods of administration cannot be used.

Contraindications.
- 3rd trimester of pregnancy (see section "Use during pregnancy and breastfeeding");
- Patient age below 18;
- Hypersensitivity to the active substance or to any of the other ingredients of the drug product;
- Hypersensitivity to active substances with similar effects, such as NSAIDs, aspirin. Meloxicam should not be prescribed to patients who have developed symptoms of asthma, nasal polyps, angioedema or urticaria after taking aspirin or other NSAIDs;
- Gastrointestinal bleeding or perforation associated with previous NSAID therapy in history;
- Active or recurrent peptic ulcer/bleeding in history (two or more separate confirmed cases of ulceration or bleeding);
- Severe hepatic failure;
- Severe renal failure, when not on dialysis;
- Gastrointestinal bleeding, history of cerebrovascular bleeding or other blood clotting disorders;
- Hemostatic disorders or concomitant use of anticoagulants (contraindications related to the route of administration);
- Severe heart failure.

Do not use the drug product for the treatment of perioperative pain in coronary artery bypass grafting (CABG).

Interaction with other medicinal products and other forms of interaction
Risks associated with hyperkalemia

Some drugs or therapeutic classes of drugs may contribute to hyperkalemia: potassium salts, potassium-sparing diuretics, angiotensin converting enzyme (ACE) inhibitors, angiotensin II receptor antagonists, non-steroidal anti-inflammatory drugs, heparins (low molecular weight or unfractionated), cyclosporine, tacrolimus, and trimethoprim.
The development of hyperkalemia may depend on the presence of associated factors. The risk of hyperkalemia is increased when the above-mentioned drugs are used concomitantly with meloxicam.
Pharmacodynamic interactions
Other non-steroidal anti-inflammatory drugs (NSAIDs) and acetylsalicylic acid ≥ 3 g/day. Combination with other NSAIDs (see section "Special warnings and precautions for use"), acetylsalicylic acid in doses ≥ 500 mg per dose or ≥ 3 g total daily dose is not recommended.
Corticosteroids (e.g. glucocorticoids). Concomitant use with corticosteroids requires caution due to increased risk of bleeding or ulceration in the gastrointestinal tract.
Anticoagulants or heparin. The risk of bleeding is significantly increased due to inhibition of platelet function and damage to the gastroduodenal mucosa. NSAIDs may enhance the effects of anticoagulants such as warfarin (see section "Special warnings and precautions for use"). Concomitant use of NSAIDs and anticoagulants or heparin is not recommended in geriatric practice or in therapeutic doses. Due to intramuscular administration, meloxicam solution for injection is contraindicated in patients receiving anticoagulant treatment (see sections "Contraindications" and "Special warnings and precautions for use").
In other cases of heparin administration (e.g. in prophylactic doses) caution is required due to the increased risk of bleeding.
Thrombolytic and antiplatelet drugs. The risk of bleeding is increased due to inhibition of platelet function and damage to the gastroduodenal mucosa.
Selective serotonin reuptake inhibitors (SSRIs). The risk of gastrointestinal bleeding is increased.
Diuretics, ACE inhibitors and angiotensin II antagonists. NSAIDs may reduce the effect of diuretics and other antihypertensive drugs. In some patients with impaired renal function (e.g. dehydrated patients or elderly patients), concomitant use of ACE inhibitors or angiotensin II antagonists and drugs that inhibit cyclooxygenase may lead to further deterioration of renal function, including acute renal failure, which is usually reversible. Therefore, this combination should be used with caution, especially in elderly patients. Patients should be adequately hydrated and renal function should be monitored after initiation of concomitant therapy and periodically thereafter (see section "Special warnings and precautions for use").
Other antihypertensive drugs (e.g. beta-blockers). The antihypertensive effect of beta-blockers may be reduced (due to inhibition of vasodilatory prostaglandins).
Calcineurin inhibitors (e.g. cyclosporine, tacrolimus). Nephrotoxicity of calcineurin inhibitors may be potentiated by NSAIDs through mediation of the effects of renal prostaglandins. Renal function should be monitored during treatment. Close monitoring of renal function is recommended, especially in elderly patients.
Deferasirox. Concomitant use of meloxicam and deferasirox increases the risk of gastrointestinal adverse reactions. Caution should be exercised when combining these drugs.
Pharmacokinetic interactions: effect of meloxicam on the pharmacokinetics of other drugs
Lithium. There are reports of NSAIDs increasing plasma lithium concentrations (by reducing renal lithium excretion) which may reach toxic levels. Concomitant use of lithium and NSAIDs is not recommended (see section "Special warnings and precautions for use"). If combination therapy is necessary, careful monitoring of plasma lithium levels is recommended at the start of treatment, during dose adjustment and when meloxicam is discontinued.
Methotrexate. NSAIDs may reduce the tubular secretion of methotrexate, thereby increasing its plasma concentrations. For this reason, concomitant use of NSAIDs is not recommended in patients receiving high doses of methotrexate (more than 15 mg/week) (see section "Special warnings and precautions for use"). The risk of interaction between NSAIDs and methotrexate should also be considered in patients receiving low doses of methotrexate, including patients

with renal impairment. If combined treatment is necessary, blood counts and renal function should be monitored. Caution should be exercised when NSAIDs and methotrexate are administered for 3 consecutive days, as plasma levels of methotrexate may raise and toxicity may be increased. Although the pharmacokinetics of methotrexate (15 mg/week) was not affected by concomitant treatment with meloxicam, it should be considered that the hematological toxicity of methotrexate may be increased by treatment with NSAIDs (see above and also section "Adverse reactions").
Pemetrexed. When meloxicam is co-administered with pemetrexed in patients with creatinine clearance between 45 and 79 mL/min, meloxicam should be discontinued 5 days before, on the day of, and for 2 days after pemetrexed administration. If the combination of meloxicam and pemetrexed is necessary, patients should be closely monitored, particularly for myelosuppression and gastrointestinal adverse reactions. In patients with severe renal impairment (creatinine clearance below 45 mL/min), concomitant use of meloxicam and pemetrexed is not recommended.
In patients with normal renal function (creatinine clearance ≥ 80 mL/min), doses of meloxicam 15 mg may reduce the elimination of pemetrexed and therefore increase the incidence of adverse reactions associated with pemetrexed. Therefore, caution should be exercised when prescribing meloxicam 15 mg concomitantly with pemetrexed in patients with normal renal function (creatinine clearance ≥ 80 mL/min).
Pharmacokinetic interactions: effect of other medicinal products on the pharmacokinetics of meloxicam
Cholestyramine accelerates the elimination of meloxicam by impairing intrahepatic circulation, resulting in a 50% increase in meloxicam clearance and a reduction in the half-life to 13 ± 3 hours. This interaction is clinically relevant.
Pharmacokinetic interactions: effect of the combination of meloxicam and other medicinal products on pharmacokinetics
Oral antidiabetic drugs (sulfonylurea derivatives, nateglinide)
Meloxicam is almost completely eliminated by hepatic metabolism, approximately two-thirds of which is mediated by cytochrome (CYP) P450 enzymes (primary CYP 2C9 and minor CYP 3A4) and one-third by other pathways, such as peroxidase oxidation. The possibility of pharmacokinetic interactions should be considered when meloxicam is co-administered with drugs that are known to inhibit or are metabolized by CYP 2C9 and/or CYP 3A4. CYP 2C9-mediated interactions can be expected with drugs such as oral antidiabetic drugs (sulfonylurea derivatives, nateglinide). This interaction may lead to increased plasma levels of these drugs and meloxicam. Patients taking meloxicam and sulfonylurea derivatives or nateglinide should be closely monitored for hypoglycemia.
No clinically significant pharmacokinetic interactions have been observed with concomitant administration of antacids, cimetidine, and digoxin.
Pediatric population
Interaction studies have only been conducted in adults.

Special warnings and precautions for use
Adverse reactions can be minimized by taking the lowest effective dose for the shortest duration necessary to control symptoms (see section "Posology and method of administration" and information on gastrointestinal and cardiovascular risks below).
The recommended maximum daily dose should not be exceeded in case of insufficient therapeutic effect, nor should additional NSAIDs be used, as this may increase toxicity while the therapeutic benefit has not been proven. Concomitant use of meloxicam with NSAIDs, including selective cyclooxygenase-2 inhibitors, should be avoided.
Meloxicam should not be used to treat patients who require relief of acute pain.
If there is no improvement after several days, the clinical benefit of treatment should be reassessed.

A history of esophagitis, gastritis and/or peptic ulcer should be considered to ensure that they have been completely treated before initiating therapy with meloxicam. Patients who have been treated with meloxicam and patients with a history of such disorders should be monitored regularly for recurrence.

Gastrointestinal disorders

As with other NSAIDs, potentially fatal gastrointestinal bleeding, ulceration or perforation may occur at any time during treatment, with or without previous symptoms or a history of serious gastrointestinal diseases.

The risk of gastrointestinal bleeding, ulceration or perforation is greater with increasing NSAID doses in patients with a history of ulcer, particularly if complicated by bleeding or perforation (see section "Contraindications"), and in the elderly. In such patients, treatment should be initiated at the lowest effective dose. For these patients, combination therapy with protective drugs (such as misoprostol or proton pump inhibitors) should be considered. This also applies to patients who require concomitant use of low-dose aspirin or other drugs that increase gastrointestinal risks (see information below and also section "Interaction with other medicinal products and other forms of interaction").

Patients with a history of gastrointestinal toxicity, particularly elderly patients, should be advised to report any unusual abdominal symptoms (especially gastrointestinal bleeding), particularly during the initial stages of treatment.

Administration of meloxicam is not recommended in patients receiving concomitant drugs that increase the risk of ulceration or bleeding, such as heparin, as a radical therapy or in geriatric practice, anticoagulants such as warfarin, other non-steroidal anti-inflammatory drugs, acetylsalicylic acid in doses ≥ 500 mg per dose or ≥ 3 g total daily dose (see section "Interaction with other medicinal products and other forms of interaction").

If gastrointestinal bleeding or ulceration occurs in patients taking meloxicam, treatment should be discontinued.

NSAIDs should be used with caution in patients with a history of gastrointestinal diseases (ulcerative colitis, Crohn's disease) as these conditions may be exacerbated (see section "Adverse reactions").

Hepatic disorders

Up to 15% of patients taking NSAIDs may have elevations in one or more liver function tests. These laboratory abnormalities may progress, remain stable, or resolve with continued treatment. Significant elevations of alanine aminotransferase [ALT] or aspartate aminotransferase [AST] (approximately three times the upper limit of normal) have been reported in 1% of patients in clinical trials with NSAIDs. In addition, rare cases of severe hepatic reactions, including jaundice and fulminant hepatitis, hepatic necrosis, and hepatic failure, some of which were fatal, have been reported.

During therapy with ELIPROB, patients with symptoms/signs of hepatic dysfunction or with abnormal liver function tests should be evaluated for the development of more severe hepatic failure. If clinical symptoms are consistent with the development of liver diseases or if systemic manifestations of the disease are observed (e.g. eosinophilia, rash), administration of ELIPROB should be discontinued.

Cardiovascular disorders

Patients with hypertension and/or a history of mild to moderate congestive heart failure should be closely monitored, as fluid retention and edema have been reported with NSAID therapy.

In patients with risk factors, clinical monitoring of blood pressure is recommended at the beginning of therapy, especially at the beginning of treatment with meloxicam.

Research and epidemiological data suggest that administration of some NSAIDs (especially at high doses and in long-term treatment) is associated with a slightly increased risk of vascular thrombotic events (such as myocardial infarction or stroke). There is insufficient evidence to exclude such a risk with meloxicam.

Patients with uncontrolled hypertension, congestive heart failure, established ischemic heart

disease, peripheral arterial disease and/or cerebrovascular disease should be treated with meloxicam only after careful examination. Such examination is necessary before starting long-term treatment in patients with risk factors for cardiovascular disease (hypertension, hyperlipidemia, diabetes mellitus, smoking, etc.).
NSAIDs increase the risk of serious cardiovascular thrombotic complications, myocardial infarction and stroke, which can be fatal. The increase in risk is associated with the duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease are at increased risk of thrombotic complications.
Skin reactions
Life-threatening severe skin lesions have been reported with meloxicam: Stevens-Johnson syndrome and toxic epidermal necrolysis. Patients should be informed of the signs and symptoms of severe skin reactions and should be closely monitored for skin reactions. The highest risk of developing Stevens-Johnson syndrome or toxic epidermal necrolysis is during the first weeks of treatment. If a patient develops symptoms or signs of Stevens-Johnson syndrome or toxic epidermal necrolysis (e.g. progressive skin rash, often with blisters or mucosal lesions), meloxicam should be discontinued.
It is important to diagnose and discontinue any drugs that may cause severe skin reactions: Stevens-Johnson syndrome or toxic epidermal necrolysis as soon as possible, as this stipulates a better prognosis. If a patient develops Stevens-Johnson syndrome or toxic epidermal necrolysis while taking meloxicam, the drug should never be restarted in the future.
Cases of fixed drug eruption have been reported with meloxicam.
Meloxicam should not be re-administered to patients who have a history of a fixed drug eruption associated with meloxicam administration.
Potential cross-reactivity with other oxicams may occur.
Anaphylactoid reactions
As with other NSAIDs, anaphylactoid reactions may occur in patients who have not previously reacted to meloxicam. ELIPROB should not be used in patients with the aspirin triad. This symptom complex occurs in patients with asthma who have developed rhinitis, sometimes with nasal polyps, or who have experienced severe, potentially fatal bronchospasm after taking aspirin or other NSAIDs. Emergency measures should be taken if an anaphylactoid reaction occurs.
Liver parameters and renal function
As with most NSAIDs, isolated cases of increased serum transaminases, serum bilirubin or other liver function parameters, increased serum creatinine and blood urea nitrogen, and other laboratory abnormalities have been reported. In most cases, these abnormalities were minor and transient. If significant or persistent confirmation of such abnormalities occurs, meloxicam should be discontinued and control tests performed.
Functional renal impairment
NSAIDs, due to inhibition of the vasodilatory effect of renal prostaglandins, can induce functional renal failure by reducing glomerular filtration. This side effect is dose-dependent. At the beginning of treatment or after increasing the dose, careful monitoring of renal function, including the volume of diuresis, is recommended in patients with the following risk factors:

- Elderly age;
- Concomitant use with ACE inhibitors, angiotensin II antagonists, sartans, diuretics (see section “Interaction with other medicinal products and other forms of interaction”);
- Hypovolemia (of any origin);
- Congestive heart failure;
- Renal failure;
- Nephrotic syndrome;
- Lupus nephropathy;
- Severe hepatic dysfunction (serum albumin < 25 g/L or Child-Pugh class ≥ 10).

In isolated cases, NSAIDs can lead to interstitial nephritis, glomerulonephritis, renal medullary necrosis or nephrotic syndrome.

The dose of meloxicam for patients with end-stage renal failure on dialysis should not exceed 7.5 mg. In patients with mild to moderate renal failure, the dose may not be reduced (creatinine clearance > 25 mL/min).

Sodium, potassium and water retention

NSAIDs may increase sodium, potassium and water retention and may influence the natriuretic effects of diuretics. In addition, the antihypertensive effect of antihypertensive drugs may be reduced (see section "Interaction with other medicinal products and other forms of interaction"). As a result, edema, heart failure or hypertension may develop or worsen in susceptible patients. Therefore, clinical monitoring is recommended in patients at risk of sodium, potassium and water retention (see sections "Posology and method of administration" and "Contraindications").

Hyperkalemia

Hyperkalemia may be precipitated by diabetes mellitus or concomitant use of drugs that increase potassium levels (see section "Interaction with other medicinal products and other forms of interaction"). In such cases, potassium levels should be monitored regularly.

Combination with pemetrexed

In patients with mild to moderate renal impairment receiving pemetrexed, meloxicam treatment should be suspended for at least 5 days before, on the day of and for at least 2 days after pemetrexed administration (see section "Interaction with other medicinal products and other forms of interaction").

Other warning and precautions

Adverse reactions are often worse tolerated in elderly, frail or debilitated patients who require close monitoring. As with other NSAIDs, caution should be exercised in elderly patients who are more likely to have decreased renal, hepatic and cardiac function. Elderly patients have a higher incidence of adverse reactions to NSAIDs, especially gastrointestinal bleeding and perforation, which may be fatal (see section "Posology and method of administration").

Meloxicam, like any other NSAID, may mask the symptoms of infectious diseases.

As with other NSAIDs administered intramuscularly, abscess or necrosis may occur at the injection site.

Administration of meloxicam may impair reproductive function and is not recommended in women attempting to get pregnant. Therefore, in women attempting to get pregnant or undergoing investigation of infertility, discontinuation of meloxicam should be considered (see section "Use during pregnancy and breastfeeding").

The drug product contains less than 1 mmol sodium (23 mg) per 1.5 mL ampoule, i.e. essentially sodium-free.

Masking of inflammation and fever

The pharmacological effect of ELIPROB, aimed at reducing fever and inflammation, may diminish the utility of diagnostic data of suspected non-infectious pain conditions.

Corticosteroid treatment

ELIPROB should not be used as a substitute for corticosteroids in the treatment of corticosteroid insufficiency.

Hematological effects

Anemia may occur in patients receiving NSAIDs, including ELIPROB. This may be due to fluid retention, gastrointestinal bleeding of unknown origin or macroscopic bleeding, or incompletely characterized effects on erythropoiesis. During long-term treatment with NSAIDs, including ELIPROB, patients should have their hemoglobin or hematocrit monitored if they develop symptoms and signs of anemia.

NSAIDs inhibit platelet aggregation and may prolong bleeding time in some patients. In contrast to aspirin, their effect on platelet function is quantitatively smaller, short, and reversible. Patients prescribed ELIPROB who may have adverse effects on platelet function, such as coagulation disorders, or patients receiving anticoagulants, require close monitoring.

Administration in patients with asthma

Patients with asthma may have aspirin-induced asthma. The use of aspirin in patients with aspirin-induced asthma has been associated with severe bronchospasm, which may be fatal. Due to cross-reactivity, including bronchospasm, between aspirin and other NSAIDs, ELIPROB should not be used in patients sensitive to aspirin and should be used with caution in patients with pre-existing asthma.

Use during pregnancy and breastfeeding

Pregnancy. Inhibition of prostaglandin synthesis may adversely affect pregnancy and/or embryonic/fetal development. Epidemiological data suggest an increased risk of miscarriage and of cardiac malformations and gastroschisis following exposure to prostaglandin synthesis inhibitors in early pregnancy. The absolute risk of cardiac malformations has been reported to increase from less than 1% to approximately 1.5%. This risk is suggested to increase with increasing dose and duration of treatment.

In animals, administration of a prostaglandin synthesis inhibitor has been shown to increase pre- and post-implantation loss and embryo-fetal mortality. In addition, animals treated with a prostaglandin synthesis inhibitor during organogenesis have been shown to have an increased incidence of various malformations, including cardiovascular malformations.

From the 20th week of gestation, meloxicam may cause oligohydramnios due to fetal renal dysfunction. This disorder may occur shortly after initiation of treatment and is usually reversible after discontinuation of treatment. In addition, there have been reports of ductus arteriosus narrowing following treatment in the second trimester, which in most cases resolved after discontinuation of treatment.

Therefore, meloxicam should not be used during the first and second trimesters of pregnancy unless clearly necessary. In women attempting to get pregnant or during the first and second trimesters of pregnancy, the dosage and duration of treatment with meloxicam should be kept to a minimum.

Antenatal monitoring for oligohydramnios and narrowing of the ductus arteriosus may be advisable after exposure to meloxicam for several days, starting from the 20th week of pregnancy. If oligohydramnios or narrowing of the ductus arteriosus is detected, meloxicam should be discontinued.

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors pose a risk of the following to the fetus:

- cardiopulmonary toxicity (with premature narrowing/closure of the ductus arteriosus and pulmonary hypertension);
- renal dysfunction (see above);

risks in the last stages of pregnancy for the mother and the newborn:

- prolongation of bleeding time, antiaggregant effect even at very low doses;
- inhibition of uterine contractions, leading to delayed or prolonged labor.

Therefore, meloxicam is contraindicated during the third trimester of pregnancy.

Breastfeeding. Although there are no specific data for ELIPROB, NSAIDs are known to pass into breast milk. Therefore, use is not recommended in women who are breastfeeding.

Fertility. Meloxicam, like other drugs that inhibit cyclooxygenase/prostaglandin synthesis, may have an adverse effect on reproductive function and is not recommended in women attempting to get pregnant. Therefore, in women planning pregnancy or undergoing investigation of infertility, discontinuation of meloxicam should be considered.

The effect on the ability to drive and use machines

There are no specific studies on the effects of the drug on the ability to drive or use machines. Given the pharmacodynamic profile and the adverse reactions observed, meloxicam is expected to have no or negligible effect on these activities. However, patients who experience visual disturbances, including blurred vision, dizziness, drowsiness, vertigo or other central nervous system disorders, are advised to refrain from driving or using machines.

Posology and method of administration

Posology

One 15 mg injection once daily.

DO NOT EXCEED the 15 mg/day dose.

Treatment should be limited to a single injection at the start of therapy with a maximum duration of up to 2-3 days in justified exceptional cases (i.e. when other methods of administration are not possible). Adverse reactions can be minimized by using the lowest effective dose for the shortest duration necessary to control symptoms (see section "Special warnings and precautions for use").

The patient's need for symptomatic relief and response to treatment should be assessed periodically.

Special patient populations

Elderly patients (see section "Pharmacokinetics")

The recommended dose for elderly patients is 7.5 mg/day (half a 1.5 mL ampoule) (see also section "Patients at increased risk of adverse reactions" below and section "Special warnings and precautions for use").

Patients at increased risk of adverse reactions (see section "Special warnings and precautions for use")

Patients at increased risk of adverse reactions, such as those with a history of gastrointestinal disease or risk factors for cardiovascular disease, should be started on a dose of 7.5 mg/day (half a 1.5 mL ampoule).

Renal failure

This drug product is contraindicated in patients with severe renal failure not on hemodialysis, see section "Contraindications".

For patients with end-stage renal failure on hemodialysis, the dose should not exceed 7.5 mg/day (half a 1.5 mL ampoule).

No dose reduction is required in patients with mild to moderate renal impairment (i.e. patients with creatinine clearance above 25 mL/min).

Hepatic failure

No dose reduction is required in patients with mild to moderate hepatic impairment. For patients with severe hepatic failure, see section "Contraindications".

Method of administration

For intramuscular administration.

Solution for injection 15 mg/1.5 mL is administered by deep intramuscular injection into the upper outer quadrant of the buttock, observing strict aseptic technique. In case of repeated administration, it is recommended to alternate the left and right buttock. Before injection, it is important to check that the needle tip does not enter a blood vessel.

The injection should be stopped immediately in case of severe pain during the injection.

If the patient has a hip prosthesis, the injection should be made in the other buttock.

Oral dosage forms of the drug product (tablets) should be used for continued treatment.

Pediatric population. ELIPROB, solution for injection 15 mg/1.5 mL, is contraindicated in children (less than 18 years of age) — see section "Contraindications".

Overdose

Symptoms. Symptoms of acute NSAID overdose are usually limited to lethargy, drowsiness, nausea, vomiting and epigastric pain, which are generally reversible with supportive therapy. Gastrointestinal bleeding may occur. Severe poisoning may result in hypertension, acute renal failure, hepatic dysfunction, respiratory depression, coma, convulsions, cardiovascular failure and cardiac arrest. Anaphylactoid reactions have been reported with therapeutic use of NSAIDs, which may also occur with overdose.

Treatment. In cases of NSAID overdose, symptomatic and supportive measures are recommended. Studies have shown that meloxicam is eliminated more rapidly with oral doses of cholestyramine 4 g 3 times a day.

Adverse reactions

Research and epidemiological data suggest that the use of some NSAIDs (especially at high doses and with long-term treatment) slightly increases the risk of vascular thrombotic events (such as myocardial infarction or stroke) (see section “Special warnings and precautions for use”).

Edema, hypertension and heart failure have been observed with NSAIDs.

Most of the observed adverse reactions of NSAIDs are gastrointestinal in origin. Peptic ulcer, perforation or gastrointestinal bleeding, sometimes fatal, may occur, especially in elderly patients (see section “Special warnings and precautions for use”). Nausea, vomiting, diarrhea, flatulence, constipation, dyspepsia, abdominal pain, melena, hematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease have been reported after administration of NSAIDs (see section “Special warnings and precautions for use”). Gastritis has been observed less frequently after administration of NSAIDs.

Severe skin reactions have been reported: Stevens-Johnson syndrome and toxic epidermal necrolysis (see section “Special warnings and precautions for use”).

The following are adverse reactions to meloxicam identified in 27 clinical trials involving 15,197 patients who received meloxicam orally at a daily dose of 7.5 mg or 15 mg for periods ranging from 14 days to one year, as well as during post-marketing use.

Criteria for assessing the frequency of adverse drug reactions: very common (≥ 1/10); common (≥ 1/100, < 1/10); uncommon (≥ 1/1,000, < 1/100); rare (≥ 1/10,000, < 1/1,000); very rare (< 1/10,000); frequency unknown (cannot be determined from the available data).

Blood and lymphatic system disorders:

uncommon — anemia;

rare — abnormal blood counts (including changes in white blood cell count), leukopenia, thrombocytopenia.

Very rare cases of agranulocytosis have been reported (see “Selected serious and/or common adverse reactions” below).

Immune system disorders:

uncommon — allergic reactions, except anaphylactic or anaphylactoid;

unknown — anaphylactic shock, anaphylactic reaction, anaphylactoid reaction including shock.

Psychiatric disorders*:*

rare — mood swings, nightmares;

unknown — confusion, disorientation, insomnia.

Nervous system disorders:

common — headache;

uncommon — dizziness, drowsiness.

Visual disorders:

rare — visual impairment, including blurred vision; conjunctivitis.

Hearing and vestibular disorders:

uncommon — dizziness;

rare — tinnitus.

Cardiac disorders:

rare — palpitations.

Heart failure associated with administration of NSAIDs has been reported.

Vascular disorders:

uncommon — increased blood pressure (see section “Special warnings and precautions for use”), flushing.

Respiratory, thoracic and mediastinal disorders:
rare — asthma in patients allergic to aspirin and other NSAIDs;
unknown — upper respiratory tract infections, cough.
Gastrointestinal disorders:
very common — digestive tract disorders: dyspepsia, nausea, vomiting, abdominal pain, constipation, flatulence, diarrhea;
uncommon — occult or macroscopic gastrointestinal bleeding, stomatitis, gastritis, belching;
rare — colitis, gastroduodenal ulcer, esophagitis;
very rare — gastrointestinal perforation;
unknown — pancreatitis.
Gastrointestinal bleeding, ulcers or perforation can be severe and potentially fatal, especially in elderly patients (see section "Special warnings and precautions for use").
Hepatobiliary disorders:
uncommon — abnormal liver function tests (e.g. increased levels of transaminases or bilirubin);
very rare — hepatitis;
unknown — jaundice, hepatic failure.
Skin and subcutaneous tissue disorders:
uncommon — angioedema, pruritus, rash;
rare — Stevens-Johnson syndrome, toxic epidermal necrolysis, urticaria;
very rare — bullous dermatitis, erythema multiforme;
unknown — photosensitivity reactions, exfoliative dermatitis, fixed drug eruption (see section "Special warnings and precautions for use").
Urinary system disorders:
uncommon — sodium and water retention, hyperkalemia (see sections "Special warnings and precautions for use" and "Interaction with other medicinal products and other forms of interaction"), changes in renal parameters (increased creatinine and/or serum urea);
very rare — acute renal failure, particularly in patients with risk factors (see section "Special warnings and precautions for use");
unknown — urinary tract infections, urinary frequency disorders.
Reproductive system and breast disorders:
unknown — female infertility, ovulation delay.
General disorders and administration site conditions:
common — injection site induration, injection site pain;
uncommon — edema, including edema of the lower extremities;
unknown — influenza-like symptoms.
Musculoskeletal disorders:
unknown — arthralgia, back pain, joint-related signs and symptoms.

Selected serious and/or common adverse reactions
Agranulocytosis has been reported very rarely in patients taking meloxicam and other potentially myelotoxic drugs (see section "Interaction with other medicinal products and other forms of interaction").
Adverse reactions common to other compounds of the class
Organic renal damage, which may lead to acute renal failure: very rare cases of interstitial nephritis, acute tubular necrosis, nephrotic syndrome and papillary necrosis have been reported (see section "Special warnings and precautions for use").

Post-marketing reporting of adverse reactions is of great importance. This allows monitoring of the benefit/risk ratio of this drug product. Healthcare and pharmaceutical professionals, as well as patients or their legal representatives, should report all cases of suspected adverse reactions and lack of efficacy of a medicinal drug through the automated pharmacovigilance information system at: https://aisf.dec.gov.ua

Shelf life. 4 years.

Storage conditions. Store at a temperature below 25°C in the original package. Keep out of the reach of children.

Package. 1.5 mL in an ampoule, 3 or 5 ampoules in a blister; 1 blister in a cardboard box.

Legal status. Prescription only.

Manufacturer. S.C. Rompharm Company S.R.L.

Manufacturer's location and business activity address
1A Eroilor Str., Otopeni, 075100, Ilfov District, Romania — Rompharm 1 and Rompharm 2 buildings.

Applicant. SALUTARIS BOUTIQUE PHARMACEUTICAL COMPANY
Limited Liability Company

Applicant's address. 9 Druzhby Narodiv Ave., Kyiv, 01042, Ukraine.

Last revision date.