SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

ETOTAC SR 600 mg Sustained Release Film Coated Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITIONActive

substance: Etodolac.....600 mg

Excipients:

Lactose Monohydrate (cow's milk sourced),.....233 mg

See Section 6.1 for excipients.

3. PHARMACEUTICAL FORM

Light grey, large oval, printless, biconvex and non-scored film coated tablets

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

- It is indicated to treatment of symptoms and signs of osteoarthritis, rheumatoid arthritis and ankylosing spondylitis,
- It is indicated for the treatment of acute gout arthritis, acute musculoskeletal pain, post-operative pain and dysmenorrhea.

2. Posology and method of administration

Posology/administration frequency and time:

The recommended dose for the ETOTAC SR Sustained Release Film Coated Tablet is 1 tabletper day (600 mg).
The lowest dose, which is effective to be in line with the treatment, should be used for the shortest period of time.
The dose and dose range should be individually adjusted according to the needs of the patient after response to initial treatment.
When different dose titrations are required, treatment with other forms of ETOTAC SR can becontinued under the supervision of a physician.
The use of more than 1200 mg per day is not proven safe.No tolerance or tachyphylaxis has been reported.

Method of administration:

ETOTAC SR can be taken orally independent or in combination with food. If the stomach is uncomfortable, it can be taken with food. Taking with food may not reduce the risk of stomach or intestinal problems (eg bleeding, ulcers). Etodolac should be used with caution in patients with persistant stomach disease.
The ETOTAC SR must be taken with a fully filled glass of water.

Additional information for specific populations

Renal/Hepatic failure: As with other drugs in this group, it should be used with caution against kidney or liver failure. Renal and liver functions should be reviewed regularly for long-term use.

Pediatric population: The use of the ETOTAC SR is not recommended for children under 18years of age (see section 4.4).

Geriatric population: Usually, the initial dose does not need to be changed in the elderly. However, it should be used with caution in elderly patients compared to young people as they may be more sensitive to gastric bleeding and kidney problems (see section 4.4. Special warnings and precautions for use).

3. Contraindications

- ETOTAC SR is contraindicated in patients known to be hypersensitive to etodolac or any substance contained in the tablet.
- In patients with previously detected allergies to any component of ETOTAC SR,
- In patients with severe heart failure, just before or after bypass and heart surgery,
- Patients with a history of active peptic ulcer or peptic ulcer disease (including gastrointestinal hemorrhage caused by other nonsteroidal anti-inflammatory drugs),
- In patients who develop allergic reactions such as acute asthma, rhinitis, urticaria, angioedema during treatment with aspirin or other nonsteroidal anti-inflammatory drugs due to possible cross-drug reactions,
- It should not be used in patients who are in the last 3 months of pregnancy.

4. Special warnings and precautions for use

- It is not recommended for use under the age of 18 since its safety and efficacy are not verified.
- It should be used more carefully in elderly patients than in young people because they may be more sensitive to stomach bleeding and kidney problems. In long-term use of etodolac, especially elderly patients should be monitored for potential side effects and the dose should be reduced if necessary.
- Kidney function should be monitored especially in elderly or in patients receiving diuretics and in patients with kidney, heart or liver failure. NSAID may reduce the production of prostaglandins depending on the dose and prepare the ground for renal failure. The lowest possible dose should be used. Liver, renal function and hematological parameters should be reviewed regularly in patients using long-term etodolac.
- Etodolac should be used with caution for patients having a history of bronchial asthma or bronchial asthma due to reports that notifying of using nonsteroidal anti-inflammatory use cause to increase of bronchospasm.
- Etodolac should be used with caution in patients with fluid retention, hypertension or heart failure.
- All such drugs that inhibit prostaglandin biosynthesis may disrupt thrombocyte function. Patients should be carefully monitored for side effects that may occur with inhibition of thrombocyte function.
- Undesirable effects can be reduced by using the lowest effective dose required to control symptoms at the shortest time.
- Etodolac can cause a high risk for serious and sometimes fatal heart and blood vessel problems (eg heart attack, crisis). If the patient already has heart problems or has been taking etodolac for a long time, the risk may be higher.
- Etodolac can cause serious and sometimes fatal gastric ulcers and bleeding with high risks. Elderly patients may have the largest group risk. This condition can develop without any preliminary symptoms.
- This medicinal product contains 233 mg of lactose per dose. Patients with rare hereditary problems of galactose intolerance, Lapp lactose deficiency or glucose-galactose malabsorption should not use this drug.
- Each medicinal product contains 45.00 mg of mannitol at each dose. No warning is required due to its dose.

5. Interactions with Other Medical Products and Other Interaction Types

- When etodolac is used in combination with anticoagulants (eg, warfarin), aspirin, corticosteroids (eg, prednisone), heparin or selective serotonin reuptake inhibitors (SSRIs) (eg, fluoxetine) risk of stomach bleeding is increased.
- Phenylbutazone or probenecid may increase the risk of side effects of etodolac.
- When cyclosporin, digoxin, lithium, methotrexate, quinolones (eg, ciprofloxacin) or sulfonylureas (eg, glipizide) are used in combination with etodolac, the risk of side effects may be increased.
- The effectiveness of angiotensin-converting enzyme (ADE) inhibitors (eg, enalapril) or diuretics (eg, furosemide, hydrochlorothiazide) can be reduced by etodolac.
- Aspirin should be used with caution when using Etodolac.
- Due to the presence of phenolic metabolites in the urine, the determination of bilirubin in urine may produce a false positive result.
- Etodolac may increase the risk of convulsion side effects of quinolones when used together.

Additional information on special populations

No interaction studies of specific populations were reported.

Pediatric population:

There is no information on the use of etodolac in children. Thus, the interaction study on pediatric population has not been reported.

6. Pregnancy and Lactation

Etodolac should not be used in pregnant women and lactation as there are no controlledclinical studies in pregnant women and lactation period.

General recommendation

Pregnancy is category C (Category D, in the 3rd trimester of pregnancy).

It may cause unexpected bleeding, severe gastrointestinal toxic effects such as ulcers and perforations in patients treat with chronic nonsteroidal anti-inflammatory. Etodolac should be discontinued immediately when signs of gastrointestinal bleeding occur.

Fertile women / Contraception

Effective contraception is recommended during the treatment of women with childbearing potential.

Pregnancy

Congenital anomalies associated with NSAID administration in humans have been reported; however, their frequency is small and they do not follow a specific pattern.

In the light of the known effects of NSAIDs on the fetal cardiovascular system (closure of ductus arteriosus), contraindicated for use in the third trimester of pregnancy. The start of birth may be delayed, with the increasing tendency of bleeding in both mother and child, the duration may be prolonged. (see section 4.3).

If the potential benefit to the patient is not greater than the potential harm to the fetus, NSAIDdrugs should not be used during the first two trimesters of pregnancy and at birth.

Breast-feeding

In the limited studies conducted so far, NSAIDs have been observed in milk at very low concentrations. If possible, use of NSAIDs should be avoided during lactation.

Please see section 4.4. "Special warnings and precautions for use" regarding female reproduction.

Fertility

The use of etodolac is not recommended for those who wish to become pregnant as it may affect fertility in females. The use of etodolac should be discontinued in patients who cannot conceive or have been investigated for infertility.

7. Effects on ability to drive and use machines

Etodolac can cause dizziness or drowsiness. These effects may be more pronounced when taken with alcohol or certain drugs. Etodolac should be handled with care, no car should be used or other potentially unsafe work should not be carried out until it is learned how to react.

4.8. Undesirable effects

According to the data obtained from clinical studies and post-surveillance studies, undesirable effects are presented according to organ classification and frequency.

Frequencies can be defined as follows: Very common (≥1 / 10); commonly (≥1 / 100, <1/10); non-widespread (≥1 / 1000, <1/100); infrequently (≥1 / 10000, <1/1000); very rare (<1/10000), unknown (unpredictable). It is reported that edema, heart failure and hypertension may develop with NSAID therapy. Clinical study and epidemiological data show that the risk of arterial thrombotic event (suchas myocardial infarction, stroke) may increase with the use of some NSAIDs for a long time and with high doses.

Blood and lymphatic system diseases:

Uncommon: Thrombocytopenia, neutropenia, agranulocytosis, aplastic anemia, hemolytic anemia

Immune system diseases:

Uncommon: Severe allergic reactions (Non-specific allergic reactions, anaphylaxis, asthma, respiratory system reactions such as bronchospasm or disapneal or urticaria, rash, itching, purpura, angioedema and very rarely include exfoliative and skin reactions such as bullous dermatosis (epidermal necrolysis and erythema multiform) have been reported during NSAID treatments.

Psychiatric diseases

Common: Depression, nervousness
Uncommon: Insomnia and sleep disorders, mental or behavioral changes, hallucinations

Diseases of the nervous system
Common: Dizziness.
Uncommon: Arm or leg numbness, unilateral weakness, severe headache, confusion

Eye diseases
Uncommon: Vision disorder, optic neuritis

Ear and inner ear diseases
Common: Tinnitus

Gastrointestinal diseases
Very common: Indigestion.
Common: Abdominal pain, constipation, diarrhea, gas, bloating, gastritis, nausea, severe vomiting, (severe gastric ulcers or bleeding with the use of etodolac may occur. Taking high doses or taking it for a long time, smoking or drinking alcohol increases the risk of these side effects. Taking the drug with food does not reduce the risk of these effects.
Uncommon: Feeling of thirst, mouth ulcers, dry mouth, hematemesis, melena, rectal bleeding,exacerbation of colitis

Hepato-biliary diseases
Uncommon: Jaundice, pancreatitis, hepatitis

Skin and subcutaneous tissue diseases
Common: Itching, skin rash, rash
Uncommon: Toxic epidermal necrolysis, bullous reactions such as Stevens-Johnson syndrome, hypersensitivity to light

Kidney and urinary tract diseases
Common: Painful urination, frequent urination.
Uncommon: Nephrotic syndrome, interstitial nephritis, nephrotoxicity such as renal failure

General disorders and diseases related to the application area

Common: Chills, fever, dizziness, sudden or unexplained weight gain, hands, swelling of the legs or feet, fatigue, weakness / fatigue

Researches
Uncommon: Increase in liver enzyme levels.

If you get any side effects, stated or not stated in the Patient Information Leaflet, talk to your doctor or pharmacist. Also, please report the side effects you have to Turkish Pharmacovigilance Center (TÜFAM) by either clicking to “Reporting Drug Side Effect” icon on www.titck.gov.tr or calling side effect reporting line via 0 800 314 00 08. By reporting the side affects you can help provide more information on the safety of this medicine.

TÜFAM	Turkish Pharmacovigilance Center www.titck.gov.tr

4.9 Overdose and treatment

Symptoms can be as following; decreasing urination, headache, nausea, vomiting, epigastric pain, gastrointestinal bleeding, rarely diarrhea, disorientation, excitation, coma, dizziness, tinnitus, fainting, very rarely convulsions and power breathing can be. The overdose is treatedsymptomatically. Gastric lavage, activated charcoal and supportive treatments can be performed.
Liver and kidney function should be closely monitored.

5. PHARMACOLOGICAL PROPERTIES
1. Pharmacodynamic properties

Pharmacotherapeutic group: non-steroidal anti-
inflammatoryATC Code: M01AB08

Etodolac indole derivative is a non-steroidal anti-inflammatory drug. Etodolac shows anti-inflammatory, analgesic and antipyretic properties.

Etodolac inhibits prostaglandin synthesis in inflamed tissue. Thus, it reduces the sensitivity of pain receptors to histamine, serotonin and quinins, which are mediators of inflammation.

Inhibition of prostaglandin synthesis and COX-2 selectivity:
All nonsteroidal antiinflammatory drugs (NSAIDs) have been shown to inhibit prostaglandin formation. This effect is responsible for both the therapeutic effects and some side effects of prostaglandins. The inhibition of prostaglandin synthesis observed with Etodolac differs from other NSAIDs. Etodalac applied in antiinflammatory effect doses in the animal model compared to other NSAIDs, decreased the cytoprotective PGE concentration in the gastric mucosa for a shorter period and at lower levels. This finding is consistent with the in vitro studies showing that the effect of etodolac on COX-1 (cytoprotective) -induced cyclooxygenase 2 (COX-2 associated with inflammation) is more selective.
Furthermore, studies on human cell models have confirmed that etodolac is selective in COX-2 inhibition.
The clinical benefits of COX-2 inhibition compare to COX-1 have just been demonstrated.

Antiinflammatory effects:
Studies have shown that etodolac has a more pronounced anti-inflammatory activity than most clinical trials with NSAIDs.

2. Pharmacokinetic properties
General features
Pharmacokinetic properties do not differ in old and young

people.Absorption

Etodolac is well absorbed when taken orally. Bioavailability does not change with food and antacids.

Distribution
The drug is highly bound to proteins.
Stable levels are reached after 3 days of treatment. The peak plasma concentration reached by600 mg / day was 7.5 microg / mL at 7.9 hours and 11.9 microg / mL at 7.8 hours.

Biotransformation
Etodolac is metabolized in the liver.

Elimination
The main pathway is urine, mainly in the form of metabolites. The average elimination half-life is 7 hours.

Linearity / non-linearity:
Recurrent etodolac intake at the therapeutic dose limits is significantly higher than the plasma concentration of plasma etodolac in a single dose of drug intake.

Characteristic of patients
Race:
No race-dependent pharmacokinetic differences were found. Clinical studies involving

different breeds were made and the response of all strains to the drug was similar.

Age:
In the clinical studies conducted for the safety and efficacy of the drug, no difference was observed between the elderly and young groups. In pharmacokinetic studies, no age-related difference was found in etodolac half-life and protein binding, and there was no change in expected drug accumulation.

Kidney failure:
There were no pharmacokinetic differences in patients with mild to moderate renal impairment. After 4 weeks of receiving etodolac in therapeutic doses, the serum uric acid level is reduced by 1-2 mg.

5.3. Preclinical safety data
NSAID-induced intoxications, primarily with gastrointestinal disorders and hemorrhage kidney disorders.

Etodolac pharmacological and toxicological properties are well known. Etodolac does not have carcinogenic or mutagenic potential. There are no embryogenic or teratogenic effects. However, there were isolated changes in limb development in rats receiving 2-14 mg / kg / day.

Carcinogenesis, mutagenesis and reproductive disorders

No carcinogenic effects of etodolac were observed orally 15 mg / kg in mice or rats per day (45 to 89 mg / m2, respectively) for less than 2 years or for 18 months, respectively. Etodolac is not mutagenic in in vitro tests with S. typhimurium and mouse lymphoma cells and in a mouse micronucleus test in vivo. In vitro human peripheral lymphocyte data, however, showed an increase in the number of spotless-clean regions (3.0 to 5.3% without displacement of the chromatid - clean region) in the etodolac added cultures (50 - 200 microg / mL) compared to negative controls (2.0%); no difference was observed between the controls and the drug-treated groups. Male and female rats treated with etodolac up to an oral dose of 16 mg / kg showed no reproductive disorder (94 mg / m^2). However, the implantation of fertilized eggs in the 8 mg / kg group decreased.

6. PHARMACEUTICAL PROPERTIES

1. List of excipients

Lactose monohydrate (originating from cow's milk),
Hydroxypropyl Methyl Cellulose (HPMC E-5)
Hydroxypropyl Methyl Cellulose (HPMC 4000 SR)
Povidone (PVP-K30, PVP K-29/32)
Mannitol pearlitol 200
Colloidal Silicon Dioxide (Anhydrous)
Magnesium Stearate
Talc
Opadry grey 20A275001 (Hydroxypropyl cellulose, Hypromellose, Titanium dioxide (E171), black iron oxide (E172), yellow iron oxide (E172), red iron oxide (E172))

2. Incompatibilities
No discrepancy was reported.

3. Shelf life

36 months

4. Special precautions for storage
Store at room temperature below 30 ° C.

5. Nature and content of packaging

Blister packaging containing PVC / PVDC and Aluminum Foil and 10 or 14 sustained releasefilm coated tablets.

6. Disposal of other medicinal products and other special measures

Unused products or waste materials must be disposed of in accordance with the Regulation on Control of Medical Wastes and Regulation on Control of Packaging and Packaging Wastes

Do not throw away any expired or unused medicines! Give to the collection system determined by the Ministry of Environment and Urbanization.

7. MARKETING AUTHORIZATION HOLDER

Pharmactive İlaç San. and Tic.
Inc.Istanbul-Turkey

8. MARKETING AUTHORIZATION NUMBER

TAN 21 HM 0234

9. FIRST LICENSE DATE / LICENSE DATE

First Registration Date: 6.03.2021
Last license renewal date:

10. RENEWAL DATE OF SUMMARY OF PRODUCT CHARACTERISTICS