SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

SOLKET "80 mg powder for oral solution"

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

A bipartite sachet contains:
Active substance: ketoprofen lysine salt 80 mg equal to 50 mg of ketoprofen
Excipients with known effects: sorbitol

For the full list of excipients, see paragraph 6.1.

3. PHARMACEUTICAL FORM

Powder for oral solution

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Adults: symptomatic treatment of inflammatory states associated to pain such as: rheumatoid arthritis, ankylosing spondylitis, painful arthrosis, extra-articular rheumatism, Post-traumatic flogosis, painful inflammatory diseases in dentistry, otorhinolaryngology, urology and pneumology.
Children: symptomatic and short-term treatment of inflammatory states associated to pain, even accompanied by pyrexia, such as those affecting osteoarticular system, post-surgery pain and otitis.

4.2 Posology and method of administration

The lowest effective dose should be used for the shortest duration necessary to relieve symptoms (see section 4.4).

Posology

Adults: one sachet of 80 mg (full dose) three times a day, during meals.

Children between 6 and 14 years old: half sachet of 40 mg (half dose) three times a day, during meals.

*Elderly: t*he dose should be carefully determined by the physician who will need to evaluate any reduction in the above dosages (see paragraph 4.4).

People with liver failure: It is advisable to set the therapy at the minimum daily dose (see paragraph 4.4).

*People with mild or moderate kidney problems: i*t is advisable to check the volume of diuresis and kidney function (see paragraph 4.4).

SOLKET should not be used in patients with severe liver and kidney dysfunction (see paragraph 4.3).
Side effects may be minimized using the shortest possible treatment time to monitor the symptoms (see paragraph 4.4).

Method of administration

Instructions on use of the sachet: by opening the sachet along the line "half dose", a dose of 40 mg is obtained. By opening the sachet along the line "full dose", a dose of 80 mg is obtained. Pour the content of a sachet or half sachet in half a glass of water and mix.

4.3 Contraindications

Ketoprofen lysine salt should not be administered in the following cases:

- Hypersensitivity to the active substance, other non-steroidal anti-inflammatory drugs (NSAIDs) or to any of the excipient listed in paragraph 6.1.
- In patients with a history of hypersensitivity reactions, such as bronchospasm, asthma attacks, rhinitis, nasal polyps, urticaria, angioneurotic edema or other allergic reactions to ketoprofen or substances with similar mechanism of action (eg acetylsalicylic acid, ASA, or other non-steroidal anti-inflammatory drugs, NSAIDs). In these patients, serious rarely fatal anaphylactic reactions have been reported (see paragraph 4.8).
- Peptic ulcer/active hemorrhage or previous anamnestic gastrointestinal haemorrhage, ulceration or perforation (two or more distinct episodes, proven by bleeding or ulceration) or chronic dyspepsia;
- Gastrointestinal bleeding or gastrointestinal perforation resulting from previous NSAIDs therapy or other active bleeding or haemorrhagic disorders.
- Crohn's disease or ulcerative colitis.
- Previous bronchial asthma.
- Serious heart failure.
- Serious liver failure.
- Serious kidney failure.
- Hemorrhagic diathesis or other defects in blood clotting, or patients undergoing anticoagulant therapy.
- Third trimester of pregnancy and breast-feeding (see paragraph 4.6);
- Children under 6 years of age.

4.4 Special warnings and precautions for use

Use with caution in patients with allergic events or history of allergy. Treatment with ketoprofen lysine salt must be discontinued at the first appearance of rash, mucous lesions or any other sign of hypersensitivity.
The side effects could be minimized with use of lowest effective dose for the shortest period of treatment to control the symptoms (see paragraph 4.2 and paragraphs below concerning gastrointestinal and cardiovascular risks).
Concomitant use of ketoprofen lysine salt with other NSAIDs, including selective cyclooxygenase-2 inhibitors, must be avoided.
Elderly: elderly patients have an increased frequency of adverse reactions to NSAIDs, especially bleeding and gastrointestinal perforations, which can be fatal (see paragraph 4.2).
As for other non-steroidal anti-inflammatory drugs, in presence of infection, the anti-inflammatory, analgesic and antipyretic effects of ketoprofen lysine salt can mask the symptoms of progression of the infection, such as fever.

Masking of symptoms of underlying infections

Solket can mask symptoms of infection, which may lead to delayed initiation of appropriate treatment and thereby worsening the outcome of the infection. This has been observed in bacterial community acquired pneumonia and bacterial complications to chicken pox. When Solket is administered for fever or pain relief in relation to infection, monitoring of infection is advised. In nonhospital settings, the patient should consult a doctor if symptoms persist or worsen.

Cardiovascular and cerebrovascular effects

Adequate monitoring and appropriate instructions are needed in patients with a history of hypertension and/or mild to moderate congestive heart failure as fluid retention and edema were found in association with treatment with NSAIDs.
Clinical studies and epidemiological data suggest that the use of some NSAIDs (especially at high doses and for long-term treatments) may be associated with a modest increase in the risk of arterial thrombotic

events (eg myocardial infarction or stroke). There is not enough data to exclude a similar risk for ketoprofen lysine salt.
Patients with uncontrolled hypertension, congestive heart failure, confirmed ischemic heart disease, peripheral arterial disease and/or Cerebrovascular illness should be treated with ketoprofen lysine salt, as well as with all NSAIDs, only after careful evaluation. Analogous considerations should be made before starting treatment of long duration in patients with risk factors for cardiovascular disease (eg hypertension, hyperlipidemia, diabetes mellitus, smoking).

Gastrointestinal effects
During treatment with all NSAIDs, at any time, with or without warning symptoms or previous history of severe gastrointestinal events, gastrointestinal haemorrhage, ulceration and perforation, that can be fatal, have been reported.
Some epidemiological evidence suggests ketoprofen lysine salt may be associated with a high risk of severe gastrointestinal toxicity, compared to other NSAIDs, especially at high doses (see also paragraph 4.2 and 4.3).
In elderly and in patients with history of ulcer, especially if complicated by hemorrhage or perforation (see paragraph 4.3), the risk of gastrointestinal bleeding, ulceration or perforation is higher with increased doses of NSAIDs. These patients should start treatment with the lowest available dose. Concomitant use of protective agents (misoprostol or inhibitors of proton pump) should be considered for these patients and also for patients taking low doses of aspirin or other medications that can increase the risk of gastrointestinal events (see below and paragraph 4.5).
Patients with history of gastrointestinal toxicity, especially the elderly, must report any unusual gastrointestinal symptoms (especially gastrointestinal haemorrhage) especially during the initial stages of treatment.
Caution should be given to patients taking concomitant medications which could increase the risk of ulceration or hemorrhage, such as oral corticosteroids, anticoagulants such as warfarin, selective inhibitors of serotonin reuptake or antiaggregating agents such as aspirin (see paragraph 4.5).
When hemorrhage or gastrointestinal ulceration occurs in patients who take ketoprofen lysine salt, treatment should be discontinued.
NSAIDs should be administered with caution in patients with a history of gastrointestinal disease (ulcerative colitis, Crohn's disease) as such conditions may be exacerbated (see paragraph 4.8).
In some pediatric patients treated with ketoprofen lysine salt, gastrointestinal haemorrhages, occasionally severe, and ulceration were reported (see paragraph 4.8); therefore, the product should be administered under close check-up of physycian that will evaluate the necessary posology chart time after time.

Effects on the skin
Serious skin reactions, some of which are fatal, including exfoliative dermatitis, Stevens-Johnson syndrome and toxic epidermal necrolysis, have been reported very rarely in association with the use of NSAIDs (see paragraph 4.8). In early stages of therapy, patients appear to be at higher risk: the onset of the reaction occurs in most cases within the first month of treatment. Ketoprofen lysine salt must be interrupted at first appearance of skin rash, mucous lesions or any other sign of hypersensitivity.

Renal and liver effects
As with all NSAIDs, the drug may increase the plasma urea nitrogen and the creatinine.
Like other prostaglandin synthesis inhibitors, the drug may be associated with adverse events on the kidney system that can lead to glomerular nephritis, renal papillary necrosis, nephrotic syndrome and kidney acute insufficiency.
Careful monitoring of renal function at the beginning of treatment should be carried out in patients with heart failure, with cirrhosis and nephrosis, in patients in diuretic therapy, with chronic renal failure,

especially if the elderly. In such patients, administration of ketoprofen lysine salt may cause a reduction of renal blood flow, caused by the inhibition of prostaglandins and lead to renal impairment.
As with other NSAIDs, the drug may cause small transient increase of some liver parameters and also significant increases in SGOTs and SGPTs (See paragraph 4.8). In the event of a significant increase in such parameters, therapy must be interrupted.
In patients with impaired hepatic function or with previous hepatic pathologies, transaminases should be evaluated on a regular basis during long-term therapies. With ketoprofen lysine salt cases of jaundice and hepatitis were reported.

Ketoprofen lysine salt should be given with caution in patients with hematopoietic alterations, systemic lupus erythematosus, or mixed affections of connective tissue.

The use of NSAIDs can compromise fertility and is not recommended in women who intend to start a pregnancy.
Ketoprofen should be discontinued in women who have difficulty conceiving or being subjected to fertility surveys.

Treatment should be discontinued in the event of visual disturbances such as blurred vision.

Asthma subjects with chronic rhinitis, chronic sinusitis and/or nasal polyposis have a higher risk of allergy to aspirin and/or NSAIDs, if compared to the rest of the population. Administration of this medicine may cause asthma attacks or bronchospasm, especially in allergic subjects to aspirin or NSAIDs (see paragraph 4.3).

To avoid any hypersensitivity or photosensitivity phenomena, it is advisable not to expose yourself to sunlight during use.

Important information about some excipients
SOLKET contains sorbitol: patients affected by rare hereditary problems of intolerance to fructose should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction
Not recommended associations:

- Other NSAIDs (included inhibitors of cyclooxygenase-2), including high doses of salicylates (≥ 3 g/die): concomitant administration of different NSAIDs may increase of rick of ulcerations and gastrointestinal bleeding, by a synergic effect.
- Anticoagulants (eg heparin and warfarin): NSAIDs may amplify the effects of the anticoagulants by increasing risk of bleeding by inhibition of platelet function and damage to the gastrointestinal mucosa (see paragraph 4.4). If concomitant administration cannot be avoided, patients should be carefully monitored.
- Antiaggregant agents (eg ticlopidine and clopidogrel): increase of the risk of gastrointestinal hemorrhage by inhibition of platelet function and damage to the gastrointestinal mucosa (see paragraph 4.4). If concomitant administration cannot be avoided, patients should be carefully monitored.
- Lithium: risk of increased plasmatic levels of lithium, that sometimes could reach toxic levels due to lower renal excretion of lithium. Where necessary, plasmatic levels of lithium should be monitored with eventual dosage adjustment during and after the therapy with NSAIDs.
- Methotrexate, at doses higher than 15 mg/week: increase of risk of hematologic toxicity due to methotrexate, especially if administered at high doses (> 15 mg/week); probably due to a shift of methotrexate from the protein bond and a decreased renal clearance.

- Idantoins and sulphonamides: the toxic effects of these substances may be increased.

Associations that require precaution:
- Corticosteroids: increase of risk of gastrointestinal ulceration or bleeding (see paragraph 4.4).
- Diuretics: Patients and especially those taking diuretics and dehydrated, are at high risk of developing secondary kidney failure due to a reduction in renal blood flow. The patients must be properly hydrated and monitoring of kidney function after the onset of concomitant therapy must be taken in consideration (see paragraph 4.4). NSAIDs may reduce the effect of diuretics.
- ACE inhibitors and angiotensin II antagonists: in some patients with impaired renal function (eg dehydrated patients or elderly patients with compromised renal function), co-administration of an ACE inhibitor or angiotensin II antagonist and agents that inhibit the cyclooxygenase system can lead to a further deterioration of renal function, which includes a possible acute renal failure. Therefore the association should be administered carefully, especially in elderly.
- Methotrexate, used at low doses, lower than 15 mg/week: during the first weeks of the combined therapy a emocromocytometric examination must be performed every week. In presence of alterations of renal function or elderly patients, the monitoring should be more frequent.
- Pentoxifylline: increase of hemorrhagic risk. It is necessary a more careful clinical monitoring and of bleeding time.
- Zidovudine: risk of increased toxicity on the red cell line, by action of its reticulocytes, with a serious anemia that occurs a week after the beginning of the treatment with the NSAID. Check the complete emocromocytometric examination and reticulocytes count one or two weeks after beginning of treatment with the NSAID.
- Sulfonylureas: NSAIDs may increase the hypoglicemic effect of sulfonylureas by displacing them from the binding sites with the plasmatic proteins.

Associations that must be taken into consideration:
- Antihypertensives (beta-blockers, inhibitors of conversion enzyme of angiotensin, diuretics): NSAIDs may reduce the effect of antihypertensive drugs, due to inhibition of the synthesis of prostaglandins.
- Thrombolytics: increase of the risk of bleeding.
- Probenecid: concomitant administration of probenecid may considerably reduce the plasmatic clearance of ketoprofen and accordingly the plasmatic concentrations of ketoprofen may be increased; this interaction could be due to an inhibitory mechanism at the site of renal tubular secretion and glucuronoconjugation, and requires adaptation of ketoprofen dose.
- Antiaggregant agents and selective serotonine reuptake inhibitors (SSRIs): increase of the risk of gastrointestinal hemorrhage (see paragraph 4.4).
- Cyclosporine, tacrolimus: risk of nephrotoxic additive effects, especially in elderly patients. Renal function should be measured during the associated therapy.

4.6 Fertility, pregnancy and lactation

Pregnancy

The inhibition of prostaglandin synthesis can negatively affect pregnancy and/or embryo/fetal development; therefore, Ketoprofen lysine salt should not be given during pregnancy. Results of epidemiological studies suggest an increased risk of abortion and cardiac malformation and gastroschisis after the use of a prostaglandin synthesis inhibitor in the early stages of pregnancy. The absolute risk of cardiac malformations increased from less than 1% to about 1.5%. It was considered that the risk increases with the dose and duration of the therapy. In animals, the administration of prostaglandin synthesis inhibitors has showed to cause an increase in pre- and post-plant loss and of embryo-fetal mortality.

In addition, an increase in incidence of various malformations, including the cardiovascular one, was reported in animals to which they had been given prostaglandin synthesis inhibitors during the organogenetic period.
From the 20th week of pregnancy onwards, the use of Solket may cause oligohydramnios resulting from foetal renal dysfunction. This condition may be seen shortly after initiation of treatment and is usually reversible upon discontinuation of treatment. In addition, there have been reports of ductus arteriosus constriction following treatment in the second trimester, most of which resolved after treatment cessation. Therefore, during the first and second trimester of pregnancy, Solket should not be given unless crearly necessary. If Solket is used by a woman attemping to conceive, or during the first and second trimester of pregnancy, the lowest possible dose should be used for the shortest duration possible.
Following exposure to Solket for several days from the 20th week of gestation onwards, antenatal monitoring for oligohydramnios and ductus arteriosus constriction should be considered. In the event of oligohydramnios or ductus arteriosus constriction, Solket treatment should be discontinued.
During the third trimester of pregnancy, all prostaglandins synthesis inhibitors can expose the fetus to:

- cardiopulmonary toxicity (premature constriction/closure of the ductus arteriosus and pulmonary hypertension);
- renal disfunction (see above);

the mother and newborn, at the end of the pregnancy, to:

- possible extension of bleeding time, and anti-aggreganting effect which may occur even at very low doses;
- inhibition of uterine contractions resulting in delayed or prolonged labour.

Consequently, Solket is contraindicated during the third trimester of pregnancy (see sections 4.3 and 5.3).

Lactation
Since no data are available on secretion of ketoprofen lysine salt in the breast milk, ketoprofen must not be administered during breast-feeding.

Fertility
The use of ketoprofen lysine salt, as any other drug that inhibits prostaglandin synthesis and cycloxigenase, is not recommended in women that intend to start a pregnancy.
Ketoprofen should be discontinued in women who have difficulty conceiving or being subjected to fertility surveys.

4.7 Effects on ability to drive and use machines
Patients must be informed about the potential occurrence of drowsiness, dizziness or convulsions and must avoid driving or carry out activities that require particular surveillance in case of such symptoms are present (see paragraph 4.8).

4.8 Undesirable effects
The experience derived from the marketing of oral formulations of ketoprofen lysine salt points out that the onset of side effects is a very rare event. Based on the estimate of exposed patients, derived from the number of packs sold, and considering the number of spontaneous reports, less than one patient per 100,000 had adverse reactions. In most cases, the symptoms were transient and resolved with the discontinuation of therapy and, in some cases, with specific pharmacological treatment.

The following adverse reactions have been observed following administration of ketoprofe lysine salt in adults.

Frequency of the adversee events is classfied as follows: very common (≥1/10); common (≥1/100, <1/10); uncommon (≥1/1000, <1/100); rare (≥1/10,000, <1/1,000); very rare (<1/10,000), unknown (it cannot be determined on the basis of the availabe data).

Pathologies of blood and lymphatic system:
Rare: anemia due to bleeding.
Unknown: Agranulocytosis, thrombocytopenia, midazular aplasia.
Single cases of leukocytosis, lymphangitis, purpura, thrombocytopenic purpura and leukocytopenia have been reported.

Immune system disorders:
Unknown: anaphylactic reactions (included shock).

Psychiatric disorders:
Unknown: mood alteration, excitability, insomnia.
There was a single case of anxiety, visual hallucinations, hyperexcitability and behavioural alteration in a pediatric patient that had taken a double dose compared to the recommended dose in the SmPC. The symptoms disappeared spontaneously within 1-2 days.

Nervous system pathologies:
Uncommon: headache, dizziness, drowsiness.
Rare: paresthesia.
Unknown: convulsions, dysgeusia.
Only occasionally, tremors, transient dyskinesia, asthenia, dizziness have been observed. There was a single case of tremors and hyperkinesis in an elderly patient treated concomitantly with a quinolone antibiotic.

Eye disorders:
Rare: blurred vision (see paragraph 4.4).
Unknown: periorbital edema.

Ear and labyrinth disorders:
Rare: tinnitus.

Cardiac pathologies:
Unknown: heart failure, palpitations, tachycardia

Vascular pathologies:
Unknown: hypertension, vasodilatation, hypotension
Exceptionally cases of vasculitis and skin redness have been reported.
Clinical studies and epidemiological data suggest that the use of some NSAIDs (especially high doses and long-term treatments) may be associated with a modest increase in the risk of arterial thrombotic events (eg myocardial infarction or stroke) (see paragraph 4.4).

Respiratory, thoracic and mediastinic pathologies:
Rare: asthma.
Unknown: broncospasm (especially in patients with known hypersensitivity to acetyl salicylic acid and other NSAIDs), rhinitis, dyspnoea, laryngeal edema, laryngospasm.
There was a single case of acute respiratory failure with fatal outcome in an asthmatic patient and sensitive to aspirin.

Most of the reactions manifested in allergic/asthmatic patients and/or with known hypersensitivity to NSAIDs were of serious nature.

Gastrointestinal pathologies:
The adverse events more commonly observed are of gastrointestinal nature. Peptic ulcers, perforation or gastrointestinal hemorrhage, sometimes fatal especially in elderly patients, may occur (see paragraph 4.4).
Common: nausea, vomiting, dyspepsia, abdominal pain.
Uncommon: constipation, diarrhea, flatulence, gastritis.
Rare: ulcerative stomatitis, peptic ulcer.
Unknown: colitis exacerbation and Crohn's disease, gastrointestinal bleeding and perforation (see paragraph 4.4).
Gastric and duodenal ulcer and erosive gastritis have been reported. In two individual cases hematemesis or melena occurred respectively. Two cases of ulcerative stomatitis and edema of the tongue have been reported.

Hepatobiliary pathologies:
Rare: hepatitis, increase of transaminases levels, high levels of serum bilirubin due to hepatic disorders.

Pathologies of skin and subcutaneous tissue:
Uncommon: rash, itch.
Unknown: photosensitization, alopecia, urticaria, angioedema, bullous eruptions, including Steven-Johnson syndrome and toxic epidermal necrolysis, erythema, esantema, maculo-papular esantema, dermatitis, skin redness, eczema.
Some NSAIDs, including ketoprofen, may cause extremely rare serious mucocutaneous reactions (such as Steven-Johnson syndrome and Lyell syndrome).

Renal and urinary pathologies:
Unknown: acute renal failure, tubular-interstitial nephritis, nephrotic syndrome, abnormal renal function tests, dysuria.
Face edema and hematuria have been reported. A single case of oliguria has been reported.

Systemic pathologies and conditions concerning the site of administration:
Uncommon: edema, fatigue.
Unknown: allergic and anaphylactoid reactions, anaphylactic shock, mouth edema.
Single cases of respectively peripheral edema and syncope have been reported.

Diagnostic tests:
Rare: weight increase.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system at the web address http://www.aifa.gov.it/content/segnalazioni-reazioni-avverse.

4.9 Overdose

Cases of overdose with dose higher than 2.5 g of ketoprofen lysine salt have beeb reported. In most cases, the observed symptoms have been of benign nature and limited to lethargy, drowsiness, nausea, vomiting and epigastric pain.

Overdose symptoms may also include: central nervous system disorders such as headache, dizziness, confusion and loss of consciousness, as well as pain, nausea and vomiting. Hypotension, respiratory depression and cyanosis may also occur.
No specific antidotes there are for an overdose of ketoprofen lysine salt. In case of suspected serious overdose, gastric lavage is recommended and institution of supporting and symptomatic therapies to compensate dehydration to monitor the renal function and correct acidosis if present.
In case of renal failure, hemodialysis can be useful for removal of the drug from circulation.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anti-inflammatory, anti-rheumatic, non-steroidal drugs. Propionic acid derivatives. ATC: M01AE03.
Ketoprofen lysine salt is the lysine salt of the 2-(3-benzoylphenyl) propionic acid, an analgesic, anti-inflammatory and anti-pyretic drug that belongs to NSAIDs class (M01AE).
Ketoprofen lysine salt is more soluble than acid ketoprofen.
The mechanism of action of NSAIDs is correlated to the reduction of prostaglandins synthesis through inhibition of cyclooxygenase enzyme.
In particular, inhibition of transformation of arachidonic acid is observed in cyclic endo-peroxides, PGG 2 and PGH 2, prostaglandins precursors PGE 1, PGE 2, PGF 2a and PGD 2 and also prostacyclin PGI 2 and thromboxanes (TxA 2 and TxB 2). In addition, inhibition of prostaglandins synthesis may interfere with other mediators like quinines, causing an indirect action that would add itself to the direct action.
Ketoprofen lysine salt makes an antipyretic activity without interfering with the normal processes of thermoregulation.
Flogistic painful manifestations are removed or attenuated, promoting joint mobility.

5.2 Pharmacokinetic properties

Ketoprofen lysine salt has more solubility respect to the acid ketoprofen.
The form for oral use permits the administration of the active substance already in water solution and therefore it leads to a rapid increase of plasmatic levels and an early achievement of peak value. This is manifested clinically with a more rapid onset and higher intensity of the antalgic and anti-inflammatory effect.
The kinetic profile in children does not differ from that of adult.
Repeated administration does not modify the kinetic of the drug and does not produce accumulation.
Ketoprofen is bonded to the plasmatic proteins for 95-99%. Significant levels of ketoprofen have been reported in tonsillar tissue and synovial liquid after systemic administration.
The elimination is rapid and essentially by renal way: the 50% of the administered product by systemic way is excreted in urines in 6 hours. Ketoprofen is extensively metabolized: about 60-80% of the product administered by systemic way is under the form metabolites in urines.

5.2 Preclinical safety data

DL_{50} of oral ketoprofen lysine salt in rat and mouse is respectively 102 and 444 mg/kg, equal to 30-120 times the dose active as anti-inflammatory and analgesic in animal. By intraperitoneal way, DL_{50} of ketoprofen lysine salt is 104 and 610 mg/kg respectively in rat and mouse.

Prolonged treatment in rat, dog and monkey, with orally administered ketoprofen lysine salt at doses equal or higher to the foreseen therapeutic doses, did not cause the appearance of toxic phenomena. At high doses, gastrointestinal and renal alterations have been observed, referable to the known side effects caused in animal by the non-steroidal anti-inflammatory drugs. In a prolonged toxicity study conducted in

rabbit by oral or rectal way the ketoprofen showed to be better tolerated when administered by rectal way respect to the oral way. In a tolerability study conducted in rabbit by intramuscular way, ketoprofen lysine salt showed to be well tolerated.

Ketoprofen lysine salt resulted to be non-mutagenic in genotoxicity tests performed “in vitro” and “in vivo”. Carcinogenesis studies with ketoprofen in mouse and rat showed the absence of carcinogenic effects.

About embryo-fetal toxicity and teratogenicity of NSAIDs in animal, see paragraph 4.6.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sorbitol (Neosorb P60), sorbitol (Neosorb P30/P60), povidone, silica colloidal anhydrous, sodium chloride, saccharin sodium, ammonium glycyrrhizinate, mint flavor.

6.2 Incompatibilities

Not applicable.

6.3 Shelf-life

3 years.

6.4 Special precautions for storage

This medicinal product does not require any special precaution for storage.

6.5 Nature and contents of container

Paper/aluminum/polythene heat-sealed sachets.
Packaging of 30 bipartite sachets of 2g.

6.6 Special precautions for disposal and handling

No special instruction.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORIZATION HOLDER

Aesculapius Farmaceutici S.r.l.
Via Cefalonia, 70
25124 Brescia

8. MARKETING AUTHORIZATION NUMBER(S)

SOLKET “80 mg powder for oral solution” 30 bipartite sachets
MA No. 038727018

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

First Authorization: 15/03/2010
Renewal of Authorization: 17/11/2015

10. DATE OF REVISION OF THE TEXT

January 2023