SUMMARY OF PRODUCT CHARACTERISTICS

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1. NAME OF MEDICINE

VIGAFEN 80 mg powder for oral solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One sachet contains:
Active substance: ketoprofen lysine salt 80 mg (equivalent of 50 mg of ketoprofen).

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for oral solution.

4. CLINICAL INFORMATION

4.1 Therapeutic indication

Adults: Symptomatic treatment of inflammation associated with pain, including: rheumatoid arthritis, ankylosing spondylitis, painful osteoarthritis, extra-articular rheumatism, post-traumatic inflammation, painful inflammatory disorders in dentistry, Otolaryngology, urology and Pneumology.

4.2 Posology and method of administration

Adults: one sachet of 80 mg (full dose) three times a day during meals.The maximum daily dose is 200 mg of ketoprofen, equivalent to 320 mg di ketoprofen lysine salt. The benefitrisk ratio should be carefully considered before starting treatment with the daily dose of 200 mg ketoprofen, and higher doses are not recommended (see also section 4.4).

Special populations

Paediatric population
VIGAFEN is contra-indicated in children and adolescents under 14 of age

Elderly: The posology should be carefully determined by the Doctor who will evaluate a possible reduction of the above dosages (see section 4.4).

Patients with hepatic impairment: it is advisable to establish therapy at a daily minimum dosage (see section 4.4).

Patients with mild or moderate renal failure: it is advisable to reduce the initial dose and to practice maintenance with the lowest effective dose. Individualized adjustments may be considered only after the good tolerability of the drug has been established. Monitor the volume of diuresis and renal function
(see section. 4.4).

Side effects can be minimized with the use of the shortest possible treatment duration that you need to control the symptoms (see 4.3).

Instructions on the use of sachet: Pour the contents of a sachet in half a glass of water and stir.

4.3 Contra-indications

VIGAFEN should not be administered in the following cases:

- Hypersensitivity to the active substance, to other non-steroidal anti-inflammatory drugs (NSAIDs) or to any of the excipients
- Patients with a history of hypersensitivity reaction such as bronchospasm, asthma attacks, acute rhinitis, urticaria, nasal polyps, angioneurotic edema or other allergic-type reactions to ketoprofen or substances with similar mechanism of action (e.g. Acetylsalicylic acid or other NSAIDs). Severe, rarely fatal anaphylactic reactions have been observed in these patients (see section 4.8)
- Patients with bronchial asthma
- severe cardiac failure
- Active peptic ulcer/bleeding, or history of bleeding/recurrent peptic ulcer (two or more distinct episodes, evidence of bleeding or ulceration)
- Previous medical history of gastrointestinal bleeding, ulceration or perforation or chronic dyspepsia
- History of gastrointestinal bleeding or perforation resulting from prior therapy with NSAIDs
- leucopaenia and thrombocytopaenia
- Patients with hemostatic disorders
- Crohn's disease or ulcerative colitis
- Gastritis
- Severe hepatic impairment (hepatic cirrhosis, severe hepatitis)
- Severe hemorrhagic diathesis renal failure and other coagulation disorders, during treatment of intensive diuretic therapy
- Third trimester of pregnancy
- Children under 14 years of age

4.4 Special warnings and precautions for use

Warnings

Side effects can be minimised with the use of the lowest effective dose for the shortest possible treatment duration that is needed to control the symptoms (see section 4.2 and the underlying paragraphs on gastrointestinal risks and Cardiovascular disease).

Concomitant use of VIGAFEN with other NSAIDs should be avoided, including selective cyclooxygenase-2 inhibitors.

Gastrointestinal hemorrhage, ulceration and perforation: During treatment with all NSAIDs, at any time, with or without symptoms of warning or previous history of severe gastrointestinal events, has been reported gastrointestinal hemorrhage , ulceration and perforation, which can be fatal.

In the elderly and in patients with history of ulcer, especially if complicated by hemorrhage or perforation (see section 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 proton pump inhibitors) should be considered for these patients and also for patients taking low doses of aspirin or other medications that may increase the risk of gastrointestinal events (See below and section 4.5).

Patients with history of gastrointestinal toxicity, in particular the elderly, must report any unusual abdominal symptom (especially gastrointestinal hemorrhage) in particular in the early stages of

treatment.
Caution should be taken to patients taking concomitant medications that could increase the risk of ulceration or hemorrhage, such as oral corticosteroids, anticoagulants such as warfarin, selective serotonin reuptake inhibitors or agents Antiplatelets such as aspirin (see section 4.5).

Elderly: Elderly patients have an increased frequency of adverse reactions to NSAIDs, especially hemorrhages and gastrointestinal perforations, which can be fatal (see section 4.2). Elderly patients are more predisposed to renal, cardiovascular or hepatic function reduction.
Patients with previous or current gastrointestinal disease should be closely monitored for the emergence of digestive disorders, especially gastrointestinal bleeding.
When bleeding or gastrointestinal ulceration occurs in patients taking VIGAFEN treatment should be suspended.

Patients with previous or current peptic ulcer desease:
NSAIDs should be administered with caution in patients with a history of gastrointestinal disease (ulcerative colitis, Crohn's disease) as these conditions can be exacerbated (see section 4.8-Side effects).

Some epidemiological evidence suggests that Ketoprofen may be associated with a high risk of severe gastrointestinal toxicity compared to other NSAIDs, especially at high doses (see also sections 4.2 and 4.3).

Skin reaction:
Severe 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 4.8). In the 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. AVIGAFEN should be interrupted at the first appearance of skin rash, mucosal lesions or any other sign of hypersensitivity.

Precautions

cardiovascular, renal and hepatic dysfunction:

The administration of Ketoprofen should be performed with particular caution in patients with impaired renal function in view of the essentially renal elimination of the drug.

At the beginning of treatment, renal function should be closely monitored in patients with heart failure, cirrhosis and nephrosis, in patients receiving diuretics or with chronic renal failure, especially if elderly. In these patients, the administration of ketoprofen may induce a reduction in renal blood flow caused by the inhibition of prostaglandins and to determine a renal failure (see section 4.3 contraindications).
Caution is also required in patients subject to diuretic therapy or probable hypovolaemic because the risk of nephrotoxicity is increased.
As with all NSAIDs, the drug can increase plasma urea nitrogen and creatinine. As with other prostaglandin synthesis inhibitors, the drug may be associated with adverse events on the renal system that may lead to glomerular nephritis, renal papillary necrosis, nephrotic syndrome and acute renal failure.

In patients with abnormal liver function tests or a history of liver disease, transaminase levels should be periodically monitored, especially in the case of long-term therapy.
As with other NSAIDs, the drug may cause small transient increments in some hepatic parameters and

also significant increases in SGOT and SGPT. In case of significant increase in these parameters, the therapy should be interrupted. Cases of jaundice and hepatitis have been reported with Ketoprofen.

Cardiovascular and cerebrovascular effects

As with other NSAIDs, patients with uncontrolled hypertension, congestive heart failure, established ischemic heart disease, peripheral arterial illness and/or cerebrovascular disease should be treated with ketoprofen lysine salt, only After careful evaluation. Similar considerations must be made before a long-term treatment is initiated in patients with risk factors for cardiovascular disease (e.g. hypertension, hyperlipid, diabetes mellitus, smoking).
Adequate monitoring and appropriate instructions are necessary in patients with a positive history of hypertension and/or mild to moderate congestive heart failure because in combination with the treatment with NSAIDs, retention of Liquids and edema have been reported.

Clinical studies and epidemiological data suggest that the use of some NSAIDs (especially at high dosages and for long-term treatments) may be associated with an increase in the risk of arterial thrombotic events (p.es. Myocardial infarction or stroke). There is insufficient data to exclude a similar risk for ketoprofen lysine salt.

An increase in the risk of atrial fibrillation associated with the use of NSAIDs has been reported.
Hyperkalemia may occur, especially in patients with underlying diabetes, renal failure, and/or concomitant treatment with hyperkalemia promoters (see section 4.5).
In these circumstances, potassium levels should be monitored.

Infection
Like other NSAIDs, in case of infectious disease, the anti-inflammatory, analgesic and antipyretic properties of ketoprofen may mask common symptoms of infection progression as fever.
Administer with caution in patients with allergic manifestations or prior allergy.
Respiratory diseas:
Like all non-steroidal medications the use of ketoprofen in patients with bronchial asthma or with allergic diathesis can make an asthmatic crisis occur.
Patients with asthma associated with chronic rhinitis, chronic sinusitis and/or nasal polyposis have a higher risk of allergy to acetylsalicylic acid and/or NSAIDs than the rest of the population.
The administration of this medicine can cause asthmatic or bronchospasm, shock and other allergic phenomena, especially in patients allergic to acetylsalicylic acid or NSAIDs (see section 4.3). For the interaction of the drug with the metabolism of arachidonic acid, in asthmatics and susceptible patients may arise bronchospasm crisis and possibly shock and other allergic phenomena.

Visually impaired
If vision disturbances are blurred, the treatment should be interrupted.

VIGAFEN should be administered with caution in patients with hematopoietic alterations, systemic lupus erythematosus or mixed connective tissue diseases.

VIGAFEN contains sorbitol: Patients suffering from rare hereditary problems of fructose intolerance should not take this medicine.

4.5 Interactions with other medicines and other forms of interaction

Associations not recommended:

- Other NSAIDs (including selective cyclooxygenase 2 inhibitors) and high doses of salicylates (≥ 3 G/day): Simultaneous administration of several NSAIDs can increase the risk of gastrointestinal ulcers and bleeding, for a synergistic effect.
- Anticoagulants (heparin and warfarin): NSAIDs can amplify the effects of anticoagulants, such as warfarin (see Section 4.4). Increased risk of bleeding by inhibition of platelet function and damage to the gastrointestinal mucosa (see Section 4.4). If co-administration cannot be avoided, the patient should be closely monitored.
- Platelet aggregation inhibitors (Ticlopidine and Clopidogrel): Increased risk of bleeding by inhibition of platelet function and damage to the gastrointestinal mucosa (see Section 4.4). If co-administration cannot be avoided, the patient should be closely monitored.
- Lithium (described with several NSAIDs): NSAIDs increase plasma levels of lithium (decreased renal excretion of lithium), which can reach toxic values. This parameter therefore requires to be monitored and the lithium dosage must be adapted in the course and following treatment with Ketoprofen and other NSAIDs.
- Methotrexate, used at doses higher than 15 mg/week: Increased blood toxicity of methotrexate, especially when administered at high doses (> 15 mg/week), probably related to the displacement of protein binding methotrexate and Decrease in renal clearance due to anti-inflammatory agents in general. Take at least 12 hours between the suspension or initiation of treatment with ketoprofen and administration of methotrexate.
- Hydantoins and Sulphonamides: The toxic effects of these substances can be increased.

Associations requiring precaution:
- Drugs or therapeutic categories that may promote hyperkalemia: Some drugs or therapeutic categories may promote hyperkalemia, e.g. Potassium salts, potassium-sparing diuretics, inhibitors of enzymatic converters (ACE inhibitors), Angiotensin Il receptor blockers, NSAIDs, heparins (low molecular weight or non-fractional), cyclosporine, Tacrolimus and Trimethoprim. The occurrence of hyperkalemia may depend on the presence of cofactors. The risk is strengthened when the above mentioned medicinesare administered concomitantly.
- Tenofovir: Concomitant administration of tcnofovir Disoproxil Fumarate and NSAIDs may increase the risk of renal failure.
- Patients who are taking diuretics and among those who are particularly dehydrated are at greater risk of developing renal failure secondary to the reduction of renal blood flow caused by the inhibition of prostaglandins. These patients should be rehydrated prior to the initation of concomitant therapy and the renal function must be monitored closely after treatment begins (see Section 4.4). NSAIDs can reduce the effect of diuretics.
- ACE inhibitors and angiotensin II antagonists: in patients with impaired renal function (e.g. dehydrated patients and elderly patients) co-administration of an ACE inhibitor or angiotensin e antagonist and agents capable of Inhibiting the cyclooxygenase may result in further deterioration of this renal function, which includes a possible acute renal failure. Therefore, the combination should be administered with caution, especially in elderly patients. Patients should be adequately hydrated and monitoring of renal function should be considered after the initiation of concomitant therapy.
- Methotrexate, Used at doses below 15 mg/week: Increased blood toxicity of methotrexate for a decrease in renal clearance due to anti-inflammatory agents in general. Perform weekly monitoring of the blood counts exam during the first weeks of the association. Increase monitoring in case of even mild worsening of renal function, as well as in the elderly.
- Corticosteroids: Increased risk of gastrointestinal ulceration or bleeding (see Section 4.4).
- Pentoxifylline: Increased risk of bleeding. Increase clinical monitoring and control bleeding time more frequently.
- Zidovudine: Risk of increased toxicity on the red Cell Line for action on reticulocytes, with severe anemia manifesting one week after initiation of treatment with NSAIDs. Check the complete

blood counts examination and the reticulocytes count one or two weeks after starting the treatment with the NSAIDs.

- Sulphonylurea: NSAIDs can increase the hypoglycemic effect of sulphonylurea by displacement from binding sites with plasma proteins.
- Cardiac glucosides: NSAIDs can exacerbate heart failure, reduce for filtration rate, and increase cardiac glycosides levels; However, the pharmacokinetic interaction between active glycosides Ketoprofen has not been demonstrated.

Associations that need to be considered:

- antihypertensive agents (Beta-blockers, ACE inhibitors, diuretics): NSAIDs can reduce the effect of antihypertensive medications. Treatment with an NSAID can decrease their antihypertensive effect by inhibiting the synthesis of vasodilatory prostaglandins.
- Mifepristone: The efficacy of the contraceptive method can, theoretically, be reduced due to the antiprostaglandiniche properties of non-steroidal anti-inflammatory drugs (NSAIDs) including aspirin (acetylsalicylic acid). There are some evidences suggesting that the simultaneous administration of NSAIDs on the day of dose of prostaglandin does not adversely affect the effects of mifepristone or prostaglandin on cervical maturation or On uterine contractility and does not reduce the clinical efficacy of medical pregnancy interruption.
- Intrauterine contraceptive devices (IUDs): The efficacy of the device may be reduced resulting in pregnancy. Ciclosporin and Tacrolimus: Simultaneous treatment with NSAIDs may lead to a greater risk of nephrotoxicity especially in elderly subjects. Thrombolytic: Increased risk of bleeding.
- Anti-aggregating agents and selective serotonin reuptake inhibitors (SSRIs): Increased risk of gastrointestinal hemorrhage (see Section 4.4).
- Probenecid: Co-administration of Probenecid can markedly reduce the plasma clearance of ketoprofen and, as a result, plasma concentrations of ketoprofen may be increased; this interaction may be due to an inhibitory mechanism at the site of renal tubular secretion and glucurono conjugation and requires an adaptation of the dose of ketoprofen.
- Quinolone antibiotics: Animal data indicate that NSAIDs can increase the risk of convulsions associated with quinolone antibiotics. Patients taking NSAIDs and quinolones may have an increased risk of developing convulsions.
- Diphenylhydantoin and Sulphonamides: Since the protein binding of the ketoprofon is high, it may be necessary to reduce the dosage of diphenylhydantoin or sulphonamidesthat should be administered at the same time.
- Gemeprost: reduced efficacy of gemeprost.

Avoid alcohol consumption

4.6 Pregnancy and lactation

Pregnancy

The use of Ketoprofen during the first and second trimesters of pregnancy should be avoided.
Inhibition of prostaglandin synthesis may adversely affect pregnancy and/or embryo/fetal development.
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 by less than 1%, up to about 1.5%. It was considered that the risk increases with the dose and duration of therapy. In animals, the administration of prostaglandin synthesis inhibitors has shown to cause an increase in the loss of pre-and post-implant and embryo-fetal mortality.
Furthemore, an increase in incidence of various malformations, including cardiovascular, was

reported in animals to which prostaglandin synthesis inhibitors were administered during the organogenic period.
During the first or second trimester of pregnancy, ketoprofen should not be administered except in strictly necessary cases.
If the ketoprofen is used by a woman who wants a pregnancy, or during the first and second trimester of pregnancy, the dose and duration of treatment must be kept as low as possible.
During the third trimester of pregnancy all prostaglandin synthesis inhibitors may expose the fetus to:

- Cardiopulmonary toxicity (with premature closure of the arterial duct and pulmonary hypertension);
- Renal dysfunction, which may progress in renal failure with oligo-idroamnios; The mother and the newborn, at the end of pregnancy, to:
- Possible prolonged bleeding time, and antiplatelet effect which may also be necessary at very low doses;
- Inhibition of uterine contractions resulting delayed or prolonged labor.

The use of the drug close to partorition may cause changes in the hemodynamics of the small circle of the unborn child with serious consequences for breathing.
Therefore, the Ketoprofen is contraindicated during the third trimester of pregnancy.

Lactation
There is no information available on the excretion of ketoprofen in breast milk. Ketoprofen is not recommended during breastfeeding.

Fertility
The use of NSAIDs can reduce female fertility and is not recommended in women who intend to start a pregnancy.
The use of VIGAFEN, as well as any inhibitory drug of prostaglandin synthesis and cyclooxygenase, is not recommended in women who intend to start a pregnancy.
The administration of NSAIDs, as well as VIGAFEN, should be suspended in women who have fertility problems or who are subjected to fertility surveys.

4.7 Effects on the ability to drive and use machines

If drowsiness, dizziness, or convulsions occur after administration of ketoprofen, the patient should avoid driving, using machines or carrying out activities requiring particular vigilance.

4.8 Side effects

Like all medicines, VIGAFEN can cause side effects, although not all people will manifest them.
The most commonly observed adverse events are of a gastrointestinal nature.
Expected frequency Classification:
Very common (1/10), common (affecting 1/100 to ≤ 1/10), uncommon (affecting 1/1000 to ≤ 1/100), rare (affecting 1/10000 to ≤ 1/1000), very rare (≤ 1/10000), frequency not known (The frequency cannot be defined on the basis of the available data).
The following adverse reactions were observed with the use of ketoprofen in adults:

Infections and infestation
Not known: aseptic meningitis, Lymphangitis.

Blood and lymphatic system disorders

Rare: Haemorrhagic anemia
Not known: Thrombocytopenia, agranulocytosis, medullary insufficiency, hemolytic anemia, severe neutropenia, aplastic anemia, leukocytosis, purpura thrombocytopenic.

Immune system disorders
Not known: anaphylactic reactions (including shock), hypersensitivity.

Disturbi del metabolismo e della nutrizione
Not known: Hyperkalemia, hyponatremia (see Sections 4.4 and 4.5).

Psychiatric disorders
Not known: depression, hallucinations, confusion, mood alterations, excitability, insomnia. In a paediatric patient who had taken a double dose compared to that recommended in CPR, anxiety, behavioural disorder, was also manifested.

Nervous system disorders
Uncommon: headache, dizziness, vertigo, drowsiness
Rare: Paraesthesia
Very rare: dyskinesia, syncope
Not known: convulsions, Dysgeusia, tremor, hyperkinesis.

Eye disorders
Rare: Blurred vision (see Section 4.4)
Not known: periorbital edema.

Ear and labyrinth disorders
Rare: ringing.

Heart disease
Not known: heart failure, atrial fibrillation, palpitations and tachycardia

Vascular disorders
Not known: hypertension, vasodilation, vasculitis (including Leukocytoclastic vasculitis)
Very rare: hypitension.

Respiratory, thoracic and mediastinal disorders
Rare: asthma
Very rare: laryngeal oedema
Not known: Bronchospasm (especially in patients with hypersensitivity to acetylsalicylic acid and other NSAIDs), rhinitis, dyspnea, laryngospasm, acute respiratory failure (a single, fatal outcome has been reported in an asthmatic patient and Sensitive to aspirin).

Gastrointestinal disease
Common: dyspepsia, nausea, abdominal pain, vomiting
Uncommon: constipation, diarrhoea, flatulence, gastritis
Rare: peptic ulceration, colitis, stomatitis
Not known: Gastralgia, exacerbation of colitis and Crohn's disease, gastrointestinal hemorrhage, gastrointestinal perforation (sometimes fatal, especially in the elderly-see Section 4.4), gastric ulcer, duodenal ulcer, gastric heartburn, mouth edema, Pancreatitis, haematemesis, hyperchlorhydria, gastric pain, erosive gastritis, edema of the tongue.

Hepatobiliary disorders
Rare: Hepatitis, increased transaminases, increased blood bilirubin, jaundice.

Skin and subcutaneous tissue disorders
Uncommon: rash, itching
Not Known: Photosensitization, Alopecia, urticaria, angioedema, bullous eruptions including Stevens-Johnson syndrome, Lyell syndrome, toxic epidermal toxic, erythema, Exanthema, Exanthema maculo-Papuleare, purpura, pustulosis acute generalized esantemica, Dermatitis.

Renal and urinary disorders
Very rare: haematuria
Not known: acute renal failure, interstitial tubule nephritis, nephritis or nephritic syndrome, nephrotic syndrome, glomerular nephritis, water/sodium retention with possible edema, acute renal failure, acute tubular necrosis, papillary necrosis Renal, oliguria, abnormal renal function tested

General Disorders and Administration Site Conditions
Uncommon: edema, tiredness, peripheral oedema, chills
Very rare: asthenia, facial oedema.

Diagnostic examination
Rare: increased weights.

Clinical studies and epidemiological data suggest that the use of some NSAIDs (especially at high dosages and for long-term treatments) may be associated with a modest increase in the risk of arterial thrombotic events (e.g. myocardial infarction or stroke) (see Section 4.4). (already present at 4.4.)

Report of suspected adverse reactions.
The reporting of suspected adverse reactions occurring after the authorisation of the medicinal product is important, as it allows a continuous monitoring of the benefit/risk ratio of the medicinal product. Healthcare professionals are required to report any suspected adverse reactions via the national reporting system to the address: Http://www.agenziafarrnaco.gov.it/it/responsabili.

4.9 Overdose

Cases of overdose with doses up to 2.5 g of ketoprofen have been reported.
In most cases, benign and limited symptoms of lethargy, drowsiness, nausea, vomiting, epigastric pain and abdominal pain, headache, dizziness and diarrhea have been observed.
In case of severe overdose, hypotension, respiratory depression and gastrointestinal bleeding were observed.
The patient should be immediately transferred to a specialist centre to initiate symptomatic treatment.
There are no specific antidotes in case of overdose of ketoprofen.
In case of suspected massive overdose we recommend a gastric lavage and to establish a symptomatic and supportive treatment to compensate for dehydration, monitor urinary excretion and, if appropriate, correct the acidosis.
In cases of renal failure, hemodialysis may be useful to remove the drug from the body.

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 2-(3-Benzoilfenil) propionic acid, an analgesic, anti-inflammatory and antipyretic that belongs to the class of NSAIDs (M01AE). Ketoprofen lysine salt is more soluble than acid ketoprofen.
The mechanism of action of NSAIDs is related to the reduction of prostaglandin synthesis by inhibition of the cyclooxygenase enzyme.
In particular, it is observed an inhibition of arachidonic acid transformation in cyclic Endoperossidi, PGG2 and PGH2, precursors of prostaglandins PGE1, PGE2, PGF2α and PGD2 and also of Prostacyclin PGI2 and Thromboxanes (TxA2 and TxB2). Moreover, inhibition of prostaglandin synthesis may interfere with other mediators such as the chini, causing an indirect action that would added to direct action.
Ketoprofen lysine salt has a pronounced analgesic effect, correlated with both its anti-inflammatory effect and with a central effect.
Ketoprofen lysine salt exerts a antipyretic activity without interfering with the normal thermoregulation processes.
Painful inflammatory manifestations are eliminated or attenuated by encouraging range of motion.

5.2. Pharmacokinetics

The Ketoprofen lysine salt has more solubility than acid ketoprofen.
The form for oral use allows the assumption of the active ingredient already in aqueous solution and therefore leads to a rapid increase of plasma levels and an early achievement of the peak value. This is extrinsic, clinically, with a faster onset and a greater intensity of the analgesic and antiphlogistic effect.
The kinetic profile in the child does not differ from that of the adult.
Repeated administration does not alter the kinetics of the drug or produce accumulation.
Ketoprofen is linked for 95-99% to plasma proteins. Significant levels of Ketoprofen were found in the tonsil tissue and synovial fluid after systemic administration.
The elimination is rapid and essentially renal: 50% of the product administered by systemic means is excreted in the urine in 6 hours. The Ketoprofen is extensively metabolized: approximately 60-80% of the systemically administered product is found in the form of metabolites in the urine.

5.3. Preclinical safety data

The LD 50 of ketoprofen lysine salt in the rat and the mouse by the oral route was respectively 102 and 444 mg/kg, equal to 30-120 times the active dose as an anti-inflammatory and analgesic in the animal. Intraperitoneally, the LD 50 of Ketoprofen lysine Salt was 104 and 610 mglkg respectively in rats and mice.
Prolonged treatment in rats, dogs and monkeys, with ketoprofen lysine salt by the oral route at doses equal to or greater than the expected therapeutic dosages, did not cause the onset of any toxic phenomena. Gastrointestinal and renal alterations have been reported at high doses due to the known side effects on the animal, from non-steroidal anti-inflammatory drugs. In a prolonged toxicity study conducted in the rabbit, orally or rectally, Ketoprofen was better tolerated when administered rectally than the oral route. In a tolerability study conducted on the Rabbit intramuscularly, ketoprofen lysine salt was well tolerated.
Ketoprofen Salt of lysine is a non-mutagenic result in the genotoxicity tests performed 'in vitro and in 'Vivo'. Carcinogenesis studies with Ketoprofen in mice and rats highlighted the absence of carcinogenic effects.
As regards the foetal toxicity and the teratogenesis of the NSAIDs in the animal, refer to par. 4.6.

6. PHARMACEUTICAL PARTICULARS

6.1. list of excipients

Sorbitol, colloidal anhydrous silica, sodium chloride, saccharin sodium, mint aroma.

6.2. incompatibility

Not known

6.3. Period of validity

36 Months

6.4. Special precautions for storage

No particular condition for storage

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

Do not use this medicine after the expiration date that is stated on the label after "exp.". The expiration date refers to the last day of that month and to the product in properly preserved intact packaging.

6.5. Nature and contents of container

lithographed cardboard box containing 30 sachets of paper/aluminium/polythene.

6.6. Special precautions for disposal and other handling

No particular instruction.
The unused medicinal product and the waste derived from this medicinal product must be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Vigapharma S.r.l. Via della Costa, 16F – Manziana (ROME) - Italy

8. MARKETING AUTHORISATION NUMBER

VIGAFEN 80 mg powder for oral solution - 30 sachets MA……

9. DATE OF THE FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10. DATE OF REVISION OF TEXT

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