1. NAME OF THE MEDICINAL PRODUCT

Airtal 100 mg powder for oral suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sachet contains 100 mg aceclofenac.

Excipients with known effect: contains 2.639 mg sorbitol (E420) and 10 mg aspartame (E951) in each sachet.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for oral suspension.

Approximately 3 g white or almost white powder.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Symptomatic treatment of pain and inflammation in osteoarthritis, rheumatoid arthritis and ankylosing spondylitis as well as other painful locomotor disorders (e.g. humeroscapular periarthritis and other extra-articular rheumatism). Analgesic in different painful conditions (including lumbar or dental pain and primary dysmenorrhoea).

4.2 Posology and method of administration

Posology

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.4).

Adults
The recommended dose is one sachet twice daily (one in the morning and one in the evening).

Paediatric population
The safety and efficacy in children and adolescents have not been established. The use of Airtal is not recommended in paediatric population.

Elderly
The elderly, who are more likely to be suffering from impaired renal, cardiovascular or hepatic function and receiving concomitant medication, are at increased risk of the serious consequences of adverse reactions. If an NSAID is considered necessary, the lowest effective dose should be used and for the shortest possible duration. The patient should be monitored regularly for GI bleeding during NSAID therapy.
The pharmacokinetics of aceclofenac is not altered in elderly patients. Generally no dose reduction is necessary; however, consider the precautions in section 4.4.

Hepatic insufficiency
The dose of aceclofenac should be reduced in patients with mild to moderate hepatic impairment. The recommended initial dose is 100 mg daily.

Renal insufficiency
There is no evidence that the dose of aceclofenac needs to be modified in patients with mild renal impairment, but as with other NSAIDs caution is advised.

Method of administration
For oral use only.
The contents of the sachets should be dissolved in approximately 40-60 ml of water and should be consumed immediately.
Simultaneous food intake slows the absorption of the active substance in the gastrointestinal tract, but does not reduce its extent.

4.3 Contraindications

Airtal is contraindicated in the following cases:
- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1;
- In patients in whom substances with a similar action (e.g. ibuprofen, acetylsalicylic acid, or other NSAIDs) precipitated attacks of asthma, bronchospasm, acute rhinitis or urticaria, or hypersensitivity to these drugs;
- History of gastrointestinal bleeding or perforation, related to previous NSAIDs therapy. Active, presumable or a history of recurrent peptic or duodenal ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding);
- Active bleeding or bleeding disorders (bleeding diathesis or coagulation disorders);
- Established congestive heart failure (NYHA II-IV), ischaemic heart disease, peripheral arterial disease and/or cerebrovascular disease;
- Severely impaired hepatic or renal function;
- Third trimester of pregnancy.

4.4 Special warnings and precautions for use

The use of Airtal with concomitant NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided (see section 4.5).

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.2, and gastrointestinal and cardiovascular risks below).

Aceclofenac should be administered with caution and under close medical surveillance to patients with the following conditions as these may be exacerbated (see section 4.8):
- Symptoms indicative of gastrointestinal disorders involving either the upper or lower gastrointestinal tract.
- A history of gastrointestinal ulceration, bleeding or perforation.
- Ulcerative colitis.
- Crohn's disease.

Haematological abnormalities, systemic lupus erythematosus (SLE), porphyria, and haematopoietic disorders.
Gastrointestinal effects
Gastrointestinal bleeding, ulceration or perforation, which can be fatal, have been reported with all NSAIDs at any time during treatment, with or without warning symptoms or a previous history of serious gastrointestinal events.

The risk of gastrointestinal bleeding, ulceration or perforation is higher with increasing NSAID doses, in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation (see section 4.3), and in the elderly. These patients should commence treatment on the lowest dose available. Combination therapy with protective agents (e.g. misoprostol or proton pump inhibitors) should be considered for these patients, and also for patients requiring concomitant low dose acetylsalicylic acid, or other drugs likely to increase gastrointestinal risk (see section 4.5).

Patients with a history of gastrointestinal toxicity, particularly when elderly, should report any unusual abdominal symptoms (especially gastrointestinal bleeding) particularly in the initial stages of treatment.

Caution should be advised in patients receiving concomitant medications which could increase the risk of ulceration or bleeding, such as systemic corticosteroids, anticoagulants such as warfarin, selective serotonin-reuptake inhibitors or anti-platelet agents such as acetylsalicylic acid (see section 4.5).

When gastrointestinal bleeding or ulceration occurs in patients receiving Airtal, the treatment should be withdrawn.

Cardiovascular and cerebrovascular effects
Appropriate monitoring and advice are required for patients with a history of hypertension and/or mild to moderate congestive heart failure as fluid retention and oedema have been reported in association with NSAID therapy.

There are insufficient data to exclude such a risk for aceclofenac.

Patients with congestive heart failure (NYHA-I) and patients with significant risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, and smoking) should only be treated with aceclofenac after careful consideration. As the cardiovascular risks of aceclofenac may increase with dose and duration of exposure, the shortest duration possible and the lowest effective daily dose should be used. The patient's need for symptomatic relief and response to therapy should be re-evaluated periodically.

Aceclofenac should also be administered with caution and under close medical surveillance to patients with a history of cerebrovascular bleeding.

Hepatic and renal effects
The administration of an NSAID may cause a dose dependent reduction in prostaglandin formation and precipitate renal failure. The importance of prostaglandins in maintaining renal blood flow should be taken into account in patients with impaired cardiac or renal function, liver dysfunction, those being treated with diuretics or recovering from major surgery, and the elderly.

Caution should be exercised in patients with mild to moderate impairment of hepatic and renal function as well as in patients with other conditions predisposing to fluid retention. In these patients, the use of NSAIDs may result in deterioration of renal function and fluid retention. Caution is also required in patients with diuretic treatment or otherwise at risk of hypovolaemia. The lowest effective dose should be used and renal function monitored regularly. Effects on renal function are usually reversible on withdrawal of aceclofenac.

Aceclofenac should be discontinued if abnormal liver function tests persist or worsen, clinical signs or symptoms consistent with liver disease develop or if other manifestations occur (e.g. eosinophilia, rash).
Hepatitis may occur without prodromal symptoms.

Use of NSAIDs in patients with hepatic porphyria may trigger an attack.

Hypersensitivity
As with other NSAIDs, allergic reactions, including anaphylactic/anaphylactoid reactions, can also occur without earlier exposure to the drug.

Skin reactions
Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, have been reported very rarely in association with the use of NSAIDs (see section 4.8). Patients appear to be at highest risk of these reactions early in the course of therapy, the onset of the reaction occurring in the majority of cases within the first month of

treatment. Airtal treatment should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

Exceptionally, varicella can trigger serious cutaneous and soft tissues infections complications. To date, the contributing role of NSAIDs in the worsening of these infections cannot be ruled out. Thus, it is advisable to avoid use of Airtal in case of varicella.

SLE and mixed connective tissue diseases
In patients with SLE and mixed connective tissue disorders there may be an increased risk of aseptic meningitis (see section 4.8).

Haematological effects
Aceclofenac may reversibly inhibit platelet aggregation (see section 4.5).

Respiratory disorders
Caution is required if administered to patients suffering from, or with a previous history of, bronchial asthma since NSAIDs have been reported to precipitate bronchospasm in such patients.

Paediatric population
The use of Airtal in children is not recommended due to lack of safety and efficacy data.

Elderly
Caution should be exercised in elderly patients, because they have increased frequency of occurrence of adverse events to NSAIDs, especially gastrointestinal bleeding and perforation, which may be fatal. In addition, elderly patients are more likely to be suffering from impaired renal, hepatic or cardiovascular function.

Long-term treatment
All patients who are receiving long-term treatment with non-steroidal anti-inflammatory drugs should be monitored as a precautionary measure (e.g. blood counts, renal and hepatic function - because elevation of hepatic enzymes may occur).

Excipients
Sorbitol
Airtal 100 mg powder for oral suspension contains 2.64 g sorbitol in each sachet. Patients with rare hereditary fructose intolerance (HFI) should not take this medicinal product.
The additive effect of concomitantly administered products containing sorbitol (or fructose) and dietary intake of sorbitol (or fructose) should be taken into account. The content of sorbitol in medicinal products for oral use may affect the bioavailability of other medicinal products for oral use administered concomitantly.

Aspartame
Airtal 100 mg powder for oral suspension contains 10 mg aspartame in each sachet.
Aspartame is hydrolysed in the gastrointestinal tract when orally ingested. One of the major hydrolysis products is phenylalanine.

Sodium
Airtal 100 mg powder for oral suspension contains 10 mg of saccharin sodium in each sachet.
This medicine contains less than 1 mmol sodium (23 mg) per sachet, that is to say essentially ‘sodium-free’.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed, except for warfarin.

Aceclofenac is metabolized through cytochrome P450 2C9 and *in vitro* data indicate that aceclofenac may be an inhibitor of this enzyme. A risk of pharmacokinetic interaction is therefore possible with

phenytoin, cimetidine, tolbutamide, phenylbutazone, amiodarone, miconazol and sulphaphenazole. As with other products within the NSAID-group, there also exists a risk of pharmacokinetic interactions with other drugs eliminated by active renal secretion, such as methotrexate and lithium. Aceclofenac is bound practically completely to plasma albumin and consequently the possibility of displacement interactions with other highly protein bound drugs must be borne in mind.

Due to the lack of pharmacokinetic interaction studies the following is based upon knowledge from other NSAIDs:

The following combinations should be avoided:

Other NSAIDs: Concomitant therapy with two or more NSAIDs (including acetylsalicylic acid) should be avoided as this combination may increase the risk of side effects including GI bleeding (see section 4.8).

NSAIDs inhibit the tubular secretion of methotrexate and a slight metabolic interaction may also occur, resulting in decreased clearance of methotrexate. Therefore, during treatment with high dose methotrexate prescription of NSAID drugs should always be avoided.

Lithium: Several NSAIDs inhibit the renal clearance of lithium, resulting in increased serum concentrations of lithium. The combination should be avoided unless frequent monitoring of lithium levels can be performed.

Anticoagulants: NSAIDs inhibit the platelet aggregation and damage the mucous membrane in the gastrointestinal tract which may enhance the activity of anticoagulants and increase the risk of gastrointestinal bleedings in patients using anticoagulant drugs. The combination of aceclofenac with oral anticoagulants of the coumarin group, ticlopidine, thrombolytics and heparin should be avoided unless careful monitoring is exercised.

Antiplatelet agents and selective serotonin reuptake inhibitors (SSRIs) combined with NSAIDs may increase the risk of gastrointestinal bleeding (see section 4.4).

Cardiac glycosides such as digoxin: NSAIDs may exacerbate cardiac failure, reduce glomerular filtration rate (GFR) and inhibit the renal clearance of glycosides, resulting in increased plasma glycoside levels. The combination should be avoided unless frequent monitoring of glycoside levels can be performed.

Mifepristone: NSAIDs should not be used for 8-12 days after mifepristone administration as NSAIDs can reduce the effect of mifepristone.

The following combinations may require dose adjustments and precautions:

Methotrexate: The possible interaction between NSAIDs and methotrexate should be born in mind also when low doses of methotrexate are used, especially in patients with decreased renal function. When combination therapy has to be used, the renal function should be monitored. Caution should be exercised if both an NSAID and methotrexate are administered within 24-hour period, since the methotrexate levels may increase and result in increased toxicity.

Cyclosporine, tacrolimus: Administration of NSAIDs together with cyclosporine or tacrolimus is thought to increase the risk of nephrotoxicity due to decreased synthesis of prostacycline in the kidney. During combination therapy it is therefore important to carefully monitor renal function.

Corticosteroids: increased risk of gastrointestinal ulceration or bleeding (see section 4.4).

Diuretics: Aceclofenac, like other NSAIDs, may inhibit the activity of diuretics. Diuretics can increase the risk of nephrotoxicity of NSAIDs. Although it was not shown to affect blood pressure control when co-administered with bendrofluazide, interactions with other diuretics cannot be ruled out.

Concomitant treatment with potassium-sparing diuretics may be associated with increased potassium levels; hence, serum potassium should be monitored.

Antihypertensives: NSAIDs may also reduce the effect of certain antihypertensive medicinal products. ACE inhibitors or angiotensin II receptor antagonists combined with NSAIDs may result in a deterioration of renal function. The risk of acute renal insufficiency, which is usually reversible, may be increased in some patients with compromised renal function such as the elderly or dehydrated. Therefore, the combination with NSAIDs should be administered with caution, especially in the elderly. Patients should be adequately hydrated and consideration should be given to monitoring of renal function after initiation of concomitant therapy, and periodically thereafter.

Antidiabetic agents: Clinical studies have shown that diclofenac can be given together with oral antidiabetic agents without influencing their clinical effect. However, there have been isolated reports of hypoglycaemic and hyperglycaemic effects. Thus for aceclofenac, consideration should be given to adjustment of the dosage of agents, that might produce hypoglycaemia.

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.

Zidovudine: When NSAIDs are given with zidovudine there is an increased risk of haematological toxicity. There are indications of an increased risk of haemoarthroses and haematoma in HIV(+) haemophiliacs receiving concurrent treatment with zidovudine and ibuprofen.

4.6 Fertility, pregnancy and lactation

Pregnancy
No clinical data on exposed pregnancies are available for aceclofenac.

Inhibition of prostaglandin synthesis may adversely affect pregnancy and/or embryo/foetal development.

Data from epidemiological studies suggest an increased risk of miscarriage and of cardiac malformation and gastroschisis after use of a prostaglandin synthesis inhibitor in early pregnancy. The absolute risk for cardiovascular malformation was increased from less than 1% up to approximately 1.5%. The risk is believed to increase with dose and duration of therapy. In animals, administration of a prostaglandin synthesis inhibitor has been shown to result in increased pre- and postimplantation loss and embryo-foetal lethality. In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period.

During the first and second trimester of pregnancy, a medicine containing aceclofenac should not be given unless clearly necessary. If aceclofenac is used by a woman attempting to conceive, or during the first and second trimester of pregnancy, the dose should be kept as low and duration of treatment as short as possible.

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose the foetus to:
- cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension);
- renal dysfunction, which may progress to renal failure with oligo-hydroamniosis;

The mother and the neonate, at the end of pregnancy, may be exposed to:
- possible prolongation of bleeding time, an anti-aggregating effect which may occur even after very low doses;
- inhibition of uterine contractions resulting in delayed or prolonged labour.

Consequently, aceclofenac is contraindicated during the third trimester of pregnancy (see sections 4.3 and 4.4).

Breast-feeding
It is not known whether aceclofenac is excreted in human milk; there was however no notable transfer of radio-labelled (14C) aceclofenac to the milk of lactating rats. The use of aceclofenac should therefore be avoided in lactation. A decision on whether to continue/discontinue breast-feeding or to continue/discontinue therapy with aceclofenac should be made taking into account the benefit of breast-feeding to the child and the benefit of aceclofenac therapy to the woman.

Fertility
The use of Airtal, as with any drug known to inhibit cyclooxygenase / prostaglandin synthesis, may impair female fertility and is not recommended in women attempting to conceive. In women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of aceclofenac should be considered.

4.7 Effects on ability to drive and use machines

Patients, who experience weakness, visual disturbances, drowsiness, dizziness, vertigo or other central nervous system disturbances while taking NSAIDs, should not drive or use machines.

4.8 Undesirable effects

Gastrointestinal: The most commonly-observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation or GI bleeding, sometimes fatal, particularly in the elderly, may occur with NSAIDs (see section 4.4). Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease (see section 4.4) have been reported following administration of NSAIDs. Less frequently, gastritis has been observed. Pancreatitis. has been reported very rarely.

Hypersensitivity: Hypersensitivity reactions have been reported following treatment with NSAIDs. These may consist of non-specific allergic reactions and anaphylaxis or respiratory tract reactivity comprising asthma, aggravated asthma, bronchospasm or dyspnoea, or assorted skin disorders, including rashes of various types, pruritus, urticaria, purpura, angiodema and, more rarely exfoliative and bullous dermatoses (including epidermal necrolysis and erythema multiforme).

Cardiovascular and cerebrovascular: Oedema, hypertension and cardiac failure have been reported in association with NSAID treatment.

Aceclofenac is both structurally related and metabolised to diclofenac for which a greater amount of clinical and epidemiological data consistently point towards an increased risk of general arterial thrombotic events (for example myocardial infarction or stroke, particularly at high doses or in long-term treatment). Epidemiological data has also found an increased risk of acute coronary syndrome and myocardial infarction associated with the use of aceclofenac (see sections 4.3 and 4.4).

The following table sums up adverse reactions obtained from clinical trials or reported during post-marketing surveillance only; the adverse events are grouped according to System Organ Classes and frequencies. Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000).

MedDRA SOC	**Common ≥1/100 to <1/10**	**Uncommon ≥1/1,000 to <1/100**	**Rare ≥1/10,000 to <1/1,000**	**Very rare <1/10,000**
Blood and lymphatic system disorders			Anaemia	Bone marrow depression Granulocytopenia Thrombocytopenia

				Neutropenia Haemolytic anaemia
Immune system disorders			Anaphylactic reaction (including shock) Hypersensitivity	
Metabolism and nutrition disorders				Hyperkalaemia
Psychiatric disorders				Depression Abnormal dreams Insomnia
Nervous system disorders	Dizziness			Paraesthesia Tremor Somnolence Headache Dysgeusia(abnormal taste)
Eye disorders			Visual disturbance	
Ear and labyrinth disorders				Vertigo Tinnitus
Cardiac disorders			Cardiac failure	Palpitations
Vascular disorders			Hypertension Hypertension aggravated	Flushing Hot flush Vasculitis
Respiratory, thoracic and mediastinal disorders			Dyspnoea	Bronchospasm Stridor
Gastrointestinal disorders	Dyspepsia Abdominal pain Nausea Diarrhoea	Flatulence Gastritis Constipation Vomiting Mouth ulceration	Melaena Gastrointestinal ulceration Diarrhoea haemorrhagic Gastrointestinal haemorrhage	Stomatitis Haematemesis Intestinal perforation Exacerbation of Crohn's disease and ulcerative colitis Pancreatitis
Hepatobiliary disorders	Hepatic enzyme increased			Hepatic injury (including hepatitis) Jaundice Blood alkaline phosphatase increased
Skin and subcutaneous tissue disorders		Pruritus Rash Dermatitis Urticaria	Angiooedema	Purpura Eczema Severe mucocutaneous skin reactions (including Stevens Johnson syndrome and Toxic epidermal necrolysis)
Renal and urinary disorders		Blood urea increased Blood creatinine increased		Nephrotic syndrome Renal failure

General disorders and administration site conditions				Oedema Fatigue Muscle spasms
Investigations				Weight increase

Other class-effects reported with NSAIDs are:
Blood and lymphatic system disorders: agranulocytosis, aplastic anaemia.

Nervous system disorders: optic neuritis, reports of aseptic meningitis (especially in patients with existing auto immune disorders, such as SLE, mixed connective tissue disease), with symptoms such as stiff neck, headache, nausea, vomiting, fever or disorientation (See section 4.4), confusion, hallucinations, malaise and drowsiness.

Renal and urinary disorders: nephritis interstitial.

Skin and subcutaneous tissue disorders: bullous reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis (very rare). Photosensitivity.

Exceptionally, occurrence of serious cutaneous and soft tissues infections complications during varicella has been reported in association with NSAID treatment.

See also sections 4.4 and 4.5.

If serious adverse reactions occur, Airtal should be withdrawn.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation 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.

4.9 Overdose

The symptoms could be: nausea, vomiting, epigastric pain, dizziness, , gastrointestinal irritation, gastrointestinal bleeding, rarely diarrhoea, disorientation, excitation, coma, drowsiness, tinnitus, hypotension, respiratory depression, fainting, occasionally convulsions. In cases of significant poisoning acute renal failure and liver damage.

The treatment of acute poisoning by non-steroid anti-inflammatory drugs basically consists of antacids when necessary and other supportive and symptomatic treatment for complications such as hypotension, renal failure, convulsions, gastro-intestinal irritation, and respiratory depression. Renal and liver function should be closely monitored. Patients should be observed for at least four hours after ingestion of potentially toxic amounts. In case of frequent or prolonged convulsions, patients should be treated with intravenous diazepam. Other measures may be indicated by the patient's clinical condition.

Treatment of acute poisoning with oral aceclofenac: consist of preventing absorption as soon as possible after overdose (within one hour of ingestion of a potentially toxic amount) by means of gastric lavage and treatment with activated charcoal in repeated doses.
Dialysis or haemoperfusion may not be able to eliminate NSAIDs due to their high rate of protein binding and extensive metabolism.
Good urine output should be ensured.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anti-inflammatory and antirheumatic products, non-steroids, ATC code: M01AB16

Aceclofenac is a non-steroidal substance with marked anti-inflammatory and analgesic effects. Its mechanism of action is thought to be due to inhibition of prostaglandin synthesis. Aceclofenac is a potent inhibitor of the enzyme cyclo-oxygenase, which is involved in the production of prostaglandins.

5.2 Pharmacokinetic properties

Absorption
After oral administration, aceclofenac is rapidly and completely absorbed and the bioavailability is almost 100%. Peak plasma concentrations are reached approximately 1.25 to 3 hours following ingestion. Food intake delays the rate of absorption, but has no influence on the extent of absorption.

Distribution
Aceclofenac is highly protein-bound (>99.7%). Aceclofenac penetrates into the synovial fluid, where the concentrations reach approximately 60% of those in plasma. The volume of distribution is approximately 30 litres.

Elimination
The mean elimination half-life is 4-4.3 hours. The elimination clearance is estimated to 5 litres per hour. Approximately two-thirds of the administered dose is excreted via the urine, mainly as conjugated hydroxyl-metabolites. Only 1% of an oral single dose is excreted unchanged. Aceclofenac is probably metabolized via CYP2C9. The main metabolite is 4-OH-aceclofenac, the contribution of which to the clinical activity is probably negligible. Diclofenac and 4-OH-diclofenac have been detected amongst many metabolites.

Characteristics in patients
No change in the pharmacokinetics of aceclofenac has been detected in the elderly.
A slower rate of elimination of aceclofenac has been detected in patients with decreased liver function after single dose of aceclofenac. In a multiple dose study using 100 mg of aceclofenac once daily, there was no difference in the pharmacokinetic parameters between subjects with mild to moderate liver cirrhosis and normal subjects.
In patients with mild to moderate renal impairment no clinically significant differences in the pharmacokinetics were observed after a single dose.

5.3 Preclinical safety data

Similarly to other NSAIDs, aceclofenac is poorly tolerated by experimental animals. Additionally, pharmacokinetic differences between animals and man make it difficult to evaluate the potential toxicity of aceclofenac. The principal target organ was the gastrointestinal tract. However, toxicity studies employing maximally tolerated dosages in the rat, a species which metabolizes aceclofenac to diclofenac, and in the monkey (some exposure to unchanged aceclofenac) showed no other toxic effects than those commonly seen with NSAIDs.

Animal studies indicate that there was no evidence of teratogenesis in rats although the systemic exposure was low and in rabbits, treatment with aceclofenac (10 mg/kg/day) resulted in a series of morphological changes in some foetuses.

Carcinogenicity studies in the mouse (systemic exposure to aceclofenac unknown) and in the rat (metabolism to diclofenac) did not show any carcinogenic effect and aceclofenac was negative in genotoxicity tests.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sorbitol (E420), sodium-saccharin, aspartame (E951), anhydrous colloidal silica, hypromellose, titanium dioxide (E171), milk essence, caramel essence, cream essence.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

4 years.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Approximately 3 g powder in paper/Al/LDPE sachet.
Box contains 20 sachets.

6.6 Special precautions for disposal and other handling

No special requirements for disposal.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Note: ✠ (single cross)
Availability: group II.
Medicinal product subject to medical prescription (V).

7. MARKETING AUTHORISATION HOLDER

Gedeon Richter Plc.
H-1103 Budapest
Gyömrői út 19-21.
Hungary

8. MARKETING AUTHORISATION NUMBER(S)

OGYI-T-6689/06	paper/Al/LDPE sachet
OGYI-T-6689/07	paper/Al/LDPE sachet

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 29. 12. 2005.

10. DATE OF REVISION OF THE TEXT

25 August 2019