SUMMARY OF PRODUCT CHARACTERISTICS

Swiss Relief Dual Release, 75 mg capsules

1. NAME OF THE MEDICINAL PRODUCT

Swiss Relief Dual Release
75 mg capsule
Diclofenac sodium

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule, hard, contains 75 mg diclofenac sodium (25 mg diclofenac sodium in gastro-resistant form, 50 mg diclofenac sodium in prolonged-release form).

For the full list of excipients, see Section 6.1.

3. PHARMACEUTICAL FORM

Capsules, hard.
Size 2 hard gelatine capsule with light blue cap and transparent body.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

As a non-steroidal anti-inflammatory analgesic in symptomatic management of rheumatoid arthritis, osteoarthritis and ankylosing spondylitis, acute musculo-skeletal disorders such as periarthritis, tendinitis, tensynovitis, bursitis, sprains, strains and dislocations, relief of pain in fractures, low back pain, acute gout, psoriatic arthropathy.
In the management of pain and inflammation associated with orthopaedic, dental and minor surgery.

4.2 Posology and method of administration

Posology:
The dose of diclofenac should be based on the severity of the condition. The recommended dose range for adults is between 50 and 150 mg diclofenac sodium per day.

Age:	Single dose: Number of Swiss Relief Dual Release capsules	Total daily dose: Number of Swiss Relief Dual Release capsules
Adults	1 (equivalent to 75 mg diclofenac sodium)	2 (equivalent to 150 mg diclofenac sodium)

Method of administration and duration of use:
Swiss Relief Dual Release is swallowed whole (without chewing) and with plenty of liquid.
Those with sensitive stomachs are recommended to take Swiss Relief Dual Release during meals.

The duration of use is decided by the treating physician.

For rheumatic diseases, it may be necessary to take Swiss Relief Dual Release over a prolonged period of time.

Adverse reactions may be minimized by administering the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.4 “Special Warnings and Precautions for Use”).

Specific patient groups:

Elderly patients:
No specific dose adjustment is required. Due to the potential adverse effect profile, elderly patients should be monitored with particular care.

Impaired renal function:
Swiss relief dual release is contraindicated in patients with renal failure (see section 4.3 Contraindications).
No specific studies have been carried out in patients with renal impairment, therefore, no specific dose adjustment recommendations can be made. Caution is advised when administering Swiss Relief Dual release to patients with mild to moderate renal impairment (see section 4.4)

Hepatic impairment
Swiss relief dual release is contraindicated in patients with hepatic failure (see section 4.3 Contraindications).
No specific studies have been carried out in patients with hepatic impairment, therefore, no specific dose adjustment recommendations can be made. Caution is advised when administering Swiss Relief Dual Release to patients with mild

to moderate hepatic impairment (see section 4.4).

Established cardiovascular disease or significant cardiovascular risk factors

Swiss Relief Dual Release is contraindicated in patients with established congestive heart failure (NYHA II-IV), ischemic heart disease, peripheral arterial disease and/or cerebrovascular disease (see section 4.3 Contraindications).

Patients with congestive heart failure (NYHA-1) and patients with significant risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking) should only be treated with the lowest effective daily dose for the shortest duration possible (see section 4.4).

Paediatric population:

For use in children and adolescents, see also section 4.3.

4.3 Contraindications

- Hypersensitivity to the active substance diclofenac or to any of the excipients listed in section 6.1
- History of bronchospasm, asthma, rhinitis or urticaria after taking acetylsalicylic acid or other non-steroidal anti-inflammatory drugs (NSAIDs)
- Unexplained blood disorders
- Active or history of recurrent peptic ulcer/hemorrhage (at least 2 distinct episodes of proven ulceration or hemorrhage)
- History of gastrointestinal hemorrhage or perforation relating to previous NSAID therapy.
- Cerebrovascular or other active hemorrhage
- Severe hepatic or renal dysfunction
- Established congestive heart failure (NYHA II-IV), ischemic heart disease, peripheral arterial disease and/or cerebrovascular disease
- Severe cardiac failure
- Last trimester of pregnancy (see section 4.6)

Swiss Relief Dual Release is not suitable for use in children under 18 years of age because the amount of active substance is too high.

4.4 Special warnings and precautions for use

Gastrointestinal safety:

Swiss Relief Dual Release should not be combined with NSAIDs, including selective cyclo-oxygenase (COX) 2 inhibitors.

Adverse reactions may be minimized by administering the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.2 as well as gastrointestinal and cardiovascular risks below).

NSAIDs, including diclofenac, may be associated with increased risk of gastrointestinal anastomotic leak. Close medical supervision and caution are recommended when using diclofenac after gastrointestinal surgery.

Elderly:

The elderly have an increased frequency of adverse reactions to NSAIDs, especially gastrointestinal hemorrhage and perforation, which may be fatal (see section 4.2).

Gastrointestinal hemorrhage, ulceration and perforation:

Gastrointestinal hemorrhage, ulceration and perforation, which can be fatal, have been reported with all NSAIDs and may occur at any time during treatment, with or without warning symptoms or a history of serious gastrointestinal events.

The risk of gastrointestinal hemorrhage, ulceration or perforation is higher with increasing NSAID doses in patients with a history of ulcer, particularly if complicated with hemorrhage or perforation (see section 4.3), and in elderly patients. Treatment in these patients should be initiated at the lowest available dose.
Combination therapy with protective agents (e.g., misoprostol or proton pump inhibitors) should be considered for these patients as well as for patients requiring concomitant use of medicinal products containing low-dose acetylsalicylic acid (aspirin) or other medicinal products that may increase gastrointestinal risk (see below and section 4.5).

Patients with a history of gastrointestinal toxicity, particularly the elderly, should report any unusual abdominal symptoms (especially gastrointestinal hemorrhage), particularly at the start of treatment.
Caution is recommended if patients receiving concomitant medicinal products that could increase the risk of ulceration or hemorrhage, such as oral corticosteroids, anticoagulants such as warfarin, selective serotonin reuptake inhibitors (SSRIs) or antiplatelet agents such as aspirin (see section 4.5).

Treatment with Swiss Relief Dual Release should be discontinued in patients experiencing gastrointestinal hemorrhage or ulceration.

NSAIDs should only be used with caution in patients with a history of gastrointestinal disorders (ulcerative colitis, Crohn's

disease), as their condition may be exacerbated (see section 4.8).

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 edema have been reported in association with NSAID therapy.

Clinical trials and epidemiological data suggest a potentially slightly increased risk of arterial thrombotic events (e.g., myocardial infarction or stroke) associated with the use of diclofenac, particularly at high dose (150 mg daily) and in long term treatment.

Patients with significant risk factors for cardiovascular events (e.g., hypertension, hyperlipidemia, diabetes mellitus, smoking) should only be treated with diclofenac after careful consideration. As the cardiovascular risks of diclofenac may increase with the 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.

Skin effects:

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome and toxic epidermal necrolysis (Lyell syndrome), have been reported very rarely under NSAID therapy (see section 4.8).
The highest risk for these reactions appears to be early in the course of therapy, with the reaction occurring within the first month of treatment in the majority of cases. Swiss Relief Dual Release should be discontinued at the first sign of skin rash, mucosal lesions or any other signs of hypersensitivity.

Hepatic effects:

Caution is indicated when starting diclofenac treatment in patients with hepatic impairment, as their condition may be exacerbated. During prolonged treatment with Swiss Relief Dual Release, regular monitoring of hepatic function is indicated as a precautionary measure. If clinical signs consistent with liver disease develop, Swiss Relief Dual Release should be discontinued immediately.

Other information:

Swiss Relief Dual Release should only be used after careful consideration of risk to benefit:

- In patients with congenital porphyrin metabolic disorders (e.g., acute intermittent porphyria).
- In patients with systemic lupus erythematosus (SLE) or mixed connective tissue disease (see section 4.8).

Close monitoring by a physician is required:

- In patients with renal impairment.
- In patients with hepatic impairment.
- Immediately after major surgery.
- In patients with seasonal allergic rhinitis, nasal polyps or chronic obstructive pulmonary diseases, as they are at an increased risk of allergic reaction, such as asthma exacerbations (referred to as analgesic-induced asthma), Quincke's edema or urticaria.
- In patients who are allergic to other substances, as they are also at an increased risk of hypersensitivity reaction when using Swiss Relief Dual release.

Severe acute hypersensitivity reactions (e.g., anaphylactic shock) have been reported very rarely. Therapy with Swiss Relief Dual Release should be discontinued at the first sign of a hypersensitivity reaction and the necessary steps taken by competent individual to alleviate symptoms.

As with other NSAIDs, allergic reactions, including anaphylactic/anaphylactoid reactions, can occur in rare cases also when using diclofenac even without earlier exposure to the drug. Hypersensitivity reactions can also progress to Kounis syndrome, a serious allergic reaction that can result in myocardial infarction. Presenting symptoms of such reactions can include chest pain occurring in association with an allergic reaction to diclofenac.

Diclofenac can temporarily inhibit platelet aggregation, so patients with coagulation disorders should be closely monitored.

As with other NSAIDs, diclofenac may mask the signs and symptoms of infection due to its pharmacodynamic properties. Patients noticing signs of an infection or worsening of an existing infection while using Swiss Relief Dual Release should seek immediate medical attention to determine whether antibiotic treatment is indicated.

During prolonged treatment with Swiss Relief Dual Release, monitoring of renal function and blood counts is required.

Prolonged use of analgesics can result in headaches that should not be treated with an increased dose of the same medicinal product.

Habitual use of analgesics in general, especially the concomitant use of multiple analgesics, can result in permanent kidney damage and even renal failure (analgesic nephropathy).

Concomitant use of NSAIDs and alcohol can potentiate adverse reactions, particularly those affecting the gastrointestinal tract or central nervous system.

For female fertility, see section 4.6.

4.5 Interaction with other medicinal products and other forms of interaction

Other NSAIDs, including salicylates:

Coadministration of multiple NSAIDs can increase the risk of gastrointestinal ulceration and hemorrhage due to synergistic effects. Concomitant use of diclofenac with other NSAIDs is not recommended (see section 4.4).

Digoxin, phenytoin, lithium:

Concomitant use of Swiss Relief Dual Release and digoxin, phenytoin or lithium can increase plasma the concentrations of these medicinal products. Monitoring of serum lithium level is required. Monitoring of serum digoxin and serum phenytoin levels is recommended.

Diuretics and antihypertensive agents:

NSAIDs may decrease the effect of diuretics and antihypertensive agents. Coadministration of an angiotensin-converting enzyme (ACE) inhibitor or an angiotensin receptor blocker (ARB) with a COX inhibitor in patients with reduced renal function (e.g., dehydrated patients or elderly patients with renal impairment) can further exacerbate renal function and even result in acute renal failure, which is usually reversible. Therefore, this combination should be administered with caution, particularly in elderly patients. Patients should be adequately hydrated and consideration should be given to regular monitoring of renal function after initiation of concomitant therapy.

Coadministration of Swiss Relief Dual Release and potassium-sparing diuretics may result in hyperkalemia. Monitoring of serum potassium level is recommended with concomitant therapy.

Corticosteroids:

Increased risk of gastrointestinal ulceration or hemorrhage (see section 4.4).

Antiplatelet agents such as acetylsalicylic acid (aspirin) and selective serotonin reuptake inhibitors (SSRIs):

Increased risk of gastrointestinal hemorrhage (see section 4.4.).

Methotrexate:

Administration of Swiss Relief Dual Release within 24 hours of administration of methotrexate may cause the blood concentration of methotrexate to rise and its toxicity to increase.

Ciclosporin:

NSAIDs (such as diclofenac sodium) may increase the nephrotoxicity of ciclosporin.

Anticoagulants and antiplatelet agents:

Caution is indicated, as coadministration may increase the risk of hemorrhage. Although clinical investigations do not appear to indicate that diclofenac affects the action of anticoagulants, there are reports of an increased risk of hemorrhage in patients receiving diclofenac and anticoagulants concomitantly. Therefore, close monitoring of such patients is recommended.

Probenecid and sulfinpyrazone:

Medicinal products containing probenecid or sulfinpyrazone may delay the elimination of diclofenac.

4.6 Fertility, pregnancy and lactation

Pregnancy:

Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or embryonic/fetal development. Data from epidemiological studies suggests an increased risk of miscarriage, cardiac malformation and gastroschisis after use of a prostaglandin synthesis inhibitor in early pregnancy. 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 post-implantation loss and embryonic/fetal lethality. In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period.

Swiss Relief Dual Release should not be administered during the first and second trimesters of pregnancy unless absolutely necessary. If Swiss Relief Dual Release is used by a woman attempting to conceive or during the first and second trimesters of pregnancy, the dose should be kept as low as possible, 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 (premature constriction/closure of the ductus arteriosus and pulmonary hypertension)
  - Renal dysfunction (see above)

- At the end of pregnancy, expose the mother and the neonate to:
  - Possible prolongation of bleeding time, an antiplatelet effect, that may occur even at very low doses
  - Inhibition of uterine contractions resulting in delayed or prolonged labor

Consequently, Swiss Relief Dual Release is contraindicated during the third trimester of pregnancy (see sections 4.3 and 5.3).

Fetal Toxicity

Premature Closure of Fetal Ductus Arteriosus:

Avoid use of NSAIDs, including Swiss Relief Dual Release, in pregnant women at about 28 weeks gestation and later. NSAIDs, including Swiss Relief Dual Release, increase the risk of premature closure of the fetal ductus arteriosus at approximately this gestational age.

Oligohydramnios/Neonatal Renal Impairment:

Use of NSAIDs, including Swiss Relief Dual Release, at about 20 weeks gestation or later in pregnancy may cause fetal renal dysfunction leading to oligohydramnios and, in some cases, neonatal renal impairment. These adverse outcomes are seen, on average, after days to weeks of treatment, although oligohydramnios has been infrequently reported as soon as 48 hours after NSAID initiation. Oligohydramnios is often, but not always, reversible with treatment discontinuation. Complications of prolonged oligohydramnios may, for example, include limb contractures and delayed lung maturation. In some postmarketing cases of impaired neonatal renal function, invasive procedures such as exchange transfusion or dialysis were required.

If NSAID treatment is necessary between about 20 weeks and 28 weeks gestation, limit Swiss Relief Dual Release use to the lowest effective dose and shortest duration possible. Consider ultrasound monitoring of amniotic fluid if Swiss Relief Dual Release treatment extends beyond 5 days. Discontinue Swiss Relief Dual Release if oligohydramnios occurs and follow up according to clinical practice.

Breastfeeding:

Diclofenac and its metabolites pass into breast milk in small amounts. Since there are to date no known adverse effects on infants, discontinuation of breastfeeding is usually not required with short-term use. Early ablactation, however, should be considered if prolonged use/increased doses are prescribed to treat inflammatory disorders.

Fertility:
As with other medicinal products known to inhibit cyclo-oxygenase/prostaglandin synthesis, the use of Swiss Relief Dual Release may impair female fertility and is not recommended in women attempting to conceive. Discontinuation of Swiss Relief Dual Release should be considered in women who have difficulties conceiving or who are undergoing investigations of infertility.

4.7 Effects on ability to drive and use machines

As the use of Swiss Relief Dual Release, particularly at higher doses, can result in adverse reactions of the central nervous system, such as fatigue and dizziness, reaction time may be affected in isolated cases and the ability to drive and operate machinery impaired, especially when combined with alcohol.

4.8 Undesirable effects

Adverse reactions are ranked under the following categories:
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); not known (frequency cannot be estimated from the available data).

It must be noted that the following undesirable effects are predominantly dependent on dose and vary by individual.

The most commonly reported adverse reactions affect the intestinal tract. Peptic ulceration, perforation or hemorrhage , sometimes fatal, can occur, particularly in elderly patients (see section 4.4). Nausea, vomiting, diarrhea, flatulence, constipation, dyspepsia, abdominal pain, melena, hematemesis, ulcerative stomatitis, and exacerbation of ulcerative colitis and Crohn's disease (see section 4.4) have been reported after use. Gastritis is less common.

Edema, hypertension and heart failure have been reported in association with NSAID treatment.

Clinical trials and epidemiological data consistently point toward an increased risk of arterial thrombotic events (e.g., myocardial infarction or stroke) associated with the use of diclofenac, particularly at high dose (150 mg daily) and in long-term treatment (see sections 4.3 and 4.4 for contraindications as well as special warnings and precautions for use).

Cardiac disorders:
Very rare: palpitations, edema, cardiac failure, myocardial infarction

Not known: Kounis syndrome

Blood and lymphatic system disorders:
Very rare: blood disorders (anemia, leukopenia, thrombocytopenia, pancytopenia, agranulocytosis), haemolytic anemia
First indications may be: fever, sore throat, superficial oral lesions, flu-like symptoms, abnormal fatigue, epistaxis and ecchymosis.

Blood count should be regularly monitored during long-term treatment.

Nervous system disorders:
Common: CNS (central nervous system) disturbances such as headache, dizziness, drowsiness, agitation, irritability, fatigue
Very rare: paresthesia, taste disturbances, memory impairment, disorientation, convulsions, tremor

Eye disorders:
Very rare: vision disturbances (blurred vision and diplopia)

Ear and labyrinth disorders:
Very rare: tinnitus, temporary hearing impairment

Gastrointestinal disorders:
Very common: gastrointestinal symptoms such as nausea, vomiting and diarrhea as well as minor gastrointestinal hemorrhage that may result in anemia in rare cases
Common: dyspepsia, flatulence, abdominal pain, anorexia, gastrointestinal ulceration (occasionally with hemorrhage and diarrhea)
Uncommon: hematemesis, melena or hemorrhagic diarrhea
Very rare: stomatitis, glossitis, oesophageal lesions, hypogastric symptoms (e.g., hemorrhagic colitis or exacerbation of ulcerative colitis/Crohn's disease), constipation, pancreatitis, diaphragm-like intestinal strictures
Not known: ischemic colitis

Patients should be advised to discontinue the medicinal product and seek immediate medical attention if they experience intense epigastric pain, melena or hematemesis.

Renal and urinary disorders:
Uncommon: edema, particularly in patients with arterial hypertension or renal failure
Very rare: renal tissue damage (interstitial nephritis, papillary necrosis), accompanied by acute renal failure, proteinuria and/or hematuria. nephrotic syndrome
Therefore, renal function should be regularly monitored.

Skin and subcutaneous tissue disorders:
Uncommon: alopecia.
Very rare: exanthema, eczema, erythema, photosensitivity reaction, purpura (including allergic purpura) and bullous skin reactions such as Stevens-Johnson syndrome and toxic epidermal necrolysis (Lyell syndrome)

Infections and parasitic disorders:
Exacerbation of infection-induced inflammation (e.g., necrotizing fasciitis) in conjunction with systemic use of NSAIDs is very rare. This may be associated with NSAIDs' mechanism of action .

Patients noticing signs of an infection or worsening uof an existing infection while using Swiss Relief Dual Release should seek immediate medical attention to determine whether antibiotic treatment is indicated.

Symptoms of aseptic meningitis with neck stiffness, headache, nausea, vomiting, fever or drowsiness are very rare when using diclofenac. Patients with autoimmune disorders (SLE, mixed connective tissue disease) may have an increased risk.

Vascular disorders:
Very rare: hypertension.

Immune system disorders:
Common: hypersensitivity reactions such as rash and pruritus
Uncommon: urticaria.

Patients should be advised to inform their physician immediately and discontinue Swiss Relief Dual Release if this occurs.

Very rare: severe allergic hypersensitivity reactions. These may manifest as face edema, glossitis, laryngeal edema with airway stenosis, dyspnea, tachycardia, hypotension or life-threating shock.

Patients should be advised to discontinue Swiss Relief Dual Release and seek immediate medical attention if any of these symptoms occurs (symptoms may occur during first use).

Very rare: hypersensitivity vasculitis and pneumonitis

Hepatobiliary disorders:
Common: increased transaminases
Uncommon: liver damage, particularly with long-term treatment, acute hepatitis, possibly with icterus (very rarely fulminant, even without prodromal symptoms)
Therefore, Hepatic levels should be regularly monitored during long-term treatment.

Psychiatric disorders:
Very rare: psychotic reactions, depression, anxiety, nightmare

Swiss Relief Dual Release may cause an allergic reaction in very rare cases.

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.
Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form https://sideeffects.health.gov.il
In addition, you can report to Padagis.co.il

4.9 Overdose

a) Symptoms of overdose:

Overdose can cause Central Nervous System (CNS) symptoms such as headache, dizziness, drowsiness, coma (including myoclonic seizures in children) as well as abdominal pain, nausea and vomiting. Gastrointestinal hemorrhage as well as hepatic and renal dysfunction are also possible. Hypotension, respiratory depression and cyanosis can also occur.

b) Therapeutic measures for overdose:

There is no specific antidote.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group:
Non-steroidal anti-inflammatory agents;
Acetic acid derivatives and related substances
ATC code: M01AB05

Diclofenac is a non-steroidal anti-inflammatory agent that has proven effective in inhibiting prostaglandin synthesis in the usual animal inflammation models. In humans, diclofenac reduces pain caused by inflammation, swelling and fever. Diclofenac also inhibits ADP- and collagen-induced platelet aggregation.

5.2 Pharmacokinetic properties

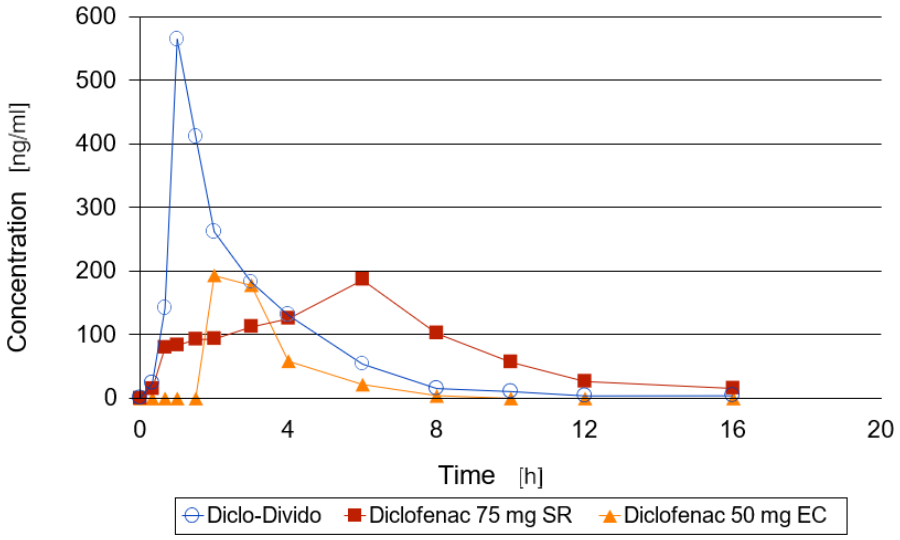
Following oral application of the usual gastro-resistant forms, diclofenac is fully absorbed after passing through the stomach. Peak plasma concentration is reached in 1-16 hours depending on duration of stomach passage with a mean of 2-3 hours. Following IM administration, peak plasma concentration is reached in 10-20 minutes; following rectal administration, approximately 30 minutes. Orally administered diclofenac undergoes a marked first-pass effect with only 35-70% of the absorbed active substance entering post-hepatic circulation unchanged. Approximately 30% of the active substance is metabolized and excreted in the feces.
Approximately 70% is excreted in the urine as pharmacologically inactive metabolites once metabolized in the liver (hydroxylation and conjugation). The elimination half-life is approximately 2 hours and is largely independent of hepatic or renal function. Plasma protein binding is approximately 99%.

Bioavailability
A bioavailability study of Diclofenac Divido 75 mg conducted in 1992 with 24 subjects determined the following compared to reference compounds (Diclofenac 50 mg EC [enteric-coated tablets] and Diclofenac 75 mg SR [sustained-release tablets]):

	Test Compound Diclofenac Divido 75 mg* Prolonged-Release Capsules	Reference Compound Diclofenac 50 mg EC	Reference Compound Diclofenac 75 mg SR
Peak Plasma Concentration (c_{max}) [ng/ml]	869.3	1,003.0	289.9
Spread:	232.1–1,652.3	0.0 – 2,152.1	144.3 – 1,160.9
Time to Peak Plasma Concentration (C_{max}) [h]	1.00	2.00	6.0
Spread:	0.67-2.00	1.5-6.00	0.33-8.00
Area Under Concentration-Time Curve ($AUC_{0-\infty}$) [h x ng/mL]	1,473.1	1315.7	1,428.4
Spread:	787.5–3,592.1	0.00–2,798.3	741.4–2,973.2

* Composition identical to Swiss Relief Dual Release

Mean plasma level curves for Diclofenac Divido 75 mg (Diclo Divido)* compared to reference compounds on a concentration-time graph:



*Composition identical to Swiss Relief Dual Release

5.3 Preclinical safety data

Preclinical data from conventional safety pharmacology, genotoxicity and carcinogenicity studies suggests no specific dangers to humans beyond those described elsewhere in this summary of product characteristics. In animal studies, the chronic toxicity of diclofenac manifested primarily as gastrointestinal lesions and ulcers. A 2-year toxicity study of rats treated with diclofenac showed a dose-dependent increase in thrombotic vascular occlusions in the heart.

In animal genotoxicity studies, diclofenac inhibited ovulation in rabbits, and disrupted implantation and early embryonic development in rats. Diclofenac prolonged gestation time and labor. The embryotoxicity of diclofenac was investigated in three animal species (rat, mouse, rabbit). Fetal death and growth retardation occurred at doses in the maternal toxicity range. Based on available data, diclofenac is not considered teratogenic. Doses below the maternal toxicity level did not affect the postnatal development of offspring.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

microcrystalline cellulose,
gelatin,
povidone K 25,
methacrylic acid ethyl acrylate copolymer (1:1) neutralized with sodium hydroxide,
talc,
ammonio methacrylate copolymer (type B),
colloidal anhydrous silica,
propylene glycol,
ammonio methacrylate copolymer (type A),
titanium dioxide E 171,
triethylcitrate,
indigocarmine E 132,
sodium lauryl sulphate,
printing ink

6.2 Incompatibilities

None known.

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.
This medicinal product should not be used past the expiration date.

6.4 Special precautions for storage

Store below 25°C.
Store in the original package in order to protect from moisture.

6.5 Nature and contents of container

Blisters made of PVC/PVDC foil and aluminium foil.
Original pack with 4, 10, 20, 56, hard capsules.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. MANUFACTURER

Swiss Caps GmbH
Grassingstrasse 9, 83043 Bad Aibling, Germany

8. REGISTRATION HOLDER

Padagis Israel Agencies Ltd., 1 Rakefet St., Shoham, Israel

9. REGISTRATION NUMBER

14210.31815

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30.6.2024