SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Voltaren® retard 100 mg – film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains: Diclofenac sodium 100 mg
Excipients with known effect: approximately 119 mg sucrose per film-coated tablet and less than 1 mmol sodium per film-coated tablet.
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablets
Pink, round, biconvex tablets with rounded edges, embossed with "CGC" on one side and "CG" on the other side

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

For the treatment of the following pain conditions:

- Painful conditions in inflammatory and degenerative rheumatic diseases such as chronic polyarthritis, ankylosing spondylitis, osteoarthritis, spondylarthrosis, and spondylarthritis;
- Spondylogenic pain syndromes;
- Extra-articular rheumatism;
- Painful, post-traumatic and postoperative inflammatory and swelling conditions;
- Painful, inflammatory conditions in gynecology (e.g., as an adjuvant in adnexitis) or in ear, nose, and throat medicine (e.g., as an adjuvant in pharyngotonsillitis, otitis)
- primary dysmenorrhea

Fever alone is not an indication.

Depending on the indication and the resulting duration of use, Voltaren retard film-coated tablets are suitable for use in long-lasting pain and inflammatory conditions.

Due to the delayed release of the active ingredient from Voltaren retard film-coated tablets, this preparation is not suitable for initiating the treatment of conditions where a rapid onset of action is required.

4.2. Dosage and method of administration

Side effects can be minimized by using the lowest effective dose for the shortest period necessary to control symptoms (see section 4.4 Special warnings and precautions for use).

The dosage should be individually adjusted to the clinical picture. The daily dose is generally divided into two single doses.

Method of administration
For oral use.
Swallow whole with sufficient liquid, preferably with meals. The film-coated tablets must not be divided or chewed.

Adults and adolescents from 14 years of age:
The recommended initial dose is 100-150 mg per day. This is achieved in the form of 1 Voltaren retard film-coated tablet, and if necessary, increased by additional use of film-coated tablets or suppositories of 50 mg. If symptoms are particularly severe during the night or in the morning, Voltaren retard film-coated tablets should be taken in the evening.
In milder cases or for long-term treatment, 1 Voltaren retard 100 mg film-coated tablet per day is generally sufficient, or Voltaren 50 mg film-coated tablets are available.

Other indications (e.g., painful postoperative inflammatory and swelling conditions):
The recommended initial dose is 100-150 mg daily. In milder cases and for adolescents over 14 years, 50 - 100 mg per day is generally sufficient.
For these patients, Voltaren film-coated tablets with a lower dosage (50 mg) are available.

Dysmenorrhea:
In primary dysmenorrhea, the dose must be individually adjusted and ranges between 50 and 150 mg daily. Initially, 50 to 100 mg daily is recommended. Start treatment at the onset of the first symptoms and continue depending on the symptomatology for a few days.

Elderly persons (from 65 years):
In elderly persons, caution is advised due to general medical considerations: It is particularly recommended to use the lowest effective dose in frail elderly and underweight patients (see section 4.4).

For low dosage in adults, Voltaren is available in other dosage forms.
Children and adolescents under 14 years:
Voltaren retard 100 mg film-coated tablets are not suitable for children and adolescents under 14 years.

Liver dysfunction
Voltaren is contraindicated in patients with severe liver insufficiency (see section 4.3 Contraindications). As no specific studies have been conducted in patients with impaired liver function, no recommendations can be made for a specific dose adjustment. Caution is advised when Voltaren is used in patients with mild to moderate liver dysfunction (see section 4.4).

Renal dysfunction
Voltaren is contraindicated in patients with severe renal insufficiency (see section 4.3 Contraindications). As no specific studies have been conducted in patients with impaired

renal function, no recommendations can be made for a specific dose adjustment. Caution is advised when Voltaren is used in patients with mild to moderate renal dysfunction (see section 4.4).

4.3 Contraindications

Voltaren retard film-coated tablets must not be used in:

- Known hypersensitivity to the active substance or any of the excipients listed in section 6.1
- Patients in whom acetylsalicylic acid, non-steroidal anti-rheumatics (NSAIDs), or other drugs with prostaglandin synthesis inhibitory effects can trigger asthma, angioedema, skin reactions, or rhinitis, i.e., NSAID-induced cross-reactions
- Hematological disorders (e.g., blood formation disorders, porphyria, hemorrhagic diathesis)
- Known heart failure (NYHA II-IV), ischemic heart disease, peripheral arterial
- Occlusive disease and/or cerebrovascular disease
- Active peptic ulcers or bleeding
- Recurrent peptic ulcers or bleeding (two or more episodes of proven ulceration or bleeding in the history)
- Gastrointestinal bleeding or perforation in the history, due to previous NSAID therapy
- Cerebrovascular bleeding
- Acute severe bleeding
- Severe liver insufficiency (see section 4.4)
- Severe renal insufficiency (see section 4.4)
- pregnancy in the last trimester and during breastfeeding (see section 4.6)
- Children and adolescents up to the age of 14, as the body weight-based dosage recommended for this patient group is not possible with the 100 mg sustained-release film-coated tablets.

4.4. Special warnings and precautions for use

The occurrence of adverse effects can be minimized by using the lowest effective dose for the shortest duration necessary to achieve symptom relief (see section 4.2 and the package leaflet and cardiovascular effects below).

The concomitant use of diclofenac with systemic NSAIDs, including selective cyclooxygenase-2 inhibitors, should be avoided due to the lack of evidence of synergistic benefits and the possibility of additive side effects.

Elderly patients:
In elderly patients (aged 65 and over), especially if they are frail or have a low body weight, adverse effects occur more frequently under NSAID therapy, particularly gastrointestinal bleeding and perforations, which can be fatal (see section 4.2).

Warnings
In connection with the use of diclofenac, very rare cases of serious skin reactions, some with fatal outcomes, including exfoliative dermatitis, Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell's syndrome), and generalized bullous fixed drug eruption have been reported

(see section 4.8). The highest risk for such reactions appears to be at the start of therapy, as these reactions occurred in the majority of cases within the first month of treatment.
Voltaren sustained-release film-coated tablets should be discontinued at the first signs of skin rash, mucosal lesions, or any other signs of hypersensitivity.
As with other NSAIDs, allergic reactions, including
anaphylactic/anaphylactoid reactions, can occur without prior exposure to diclofenac.
Hypersensitivity reactions can also progress to Kounis syndrome, a severe allergic reaction that can lead to a heart attack.
Symptoms of such reactions when the patient presents can include
chest pain associated with an allergic reaction to diclofenac.

Like other NSAIDs, Voltaren sustained-release film-coated tablets can mask the signs and symptoms of an infection due to their pharmacodynamic profile.

Precautions
In elderly patients, caution is advised due to general medical considerations. It is particularly recommended to use the lowest effective dosage in frail elderly and underweight patients.

Pre-existing asthma:
In patients suffering from asthma, hay fever, nasal mucosal swelling (so-called nasal polyps), chronic obstructive airway diseases, or chronic respiratory infections (especially associated with hay fever-like symptoms), reactions to NSAIDs, such as exacerbated asthma (so-called analgesic intolerance/analgesic asthma), angioedema, or urticaria
(Urticaria) more frequently than in other patients. Therefore, special caution is advised for such patients (emergency readiness). The same applies to patients who are hypersensitive (allergic) to other substances, e.g., with skin reactions, itching, or hives.

Gastrointestinal effects:
As with all NSAIDs, when prescribing diclofenac to patients with symptoms suggesting gastrointestinal disorders or with a history indicating gastric or intestinal ulceration, bleeding, or perforation, special caution and specific monitoring are required (see section 4.3).
Gastrointestinal bleeding, ulcers, or perforations, including those with fatal outcomes, have been reported with all NSAIDs, including diclofenac. They occurred with or without prior warning symptoms or serious gastrointestinal events in the history at any time during therapy.

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

The risk of gastrointestinal bleeding, ulceration, or perforation is higher with increasing NSAID doses, in patients with a history of ulcers, especially with complications such as bleeding or perforation (see section 4.3), and in older patients. These patients should start and continue treatment with the lowest available dose. Older patients show a higher frequency of adverse effects under NSAIDs, particularly gastrointestinal bleeding and perforation, which can be fatal.
For these patients, as well as for patients requiring concomitant therapy with low-dose acetylsalicylic acid

(ASA) or other medications that may increase gastrointestinal risk (see section 4.5), a combination therapy with protective medications (e.g., misoprostol or proton pump inhibitors) should be considered (see below and section 4.5).

Patients with a history of gastrointestinal complaints, especially older patients, should report any unusual abdominal symptoms (especially gastrointestinal bleeding) to their doctor. Caution is also recommended for patients receiving concomitant medications that could increase the risk of gastrointestinal ulceration or bleeding, such as systemic corticosteroids, anticoagulants (e.g., warfarin), antiplatelet agents, or selective serotonin reuptake inhibitors (see section 4.5).

If gastrointestinal bleeding or ulceration occurs in patients under treatment with diclofenac, the treatment must be discontinued immediately.

NSAIDs should be used with caution in patients with a history of gastrointestinal disease (ulcerative colitis, Crohn's disease) as their condition may worsen (see section 4.8).

Cardiovascular and cerebrovascular effects:
Appropriate monitoring and advice are required for patients with hypertension and/or mild to moderate congestive heart failure in the history, as fluid retention and edema have been reported in connection with NSAID therapy.

Clinical studies and epidemiological data consistently indicate an increased risk of arterial thrombotic events (e.g., heart attack or stroke) associated with the use of diclofenac, especially at a high dose (150 mg daily) and with long-term use (see section 4.3 Contraindications).

Patients with significant risk factors (e.g., hypertension, hyperlipidemia, diabetes mellitus, smoking) for cardiovascular events should only be treated with diclofenac after careful consideration. Since the cardiovascular risks of diclofenac may increase with dose and duration of use, the lowest effective daily dose should be used for the shortest possible period. It should be regularly reviewed whether the patient still requires symptom relief and how they respond to the therapy.
This is particularly true if the treatment lasts more than 4 weeks. Patients should be vigilant for signs and symptoms of arterial thrombotic events (e.g., chest pain, shortness of breath, weakness, slurred speech), which can occur without warning. Patients should be advised to seek medical attention immediately if such an event occurs.

Hepatic effects:
Patients with liver dysfunction require careful medical monitoring, as their condition could worsen.
As with other NSAIDs, including diclofenac, the levels of one or more liver enzymes may increase. As a precaution, regular liver function tests are indicated during prolonged treatment with Voltaren retard film-coated tablets. Voltaren retard film-coated tablets should be discontinued if liver function impairment persists or worsens, if clinical signs of liver disease are detected, or if other manifestations occur (e.g., eosinophilia, rash). Hepatitis can occur without preceding symptoms.

Caution is advised when using Voltaren retard film-coated tablets in patients with hepatic porphyria, as an attack may be triggered.

Renal effects:
Fluid retention and edema have been reported with the use of NSAIDs, including diclofenac. Therefore, special caution is advised for the following patients:
Patients with impaired cardiac or renal function, patients with a history of hypertension, elderly patients, patients receiving concomitant treatment with diuretics or drugs that significantly affect renal function, patients with a significant reduction in extracellular volume due to various causes, e.g., before or after major surgery (see section 4.3).
As a precaution, renal function should be determined in these cases. Discontinuation of therapy usually leads to a restoration of the pre-treatment condition.

Hematological effects:
In the case of prolonged use, monitoring of the blood count is recommended as with all NSAIDs.
As with other NSAIDs, temporary inhibition of platelet aggregation may occur with treatment with Voltaren retard film-coated tablets. Patients with impaired hemostasis should be carefully monitored.

Skin reactions:
Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, toxic epidermal necrolysis, and generalized bullous fixed drug eruption have been reported in very rare cases in connection with the use of diclofenac (see section 4.8).
Patients appear to be at the highest risk for these reactions early in the course of therapy, with the onset of the reaction occurring in most cases within the first month of treatment.
Voltaren should be discontinued at the first appearance of skin rash, mucosal lesions, or any other signs of hypersensitivity.
As with other NSAIDs, allergic reactions, including anaphylactic/anaphylactoid reactions, may occur in rare cases without prior exposure to diclofenac.

General information
Due to its pharmacodynamic properties, diclofenac - like other NSAIDs - can mask the symptoms of an infection (e.g., fever, pain). Patients should be informed to seek medical advice immediately if pain or other signs of inflammation persist or worsen, such as a deterioration in general well-being or the occurrence of fever during therapy.

Analgesic-induced headache
Prolonged high-dose, non-compliant use of painkillers can cause headaches that should not be treated with increased doses of the medication. Patients should be informed accordingly if necessary.

Renal damage
Habitual intake of painkillers can lead to permanent kidney damage with the risk of kidney failure. Patients should be informed accordingly if necessary.

Sucrose intolerance:

Voltaren retard film-coated tablets contain sucrose. Patients with the rare hereditary fructose/galactose intolerance, glucose-galactose malabsorption, or sucrase-isomaltase insufficiency should not take this medication.

This medicine contains less than 1 mmol sodium (23 mg) per film-coated tablet, i.e., it is almost "sodium-free".

4.5. Interactions with other medicinal products and other forms of interaction

The following interactions have been reported (including those described with Voltaren retard film-coated tablets and/or other forms of Voltaren):

Strong CYP2C9 inhibitors
Caution is advised when diclofenac is prescribed concurrently with strong CYP2C9 inhibitors (such as sulfinpyrazone and voriconazole); this could lead to a significant increase in peak plasma concentrations and diclofenac exposure due to inhibition of diclofenac metabolism.

CYP2C9 inducers
Caution is advised when prescribing diclofenac concurrently with CYP2C9 inducers (e.g., rifampicin). It may lead to a significant decrease in plasma concentration and exposure of diclofenac.

Lithium/Digoxin/Phenytoin
Concurrent use of diclofenac may increase plasma levels of lithium, digoxin, or phenytoin. Monitoring of serum levels is therefore recommended.

Diuretics/Antihypertensives
Like other non-steroidal anti-inflammatory drugs (NSAIDs), diclofenac may attenuate the antihypertensive effect when used concurrently with diuretics or antihypertensives (e.g., beta-blockers, ACE inhibitors). Therefore, the combination should be used with caution, and patients, especially the elderly, should have their blood pressure regularly monitored. Patients should be adequately hydrated, and renal function should be monitored after initiating concomitant therapy and periodically thereafter, particularly for diuretics and ACE inhibitors due to the increased risk of nephrotoxicity.

Medicines known to cause hyperkalemia
Concomitant treatment with potassium-sparing diuretics, ciclosporin, tacrolimus, or trimethoprim may be associated with increased serum potassium levels; these levels should therefore be frequently monitored (see section 4.4).

Other NSAIDs and corticosteroids
Concurrent administration of diclofenac with corticosteroids or other NSAIDs increases the risk of gastrointestinal side effects (see section 4.4). Concomitant medication with acetylsalicylic acid leads to a reduction in the concentration of diclofenac in the serum.

Methotrexate
Diclofenac can inhibit the tubular renal clearance of methotrexate, leading to an increase in methotrexate levels. Caution is advised when NSAIDs, including diclofenac, are used less

than 24 hours before or after administration of methotrexate, as the concentration of methotrexate in the blood may increase, thereby enhancing its toxic effect.

Ciclosporin and tacrolimus
The effect of NSAIDs on renal prostaglandins can increase the nephrotoxicity of ciclosporin and tacrolimus. Therefore, NSAIDs should be administered in lower doses when used concurrently with ciclosporin or tacrolimus.

Quinolone antibiotics
Isolated cases of seizures have been reported, which may have been due to the concurrent use of quinolones and NSAIDs.

Colestipol and Cholestyramine
These substances can cause delayed or reduced absorption of diclofenac. Therefore, it is recommended to take diclofenac at least 1 hour before or 4 to 6 hours after taking colestipol/cholestyramine.

Anticoagulants and antiplatelet agents
Caution is advised as concurrent administration may increase the risk of bleeding (see section 4.4). Although clinical studies do not seem to indicate that diclofenac affects the action of anticoagulants, there are reports of an increased risk of bleeding in patients receiving both diclofenac and anticoagulants. Therefore, close monitoring of these patients is recommended (monitoring of coagulation status).

Selective serotonin reuptake inhibitors (SSRIs)
The concurrent use of systemic NSAIDs, including diclofenac, with SSRIs may increase the risk of gastrointestinal bleeding (see section 4.4).

Antidiabetics
Clinical studies have shown that diclofenac can be administered concurrently with oral antidiabetics without affecting their clinical effect. However, isolated cases of hypo- and hyperglycemic reactions have been reported following the administration of diclofenac, necessitating an adjustment of the antidiabetic dosage. Therefore, monitoring of blood glucose levels is recommended during concurrent therapy.
There have also been isolated reports of metabolic acidosis when diclofenac was administered with metformin, especially in patients with pre-existing renal dysfunction.

Probenecid/Sulfinpyrazone
Medicines containing probenecid or sulfinpyrazone can delay the excretion of diclofenac.

4.6. Fertility, pregnancy, and lactation

Pregnancy
Inhibition of prostaglandin synthesis may adversely affect pregnancy and/or embryofetal development. Data from epidemiological studies suggest an increased risk of miscarriage as well as cardiac malformations and gastroschisis following the use of a prostaglandin synthesis inhibitor in early pregnancy. The absolute risk of a cardiovascular malformation increased from less than 1% to about 1.5%. It is believed that the risk increases with the dose and duration of therapy.

In animals, it has been shown that the administration of a prostaglandin synthesis inhibitor leads to increased pre- and post-implantation loss and embryofetal lethality. Furthermore, increased incidences of various malformations, including cardiovascular malformations, have been reported in animals that received a prostaglandin synthesis inhibitor during the organogenesis phase (see also section 5.3).

From the 20th week of pregnancy, the use of diclofenac can cause oligohydramnios, which is triggered by fetal renal dysfunction. This can occur shortly after the start of treatment and is usually reversible after discontinuation of treatment. Additionally, there have been reports of ductus arteriosus constriction during treatment in the second trimester, most of which disappeared after
discontinuation of treatment. During the first and second trimester of pregnancy, diclofenac is only given if absolutely necessary. If diclofenac is used by a woman trying to conceive or during the first or second trimester of pregnancy, the dose should be as low and the duration of treatment as short as possible. After several days of exposure to diclofenac, prenatal monitoring for oligohydramnios and ductus arteriosus constriction should be considered from the 20th week of pregnancy. Diclofenac should be discontinued if oligohydramnios or ductus arteriosus constriction is detected.

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors:

- expose the fetus to the following risks:
  cardiopulmonary toxicity (premature constriction/closure of the ductus arteriosus and pulmonary hypertension);
  renal dysfunction (see above);

- expose the mother and the child, at the end of pregnancy, to the following risks:
  possible prolongation of bleeding time, an anti-platelet aggregation effect that can occur even at very low doses;
  inhibition of uterine contractions, resulting in delayed or prolonged labor.

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

Lactation
Like other NSAIDs, diclofenac passes into breast milk in small amounts. To avoid adverse effects on the infant, diclofenac should not be used during breastfeeding.

Fertility
Female fertility:
As with other NSAIDs, the use of diclofenac may impair female fertility and is therefore not recommended in women planning to become pregnant. In women who have difficulty conceiving or are undergoing investigation of infertility, discontinuation of Voltaren retard film-coated tablets should be considered.

Male fertility:
There are no human data on the effect of Voltaren on male fertility (see section 5.3).

4.7. Effects on ability to drive and use machines

Patients experiencing side effects such as visual disturbances, dizziness, vertigo, drowsiness, or other central nervous system disorders while taking Voltaren retard film-coated tablets should not drive or operate machinery.

4.8. Undesirable effects

The most commonly observed side effects affect the gastrointestinal tract. Peptic ulcers, perforations, or gastrointestinal bleeding – sometimes fatal, especially in the elderly – occur. Nausea, vomiting, diarrhea, flatulence, constipation, dyspepsia, abdominal pain, melena, hematemesis, ulcerative stomatitis, exacerbation of ulcerative colitis, and Crohn's disease have been reported following the use of NSAIDs. (see also section 4.4). Gastritis has been observed less frequently.
Edema, hypertension, and heart failure have been reported in connection with NSAID treatment. Clinical studies and epidemiological data consistently indicate an increased risk of arterial thrombotic events (such as heart attack or stroke) associated with the use of diclofenac, especially at a high dose (150 mg daily) and with long-term use (see sections 4.3 and 4.4 Contraindications and Special warnings and precautions for use).
The side effects from clinical studies and from spontaneous reports or literature reports are listed below by MedDRA system organ classes and ranked according to frequency. Within each frequency group, side effects are listed in decreasing order of severity, with the most common first, based on the following frequency estimates:

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)

Within each frequency group, side effects are listed in decreasing order of severity. For adverse drug reactions in the post-marketing phase, the frequency cannot be estimated. Therefore, it has been categorized as not known.

The following side effects include those reported with Voltaren retard film-coated tablets and/or other forms of diclofenac in short-term or long-term use:

Blood and lymphatic system disorders:
Very rare: Blood formation disorders (hemolytic and/or aplastic anemia, leukopenia, thrombocytopenia, pancytopenia, agranulocytosis).
Initial signs may include: fever, sore throat, superficial wounds in the mouth, flu-like symptoms, severe fatigue, nosebleeds, and skin bleeding. Therefore, blood counts should be regularly monitored during long-term therapy.

Immune system disorders:

Common:	Hypersensitivity reactions such as rash and itching
Uncommon:	Urticaria
Very rare:	Severe general hypersensitivity reactions. They may manifest as:

	Angioedema (including facial edema), tongue swelling, internal laryngeal swelling with airway constriction, shortness of breath, palpitations, blood pressure drop up to life-threatening shock

Psychiatric disorders
Very rare: Disorientation, depression, insomnia, anxiety, nightmares, irritability, psychotic disorders

Nervous system disorders:

Common:	Headaches, irritability, fatigue, drowsiness, dizziness, agitation
Rare:	Restlessness, drowsiness
Very rare:	Sensory disturbances, paresthesia, memory disorders, convulsions, tremors, taste disturbances, cerebrovascular events. Symptoms of aseptic meningitis with neck stiffness, headache, nausea, vomiting, fever, and clouding of consciousness. Patients with autoimmune diseases (systemic lupus erythematosus, mixed connective tissue disease) seem to be predisposed.

Eye disorders:
Occasionally: Visual disturbances (blurred or double vision)

Ear and labyrinth disorders:
Common: Dizziness
Rare: Temporary hearing disorders, tinnitus

Heart diseases:
Occasionally: Myocardial infarction, heart failure, palpitations, chest pain, edema, Kounis syndrome

Vascular diseases:
Very rare: Hypertension, vasculitis

Respiratory, thoracic and mediastinal disorders:
Rare: Asthma (including dyspnea)
Very rare: Pneumonitis

Gastrointestinal disorders:

Very common:	Nausea, vomiting, diarrhea, minor blood loss
Common:	Dyspepsia, abdominal pain, abdominal cramps, flatulence, loss of appetite
Rare:	Gastritis, gastrointestinal bleeding, hematemesis, melena, bloody diarrhea, gastrointestinal ulcers (possibly with bleeding and perforation)
Very rare:	Pancreatitis, colitis (including bleeding colitis and exacerbation of ulcerative colitis or Crohn's disease), constipation, stomatitis, glossitis, esophageal lesions, diaphragm-like intestinal strictures (with oral DF)
Unknown	Ischemic colitis

Liver and biliary disorders:

Common:	Liver function disorders (elevation of serum transaminases)

Occasional:	Hepatitis, jaundice, liver damage of varying severity
Very rare:	Fulminant hepatitis (even without prodromal symptoms), hepatic necrosis, liver failure

Skin and subcutaneous tissue disorders:
Common: Rash
Rare: Urticaria
Very rare: Bullous dermatitis, eczema, erythema, severe forms of skin reactions (Erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, Lyell-Syndrome, exfoliative dermatitis), alopecia, photosensitization, (allergic) purpura, pruritus
Not known: Fixed drug eruption, generalized bullous fixed drug eruption Disorders of the kidneys and urinary tract:

Occasionally:	Development of edema (especially in patients with arterial hypertension or renal insufficiency)
Very rare:	Acute renal failure, hematuria, proteinuria, tubulointerstitial nephritis, nephrotic syndrome, papillary necrosis

Infections and parasitic diseases:
Very rare: A worsening of infection-related inflammations (e.g., development of necrotizing fasciitis) has been described in temporal association with the systemic use of NSAIDs. This may be related to the mechanism of action of NSAIDs.

General disorders and administration site conditions:
Rare: Edema

Description of selected side effects
A meta-analysis and pharmacoepidemiological data suggest a slightly increased risk of arterial thrombotic events (such as myocardial infarction) associated with the use of diclofenac, especially at high doses (150 mg/day) and during long-term use (see section 4.4).

Reporting of suspected adverse reactions
The reporting of suspected adverse reactions after approval is of great importance. It allows continuous monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are encouraged to report any suspected adverse reactions via the national reporting system:

Federal Office for Safety in Health Care
Traisengasse 5
1200 VIENNA
AUSTRIA
Fax: + 43 (0) 50 555 36207
Website: http://www.basg.gv.at/

4.9. Overdose

Symptoms:
A typical clinical picture of a diclofenac overdose is not known. An overdose may lead to symptoms such as vomiting, gastrointestinal bleeding, diarrhea, dizziness, tinnitus, or

seizures. In cases of severe poisoning, acute renal failure and liver damage, as well as hypotension, respiratory depression, and cyanosis are possible.

Treatment:
The treatment of acute poisoning with NSAIDs, including diclofenac, is essentially supportive and symptomatic. A specific antidote does not exist. Supportive measures and symptomatic treatment should be employed in the event of complications such as hypotension, renal failure, seizures, gastrointestinal disorders, and respiratory depression.
Specific measures such as forced diuresis, dialysis, or hemoperfusion are most likely not useful in the elimination of NSAIDs, including diclofenac, due to the high protein binding and extensive metabolism of NSAIDs.
The administration of activated charcoal may be considered after the ingestion of a potentially toxic overdose, as well as gastric decontamination (e.g., inducing vomiting, gastric lavage) after a potentially life-threatening overdose.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Non-steroidal anti-inflammatory and antirheumatic products, acetic acid derivatives and related substances; ATC code: M01AB05

Diclofenac is a non-steroidal active substance with antirheumatic, anti-inflammatory, analgesic, and antipyretic properties, primarily through the inhibition of prostaglandin synthesis. In high doses (200 mg), experimentally induced platelet aggregation is temporarily inhibited.

5.2. Pharmacokinetic properties

Absorption
Judging by the amount of unchanged diclofenac and its hydroxylated metabolites found in the urine, the same amount of diclofenac is released and absorbed from Voltaren retard film-coated tablets as from enteric-coated film-coated tablets of Voltaren. However, the systemic availability of diclofenac from Voltaren retard film-coated tablets is on average about 82% of that achieved with the same dose of Voltaren in the form of enteric-coated film-coated tablets (possibly due to the metabolism dependent on the
release rate during the first liver passage). Due to the slower release of the active substance from Voltaren retard film-coated tablets, lower plasma peak concentrations are achieved than after administration of enteric-coated film-coated tablets.
Mean plasma peak concentrations of 0.5 µg/ml (1.6 µmol/l) are reached on average four hours after administration of a film-coated tablet with modified release of 100 mg. Taking with a meal has no significant effect on the absorption and systemic availability of Voltaren retard film-coated tablets.
On the other hand, 24 hours after taking Voltaren retard 100 mg film-coated tablets, mean plasma concentrations of 13 ng/ml (40 nmol/l) are measured. There is a linear relationship between the absorbed and administered amount.
The active ingredient is metabolized to about half during the first liver passage (= "first-pass effect"), which results in different availability for oral and rectal administration compared to

parenteral administration. With repeated administration, the kinetics do not change. There is no accumulation if the recommended dosing intervals are observed.

Distribution
Protein binding: 99.7%, mainly to albumin. The apparent volume of distribution can be calculated and is therefore 0.12 - 0.17 l/kg.
Diclofenac penetrates into the synovial fluid. Peak concentrations are measured there 2-4 hours after reaching the maximum plasma concentrations. The apparent half-life from the synovial fluid is 3-6 hours. Already 2 hours after reaching the maximum plasma concentration, the concentration of the active ingredient in the synovial fluid is higher than in the plasma and remains higher for up to 11 hours.
Diclofenac was detected in low concentrations in the breast milk of a nursing mother. The amount ingested by a breastfed infant corresponds to an estimated dose of 0.03 mg/kg/day.

Biotransformation
The biotransformation of diclofenac occurs partly through glucuronidation of the intact molecule, but mainly through simple and multiple hydroxylation and methoxylation. This results in several phenolic metabolites, which are then largely conjugated to glucuronic acid. Two of these phenolic metabolites are pharmacologically active, although significantly less so than diclofenac.

Elimination
The elimination of diclofenac from the plasma occurs with a systemic clearance of 263 ± 56 ml/min
(mean ± SD). The terminal half-life is 1-2 hours. Four of the metabolites, including the two active metabolites, also have a short half-life of 1-3 hours. The practically inactive metabolite 3'-hydroxy-4'-methoxy-diclofenac has a significantly longer half-life.
About 60% of the administered dose is excreted in the urine, as glucuronide of the intact molecule and in the form of metabolites, which are also predominantly conjugated to glucuronic acid. Less than 1% is excreted unchanged. The rest of the dose is excreted in the form of metabolites via the bile in the feces.
Absorption, biotransformation, and elimination are age-independent.

5.3. Preclinical safety data

Based on conventional studies with diclofenac on safety pharmacology, toxicity with single and repeated administration, genotoxicity, and carcinogenic potential, the preclinical data do not reveal any special hazards for humans.
Reproduction and developmental studies in animals showed that the administration of diclofenac has no teratogenic effect during organogenesis despite the induction of maternal and fetal toxicity in mice at oral doses of up to 20 mg/kg/day (corresponding to 0.41 times the maximum recommended
human dose [MRHD] of Voltaren (= 200 mg/day) based on the comparison of body surface area (BSA)), and in rats and rabbits at oral doses of up to 10 mg/kg/day (0.41 and 0.81 times the MRHD based on the comparison of BSA). Regarding chronic toxicity, studies are available in various animal species.
Diclofenac, administered to male and female rats at a dose of 4 mg/kg/day (approximately 0.16 times the MRHD based on BSA), had no effect on fertility or the pre-, peri-, and postnatal development of the offspring. The administration of NSAIDs (including diclofenac) inhibited

ovulation in rabbits, implantation and placentation in rats, and led to premature closure of the ductus arteriosus Botalli in pregnant rats. In a study where pregnant rats were given from the 15th.
gestation to the 21st lactation day 2 or 4 mg/kg diclofenac (0.08 or 0.16 times the MRHD based on BSA) orally, significant maternal mortality (caused by gastrointestinal ulcerations, peritonitis, and changes in blood count) was observed. Doses of diclofenac toxic to the mother animals were associated with dystocia, prolonged gestation, reduced fetal survival, and delayed intrauterine growth in rats. The minor effects of diclofenac on reproductive parameters and birth, as well as the constriction of the ductus arteriosus Botalli in utero, are pharmacological consequences of this class of prostaglandin synthesis inhibitors.
In various studies, no mutagenic effects were found either in vitro or in vivo, and long-term studies in rats and mice showed no carcinogenic potential.
At concentrations corresponding to those reached in human plasma or synovial fluid, diclofenac sodium does not cause suppression of proteoglycan biosynthesis in cartilage in vitro (rabbit cells).

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Tablet core: Sucrose, colloidal silicon dioxide, cetyl alcohol, magnesium stearate, polyvinylpyrrolidone

Film coating: Sucrose, hydroxypropylmethylcellulose, polysorbate 80, red iron oxide (E 172), purified talc, titanium dioxide (E 171), polyethylene glycol 8000;

6.2. Incompatibilities

None known

6.3. Shelf life

3 years

6.4. Special precautions for storage

No special storage conditions are required for this medicinal product.

6.5. Nature and contents of container

Blister packs of aluminum/PVC/PE/PVDC, carton box made of paper
Packs of 10, 30, and 50 pieces

Not all pack sizes may be marketed.

6.6. Special precautions for disposal and other handling

Unused medicinal product or waste material must be disposed of in accordance with national requirements.

MARKETING AUTHORIZATION HOLDER

Novartis Pharma GmbH, Vienna

MARKETING AUTHORIZATION NUMBER

Z.Nr.: 1-16856

9. DATE OF AUTHORIZATION/RENEWAL OF AUTHORIZATION

Date of authorization: December 23, 1980
Date of last renewal of authorization: 04.06.2014

10. DATE OF REVISION OF THE TEXT

07/2025

PRESCRIPTION/PHARMACY ONLY

Prescription and pharmacy only.