AUSTRALIAN PI – VOLTAREN® RAPID (DICLOFENAC POTASSIUM) TABLETS

1 NAME OF THE MEDICINE

Active ingredient: Diclofenac Potassium

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Voltaren Rapid tablets contain 50 mg of diclofenac potassium.

Diclofenac potassium is a white or slightly yellowish, crystalline powder, slightly hygroscopic, sparingly soluble in water, freely soluble in methanol, soluble in alcohol, slightly soluble in acetone.

Excipients: Each diclofenac potassium 50 mg tablet contains 5.8 mg of potassium.

For the full list of excipients, see section 6.1 'LIST OF EXCIPIENTS'.

3 PHARMACEUTICAL FORM

Tablets (reddish-brown, round, biconvex sugar-coated tablets).

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

- As short-term treatment (up to one week) for the relief of acute pain states in which there is an inflammatory component.
- Treatment of acute migraine attacks (with or without aura)
- Symptomatic treatment of primary dysmenorrhoea.

4.2 DOSE AND METHOD OF ADMINISTRATION

Pregnancy: see Section 4.3 CONTRAINDICATIONS and Section 4.6 FERTILITY, PREGNANCY and LACTATION.

After assessing the risk/benefit ratio in each individual patient, the lowest effective dose for the shortest possible duration should be used. Adverse effects may be minimized by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.4 'SPECIAL WARNINGS AND PRECAUTIONS'). Patients on long term treatment should be reviewed regularly with regards to efficacy, risk factors and ongoing need for treatment.

The tablets should be swallowed whole with liquid, preferably before meals, and must not be divided or chewed.

Dose

Adults

Acute pain states with an inflammatory component

As a rule, the initial daily dosage for adults is 100 to 150 mg. In milder cases, as well as for children over 14 years of age, 75 to 100 mg daily is usually sufficient. The total daily dosage should generally be prescribed in 2 or 3 fractional doses. Treatment is to continue for a maximum of 7 days. If the pain has not resolved satisfactorily after 7 days' treatment, the patient should be instructed to return for review by the doctor.

Acute migraine

In migraine, an initial dose of 50 mg should be taken at the first signs of an impending attack. If the pain is not relieved within 2 hours of this initial dose, a further dose of 50 mg may be taken. If needed, further doses of 50 mg may be taken at intervals of 4-6 hours. The total dose to treat an acute migraine should not exceed 200 mg. The total daily dose should not exceed 200 mg. Diclofenac potassium should not be used for migraine prophylaxis.

Symptomatic treatment of primary dysmenorrhoea

In primary dysmenorrhoea, initially a dose of 50 or 100 mg should be given followed by 50 mg three times daily for 3 days. Treatment should be started upon appearance of the first symptoms and, depending on their duration and severity, continued for up to three days. If the pain has not resolved satisfactorily after 3 days' treatment, the patient should be instructed to return for review by the doctor.

Children

Voltaren Rapid is not recommended for use in children.

Method of administration

Voltaren Rapid tablets should be taken with liquid, preferably before meals.

4.3 CONTRAINDICATIONS

- Gastric or duodenal ulcer, gastrointestinal bleeding or perforation.
- Patients who are hypersensitive to the active ingredient, diclofenac, or any of the excipients contained in the tablets.
- Third trimester of pregnancy. (see section 4.6 'FERTILITY, PREGNANCY AND LACTATION')
- Patients with severe hepatic impairment (see section 4.4 'SPECIAL WARNINGS AND PRECAUTIONS FOR USE).
- Renal failure (see section 4.4 'SPECIAL WARNINGS AND PRECAUTIONS FOR USE)
- Severe cardiac failure (see section 4.4 'SPECIAL WARNINGS AND PRECAUTIONS FOR USE) Treatment of perioperative pain in setting of coronary artery bypass surgery (CABG)
- Patients in whom diclofenac, aspirin or other NSAIDs induce asthma, angioedema, urticaria or other allergic-type reactions because severe, rarely fatal, anaphylactic type reactions to diclofenac have been reported in such patients.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Cardiovascular Thrombotic Events

Observational studies have indicated that non-selective NSAIDs may be associated with an increased risk of serious cardiovascular events including myocardial infarction and stroke, which may increase

with dose or duration of use. Patients with cardiovascular disease, history of atherosclerotic cardiovascular disease or cardiovascular risk factors may also be at greater risk. (see section 4.2 'DOSE AND METHOD OF ADMINISTRATION').

Treatment with Voltaren Rapid is generally not recommended in patients with established cardiovascular disease (congestive heart failure, established ischemic heart disease, peripheral arterial disease) or uncontrolled hypertension. If needed, patients with established cardiovascular disease, uncontrolled hypertension or significant risk factors for cardiovascular disease (e.g. hypertension, hyperlipidemia, diabetes mellitus and smoking) should be treated with Voltaren Rapid only after careful consideration and only at doses ≤100 mg daily when treatment continues for more than 4 weeks.

As the cardiovascular risks of diclofenac may increase with dose and duration of exposure, the lowest effective daily dose should be used for the shortest duration possible. The patient's need for symptomatic relief and response to therapy should be re-evaluated periodically, especially when treatment continues for more than 4 weeks.

Physicians and patients should remain alert for the signs and symptoms of serious arteriothrombotic events (e.g. chest pain, shortness of breath, weakness, slurring of speech), which can occur without warnings. Patients should be informed about signs and/or symptoms of serious cardiovascular toxicity and be instructed to see a physician immediately in case of such an event.

There is no consistent evidence that the concurrent use of aspirin mitigates the possible increased risk of serious cardiovascular thrombotic events associated with NSAID use.

Hypertension

NSAIDs may lead to the onset of new hypertension or worsening of pre-existing hypertension and patients taking anti-hypertensives with NSAIDs may have an impaired anti-hypertensive response. Caution is advised when prescribing NSAIDs to patients with hypertension. Blood pressure should be monitored closely during initiation of NSAID treatment and at regular intervals thereafter.

Heart Failure:

Fluid retention and oedema have been observed in some patients taking NSAIDs, including diclofenac, therefore caution is advised in patients with fluid retention or heart failure.

Gastrointestinal Effects

Close medical surveillance is imperative and particular caution should be exercised when prescribing NSAIDs, including diclofenac, in patients with symptoms indicative of gastrointestinal disorders (GI) or, with a history suggestive of gastrointestinal ulceration, bleeding or perforation (see section 4.8 'ADVERSE EFFECTS').

Upper GI ulcers, gross bleeding or perforation caused by NSAIDs, including diclofenac, occur in approximately 1% of patients treated for 3-6 months and in about 2-4% of patients treated for one year. The risk of GI bleeding is higher with increasing NSAID doses, with increasing duration of use and in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation and in the elderly.

Gastric or duodenal ulceration, perforation or gastrointestinal bleeding, which can be fatal, have been reported in patients receiving diclofenac potassium tablets. Studies to date have not identified any subset of patients who are not at risk of developing these problems.

Caution is advised in patients with risk factors for gastrointestinal events who may be at greater risk of developing serious gastrointestinal events, e.g. the elderly, those with a history of serious gastrointestinal events, smoking and alcoholism.

The concurrent use of aspirin and NSAIDs, including diclofenac, also increases the risk of serious gastrointestinal adverse events.

To reduce the risk of GI toxicity in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation, and in the elderly, the treatment should be initiated and maintained at the lowest effective dose. Gastrointestinal bleeding, ulceration and perforation in general have more serious consequences in the elderly. They can occur at any time during treatment with or without warning symptoms or a previous history. In instances where gastrointestinal bleeding or ulcerations occur in patients receiving Voltaren Rapid, the drug should be withdrawn immediately. Physicians should warn patients about the signs and symptoms of serious gastrointestinal toxicity and what steps to take if they occur.

Combination therapy with protective agents (e.g. proton pump inhibitors or misoprostol) should be considered for these patients, and also for patients requiring concomitant use of medicinal products containing low-dose acetylsalicylic acid (ASA)/aspirin or other medicinal products likely to increase gastrointestinal risk.

Patients with a history of GI toxicity, particularly the elderly, should report any unusual abdominal symptoms (especially GI bleeding). Caution is recommended in patients receiving concomitant medications which could increase the risk of ulceration or bleeding, such as systemic corticosteroids, anticoagulants, anti-platelet agents or selective serotonin-reuptake inhibitors (see section 4.4 ‘SPECIAL WARNINGS AND PRECAUTIONS FOR USE) .

Close medical surveillance and caution should also be exercised in patients with ulcerative colitis, or with Crohn's disease, as well as in patients suffering from pre-existing dyshaemopoiesis or disorders of blood coagulation, as their condition may be exacerbated (see section 4.8 ‘ADVERSE EFFECTS’).

NSAIDs, including diclofenac, may be associated with increased risk of gastro-intestinal anastomotic leak. Close medical surveillance and caution are recommended when using Voltaren after gastro-intestinal surgery.

Serious Skin Reactions

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, toxic epidermal necrolysis, Drug Reaction with Eosinophilia with Systemic Symptoms (DRESS) (see Drug Reaction with Eosinophilia with Systemic Symptoms (DRESS)) and generalised bullous fixed drug eruption have been reported very rarely in association with the use of NSAIDs, including Voltaren Rapid (see section 4.8 ‘ADVERSE EFFECTS’). These serious adverse events are idiosyncratic and are independent of dose or duration of use. 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. Patients should be advised of the signs and symptoms of serious skin reactions and to consult their doctor at the first appearance of skin rash, mucosal legion or any other sign of hypersensitivity, and Voltaren Rapid should be discontinued.

Drug Reaction with Eosinophilia with Systemic Symptoms (DRESS)

DRESS has been reported in patients taking NSAIDs. Some of these events have been fatal or life-threatening. DRESS typically, although not exclusively, presents with fever, rash, lymphadenopathy, and/or facial swelling. Other clinical manifestations may include hepatitis, nephritis, haematological abnormalities, myocarditis, or myositis. Sometimes symptoms of DRESS may resemble an acute viral infection. Eosinophilia is often present. Because this disorder is variable in its presentation, other organ systems not noted here may be involved. It is important to note that early manifestations of hypersensitivity, such as fever or lymphadenopathy, may be present even though rash is not evident. If such signs or symptoms are present, discontinue the NSAID and evaluate the patient immediately.

Pre-existing Asthma

In patients with asthma, seasonal allergic rhinitis, swelling of the nasal mucosa (i.e. nasal polyps), chronic obstructive pulmonary diseases or chronic infections of the respiratory tract (especially if linked to allergic rhinitis-like symptoms), reactions to NSAIDs such as asthma exacerbations (so-called intolerance to analgesics / analgesics-asthma), Quincke's oedema or urticaria are more frequent than in other patients. Therefore, special precaution is recommended in such patients. This is applicable as well for patients who are allergic to other substances, e.g. with skin reactions, pruritus or urticaria.

Infection:

Like other NSAIDs, Voltaren Rapid may mask the usual signs and symptoms of infection due to its pharmacodynamic properties.

Hypersensitivity:

As with other NSAIDs, allergic reactions, including anaphylactic/anaphylactoid reactions have been reported with diclofenac. These reactions can occur without earlier exposure to the drug.

Sucrose:

Voltaren Rapid tablets contain sucrose and therefore are not recommended for patients with rare hereditary problems of fructose intolerance, or glucose-galactose malabsorption or sucrase-isomaltase insufficiency.

Use in hepatic impairment

Close medical surveillance is required when prescribing Voltaren Rapid to patients with impaired hepatic function, as their condition may be exacerbated (see section 4.3 'CONTRAINDICATIONS').

As with other NSAIDs, including diclofenac, elevations of one or more liver enzymes may occur during Voltaren Rapid therapy. These laboratory abnormalities may progress, remain unchanged, or revert to normal despite continued therapy. Borderline elevations (i.e. 1.2 to 3 times the upper limit of normal (ULN), or greater elevations of transaminases occurred in about 15% of Voltaren-treated patients. In clinical trials, meaningful elevations (i.e. more than 3 times the ULN) of AST and/or ALT

occurred in about 4% of patients treated for several months, including marked elevations (i.e. more than 8 times the ULN) in about 1% of patients.

Transaminase elevations were reversible on cessation of therapy, and even among patients with marked elevations, signs and symptoms of liver disease occurred only in isolated cases. Most patients with borderline elevations did not have therapy interrupted, and transaminase elevations in most of these cases disappeared or did not progress. There were no identifying features to distinguish those patients who developed marked elevations from those who did not.

Severe hepatotoxicity may develop without prodromal symptoms. If, contrary to its recommended use for short term treatment, Voltaren Rapid is administered for a more prolonged period, monitoring of hepatic function is indicated as a precautionary measure. If abnormal liver tests persist or worsen, if clinical signs and/or symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g., eosinophilia, rash, etc.), Voltaren Rapid should be discontinued.

Physicians should inform patients of the warning signs and symptoms of hepatotoxicity (e.g., nausea, fatigue, lethargy, pruritus, jaundice, abdominal tenderness in the right upper quadrant and "flu-like" symptoms) and the appropriate action to take should these signs and symptoms appear.

Caution should be exercised when using Voltaren Rapid in patients with hepatic porphyria, since Voltaren Rapid may trigger an attack.

Use in renal impairment

As a class, NSAIDs have been associated with renal papillary necrosis and other renal pathology during long-term administration in animals.

Fluid retention and oedema have been reported in association with Voltaren Rapid therapy. Owing to the importance of prostaglandins for maintaining renal blood flow, particular caution is called for in patients with impaired cardiac or renal function, history of hypertension, in the elderly, in patients being treated with diuretics or medicinal products that can significantly impact renal function, and in those with extracellular volume depletion from any cause, e.g. in the peri or post-operative phase of major surgical operations (see section 4.3 'CONTRAINDICATIONS'). Monitoring of renal function as a precautionary measure is therefore recommended when using Voltaren Rapid in such cases. Discontinuation of therapy is typically followed by recovery to the pre-treatment state.

Combination Use of ACE Inhibitors or Angiotensin Receptor Antagonist, Anti-inflammatory Drugs and Thiazide Diuretics:

The use of an ACE inhibiting drug (ACE-inhibitors or angiotensin receptor antagonist), an anti-inflammatory drug (NSAID or COX-2 inhibitor) and a thiazide diuretic at the same time increases the risk of renal impairment. This includes use in fixed combination products containing more than one class of drug. Combined use of these medications should be accompanied by increased monitoring of serum creatinine, particularly at the institution of the combination. The combination of drugs from these three classes should be used with caution particularly in elderly patients or those with pre-existing renal impairment.

Use in the elderly

In patients of advanced age, caution is indicated on basic medical grounds. In particular it is recommended that the lowest effective dosage be used in frail elderly patients or those with low body weight.

Treatment with Voltaren Rapid in the elderly usually proves necessary only for a few days.

Paediatric use

Voltaren Rapid is not recommended for use in children as safety and efficacy in this age group have not been established.

Effects on laboratory tests

Haematological Effects

Use of Voltaren Rapid is recommended only for short-term treatment. If, however, Voltaren Rapid is used for a prolonged period, monitoring of the blood count is recommended.

Like other NSAIDs, Voltaren Rapid may temporarily inhibit platelet aggregation. Patients with haemostatic disorders should be carefully monitored.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

The following interactions include those observed with Voltaren Rapid and/or other pharmaceutical forms of diclofenac.

Lithium/digoxin: When given together with preparations containing lithium or digoxin, diclofenac may raise their plasma concentrations and these concentrations should be monitored during treatment with Voltaren Rapid.

Diuretics and antihypertensive agents: Like other NSAIDs, concomitant use of diclofenac with diuretics or antihypertensive agents (e.g. beta-blockers, angiotensin converting enzyme (ACE) inhibitors) may cause a decrease in their antihypertensive effect. Therefore, the combination should be administered with caution and patients, especially the elderly, should have their blood pressure periodically monitored. When NSAIDs, including diclofenac are combined with diuretics, ACE inhibitors or angiotensin II receptor antagonists, the risk of worsening of renal function, including possible acute renal failure (which is usually reversible) may be increased in some patients, especially when renal function is compromised (e.g. dehydrated or elderly patients). Patients should be adequately hydrated and monitoring of renal function is recommended after initiation of concomitant therapy and periodically thereafter (see section 4.4 'SPECIAL WARNINGS AND PRECAUTIONS').

Other NSAIDs and corticosteroids: The concomitant use of diclofenac with systemic NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided due to the absence of any evidence demonstrating synergistic benefits and the potential for additive undesirable effects. Concomitant administration of diclofenac and other systemic NSAIDs or corticosteroids may increase the frequency of gastrointestinal undesirable effects. Concurrent treatment with aspirin lowers the plasma concentration, peak plasma levels and AUC values of diclofenac. The use of both drugs concurrently is not recommended.

Anticoagulants and anti-platelet agents: Caution is recommended since concomitant administration could increase the risk of bleeding (see section 4.4 'SPECIAL WARNINGS AND PRECAUTIONS'). The concurrent use of NSAIDs and warfarin has been associated with severe, sometimes fatal, haemorrhage. The exact mechanism of the interaction between NSAIDs and warfarin is unknown, but may involve enhanced bleeding from NSAID-induced gastrointestinal ulceration or an additive effect of anticoagulation by warfarin and inhibition of platelet function by NSAIDs. Diclofenac should be used with caution in combination with warfarin and such patients should be closely monitored.

Selective serotonin reuptake inhibitors (SSRIs): Concomitant administration of systemic NSAIDs, including diclofenac, and SSRIs may increase the risk of gastrointestinal bleeding (see section 4.4 'SPECIAL WARNINGS AND PRECAUTIONS').

Antidiabetic agents: Diclofenac can be given together with oral antidiabetic agents without influencing their clinical effect. However, there are isolated reports of both hypoglycaemic and hyperglycaemic effects in the presence of diclofenac which necessitated changes in the dosage of the antidiabetic agents. For this reason, monitoring of the blood glucose level is recommended as a precautionary measure during concomitant therapy.

There have also been isolated reports of metabolic acidosis when diclofenac was co-administered with metformin, especially in patients with pre-existing renal impairment.

Methotrexate: Caution should be exercised when NSAIDs, including diclofenac, are administered less than 24 hours before or after treatment with methotrexate, since the blood concentration of methotrexate may rise and the toxicity of this substance be increased.

Cyclosporin and tacrolimus: Nephrotoxicity of cyclosporin may be enhanced through effects of NSAIDs, including diclofenac, on renal prostaglandins. Therefore, diclofenac should be given at doses lower than those that would be used in patients not receiving cyclosporin or tacrolimus.

Drugs known to cause hyperkalaemia: Concomitant treatment with potassium-sparing drugs (e.g. diuretics, cyclosporine, tacrolimus or trimethoprim) may be associated with increased serum potassium levels, which should therefore be monitored frequently (see section 4.4 'SPECIAL WARNINGS AND PRECAUTIONS').

Glucocorticoids: The addition of glucocorticoids to NSAIDs, though sometimes necessary for therapeutic reasons, may aggravate gastrointestinal side effects.

Quinolone antibacterials: There have been isolated reports of convulsions which may have been due to concomitant use of quinolones and NSAIDs.

CYP2C9 inhibitors: Caution is recommended when co-prescribing diclofenac with potent CYP2C9 inhibitors (such as sulfinpyrazone and voriconazole), which could result in a significant increase in peak plasma concentrations and exposure to diclofenac due to inhibition of diclofenac metabolism. Concomitant administration of voriconazole with diclofenac may increase plasma diclofenac levels.

CYP2C9 inducers: Caution is recommended when co-prescribing diclofenac with CYP2C9 inducers (such as rifampicin), which could result in a significant decrease in plasma concentration and exposure to diclofenac

Phenytoin: When using phenytoin concomitantly with diclofenac, monitoring of phenytoin plasma concentrations is recommended due to an expected increase in exposure to phenytoin.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

The use of Voltaren Rapid 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 Voltaren Rapid should be considered.

Use in pregnancy – Pregnancy Category C

The use of diclofenac in pregnant women has not been studied and safety in pregnancy has not been established. Therefore Voltaren Rapid should not be used in pregnant women during the first two trimesters or in women who are likely to become pregnant unless the potential benefit to the mother outweighs the risk to the foetus.

Data from epidemiological studies suggest an increased risk of miscarriage after the use of a prostaglandin synthesis inhibitor in early pregnancy.

Dysmorphogenic effects (rib defects in 1 rat foetus at 4 mg/kg and in 1 mouse foetus at 1 and 4 mg/kg doses) were observed at 1 of 3 laboratories in which embryogenesis studies were conducted.

NSAIDs inhibit prostaglandin synthesis and, when given during the latter part of pregnancy, may cause closure of the foetal ductus arteriosus, foetal renal impairment, inhibition of platelet aggregation, and delay labour and birth.

Use of Voltaren Rapid during the third trimester of pregnancy is contraindicated owing to the possibility of uterine inertia, premature closure of the ductus arteriosus and oligohydramnios and neonatal renal impairment (see Oligohydramnios and neonatal renal impairment).

<u>Oligohydramnios and Neonatal Renal Impairment:</u>

Use of NSAIDs from about 20 weeks gestation may cause foetal 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 post-marketing cases of impaired neonatal renal function, invasive procedures such as exchange transfusion or dialysis were required.

If, after careful consideration of alternative treatment options for pain management, NSAID treatment is necessary from about 20 weeks to the end of the second trimester, limit use to the lowest effective dose and shortest duration possible. Use of Voltaren Rapid during the third trimester of pregnancy is contraindicated (see Use in pregnancy – Pregnancy Category C). Consider ultrasound monitoring of amniotic fluid if treatment extends beyond 48 hours. Discontinue treatment with NSAIDs if oligohydramnios occurs.

Use in lactation

Following oral doses of 50 mg administered every 8 hours, the active substance; diclofenac passes into human milk. As with other drugs that are excreted in milk, Voltaren Rapid is not recommended for use in nursing women.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Patients experiencing visual disturbances, dizziness, vertigo, somnolence or other central nervous disturbances while taking Voltaren Rapid should refrain from driving a vehicle or operating machines.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Whilst not all the reactions listed have been reported specifically with Voltaren rapid, similarities between the NSAIDs as a group require them to be considered possible.

Adverse reactions are ranked under heading of frequency, the most frequent first, using the following convention: common (≥ 1/100, < 1/10); uncommon (≥ 1/1,000, < 1/100); rare (≥ 1/10,000, < 1/1,000); very rare (< 1/10,000), including isolated reports.

The following undesirable effects include those reported with Voltaren Rapid and/or other pharmaceutical forms of diclofenac, with either short-term or long-term use.

Blood and lymphatic system disorders

Very rare: Thrombocytopenia, leucopoenia, anaemia (including haemolytic and aplastic anaemia), agranulocytosis, positive Coombs' test.

Immune system disorders

Rare: Hypersensitivity, anaphylactic and anaphylactoid reactions (including hypotension and shock).

Very rare: Angioneurotic oedema (including face oedema).

Psychiatric disorders

Very rare: Disorientation, depression, insomnia, nightmare, irritability, psychotic disorder.

Nervous system disorders

Common: Headache, dizziness.

Rare:	Somnolence.
Very rare:	Paraesthesia, memory impairment, convulsion, anxiety, tremor, aseptic meningitis, taste disturbances, cerebrovascular accident, myoclonic encephalopathy (described in two patients).

Eye disorders

Very rare:	Visual disturbance, blurred vision, diplopia.

Ear and labyrinth disorders

Common:	Vertigo.
Very rare:	Tinnitus, impaired hearing.

Cardiac disorders

Uncommon*:	Myocardial infarction, cardiac failure, palpitations, chest pain.
Frequency unknown:	Kounis syndrome

Vascular disorders

Very rare:	Hypertension, vasculitis.

Respiratory, thoracic and mediastinal disorders

Rare:	Asthma (including dyspnoea).
Very rare:	Pneumonitis.

Gastrointestinal disorders

Common:	Nausea, vomiting, diarrhoea, dyspepsia, abdominal pain, flatulence, anorexia.
Rare:	Gastritis, gastrointestinal haemorrhage, haematemesis, haemorrhagic diarrhoea, melaena, gastrointestinal ulcer (with or without bleeding or perforation) gastrointestinal stenosis, or perforation, which may lead to peritonitis.

Very rare: Colitis (including haemorrhagic colitis, ischemic colitis and exacerbation of ulcerative colitis or Crohn's disease), constipation, stomatitis, glossitis, oesophageal disorder, diaphragm-like intestinal strictures, pancreatitis.

Hepatobiliary disorders

Common: Elevation of serum aminotransferase (AST, ALT).

Rare: Hepatitis, jaundice, liver disorder.

Very rare: Fulminant hepatitis, hepatic necrosis, hepatic failure.

Pregnancy, puerperium and perinatal conditions

Unknown: Oligohydramnios, neonatal renal impairment

Skin and subcutaneous tissue disorders

Common: Rashes or skin eruptions.

Rare: Urticaria.

Very rare: Bullous eruptions, eczema, erythema, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell's syndrome), exfoliative dermatitis, loss of hair, photosensitivity reaction, purpura, allergic purpura, pruritus.

Unknown: Drug Reaction with Eosinophilia with Systemic Symptoms (DRESS), fixed drug eruption, generalised bullous fixed drug eruption.

Renal and urinary disorders

Very rare: Acute kidney injury (acute renal failure), haematuria, proteinuria, nephrotic syndrome, interstitial nephritis, renal papillary necrosis.

General disorders and administration site conditions

Rare: Oedema.

Very rare: Impotence (association with Voltaren Rapid intake is doubtful).

* The frequency reflects data from long-term treatment with a high dose (150 mg/day).

Description of selected adverse drug reactions

Arteriothrombotic events

Meta-analysis and pharmacoepidemiological data point towards an increased risk of arteriothrombotic events (for example myocardial infarction) associated with the use of diclofenac, particularly at a high dose (150 mg daily) and during long-term treatment (see section 4.4 'SPECIAL WARNINGS AND PRECAUTIONS'). A recent meta-analysis (CNT) estimates that, in comparison with placebo, allocation to diclofenac caused around 3 additional major vascular events per 1000 participants per year. This estimate reflects data from long term treatment with high dose diclofenac (150 mg/day).

Visual effects

Visual disturbances such as visual impairment, blurred vision or diplopia appear to be NSAID class effects and are usually reversible on discontinuation. A likely mechanism for the visual disturbances is the inhibition of prostaglandin synthesis and other related compounds that alter the regulation of retinal blood flow resulting in potential changes in vision. If such symptoms occur during diclofenac treatment, an ophthalmological examination may be considered to exclude other causes.

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration 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 at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

Management of acute poisoning with NSAIDs, including diclofenac, consists essentially of supportive and symptomatic measures. There is no typical clinical picture resulting from an overdosage of diclofenac. Overdosage can cause symptoms such as vomiting, gastrointestinal haemorrhage, diarrhoea, dizziness, tinnitus or convulsions. In the event of significant poisoning, acute renal failure and liver damage are possible. The therapeutic measures to be taken in cases of overdosage are as follows:

Activated charcoal may reduce absorption of the medicine if given within one or two hours after ingestion. In patients who are not fully conscious or have impaired gag reflex, consideration should be given to administering activated charcoal via nasogastric tube, once the airway is protected.

Supportive and symptomatic treatment should be given for complications such as hypotension, renal failure, convulsions, gastrointestinal disorder, and respiratory depression. Haematological and biochemical parameters, and the presence or absence of blood in the stools, should be monitored.

Specific therapies such as forced diuresis, dialysis, or haemoperfusion are probably of no help in eliminating NSAIDs, including diclofenac, because of their high protein-binding and extensive metabolism.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

Voltaren Rapid is a non-steroidal anti-inflammatory drug (NSAID) and contains the potassium salt of diclofenac. In Voltaren Rapid, the sodium ion of diclofenac sodium (Voltaren®) has been replaced by a potassium ion. The active principle is thus the same as in Voltaren. The preparation possesses analgesic, anti-inflammatory, and antipyretic properties.

Voltaren Rapid tablets have a rapid onset of action which makes them particularly suitable for the treatment of acute painful and inflammatory conditions.

As with other NSAIDs, its mode of action is not known; however, their ability to inhibit prostaglandin synthesis may be involved in the anti-inflammatory effect.

Clinical trials

In clinical trials Voltaren Rapid has also been found to exert an analgesic effect in moderately and severely painful states in the presence of inflammation, e.g. due to trauma or after surgical operations. It rapidly relieves both spontaneous pain and pain on movement and diminishes inflammatory swelling and wound oedema. In addition, the active substance is capable of relieving pain in primary dysmenorrhoea and may reduce the extent of bleeding.

In migraine attacks, Voltaren Rapid has been shown to be effective in relieving the headache. It may improve the accompanying symptoms of nausea and vomiting.

Low concentrations of diclofenac inhibit the aggregation of platelets induced in vitro by collagen and by adenosine diphosphate.

5.2 PHARMACOKINETIC PROPERTIES

Absorption

Diclofenac is rapidly and completely absorbed from diclofenac potassium tablets. The quantity of active substance absorbed is not diminished when the tablets are taken together with food. After ingestion of one tablet of 50 mg, plasma concentrations of diclofenac attain a mean peak value of 3.9 µmol/L after 20 to 60 minutes. The plasma concentrations show a linear relationship to the size of the dose.

Roughly half of the active substance is metabolised during its first passage through the liver ("first-pass" effect); consequently, the areas under the concentration curves (AUCs) after an oral dose are only about one-half as large as after parenteral administration of a dose of the same size.

Repeated oral administration of diclofenac for 8 days in daily doses of 50 mg t.i.d. does not lead to accumulation of diclofenac in plasma.

Distribution

Diclofenac is bound to serum proteins at 99.7%, mainly to albumin (99.4%).

Metabolism

The biotransformation of diclofenac involves partly glucuronidation of the intact molecule but mainly single and multiple hydroxylation followed by glucuronidation.

Excretion

The total systemic clearance of diclofenac from plasma is 263 ± 56 mL/min (mean value ± SD). The terminal half-life in plasma is 1 to 2 hours. Approximately 60% of the dose administered is excreted in the urine in the form of metabolites from one of these two processes. Less than 1% is excreted as unchanged substance. The remainder of the dose is eliminated as metabolites through the bile in the faeces.

Special patient populations

No relevant age-dependent differences in the absorption, metabolism, or excretion of diclofenac have been observed.

In patients suffering from renal impairment, no accumulation of the unchanged active substance can be inferred from the single-dose kinetics when applying the usual dosage schedule. At a creatinine clearance of <10 mL/min, the theoretical steady-state plasma concentrations of metabolites are about four times higher than in normal subjects. However, the metabolites are ultimately cleared through the bile.

In the presence of impaired hepatic function (chronic hepatitis, non-decompensated cirrhosis), the kinetics and metabolism of diclofenac are the same as in patients without liver disease.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

Diclofenac showed no mutagenic, or teratogenic effects in the studies conducted, despite the induction of maternal and foetal toxicity.

Carcinogenicity

Diclofenac showed no carcinogenic or teratogenic effects in the studies conducted, despite the induction of maternal and foetal toxicity.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Silica colloidal anhydrous, calcium phosphate, magnesium stearate, starch maize, povidone, sodium starch glycollate, cellulose microcrystalline, iron oxide red (CI No. 77491), macrogol 8000, sucrose, talc purified and titanium dioxide.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Voltaren Rapid tablets should be protected from heat and moisture and stored below 30°C.

6.5 NATURE AND CONTENTS OF CONTAINER

Voltaren Rapid tablets: PVC/Aluminium foil blister packs containing 20 coated tablets of 50 mg diclofenac potassium.

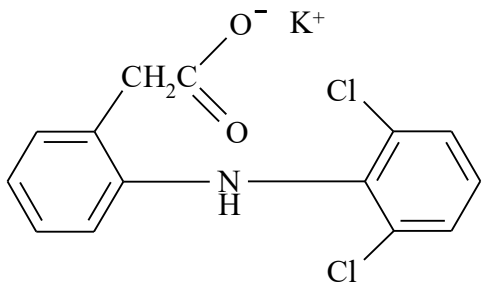
6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure

Diclofenac Potassium



Chemical name: potassium-[2-{(2, 6-dichlorophenyl) -amino}-phenyl]-acetate

CAS number

15307-81-0

7 MEDICINE SCHEDULE (POISONS STANDARD)

Prescription only medicine (Schedule 4)

8 SPONSOR

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9 DATE OF FIRST APPROVAL

27 May 1993

10 DATE OF REVISION

11 November 2025

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
4.4	Addition of “generalised bullous fixed drug eruption” in Skin reactions.
4.8	Addition of “fixed drug eruption, generalised bullous fixed drug eruption” of unknown frequency in Skin and subcutaneous tissue disorders.

Internal document code

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