AUSTRALIAN PRODUCT INFORMATION

VOLTAREN RAPID 12.5 (DICLOFENAC POTASSIUM) TABLET

1 NAME OF THE MEDICINE

Diclofenac potassium

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient: diclofenac potassium 12.5mg/tablet.

Each Voltaren Rapid 12.5 tablet contains 1.5 mg of potassium.

Contains: Sugars as lactose monohydrate (200.7 mg per maximum recommended daily dose)

For the full list of excipients, see Section 6.1 List of excipients.

3 PHARMACEUTICAL FORM

White oblong (capsule-shaped) film-coated tablets.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

- Relief of headache, dental pain, period pain, rheumatic and muscular pain, backache.
- Relief of symptoms of colds and flu, including aches and pains, sore throat pain.
- Reduction of fever

4.2 DOSE AND METHOD OF ADMINISTRATION

After assessing the risk/benefit ratio in each individual patient, the lowest effective dose for the shortest duration should be used. Adverse effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see Section 4.4 'Special warnings and precautions for use').

The tablets should be swallowed whole with water and must not be divided or chewed. It is preferable to take the tablets before meals (see section 5.2 Pharmacokinetic Properties – Absorption).

Voltaren Rapid 12.5 should not be used for more than a few days at a time unless on medical advice, in which case the patient should be reviewed regularly with regards to efficacy, risk factors and ongoing need for treatment.

Adults and children aged 14 years and over:

The initial dosage is 25 mg. If needed, further doses of 12.5 to 25 mg may be taken every 4 to 6 hours. No more than 75 mg should be taken in 24 hours. Do not exceed the stated dose.

If the pain has not resolved after a few days, the patient should be instructed to return for review by the healthcare professional.

Children under 14 years of age:

Voltaren Rapid 12.5 is not recommended for use in children under 14 years of age.

Pregnancy:

See Section 4.3 Contraindications and Section 4.6 Fertility, pregnancy and lactation

4.3 CONTRAINDICATIONS

- Known hypersensitivity to diclofenac or to any of the excipients (see Section 4.4 'Special warnings and precautions for use – hypersensitivity')
- Patients in whom attacks of asthma, angioedema, urticaria, or acute rhinitis are precipitated by aspirin or other NSAIDs (see Section 4.4 'Special warnings and precautions for use – pre-existing asthma')
- Active gastric or intestinal ulcer, bleeding or perforation (see Section 4.4 'Special warnings and precautions for use – gastrointestinal effects')
- Cardiac failure (see Section 4.4 'Special warnings and precautions for use – fluid retention').
- Severe hepatic impairment (see Section 4.4 'Special warnings and precautions for use – hepatobiliary effects')
- Renal impairment (see Section 4.4 'Special warnings and precautions for use – renal effects')
- Last trimester of pregnancy (see Section 4.6 Fertility, pregnancy and lactation).
- Treatment of perioperative pain in setting of coronary artery bypass surgery (CABG)

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.

Treatment with Voltaren Rapid is generally not recommended in patients with established cardiovascular disease (congestive heart failure, established ischaemic heart disease, peripheral arterial disease) or uncontrolled hypertension. If needed patients with established cardiovascular disease, uncontrolled hypertension or significant risk factors for cardiovascular disease (eg hypertension, hyperlipidaemia, diabetes mellitus and smoking) should be treated with Voltaren Rapid only after careful consideration.

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 possible duration (see Section 4.2 'Dosage and method of administration'). Patients should be advised to seek further medical advice if symptoms persist or do not improve within the recommended duration of treatment.

Patients should remain alert for the signs and symptoms of serious arteriothrombotic events (eg chest pain, shortness of breath, weakness, slurring of speech), which can occur without warning. Patients should be instructed to see a doctor 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.

Fluid retention

Fluid retention and oedema have been observed in some patients taking NSAIDs, including diclofenac, therefore caution is advised in patients with fluid retention. Use of Voltaren Rapid 12.5 in patients with heart failure is not recommended (see Section 4.3 'Contraindications').

Gastrointestinal effects

As with all NSAIDs, including diclofenac, close medical surveillance is imperative and particular caution should be exercised when prescribing NSAIDs, including diclofenac in patients with symptoms indicative of gastrointestinal (GI) disorders or with a history suggestive of gastrointestinal ulceration, bleeding or perforation (see Section 4.8 'Adverse effects (undesirable effects)'). The risk of GI bleeding is higher with increasing NSAID doses and in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation and in the elderly.

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 severe impairment of hepatic function, or with pre-existing dyshaemopoiesis or disorders of blood coagulation as their condition may be exacerbated (see Section 4.8 'Adverse effects (undesirable effects)').

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

Except for a history of serious gastrointestinal events and other risk factors known to be associated with gastrointestinal ulceration, such as alcoholism, smoking, etc., no other factors (e.g. age, sex) have been associated with increased risk.

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 12.5, the drug should be withdrawn immediately. Patients should be warned 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 4.5 'Interactions with other medicines and other forms of interactions').

Serious skin reactions

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome and toxic epidermal necrolysis, and Drug Reaction with Eosinophilia with Systemic Symptoms (DRESS) have been reported very rarely in association with the use of NSAIDs, including diclofenac (see Section 4.8 'Adverse effects (undesirable 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 lesion or any other sign of hypersensitivity, and diclofenac should be discontinued.

Drug Reaction with Eosinophilia with Systemic Symptoms (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.

Respiratory effects (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 also applicable to patients who are allergic to other substances, e.g. with skin reactions, pruritus or urticaria.

Infection

Like other NSAIDs, Voltaren Rapid 12.5 may mask the usual signs and symptoms of infection due to its pharmacodynamic properties.

Haematological effects

Use of Voltaren Rapid 12.5 is recommended only for short-term treatment. If, however, Voltaren Rapid 12.5 is used for a prolonged period, monitoring of the blood count is recommended.

Like other NSAIDs, Voltaren Rapid 12.5 may temporarily inhibit platelet aggregation. Patients with haemostatic disorders should be carefully monitored.

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.

Lactose sensitivity

Voltaren Rapid 12.5 tablets contain lactose and therefore are not recommended for patients with rare hereditary problems of galactose intolerance, of severe lactase deficiency or of glucose-galactose malabsorption.

Use in hepatic impairment

Close medical surveillance is required when prescribing diclofenac 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 diclofenac therapy. These laboratory abnormalities may progress, remain unchanged, or revert to normal despite continued therapy. Borderline elevations (i.e. 1.2-3 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 (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 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 12.5 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 (eosinophilia, rash), diclofenac should be discontinued.

Physicians should inform patients of the warning signs and symptoms of hepatotoxicity (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 diclofenac in patients with hepatic porphyria, since it 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 NSAID therapy, including diclofenac. Owing to the importance of prostaglandins for maintaining renal blood flow, particular caution is called for in patients with impaired cardiac 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, 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 diclofenac in such cases. Discontinuation of therapy is typically followed by recovery to the pre-treatment state. Use of Voltaren Rapid 12.5 in patients with heart failure is not recommended (see Section 4.3 'Contraindications').

Combination use of ACE inhibitors or angiotensin receptor antagonist, anti-inflammatory drugs and thiazide diuretics

The concurrent use of an angiotensin-converting enzyme (ACE)inhibitor or angiotensin II receptor antagonist with an anti-inflammatory drug (NSAID or COX-2 selective 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 12.5 in the elderly usually proves necessary only for a few days.

Paediatric use

Voltaren Rapid 12.5 is not recommended for use in children under 14 years of age as safety and efficacy in this age group have not been established.

Effects on laboratory tests

No data available.

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 12.5 tablets and/or other pharmaceutical forms of diclofenac.

Lithium: When used concomitantly, diclofenac may raise plasma concentrations of lithium and monitoring of serum lithium level is recommended during treatment with Voltaren Rapid 12.5.

Digoxin: When used concomitantly, diclofenac may raise plasma concentrations of digoxin and monitoring of serum digoxin level is recommended during treatment with Voltaren Rapid 25.

Other NSAIDs and corticosteroids: The concomitant use of diclofenac with systemic NSAIDSs 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 undesirable gastrointestinal 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 antiplatelet agents: Caution is recommended since concomitant administration could increase the risk of bleeding (see Section 4.4 'Special warnings and precautions for use – gastrointestinal effects'). 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 for use – gastrointestional effects').

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 its toxicity increased.

Cyclosporin/ciclosporin: 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/ciclosporin.

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

Potent CYP2C9 inhibitors: Caution is recommended when diclofenac is concomitantly used with potent CYP2C9 inhibitors (such as voriconazole), which could result in a significant increase in peak plasma concentrations and exposure to diclofenac due to inhibition of diclofenac metabolism.

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

Diuretics and antihypertensive drugs: Like other NSAIDs, concomitant use of diclofenac with diuretics or antihypertensive drugs (eg 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. Patients should be adequately hydrated and consideration should be given to monitoring of renal function after initiation of concomitant therapy, and periodically thereafter. (see Section 4.4 'Special warnings and precautions for use - renal effects').

Drugs known to cause hyperkalemia: Concomitant treatment with potassium-sparing drugs (eg diuretics, cyclosporin/ciclosporin, 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 for use – renal effects).

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.

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

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

As with other NSAIDs, the use of Voltaren Rapid 12.5 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 diclofenac should be considered.

Use in pregnancy – Pregnancy Category C

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

The use of diclofenac in pregnant women has not been studied and safety in pregnancy has not been established. Therefore Voltaren Rapid 12.5 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. Use of Voltaren Rapid 12.5 during the third trimester of pregnancy is contraindicated due to the possibility of uterine inertia and/or premature closure of the ductus arteriosus. (see Section 4.3 'Contraindications').

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.

Oligohydramnios and Neonatal Renal Impairment:

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, limit use to the lowest effective dose and shortest duration possible. 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 12.5 is not recommended for use in breastfeeding women.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

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

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

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.

While not all the reactions listed have been reported specifically with Voltaren Rapid 12.5, similarities between the NSAIDs as a group require them to be considered a possibility.

The adverse reactions listed below include those associated with long term use of higher strength dosage forms of diclofenac.

Adverse reactions are listed below by system organ class and frequency. Frequencies are defined as: common (≥ 1/100, < 1/10); uncommon (≥ 1/1,000, < 1/100); rare (≥ 1/10,000, < 1/1,000); very rare (< 1/10,000), or not known (cannot be estimated from available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

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

Blood and lymphatic system disorders

Very rare: Thrombocytopenia, leukopenia, 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: Angioedema (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, meningitis aseptic, dysgeusia, cerebrovascular accident, myoclonic encephalopathy (described in two patients).

Eye disorders

Very rare: Visual impairment, vision blurred, diplopia.

Ear and labyrinth disorders
Common: Vertigo.
Very rare: Tinnitus, hearing impaired.

Cardiac disorders
Uncommon*: Myocardial infarction, cardiac failure, palpitations, chest pain.
* the frequency reflects data from long-term treatment with a high dose (150 mg/day)
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, decreased apetite.
Rare: Gastritis, gastrointestinal haemorrhage, haematemesis, diarrhoea haemorrhagic, melaena, gastrointestinal ulcer (with or without bleeding), 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, intestinal diaphragm disease, pancreatitis.

Hepatobiliary disorders
Common: Rash, transaminases increased.
Rare: Hepatitis, jaundice, liver disorder.
Very rare: Hepatitis Fulminant, hepatic necrosis, hepatic failure.

Skin and subcutaneous tissue disorders
Common: Rash.
Rare: Urticaria.
Very rare: Dermatitis Bullous, eczema, erythema, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell's syndrome), Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), dermatitis exfoliative, alopecia, photosensitivity reaction, purpura, Henoch-Schonlein purpura, pruritus.

Renal and urinary disorders
Very rare: Renal failure acute, haematuria, proteinuria, nephrotic syndrome, tubulointerstitial nephritis, renal papillary necrosis.

General disorders and administration site conditions
Rare: Oedema.
Very rare: Impotence (association with Voltaren Rapid intake is doubtful).

Pregnancy, puerperium and perinatal conditions
Unknown: Oligohydramnios, neonatal renal impairment

Description of selected adverse drug reactions
Arteriothrombotic events
Meta-analysis and pharmacoepidemiological data point towards a small increased risk of arterial thrombotic events (for example myocardial infarction) associated with the use of diclofenac, particularly at high dose (150 mg daily) and during long-term treatment (see Section 4.4 'Special Warnings and Precautions for Use').

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.

4.9 OVERDOSE

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

Symptoms

There is no typical clinical picture resulting from an overdosage of diclofenac. Overdose 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.

Treatment

Management of acute poisoning with NSAIDs consists essentially of supportive and symptomatic measures.

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, GI 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.

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

MECHANISM OF ACTION

Pharmacotherapeutic group: Anti-inflammatory and antirheumatic products, non-steroids, acetic acid derivatives and related substances (ATC code M01A B05).

Voltaren Rapid 12.5 is a non-steroidal anti-inflammatory drug (NSAID) and contains the potassium salt of diclofenac. The preparation possesses analgesic, anti-inflammatory and antipyretic properties.

Voltaren Rapid 12.5 tablets have a rapid onset of action which makes them particularly suitable for the treatment of acute painful and inflammatory conditions and reduction of fever.

As with other NSAIDs, inhibition of prostaglandin biosynthesis is considered to be fundamental to the mechanism of action.

Clinical trials

In clinical trials, Voltaren Rapid 12.5 has been found to exert an analgesic effect in pain states, such as headache, dental pain, mild or moderate period pain, rheumatic and muscular pain and backache. Voltaren Rapid 12.5 has also been shown to provide temporary relief of the symptoms of colds and flu, including aches and pains and the pain of sore throat. In addition, Voltaren Rapid 12.5 has been shown to be useful in the reduction of fever.

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 the tablets. When taken with food, the rate of absorption of diclofenac was reduced. On this basis, for maximum efficacy, the tablets should not be taken directly with, or immediately after, meals.

Since about half of diclofenac is metabolised during its first passage through the liver ("first pass" effect), the area under the concentration curve is about half as large following oral administration as it is following a parenteral dose of equal size.

Distribution

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

Diclofenac enters the synovial fluid, where maximum concentrations are measured 2 to 4 hours after peak plasma values have been reached. The apparent half-life for elimination from the synovial fluid is 3 to 6 hours. Two hours after reaching peak plasma levels, concentrations of the active substance are already higher in the synovial fluid than in the plasma, and they remain higher for up to 12 hours.

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

Metabolism

The biotransformation of diclofenac involves partly glucuronidation of the intact molecule, but mainly by single and multiple hydroxylation and methoxylation, resulting in several phenolic metabolites, most of which are converted to glucuronide conjugates. Two of these phenolic metabolites are biologically active, but to a much smaller extent than diclofenac.

Excretion

The total systemic clearance of diclofenac from plasma is 263 ± 56 mL/min (mean value ± SD). The terminal plasma half-life is 1 to 2 hours. Four of the metabolites, including the two active ones, also have short plasma half-lives of 1-3 hours. One metabolite, 3'-hydroxy-4'-methoxy-diclofenac, has a much longer plasma half-life. This metabolite is virtually inactive.

About 60% of the administered dose is excreted in the urine as the glucuronide conjugate of the intact molecule and as metabolites, most of which are also converted to glucuronide conjugates. Less than 1% is excreted as unchanged substance. The remainder of the dose is eliminated as metabolites through the bile in the faeces.

Special populations

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

Impaired renal function: 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/minute, the calculated steady-state plasma concentrations of metabolites are about four times higher than in normal subjects. However, the metabolites are ultimately cleared through the bile.

Impaired hepatic function: In patients with chronic hepatitis or 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 mutagenic, carcinogenic, or teratogenic effects in the studies conducted, despite the induction of maternal and fetal toxicity.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Silica –colloidal anhydrous, lactose monohydrate, starch - maize, sodium starch glycollate, povidone, magnesium stearate, hypromellose, titanium dioxide, stearic acid, cellulose – microcrystalline.

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

6.5 NATURE AND CONTENTS OF CONTAINER

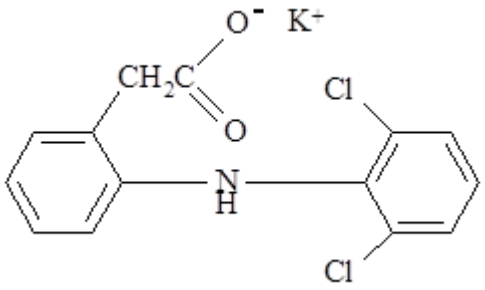
Packaged in PVC/PCTFE/PVC/aluminium foil blister packs of 10 and 20 tablets.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure



CAS number

15307-81-0

7 MEDICINE SCHEDULE (POISONS STANDARD)

Schedule 2 (Pharmacy Medicine)

8 SPONSOR

GlaxoSmithKline Consumer Healthcare
Level 48, 8 Parramatta Square,
10 Darcy Street, Parramatta NSW 2150
FREECALL Australia: 1800 028 533
Website: www.gsk.com.au

9 DATE OF FIRST APPROVAL

15 January 2010

10 DATE OF REVISION

July 2022

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
4.2	Addition of Pregnancy
4.4	Addition of Drug Reaction with Eosinophilia with Systemic Symptoms (DRESS)
4.6	Addition of information on oligohydramnios and neonatal renal impairment
4.8	Addition of adverse events in pregnancy
8	Update of sponsor address