NEW ZEALAND DATA SHEET

1. PRODUCT NAME

VOLTAREN RAPID EXTRA STRENGTH

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient:
Diclofenac potassium 25 mg per tablet

Excipients:
For full list of excipients, see section 6.1.

Each Voltaren Rapid Extra Strength tablet contains 2.9 mg of potassium.

3. PHARMACEUTICAL FORM

Voltaren Rapid Extra Strength tablets are pale red, round, biconvex and sugar-coated. The diameter is approximately 7.7 mm with a thickness of about 5.0 mm.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Short-term treatment in the following acute conditions:

- post-traumatic pain, inflammation and swelling, e.g. due to sprains
- post-operative pain, inflammation and swelling, e.g. following dental or orthopaedic surgery
- painful and/or inflammatory conditions in gynaecology, e.g. primary dysmenorrhoea or adnexitis
- migraine attacks
- painful syndromes of the vertebral column
- non-articular rheumatism
- as an adjuvant in severe painful inflammatory infections of the ear, nose, or throat, e.g. pharyngotonsillitis, otitis. In keeping with general therapeutic principles, the underlying disease should be treated with basic therapy, as appropriate. Fever alone is not an indication.

4.2 Dose and method of administration

After assessing the risk/benefit ratio in each individual patient, the lowest effective dose for the shortest possible duration should be used, which may minimise adverse effects.

Voltaren Rapid Extra Strength should be swallowed whole with liquid, preferably before meals.

Adults

Acute pain states with an inflammatory component

Following an initial loading dose of 50 mg, 25-50 mg is to be taken every 8 hours if necessary. The maximum daily dose is 150 mg.

Migraine

Following an initial loading dose of 50 mg, a further dose of 25-50 mg may be taken after 2 hours if necessary. Further doses of 25-50 mg may be taken at intervals of 4-6 hours, if needed. The maximum daily dose is 150 mg.

Children

Children 14 years of age and over: up to 75 mg daily in divided doses. The maximum daily dose is 75 mg.

The dosage strength is such that Voltaren Rapid Extra Strength is not recommended for use in children under 14 years of age.

Voltaren Rapid Extra Strength 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.

4.3 Contraindications

- Known hypersensitivity to diclofenac or to any of the excipients (see 'Special warnings and precautions for use – Hypersensitivity)
- Patients in whom attacks of asthma, urticaria or acute rhinitis are precipitated by aspirin or other NSAIDs (see 'Special warnings and precautions for use – Pre-existing asthma')
- Patients with previous myocardial infarction, within the last 6 to 12 months (see 'Special warnings and precautions for use – Cardiovascular events')
- Cardiac failure (see 'Special warnings and precautions for use – Use in cardiac failure')
- Severe hepatic impairment (see 'Special warnings and precautions for use – Hepatobiliary effects')
- Renal impairment (see 'Special warnings and precautions for use – Renal effects')
- Active gastric or intestinal ulcer, bleeding or perforation (see 'Special warnings and precautions for use – Gastrointestinal effects')
- Last trimester of pregnancy (see 'Special warnings and precautions for use – Use in pregnancy')
- Treatment of perioperative pain in setting of coronary artery bypass surgery (CABG)

4.4 Special warnings and precautions for use

General

Diclofenac tablets should only be used when the benefits are considered to outweigh the potential risks.

Voltaren Rapid Extra Strength is recommended for short-term treatment. However, patients receiving long term diclofenac treatment should be advised of the need to be regularly reviewed with regards to efficacy, adverse effects, the development of risk factors and the ongoing need for therapy. Consideration should be given to monitoring blood pressure, haemoglobin levels and renal function in long term use.

Cardiovascular thrombotic events

Treatment with NSAIDs, including diclofenac, particularly at high dose and in long-term use, may be associated with a small increased risk of serious cardiovascular thrombotic events (including myocardial infarction and stroke). Patients with previous myocardial infarction (within the last 6 to 12 months) should not use diclofenac.

Patients with established cardiovascular disease, or significant risk factors for cardiovascular disease (e.g. hypertension, hyperlipidaemia, diabetes mellitus or smoking) should be treated with diclofenac tablets 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 duration possible. Patients should be advised to seek further medical advice if symptoms persist or do not improve within the recommended duration of treatment.

Healthcare professionals should inform patients with risk factors for cardiovascular disease of the possible increased risk of cardiovascular events when recommending diclofenac tablets, particularly if diclofenac is used at high doses and for long periods of time.

Patients should remain alert for the signs and symptoms of cardiovascular events (e.g. chest pain, shortness of breath, weakness, slurring of speech), which can occur without warning. Patients should be informed about signs and/or symptoms of serious cardiovascular toxicity and should be instructed to seek medical attention immediately if any of these symptoms occur.

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.

Cardiac failure

Voltaren Rapid Extra Strength is contraindicated in patients with severe cardiac failure (see 'Contraindications'). 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.

Hypertension

Treatment is generally not recommended in patients with uncontrolled 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 NSAIDs are used by patients with hypertension. Blood pressure should be monitored closely during initiation of Voltaren Rapid Extra Strength treatment and at regular intervals thereafter.

Gastrointestinal effects

Close medical surveillance is imperative and particular caution should be exercised when NSAIDs, including diclofenac, are used by patients with symptoms indicative of gastrointestinal (GI) disorders or with a history suggestive of GI ulceration, bleeding or perforation (see 'Undesirable effects'). The risk of GI bleeding is higher with increasing NSAID doses. Caution is advised in patients with GI risk factors who may be at greater risk of developing serious GI events, e.g. the

elderly, those with a history of serious GI events or ulcer, particularly if complicated by haemorrhage or perforation, or a history of smoking or alcoholism.

Close medical surveillance should also be exercised in patients with ulcerative colitis, Crohn's disease, pre-existing dyshaemopoiesis or disorders of blood coagulation, as their condition may be exacerbated (see 'Undesirable effects').

Gastric or duodenal ulceration, GI bleeding or perforation, which can be fatal, has 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.

In instances where gastrointestinal bleeding or ulcerations occur in patients receiving Voltaren Rapid Extra Strength, the drug should be withdrawn immediately. Patients should be warned about the signs and symptoms of serious GI toxicity and what steps to take if they occur.

To reduce the risk of GI toxicity in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation, or in the elderly, treatment should be initiated and maintained at the lowest effective dose. GI bleeding, ulceration and perforation in general have more serious consequences in the elderly. These events can occur at any time during treatment with or without warning symptoms or a previous history. 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. The concurrent use of aspirin and NSAIDs also increases the risk of serious gastrointestinal events (see 'Interaction with other medicines and other forms of interaction').

Combination therapy with protective agents (e.g. proton pump inhibitors or misoprostol) should be considered for at risk patients, and also for patients requiring concomitant use of low-dose aspirin or other medicines likely to increase gastrointestinal risk.

<u>Serious skin reactions</u>

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) (see Drug Reaction with Eosinophilia with Systemic Symptoms (DRESS)) have been reported very rarely in association with the use of NSAIDs, including diclofenac potassium (see '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, with an onset of reaction occurring within the first month of treatment in the majority of cases. 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 lesions or any other sign of hypersensitivity, and Voltaren Rapid Extra Strength should be discontinued.

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome

DRESS syndrome has been reported in patients taking NSAIDs. Some of these events have been fatal or life-threatening. DRESS syndrome 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

syndrome 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)

Reactions to NSAIDs such as asthma exacerbations (also called analgesic intolerance or aspirin-induced asthma), Quincke's oedema (angioedema) or urticaria are more frequent in patients with asthma, seasonal allergic rhinitis, swelling of the nasal mucosa (i.e. nasal polyps), chronic obstructive pulmonary disease or chronic infections of the respiratory tract (especially if linked to allergic rhinitis-like symptoms) than in other patients. Therefore, special caution is recommended in such patients (readiness for emergency). This is also applicable to patients who are allergic to other substances, e.g. with skin reactions, pruritus or urticaria.

Hepatobiliary effects

Voltaren Rapid Extra Strength is contraindicated in patients with hepatic failure (see 'Contraindications'). Close medical surveillance is required in patients with impaired hepatic function when using Voltaren Rapid Extra Strength, as the condition may be exacerbated.

As with other NSAIDs, including diclofenac, elevations of one or more liver enzymes may occur during Voltaren Rapid Extra Strength 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 (U LN), 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 Extra Strength 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 other manifestations occur (eosinophilia, rash), Voltaren Rapid Extra Strength should be discontinued.

Healthcare professionals 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 or symptoms appear.

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

Renal effects

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. Voltaren Rapid Extra Strength is contraindicated in patients with renal failure (see 'Contraindications'). Due to the importance of prostaglandins in maintenance of renal blood flow, particular caution should be taken in the elderly, or in patients: with impaired cardiac function, with a history of hypertension, using diuretics or other medications that can significantly affect renal function, with extracellular volume depletion from any cause, or in the peri- or post-operative phase of major surgical operations (see 'Contraindications').

Monitoring of renal function as a precautionary measure is therefore recommended when using Voltaren Rapid Extra Strength in such cases. Discontinuation of therapy typically results in a return to the pre-treatment state. Use of Voltaren Rapid Extra Strength in patients with kidney impairment or heart failure is not recommended (see 'Contraindications').

Combination use of ACE inhibitors or angiotensin receptor antagonists, 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 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 monitoring of serum creatinine, particularly frequently 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 infection

Like other NSAIDs, Voltaren Rapid Extra Strength may mask the usual signs and symptoms of infection.

Haematological effects

Use of Voltaren Rapid Extra Strength is recommended only for a few days. If, however, Voltaren Rapid Extra Strength is used for a prolonged period, monitoring of the blood count is recommended.

Like other NSAIDs, Voltaren Rapid Extra Strength 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.

Sucrose sensitivity

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

Paediatric use

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

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 Extra Strength in the elderly usually proves necessary for only a few days.

4.5 Interaction with other medicines and other forms of interaction

Pharmacokinetic interactions

The following interactions include those observed with other pharmaceutical forms of diclofenac at high doses.

Lithium: When used concomitantly, diclofenac may increase plasma concentrations of lithium. Plasma concentrations of lithium should be monitored during treatment with Voltaren Rapid Extra Strength.

Digoxin: When used concomitantly, diclofenac may increase plasma concentrations of digoxin. Plasma concentrations of digoxin should be monitored during treatment with Voltaren Rapid Extra Strength.

Other NSAIDs and corticosteroids: The concomitant use of Voltaren Rapid Extra Strength with other systemic NSAIDs, including COX-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 Voltaren Rapid Extra Strength and other systemic NSAIDs or corticosteroids may increase the incidence 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 '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. Voltaren Rapid Extra Strength 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 'Special warnings and precautions for use – Gastrointestinal effects').

Methotrexate: Caution should be exercised when NSAIDs, including Voltaren Rapid Extra Strength, are administered less than 24 hours before or after treatment with methotrexate, since the blood concentration of methotrexate may rise and increase its toxicity.

Cyclosporin (ciclosporin): The effects of NSAIDs on renal prostaglandins may increase the nephrotoxicity of cyclosporin. In patients taking cyclosporin, dose reduction of Voltaren Rapid Extra Strength is required.

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 Voltaren Rapid Extra Strength is concomitantly used with potent CYP2C9 inhibitors (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 Voltaren Rapid Extra Strength, monitoring of phenytoin plasma concentrations is recommended due to an expected increase in exposure to phenytoin.

Diuretics and antihypertensive agents: Like other NSAIDs, concomitant use of diclofenac with diuretics or antihypertensive agents, e.g. beta-blockers or 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 renal function may be increased in some patients, especially when renal function is compromised, e.g. dehydrated or elderly patients. This includes possible acute renal failure, which is usually reversible. Patients should be adequately hydrated and consideration should be given to monitoring of renal function after initiation of concomitant therapy and periodically thereafter (see 'Special warnings and precautions for use – Renal effects').

Drugs known to cause hyperkalaemia: Concomitant treatment with potassium-sparing diuretics, cyclosporin/ciclospirin, tacrolimus or trimethoprim may be associated with increased serum potassium levels, which should therefore be monitored frequently (see '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.

<u>Pharmacodynamic interactions</u>

When taken with food, the rate of absorption of diclofenac was reduced (lower C_{max} and longer t_{max}).

4.6 Fertility, pregnancy and lactation

Fertility

As with other NSAIDs, the use of diclofenac 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.

Pregnancy (Category C)

Voltaren Rapid Extra Strength is contraindicated in 3rd trimester of pregnancy.

Voltaren Rapid Extra Strength should not be used during the first two trimesters of pregnancy unless the expected benefits to the mother outweigh the risks to the fetus. If there is a compelling need for NSAID treatment during the first or second trimester, limit use to the lowest effective dose and shortest duration possible.

Data from epidemiological studies suggest an increased risk of miscarriage and congenital malformation associated with NSAID use in early pregnancy.

Use of NSAIDs in the second or third trimester may cause fetal renal dysfunction leading to oligohydramnios and, in some cases, neonatal renal impairment. Oligohydramnios is generally seen after days to weeks of treatment, although it has been reported as soon as 48 hours after NSAID initiation. Oligohydramnios is usually, but not always, reversible after treatment discontinuation. Consider ultrasound monitoring of amniotic fluid if treatment extends beyond 48 hours. Discontinue treatment with [NSAID] if oligohydramnios occurs.

NSAID use during the third trimester may cause premature closure of the fetal ductus arteriosus, fetal renal impairment, inhibition of platelet aggregation, and may delay labour and birth. NSAID use in the third trimester of pregnancy is therefore contraindicated.

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

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 Extra Strength is not recommended for use in breastfeeding women.

4.7 Effects on ability to drive and use machines

Voltaren Rapid Extra Strength is unlikely to produce an effect on ability to drive or operate machinery at the recommended dose and duration of treatment. Patients experiencing visual disturbances, dizziness, vertigo, somnolence or other central nervous disturbances while taking Voltaren Rapid Extra Strength should refrain from driving a vehicle or operating machines.

4.8 Undesirable effects

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

Adverse reactions are listed below by system organ class and frequency. Frequencies are defined as: *common* (≥ 1%); *uncommon* (< 1% but ≥ 0.1%); *rare* (< 0.01% but ≥ 0.01%); and *very rare* (< 0.001%, including isolated reports). Within each frequency, adverse effects are presented in order of decreasing seriousness.

The following adverse effects include those reported with long-term use of higher doses of diclofenac.

Blood and lymphatic system disorders

Very rare: Thrombocytopenia, leukopenia, anaemia (including haemolytic and aplastic anaemia), agranulocytosis.

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.

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 daily). The frequency is expected to be lower for short-term treatment with lower dose.

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 appetite.
Rare: Gastritis, gastrointestinal haemorrhage, haematemesis, diarrhoea haemorrhagic, melaena, gastrointestinal ulcer (with or without bleeding or perforation), gastrointestinal stenosis, or perforation, which may lead to peritonitis.
Very rare: Colitis (including haemorrhagic colitis and exacerbation of ulcerative colitis or Crohn's disease), constipation, stomatitis, glossitis, oesophageal disorder, intestinal diaphragm disease, pancreatitis.

Hepatobiliary disorders

Common: 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), dermatitis exfoliative, alopecia, photosensitivity reaction, purpura, Henoch-Schönlein purpura, pruritus.
Unknown: Drug reaction with eosinophilia with systemic symptoms (DRESS)

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.

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 ‘Special warnings and precautions for use’).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://pophealth.my.site.com/carmreportnz/s/.

4.9 Overdose

Symptoms and signs

There is no typical clinical picture resulting from an overdose of diclofenac. Overdose can cause symptoms such as vomiting, gastrointestinal haemorrhage, diarrhoea, dizziness, tinnitus or convulsions and lead to complications such as hypotension, and respiratory depression. In the event of significant poisoning, acute renal failure and liver damage are possible.

Treatment

For information on the management of overdose, contact the National Poisons Centre on 0800 764 766 (New Zealand).

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

The therapeutic measures to be taken in cases of overdose are as follows:

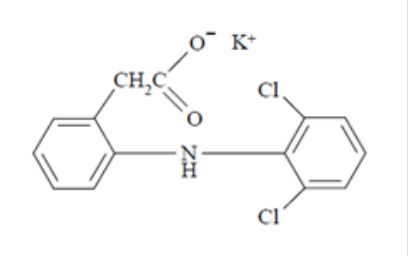
Activated charcoal may reduce absorption of the medicine if given within 1 or 2 hours after ingestion. In patients who are not fully conscious or who have impaired gag reflex, consideration should be given to administering activated charcoal via a nasogastric tube, once the airway is protected.

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 unlikely to be helpful in eliminating NSAIDs, including diclofenac, due to high protein binding and extensive metabolism.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties



Chemical Structure: Diclofenac potassium = potassium-[0-{(2, 6-dichlorophenyl)-amino}-phenyl]-acetate potassium).

Pharmacotherapeutic group: Anti-inflammatory and antirheumatic products, non-steroids, acetic acid derivatives and related substances (ATC code M01AB05).

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

As with other NSAIDs, inhibition of prostaglandin biosynthesis is considered to be fundamental to the mechanism of action. Prostaglandins play a major role in causing inflammation, pain and fever.

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

Voltaren Rapid Extra Strength has a rapid onset of action which makes it particularly suitable for the treatment of acute painful and inflammatory conditions. Voltaren Rapid Extra Strength has been shown to have an onset of pain relief from 15 minutes and a duration of up to 8 hours.

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. When taken with food, the rate of absorption of diclofenac was reduced (lower Cmax and longer tmax). On this basis, for maximum efficacy, Voltaren Rapid Extra Strength should not be taken directly with, or immediately after, meals.

Following ingestion in the fasted state of one Voltaren Rapid Extra Strength tablet, a mean peak plasma concentration of 1.8 µmol/L is reached after 35 minutes. The extent of absorption is in linear proportion to the size of the dose.

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.

Pharmacokinetic behaviour does not change after repeated administration. No accumulation occurs provided the recommended dosage intervals are observed.

Distribution

Diclofenac is highly bound to serum proteins (99.7%), predominantly albumin (99.4%). The apparent volume of distribution is calculated as 0.12-0.17 L/kg.

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

Metabolism

The biotransformation of diclofenac takes place partly by 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 lesser extent than diclofenac.

Elimination

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. Four of the metabolites, including the two active ones, also have short plasma half-lives of 1 to 3 hours. A fifth metabolite, 3'-hydroxy-4'-methoxy-diclofenac, has a much longer plasma half-life. This metabolite is virtually inactive.

Approximately 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, via bile in the faeces.

Special populations

Paediatric patients: There are no data concerning any pharmacokinetic parameters related to the use of diclofenac in children under 14 years of age.

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

Patients with 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 calculated steady-state plasma concentrations of metabolites are about four times higher than in patients with normal renal function. However, the metabolites are ultimately cleared through the bile.

Patients with hepatic impairment: 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

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

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Magnesium stearate, povidone, silica – colloidal anhydrous, sodium starch glycollate, starch – pregelatinised maize, calcium phosphate, cellulose – microcrystalline, macrogol 8000, iron oxide red, titanium dioxide, talc – purified, sucrose.

6.2 Incompatibilities

Not known.

6.3 Shelf life

30 months.

6.4 Special precautions for storage

Store below 30°C.
Protect from moisture and heat.

6.5 Nature and contents of container

Blister packs of 10, 20 and 30 tablets.

(Not all pack sizes may be marketed.)

7. MEDICINE SCHEDULE

Pharmacist Only Medicine

8. SPONSOR

Haleon New Zealand ULC,
Level 1 1.04
12 Madden Street
Auckland Central 1010
Tel 0800 540 144

9. DATE OF FIRST APPROVAL

22 November 2001

10. DATE OF REVISION OF TEXT

23 August 2024

Summary table of changes

Section changes	Summary of new changes
4.8 Undesirable effects	Additional undesirable effects included under cardiac disorders and gastrointestinal disorders. Update reporting URL to https://pophealth.my.site.com/carmreportnz/s/
4.9 Overdose	Additional information included under symptoms and signs.
10 date of revision of text	Updated date of revision of text