SCHEDULING STATUS

S2

1. NAME OF THE MEDICINE

DICLOFENAC 50 mg CLICKS, tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each enteric-coated tablet contains 50 mg diclofenac sodium.

Sugar free.

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets.

Tan coloured, round, biconvex, enteric (film) coated tablets.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For the treatment of fever and mild to moderate pain of inflammatory origin; as well as the emergency treatment of acute gout attacks.

4.2 Posology and method of administration

Posology

- Usual adult dose: Dosage for fever and mild to moderate pain of inflammatory origin is a maximum daily dose of 75 mg for a maximum treatment period of 5 days.
- Dosage for an acute gout attack is a maximum daily dose of 150 mg for a maximum treatment period of 3 days. That is 50 mg tablets three times daily after meals.
- Use the lowest effective dose for the shortest possible duration of treatment.

Paediatric population

DICLOFENAC 50 mg CLICKS is not recommended for use in children as safety and efficacy have not been established.

Method of administration

For oral administration.

4.3 Contraindications

- Diclofenac sodium is contraindicated in patients with known hypersensitivity to diclofenac and in patients who respond to aspirin and aspirin-type drug with sensitivity reactions like asthma, acute rhinitis and urticaria.
- Diclofenac sodium is absolutely contraindicated in patients with history of gastrointestinal perforation, ulceration or bleeding (PUBs) related to previous NSAIDs, including DICLOFENAC 50 mg CLICKS.
- Renal or hepatic insufficiency.
- Heart failure, established ischaemic heart disease and/or cerebrovascular disease (stroke) and peripheral arterial disease.
- Active or history of recurrent ulcer/heamorrhage/perforations.
- Avoid use of NSAIDs in women around 30 weeks gestation and later in pregnancy due to the risks of oligohydramnios/foetal renal dysfunction and premature closure of the foetal ductus arteriosus (see section 4.4 and 4.6).

4.4 Special warnings and precautions for use

- Gastro-intestinal bleeding or ulceration / perforation can occur at any time with or without symptoms. They generally have more serious consequences in the elderly. Strict accuracy of diagnosis and close medical surveillance are imperative in patients with symptoms indicative of gastro-intestinal ulceration, ulcerative colitis and Crohn’s disease in patients suffering from impaired hepatic function, pre-existing dyshaematopoiesis or disorders of blood coagulation.

- Blood counts and monitoring of hepatic and renal function are advised during prolonged therapy with DICLOFENAC 50 mg CLICKS as blood dyscrasias have been reported.
- DICLOFENAC 50 mg CLICKS should be given with care to patients with bleeding disorders, cardiovascular disease, and in those who are receiving coumarin anticoagulants. Patients who are sensitive to aspirin generally should not be given DICLOFENAC 50 mg CLICKS.
- Serious interactions have been reported after concomitant use of methotrexate and diclofenac. Allergic reactions, including anaphylactic reactions, including hypotension, vasculitis and pneumonitis, can occur without previous exposure to diclofenac.
- Caution is required in patients with a history of hypertension and/or heart failure as fluid retention and oedema have been reported in association with DICLOFENAC 50 mg CLICKS, therapy. In view of the DICLOFENAC 50 mg CLICKS's inherent potential to cause fluid retention, heart failure may be precipitated in some compromised patients.
- Caution is required in patients with significant risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking) and should only be treated with diclofenac after careful consideration.
- Elderly: The elderly have an increased frequency of adverse reactions to NSAIDs including DICLOFENAC 50 mg CLICKS, especially gastrointestinal perforation, ulceration and bleeding (PUBs) which may be fatal.
- The risk of gastrointestinal perforation, ulceration or bleeding (PUBs) is higher with increasing doses of DICLOFENAC 50 mg CLICKS, in patients with a history of ulcers, and the elderly.
- When gastrointestinal bleeding or ulceration occurs in patients receiving DICLOFENAC 50 mg CLICKS, treatment with DICLOFENAC 50 mg CLICKS should be stopped.
- DICLOFENAC 50 mg CLICKS should be given with caution to patients with a history of gastrointestinal disease (e.g. ulcerative colitis, Crohn’s disease, hiatus hernia, gastro-oesophageal reflux disease, angiodysplasia) as the condition may be exacerbated.
- Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolyis have been reported. DICLOFENAC 50 mg CLICKS should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

- Regular use of NSAIDs such as DICLOFENAC 50 mg CLICKS during the third trimester of pregnancy, may result in premature closure of the foetal ductus arteriosus *in utero*, and possibly, in persistent pulmonary hypertension of the new-born. The onset of labour may be delayed and its duration increased.
- Foetal Toxicity: Limit use of NSAIDs, including DICLOFENAC 50 mg CLICKS, between 20 and 30 weeks of pregnancy due to the risk of oligohydramnios/foetal renal dysfunction. Avoid use of NSAIDs in women around 30 weeks gestation and later in pregnancy due to the risks of oligohydramnios/foetal renal dysfunction and premature closure of the foetal ductus arteriosus.
- If NSAID treatment is necessary between 20 weeks and 30 weeks gestation, limit DICLOFENAC 50 mg CLICKS use to the lowest effective dose and shortest duration possible. Consider ultrasound monitoring of amniotic fluid if DICLOFENAC 50 mg CLICKS treatment extends beyond 48 hours. Discontinue DICLOFENAC 50 mg CLICKS if oligohydramnios occurs and follow up according to clinical practice (see section 4.3 and 4.6).

4.5 Interactions with other medicines and other forms of interaction

- Serious interactions have been reported after the use of high dose methotrexate with diclofenac.
- Blood concentrations of lithium are increased when DICLOFENAC 50 mg CLICKS is administered concomitantly.
- NSAIDs: use of two or more NSAIDs concomitantly could result in an increase in side effects.
- Corticosteroids: increased risk of gastrointestinal perforation, ulceration or bleeding (PUBs).
- Anti-coagulants: DICLOFENAC 50 mg CLICKS may enhance the effects of anti-coagulants such as warfarin.
- Anti-platelet medicines and selective serotonin reuptake inhibitors (SSRIs): increased risk of gastrointestinal bleeding.

4.6 Fertility, pregnancy and lactation

Pregnancy

- The safe use of DICLOFENAC 50 mg CLICKS in pregnancy has not been demonstrated.
- Regular use of NSAID's during the third trimester of pregnancy may result in premature closure of the foetal ductus arteriosus *in utero* and possibly in persistent pulmonary hypertension of the new-born. The onset of labour may be delayed and its duration increased (see section 4.4).
- Use of NSAIDs, including DICLOFENAC 50 mg CLICKS, can cause premature closure of the foetal ductus arteriosus and foetal renal dysfunction leading to oligohydramnios and, in some cases, neonatal renal impairment. Because of these risks, the use of DICLOFENAC 50 mg CLICKS dose and duration between 20 and 30 weeks of gestation should be limited and avoided at around 30 weeks of gestation and later in pregnancy (see section 4.3 and 4.4).

Fertility

No data on male and female fertility is available

4.7 Effects on ability to drive and use machines

- DICLOFENAC 50 mg CLICKS has moderate influence on the ability to drive and use machines (see section 4.8).
- It is not always possible to predict to what extent DICLOFENAC 50 mg CLICKS may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which DICLOFENAC 50 mg CLICKS affects them.

4.8 Undesirable effects

a. Summary of the safety profile

In view of the product's inherent potential to cause fluid retention, heart failure may be precipitated in some compromised patients.

The most commonly observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation or gastrointestinal bleeding, sometimes fatal.

b. Tabulated summary of adverse reactions

SYSTEM ORGAN CLASS	FREQUENCY	ADVERSE REACTIONS
Blood and lymphatic system disorders	Less frequent	Thrombocytopenia, leucopoenia, haemolytic anaemia, aplastic anaemia, agranulocytosis.
Nervous system disorders	Frequent	Headache, dizziness, vertigo, nervousness.
	Less frequent	Drowsiness.
Eye disorders	Less frequent	Disturbance of vision, blurred vision, diplopia.
Ear and labyrinth disorders	Less frequent	Impaired hearing, tinnitus, taste alteration disorders.
Cardiac disorders	Less frequent	Palpitations, oedema, chest pain, hypertension, congestive heart failure.
Gastrointestinal disorders	Frequent	Epigastric pain and other gastro-intestinal disorders such as nausea, diarrhoea, vomiting, abdominal pain, constipation, dyspepsia, flatulence and anorexia.
	Less frequent	Gastric or intestinal ulceration with associated bleeding. Aphthous stomatitis, glossitis, oesophageal lesions, diaphragm-like intestinal structures, lower gut disorders such as non-specific haemorrhagic colitis and exacerbation of ulcerative colitis or Crohn’s disease, constipation,

		pancreatitis, melaena, haematemesis, ulcerative stomatitis.
Hepato-biliary disorders	Frequent	Elevation of serum aminotransferase values (SGOT, SGPT).
	Less frequent	Hepatitis with or without jaundice, fulminant hepatitis.
Skin and subcutaneous tissue disorders	Frequent	Rashes and skin eruptions.
	Less frequent	Urticaria, pruritus bullous eruptions, eczema, erythema multiforme, Stevens-Johnson syndrome, Lyell's syndrome (toxic epidermal necrolysis), erythrodermia (exfoliative dermatitis), loss of hair, photosensitivity reactions, and purpura, including allergic purpura.
Renal and urinary disorders	Less frequent	Oedema, acute renal failure, urinary abnormalities such as haematuria and proteinuria, intestinal nephritis, nephrotic syndrome, papillary necrosis, nephropathy with long term 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 to SAHPRA via the **"6.04 Adverse Drug Reaction Reporting Form"**, found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

Treatment is symptomatic and supportive.

In overdose, side effects can be precipitated and/or be of increased severity (see section 4.8).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 3.1 Antirheumatics (anti-inflammatory agents).

Diclofenac sodium is a non-steroidal compound, a phenylacetic acid derivative, with analgesic, antipyretic and anti-inflammatory effects. Diclofenac sodium inhibits the biosynthesis and release of prostaglandins, which are known to be implicated in the pathogenesis of inflammation, pain and fever.

5.2 Pharmacokinetic properties

DICLOFENAC 50 mg CLICKS tablets are enteric-coated so that absorption occurs in the gastrointestinal tract to give peak plasma concentrations approximately 2 hours after ingestion. There is at least 99 % binding to plasma proteins and excretion of metabolites is mainly in the urine.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maize starch

Calcium sulphate dihydrate

Sodium starch glycolate

Docusate sodium

Magnesium stearate

HPMC (Hydroxy propyl methyl cellulose) E-5

Polyethylene glycol 600

Acryl EZE yellow (93A82339)

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at or below 25 °C.

Protect from light and moisture.

6.5 Nature and contents of container

9 tablets in white polypropylene securitainers with LDPE (low density polyethylene) closures and PVC film / printed aluminium foil blister packs.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Adcock Ingram Limited

1 New Road

Erand Gardens

Midrand, 1685

Customer Care: 0860 ADCOCK / 232625

Marketed by: Unicorn Pharmaceuticals (Pty) Ltd.

8. REGISTRATION NUMBER

U/3.1/182

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

February 1990

10. DATE OF REVISION OF THE TEXT

18 June 2021