Professional Information

SCHEDULING STATUS

S2

1. NAME OF THE MEDICINE

ADCO-MEFENAMIC ACID 250 mg**,** hard gelatine capsules.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each hard gelatine capsule contains 250 mg mefenamic acid.

Sugar free.

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Hard gelatine capsules.

A hard gelatine capsule of size ‘1’ with opaque, yellow body and opaque, blue cap containing a white powder.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

- Mefenamic acid is used for the treatment of post traumatic conditions such as pain, swelling and inflammation, for a maximum period of 5 days; and
- For the treatment of primary dysmenorrhoea subject to a maximum daily dose of 500 mg mefenamic acid 3 times a day and a maximum treatment period of 3 days.

4.2 Posology and method of administration

Posology

Adult dose: Take 500 mg (2 x 250 mg) of ADCO-MEFENAMIC ACID 250 mg capsules three times daily, with food. The dosage may be reduced to 250 mg three times daily.

Mefenamic acid should not be used for longer than 5 days at a time.

Use the lowest effective dose for the shortest possible duration of treatment.

Special populations

No information available.

Paediatric population

No information available.

Method of administration

For oral administration.

4.3 Contraindications

- Hypersensitivity to mefenamic acid or to any of the inactive ingredients (excipients) of ADCO-MEFENAMIC ACID 250 mg (see section 6.1).
- Mefenamic acid is contraindicated in patients with known sensitivity and in patients who respond to aspirin and aspirin like medicines with sensitivity reactions like bronchoconstriction, skin rashes and urticaria.
- Mefenamic acid is contraindicated in patients with a history of gastrointestinal perforation, ulceration or bleeding (PUBs) and/or inflammatory bowel disease, related to previous non-steroidal anti-inflammatory agents (NSAIDs), including ADCO-MEFENAMIC ACID 250 mg.
- Active or history of recurrent ulcer/haemorrhage/perforations.
- Safety in pregnancy and lactation has not been established.
- 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).
- Do not use in epileptic patients or in patients with impaired hepatic function.
- ADCO-MEFENAMIC ACID 250 mg is contraindicated in heart failure.

4.4 Special warnings and precautions for use

ADCO-MEFENAMIC ACID 250 mg may enhance the effects of the coumarin anticoagulants.
Therapy should be discontinued if diarrhoea or skin rash occur.
Reported haematological effects include haemolytic anaemia, agranulocytosis, pancytopenia, thrombocytopenia or thrombocytopenia purpura and bone marrow aplasia.

Allergic glomerulonephritis has occurred as well as abnormalities of hepatic and renal function. Therefore, blood counts and monitoring of hepatic and renal function are advised during prolonged therapy with mefenamic acid.

Bronchoconstriction may occur in asthmatic patients with aspirin sensitivity. ADCO-MEFENAMIC ACID 250 mg affects platelet function and it may enhance the effect of anticoagulant therapy.

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 ADCO-MEFENAMIC ACID 250 mg therapy. In view of ADCO-MEFENAMIC ACID 250 mg'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 has an increased frequency of adverse reactions to NSAIDs including ADCO-MEFENAMIC ACID 250 mg 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 ADCO-MEFENAMIC ACID 250 mg in patients with a history of ulcers, and the elderly.
When gastrointestinal bleeding or ulceration occurs in patients receiving ADCO-MEFENAMIC ACID 250 mg treatment with ADCO-MEFENAMIC ACID 250 mg should be stopped.

ADCO-MEFENAMIC ACID 250 mg 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 necrolysis have been reported. ADCO-MEFENAMIC ACID 250 mg should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

Foetal Toxicity:
Regular use of NSAIDs such as ADCO-MEFENAMIC ACID 250 mg 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.

Limit use of NSAIDs, including ADCO-MEFENAMIC ACID 250 mg, between 20 to 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 ADCO-MEFENAMIC ACID 250 mg use to the lowest effective dose and shortest duration possible. Consider ultrasound monitoring of amniotic fluid if ADCO-MEFENAMIC ACID 250 mg treatment extends beyond 48 hours. Discontinue ADCO-MEFENAMIC ACID 250 mg if oligohydramnios occurs and follow up according to clinical practice (see section 4.3 and 4.6).

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) has been reported in patients taking NSAIDs such as ADCO-MEFENAMIC ACID 250 mg. 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 ADCO-MEFENAMIC ACID 250 mg and evaluate the patient immediately.

4.5 Interactions with other medicines and other forms of interaction

Non-Steroidal Anti-inflammatories (NSAIDs):

The 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:

ADCO-MEFENAMIC ACID 250 mg may enhance the effects of anti-coagulants such as warfarin.

Anti-platelet medicines and selective serotonin reuptake inhibitors (SSRIs):

Increased risk of gastrointestinal bleeding.

Paediatric population

No information available.

4.6 Fertility, pregnancy and lactation

Pregnancy

Use of NSAIDs, including ADCO-MEFENAMIC ACID 250 mg, 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 ADCO-MEFENAMIC ACID 250 mg 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).

Breastfeeding

No information available.

Fertility

No information available.

4.7 Effects on ability to drive and use machines

No information available.

Refer to section 4.8.

4.8 Undesirable effects

a. Summary of the safety profile

The most frequently reported side effects are gastrointestinal disturbances and include dyspepsia, upper gastrointestinal discomfort as well as peptic ulceration and gastrointestinal bleeding.

b. Tabulated summary of adverse reactions

SYSTEM ORGAN CLASS	**FREQUENCY**	**ADVERSE REACTIONS**
Blood and lymphatic system disorders	Frequency unknown	Prothrombin concentration may decrease and enhance the effect of anticoagulant therapy; haemolytic anaemia, agranulocytosis, pancytopenia, thrombocytopenia or thrombocytopenia purpura and bone marrow aplasia.
Nervous system disorders	Less frequent	Headache, drowsiness, dizziness, nervousness.
Eye disorders	Less frequent	Visual disturbances.
Cardiac disorders	Frequency unknown	Oedema, hypertension, and cardiac failure.
Respiratory, thoracic and mediastinal disorders	Frequency unknown	Bronchoconstriction in asthmatic patients with aspirin sensitivity.
Gastrointestinal disorders[1]	Frequent	Dyspepsia, upper gastrointestinal discomfort as well as peptic ulceration and gastrointestinal bleeding.

	Less frequent	Diarrhoea.
Skin and subcutaneous tissue disorders	Less frequent	Drug reaction with eosinophilia and systemic symptoms (DRESS) (see section 4.4).
	Frequency unknown	Skin rash may be a sensitivity reaction and urticaria. Bullous reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis.
Renal and urinary disorders	Frequency unknown	Allergic glomerulonephritis.

Post marketing experience

No information available.

c. Description of selected adverse reactions

[1]Gastrointestinal system disorders: The most commonly observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation, or gastrointestinal bleeding, sometimes fatal. Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease, gastritis.

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

Mefenamic acid has a marked tendency to induce tonic-clonic (grand mal) convulsions in over dosage. Acute erosion or ulceration of the gastrointestinal mucosa may be a delayed manifestation.

Treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 2.7 Antipyretic or antipyretic and anti-inflammatory analgesics.

Mechanism of action

Mefenamic acid has analgesic, anti-inflammatory and antipyretic properties. It inhibits the synthesis of prostaglandins. Mefenamic acid shows central and peripheral action, and it owes these properties to its capacity to inhibit cyclooxygenase.

5.2 Pharmacokinetic properties

No information available.

5.3 Preclinical safety data

No information available.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Colloidal silicon dioxide
Magnesium stearate
Polyvinylpyrrolidone
Sodium lauryl sulphate
Sodium starch glycolate
Starch

ADCO-MEFENAMIC ACID 250 mg, hard gelatine capsules:
Gelatine
Indigo carmine (cap)
Quinoline yellow (body)
Titanium dioxide

6.2 Incompatibilities

No data available.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store at or below 25 °C in the original packaging.

6.5 Nature and contents of container

18 capsules are packed into either LDPE, white securitainers with a white lid, or an amber, round glass bottle with a white, polypropylene cap, or blister packs with transparent PVC/PVDC film on aluminium foil.

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

8. REGISTRATION NUMBER(S)

28/2.7/0019

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of registration: 29 October 1999

10. DATE OF REVISION OF THE TEXT

19 September 2022

Namibia: NS2 05/2.7/0212