PROFESSIONAL INFORMATION

SCHEDULING STATUS S2

1. NAME OF THE MEDICINE

FENAMIN-500, 500 mg (film-coated tablets)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film coated tablet contains:

Mefenamic acid 500 mg

Contains sugar:

Lactose monohydrate 143 mg

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets.

A pale yellow, round, film-coated, bevelled edge biconvex tablet.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

FENAMIN – 500 is indicated for:

- Treatment of primary dysmenorrhoea, for a maximum treatment period of 3 days.

4.2 Posology and method of administration

Posology

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

FENAMIN – 500 must be taken with meals.

FENAMIN – 500 should not be given for longer than 3 days.

Adults

FENAMIN - 500

Treatment of primary dysmenorrhoea:

A maximum daily dose of 500 mg every 8 hours orally.

Paediatric population

FENAMIN - 500 is not indicated for use in children.

4.3 Contraindications

FENAMIN - 500 is contraindicated in:

- Hypersensitivity to mefenamic acid and other NSAIDs, with prostaglandin synthetase inhibiting activity or to any of the ingredients of FENAMIN - 500 (see section 6.1).
- Because of the possibility of cross-sensitivity among NSAIDs exists, FENAMIN – 500 should not be given to patients in whom these medicines induce symptoms of bronchospasm, allergic rhinitis, or urticaria.
- History of gastrointestinal perforation, ulceration, or bleeding (PUBs) related to previous NSAIDs, including FENAMIN - 500.
- Patients with an active or a history of recurrent peptic and/or intestinal ulceration /haemorrhage/perforations.
- Chronic inflammation of either the upper or lower gastrointestinal tract such as Inflammatory bowel disease.
- Epilepsy.
- Patients with impaired hepatic or renal functions.
- Heart failure.
- Treatment of pain after coronary artery bypass graft (CABG) surgery.
- 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

Blood counts and liver function should be monitored during long-term therapy with FENAMIN - 500. FENAMIN - 500 may enhance the effects of warfarin (see INTERACTIONS section 4.5).

Drug reaction with Eosinophilia and Systemic Symptoms (DRESS):

DRESS has been reported in patients taking NSAIDs such as FENAMIN - 500. 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 FENAMIN - 500 and evaluate the patient immediately.

Elderly:
The elderly have an increased frequency of adverse reactions to NSAIDs such as FENAMIN - 500, especially gastrointestinal perforation, ulceration, and bleeding (PUBs) which may be fatal.
The risk of gastrointestinal perforation, ulceration, and bleeding (PUBs) is higher with increasing doses of FENAMIN - 500, in patients with a history of ulcers, and the elderly. FENAMIN - 500 is best avoided in elderly patients with dehydration or pre-existing renal disease.

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control the condition treated.
Patients on prolonged therapy with FENAMIN - 500 should be kept under regular surveillance with particular attention to liver dysfunction, rash, blood dyscrasias or development of diarrhoea. Appearance of any of these symptoms should be regarded as an indication to stop therapy immediately.

Precaution should be taken in patients suffering from dehydration and renal disease, particularly the elderly.
FENAMIN - 500 and its metabolites may give a false positive reaction to certain urine tests for the presence of bile.

Respiratory disorders:
Caution is required if administered to patients suffering from, or with a previous history of, bronchial asthma since NSAIDs have been reported to precipitate bronchospasm in such patients. Bronchoconstriction may occur with FENAMIN - 500 in asthmatic patients with aspirin sensitivity.

Cardiovascular, renal, and hepatic impairment:
The administration of FENAMIN - 500 may cause a dose-dependent reduction in prostaglandin formation and precipitate renal failure. Patients at greatest risk of this reaction are those with impaired renal function, cardiac impairment, liver dysfunction, those taking diuretics and the elderly. Renal function should be monitored in these patients. FENAMIN - 500 may enhance the effects of warfarin.

Toxicity has also been seen in patients with pre-renal conditions leading to a reduction in renal blood flow or blood volume. Patients at greatest risk are those with impaired renal function, heart failure, liver dysfunction, those taking diuretics, and the elderly.

Liver function tests must be carried out regularly to monitor elevation of enzymes and bilirubin.

Cardiovascular and cerebrovascular effects:
Appropriate monitoring and advice are required for patients with a history of hypertension and/or mild to moderate congestive heart failure as fluid retention and oedema have been reported in association with NSAID therapy such as FENAMIN - 500.
Use of some NSAIDs such as FENAMIN - 500 (particularly at high doses and in long-term treatment) may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke). There are insufficient data to exclude such a risk for FENAMIN - 500.

Patients with uncontrolled hypertension, established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with FENAMIN - 500 after careful consideration. Similar consideration should be made before initiating longer-term treatment of patients with risk factors for cardiovascular disease (e.g., hypertension, hyperlipidaemia, diabetes mellitus, smoking).
As NSAIDs such as FENAMIN - 500 can interfere with platelet function, they should be used in caution in patients with intracranial haemorrhage and bleeding diathesis.

Gastrointestinal bleeding, ulceration, and perforation:
Gastrointestinal perforation, ulceration, or bleeding (PUB) which can be fatal, has been reported with all NSAIDs such as FENAMIN - 500 at any time during treatment, with or without warning symptoms or a previous history of serious gastrointestinal events. Smoking and alcohol use are added risk factors.
The risk of gastrointestinal perforation, ulceration or bleeding is higher with increasing FENAMIN - 500 doses, in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation and in the elderly.
FENAMIN - 500 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. If diarrhoea occurs, use of FENAMIN - 500 should be discontinued immediately.

Combination therapy with protective medicines (e.g., misoprostol or proton pump inhibitors) should be considered for patients at risk of gastrointestinal bleeding such as the elderly, and also for patients requiring concomitant low dose aspirin, or other medicines likely to increase gastrointestinal risk.
Patients with a history of gastrointestinal toxicity, particularly the elderly, should report any unusual abdominal symptoms (especially gastrointestinal bleeding) particularly in the initial stages of FENAMIN - 500 treatment.
Caution should be advised in patients receiving concomitant medicines which could increase the risk of gastrointestinal side effects or bleeding such as corticosteroids, anticoagulants such as warfarin, selective serotonin reuptake inhibitors or anti-platelet medicines such as aspirin.
When gastrointestinal perforation, ulceration or bleeding occurs in patients receiving FENAMIN - 500, FENAMIN - 500 should be withdrawn.

Diarrhoea may occur within 24 hours following usual FENAMIN - 500 dosage. When diarrhoea occurs, FENAMIN - 500 should be discontinued immediately.

Temporary lowering of the white blood cell count has occurred but does not appear to be dose-related. Blood counts should be performed at regular intervals during long-term administration of FENAMIN - 500.

SLE and mixed connective tissue disease:
In patients with systemic lupus erythematosus (SLE) and mixed connective tissue disorders there may be an increased risk of aseptic meningitis.

Skin reactions:
Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, have been reported in association with use of NSAIDs such as FENAMIN - 500. Patients appear to be at highest risk of these reactions early in the course of therapy, the onset of the reactions occurring in the majority of cases within the first month of treatment. FENAMIN - 500 should be stopped at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

Cross-sensitivity:
Because of the possibility of cross-sensitivity due to structural relationships which exist among nonsteroidal anti-inflammatory medicines, acute allergic reactions may be more likely to occur in patients who have exhibited allergic reactions to these compounds.

Occurrence of rash is a definite reason for stopping FENAMIN – 500 because exfoliative dermatitis has been reported on continued use after development of a rash.
In dysmenorrhoea and menorrhagia lack of response should alert the medical practitioner to investigate other causes.

Poor CYP2C9 metabolisers:
In patients who are known or suspected to be poor CYP2C9 metabolisers based on previous history/experience with other CYP2C9 substrates, FENAMIN - 500 should be administered with caution as they may have abnormally high plasma levels due to reduced metabolic clearance.

Foetal Toxicity:
Limit use of NSAIDs, including FENAMIN – 500, 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 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 4.6).

If NSAID treatment is necessary between 20 weeks and 30 weeks gestation, limit FENAMIN – 500 use to the lowest effective dose and shortest duration possible. Consider ultrasound monitoring of amniotic fluid if FENAMIN – 500 treatment extends beyond 48 hours. Discontinue FENAMIN – 500 if oligohydramnios occurs and follow up according to clinical practice.

Excipients
FENAMIN - 500 contains lactose monohydrate which may have an effect on the glycaemic control of patients with diabetes mellitus.
Patients with rare hereditary problems of galactose intolerance e.g., galactosaemia, Lapp lactase deficiency, glucose-galactose malabsorption or fructose intolerance should not take FENAMIN – 500.

4.5 Interactions with other medicines and other forms of interaction
Warfarin: FENAMIN - 500 may enhance the effects of warfarin.

Anti-platelet medicines and selective serotonin reuptake inhibitors (SSRIs): Increased risk of gastrointestinal bleeding.
Corticosteroids: increased risk of gastrointestinal perforation, ulceration, or bleeding (PUBs)
Lithium: Patients receiving lithium concurrently with non-steroidal anti-inflammatory medicines, including FENAMIN - 500, have produced an elevation of plasma lithium levels and a reduction in renal lithium clearance. Thus, when FENAMIN - 500 and lithium are administered concurrently, patients should be observed carefully for signs of lithium toxicity.
NSAIDs: Use of two or more NSAIDs concomitantly could result in an increase in side effects.

4.6 Fertility, pregnancy, and lactation

Pregnancy

Use of NSAIDs, including FENAMIN - 500, can cause premature closure of the foetal ductus arteriosus, persistent pulmonary hypertension of the new-born, foetal renal dysfunction leading to oligohydramnios and, in some cases, neonatal renal impairment. Because of these risks, the use of FENAMIN - 500 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. The onset of labour may be delayed, and its duration increased.

Lactation

Trace amounts of mefenamic acid may be present in breast milk and transmitted to the breastfeeding infants. Therefore, FENAMIN - 500 should not be taken by mothers breastfeeding their infants.

Fertility

The use of FENAMIN - 500 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 FENAMIN - 500 should be considered.

4.7 Effects on ability to drive and use machines

Undesirable effects such as dizziness, drowsiness, fatigue, and visual disturbances are possible after taking NSAIDs such as FENAMIN - 500. If affected, patients should not drive or operate machinery.

4.8 Undesirable effects

a. Summary of the safety profile

The most frequent side effects occurring with FENAMIN – 500 are gastrointestinal disturbances.

b. Tabulated summary of adverse reactions

SYSTEM ORGAN CLASS	**FREQUENCY**	**ADVERSE REACTIONS**
Blood and the lymphatic system disorders	Less frequent	Haemolytic anaemia, decreased haematocrit, leucopoenia, eosinophilia, thrombocytopenia or thrombocytopenic purpura, agranulocytosis, pancytopenia, aplastic anaemia, bone marrow aplasia.
Immune system disorders	Less frequent	Acute hypersensitivity reactions (urticaria, bronchospasm, anaphylaxis).
Metabolism and nutrition disorders	Less frequent	Glucose intolerance in diabetic patients, hyponatraemia.
Psychiatric disorders	Less frequent	Nervousness.
Nervous system disorders	Less frequent	Drowsiness, dizziness, headache, convulsions, insomnia.
Eye disorders	Frequency unknown	Visual disturbances.
Ear and labyrinth disorders	Less frequent	Ear pain.
Cardiac disorders	Less frequent	Palpitations, oedema, hypertension, and cardiac failure.
Vascular disorders	Less frequent	Hypotension.
Respiratory, thoracic, and mediastinal disorders	Less frequent	Asthma may be precipitated, bronchospasm, dyspnoea.

Gastrointestinal disorders	Frequent	Diarrhoea, nausea with or without vomiting, abdominal pain.
	Less frequent	Anorexia, pyrosis, flatulence, enterocolitis, colitis, steatorrhea, cholestatic jaundice, hepatitis, pancreatitis, hepato-renal syndrome, mild hepatic toxicity, constipation, peptic ulceration, perforation with or without gastrointestinal haemorrhage.
	Frequency unknown	Dyspepsia, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease, gastritis.
Skin and subcutaneous tissue disorders	Less frequent	Drug reaction with eosinophilia and systemic symptoms (DRESS) (see section 4.4). Angioedema, oedema of the larynx, Stevens-Johnson syndrome, Lyell's syndrome (toxic epidermal necrolysis), erythema multiforme, perspiration, pruritus, urticaria, skin rash, facial oedema.
	Frequency unknown	Bullous reactions.
Renal and urinary disorders	Less frequent	Renal failure, papillary necrosis, acute interstitial nephritis with haematuria, dysuria, proteinuria, allergic glomerulonephritis.

	Frequency unknown	Nephrotic syndrome, elevations in blood urea.

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. Health care 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.

Adverse reactions can also be reported to the Adcock Ingram Pharmacovigilance department by e-mail to Adcock.Aereports@adcock.com , fax to +27 86 553 0128 or call 011 635 0134.

4.9 Overdose

Refer also to section 4.8.

Symptoms

Mefenamic acid such as in FENAMIN - 500 has a marked tendency to induce tonic-clonic (grand mal) convulsions in overdosage. Dyskinesia, acute renal failure, and coma have been reported. Overdose has led to fatalities.

Treatment

Treatment is symptomatic and supportive. Following accidental overdosage, the stomach should be emptied immediately by inducing emesis followed by administration of activated charcoal. Vital functions should be monitored and supported. Haemodialysis is of little value since mefenamic acid, and its metabolites are firmly bound to plasma proteins.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 2.7 Antipyretic and anti-inflammatory analgesics

Mechanism of action

Mefenamic acid is a non-steroidal anti-inflammatory drug (NSAID) with antipyretic and analgesic properties. It has a central as well as peripheral analgesic actions. Mefenamic acid inhibit cyclo-oxygenase non-selectively and thereby antagonising certain effects of prostaglandins in analgesia.

5.2 Pharmacokinetic properties

Mefenamic acid is well absorbed from the gastrointestinal tract. Peak plasma concentrations occur in about 2 to 4 hours, with a half-life of 2 to 4 hours. Plasma levels are proportional to dose. Accumulation does not occur following repeated doses. Mefenamic acid is extensively bound to plasma proteins. Over 50 % of the dose may be recovered in the urine as unchanged substance or as conjugated metabolites.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Croscarmellose sodium
Iron oxide yellow (C.I. 77492) (E172),
Lactose monohydrate
Macrogol
Magnesium stearate
Polyvinyl alcohol
Povidone K25
Purified talc
Titanium dioxide (C.I. 77891) (E 171)

6.2 Incompatibilities

No data available

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store in a cool dry place at or below 25 °C.
Protect from light.
Keep in original packaging until required for use.

6.5 Nature and contents of container

FENAMIN - 500:
9 tablets are packed in a white, polypropylene container and sealed with a white low-density polyethylene cap together with a white foam insert and rayon. The container is packed with a leaflet.
9 tablets are packed in a white, polypropylene container and sealed with a white low-density polyethylene cap. The container is packed with a leaflet.

9 tablets are packed in a clear polyvinylchloride film sealed with an aluminium foil backing. The blister strips are packed into an outer cardboard carton together with a leaflet.

Not all packs and pack sizes are necessarily 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: 0860ADCOCK/232625

8. REGISTRATION NUMBER

27/2.7/0282

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

01 June 1993

10. DATE OF REVISION OF THE TEXT

18 August 2023

Namibia: NS2 04/2.7/0050