Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

Menozip MF 500mg/250mg tablet.

2. Qualitative and quantitative composition

Each Un-coated tablet contains:
Mefenamic Acid BP 250mg
Tranexamic Acid BP 500mg

Excipient with known effect
Lactose

For a full list of excipients, see section 6.1

3. Pharmaceutical form

A yellow-coloured un-coated tablet

4. Clinical particulars

4.1 Therapeutic indications

Mefenamic & Tranexamic acid (250/500 mg) Tablet is a combination of Mefenamic acid and Tranexamic acid. It is used to treat pain and heavy bleeding during menstruation. It prevents the breakdown of blood clots, which helps to reduce heavy menstrual flow. It also blocks the production of specific chemical substances responsible for causing pain.

4.2 Posology and method of administration

Posology
Tranexamic Acid
Adults:

- Local Fibrinolysis: The recommended standard dose is 15-25mg/kg bodyweight (i.e. 2-3 tablets) two to three times daily. For the indications listed below the following doses may be used:
  1a. Prostatectomy: Prophylaxis and treatment of haemorrhage in high-risk patients should commence per- or post-operatively with an injectable form; thereafter 2 tablets three to four times daily until macroscopic haematuria is no longer present.
  1b. Menorrhagia: Recommended dosage is 2 tablets 3 times daily as long as needed for up to 4 days. If very heavy menstrual bleeding, dosage may be increased. A total dose of 4g daily (8 tablets) should not be exceeded. Treatment with tranexamic acid should not be initiated until menstrual bleeding has started.
  1c. Epistaxis: When repeated bleeding is anticipated oral therapy (2 tablets three times daily) should be administered for 7 days.
  1d. Cervix Conisation: 3 tablets three times daily
  1e. Traumatic Hyphaemia: 2-3 tablets 3 times daily. The dose is based on 25mg/kg three times a day.

- Haemophilia: In the management of dental extractions 2-3 tablets every eight hours. The dose is based on 25mg/kg.
- Hereditary angioneurotic oedema: Some patients are aware of the onset of illness; suitable treatment for these patients is intermittently 2-3 tablets two to three times daily for some days. Other patients are treated continuously at this dosage.

Paediatric population:

- This should be calculated according to bodyweight at 25mg/kg per dose at the adult dosing frequencies. However, data on efficacy, posology and safety for these indications are limited.
- Elderly:
  No reduction in dosage is necessary unless there is evidence of renal failure
  Renal insufficiency
  By extrapolation from clearance data relating to the intravenous dosage form, the following reduction in the oral dosage is recommended for patients with mild to moderate renal insufficiency:

Serum Creatinine(µmol/l)	Oral Dose	Dose Frequency
120-249	15 mg/kg body weight	twice daily
250-500	15 mg/kg body weight	daily

Method of administration
Its administered orally after a meal swallowed whole with water or a fluid.
Mefenamic acid
Adults**:** 1 tablet (500 mg) three times daily.
In menorrhagia to be administered on the first day of excessive bleeding and continued according to the judgement of the physician.
In dysmenorrhoea to be administered at the onset of menstrual pain and continued according to the judgement of the physician.
Elderly (over 65 years)
As for adults.
Whilst no pharmacokinetic or clinical studies specific to the elderly have been undertaken with mefenamic acid, it has been used at normal dosage in trials which included many elderly patients.
The elderly are at increased risk of the serious consequences of adverse reactions. If an NSAID is considered necessary, the lowest effective dose should be used and for the shortest possible duration. The patient should be monitored regularly for GI bleeding during NSAID therapy.
Mefenamic acid should be used with caution in elderly patients suffering from dehydration and renal disease. Non-oliguric renal failure and proctocolitis have been reported mainly in elderly patients who have not discontinued mefenamic acid after the development of diarrhoea.

Paediatric population
It is recommended that children under 12 years of age should be given Mefenamic Acid Suspension (50 mg/5ml).
Method of administration
For oral administration.: Mefenamic acid should be taken preferably with or after food.

4.3 Contraindications

Tranexamic

Severe renal impairment because of risk of accumulation.

Hypersensitivity to tranexamic acid or any of the excipients, listed in section 6.1.

Active thromboembolic disease.

History of venous or arterial thrombosis.

Fibrinolytic conditions following consumption coagulopathy.

History of convulsions.

Mefenamic

Hypersensitivity to the active substance or any of the excipients listed
Inflammatory bowel disease
History of gastrointestinal bleeding or perforation, related to previous NSAIDs therapy.
Active, or history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding).
Severe heart failure, hepatic failure and renal failure
Because the potential exists for cross-sensitivity to aspirin, ibuprofen, or other non-steroidal anti-inflammatory drugs, mefenamic acid must not be given to patients who have previously shown hypersensitivity reaction (e.g. asthma, bronchospasm, rhinitis, angioedema or urticaria) to these medicines.
During the last trimester of pregnancy
Treatment of pain after coronary artery bypass graft (CABG) surgery

4.4 Special warnings and precautions for use

- Peptic ulcer: Peptic ulcers are open sores that develop in your stomach when there is excess production of stomach acid. You should take Mefenamic & Tranexamic acid (250/500 mg) Tablet with extreme caution if you are suffering from peptic ulcer disease as this medicine can increase the risk of severe stomach bleeding.
- Allergic skin reactions: Mefenamic & Tranexamic acid (250/500 mg) Tablet may cause serious skin allergies. If you notice any signs and symptoms like rashes, hives (itchy, painful eruptions that sting), or other allergic symptoms, report them immediately to your doctor. You may discontinue the treatment on your doctor's recommendation.

- Use of hormonal contraceptives: If you are taking any hormonal contraceptives (birth control) like pills, patches, vaginal rings, or injections, avoid taking Mefenamic & Tranexamic acid (250/500 mg) Tablet. This medicine may increase the risk of serious side effects in such cases. The risk is more if you are overweight, smoke cigarettes, or are above the age of 35.
- Eye disorders: If you have problems related to the eyes, take Mefenamic & Tranexamic acid (250/500 mg) Tablet with caution as it can increase the risk of visual disturbances. You should get a regular eye test performed before starting the medication and also at regular intervals throughout the treatment.
- Use in children
- Mefenamic & Tranexamic acid (250/500 mg) Tablet is not recommended for use in children less than 14 years of age.
- Driving or operating machinery: You may experience blurred vision or dizziness after taking Mefenamic & Tranexamic acid (250/500 mg) Tablet. Hence, it is advised not to drive vehicles and operate any machines after taking this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Mefenamic acid

Concurrent therapy with other plasma protein binding drugs may necessitate a modification in dosage.

Anti-coagulants: NSAIDs may enhance the effects of anti-coagulants, such as warfarin (see section 4.4). Concurrent administration of mefenamic acid with oral anti-coagulant drugs requires careful prothrombin time monitoring.

It is considered unsafe to take NSAIDs in combination with warfarin or heparin unless under direct medical supervision.

Lithium: A reduction in renal lithium clearance and elevation of plasma lithium levels. Patients should be observed carefully for signs of lithium toxicity.

The following interactions have been reported with NSAIDs but have not necessarily been associated with Mefenamic Acid Tablets:

Other analgesics including cyclooxygenase-2 selective inhibitors: Avoid concomitant use of two or more NSAIDs (including aspirin) as this may increase the risk of adverse effects (see section 4.4).

Antidepressants: Selective serotonin reuptake inhibitors (SSRIs): Increased risk of gastrointestinal bleeding (see section 4.4).

Antihypertensives and diuretics: A reduction in antihypertensive and diuretic effect has been observed. Diuretics can increase the nephrotoxicity of NSAIDs.

ACE inhibitors and angiotensin-II-receptor antagonists**:** A reduction in antihypertensive effect and an increased risk of renal impairment especially in elderly patients. Patients should be adequately hydrated, and the renal function assessed in the beginning and during concomitant therapy.

Aminoglycosides: Reduction in renal function in susceptible individuals, decreased elimination of aminoglycoside and increased plasma concentrations.

Anti-platelet agents: Increased risk of gastrointestinal ulceration or bleeding (see section 4.4).

Acetylsalicylic Acid: Experimental data implies that mefenamic acid interferes with the anti- platelet effect of low-dose aspirin when given concomitantly, and thus may interfere with aspirin's prophylactic treatment of cardiovascular disease. However, the limitations of this experimental data and the uncertainties regarding extrapolation of *ex vivo* data to the clinical situation imply that no firm conclusions can be made for regular mefenamic acid use.

Cardiac glycosides: NSAIDs may exacerbate cardiac failure, reduce GFR and increase plasma cardiac glycoside levels.

Ciclosporin: The risk of nephrotoxicity of ciclosporin may be increased with NSAIDs.

Corticosteroids: Concomitant use may increase the risk of gastrointestinal ulceration or bleeding (see section 4.4).

Oral hypoglycaemic agents: Inhibition of metabolism of sulfonylurea drugs, prolonged half- life and increased risk of hypoglycaemia.

Methotrexate: Elimination of the drug can be reduced, resulting in increased plasma levels.

Mifepristone: NSAIDs should not be taken for 8-12 days after mifepristone administration, NSAIDs can reduce the effects of mifepristone.

Probenecid: Reduction in metabolism and elimination of NSAIDs and metabolites.

Quinolone antibiotics: Animal data indicates that NSAIDs can increase the risk of convulsions associated with quinolone antibiotics. Patients taking NSAIDs and quinolones may have an increased risk of developing convulsions.

Tacrolimus: Possible increased risk of nephrotoxicity when NSAIDS are given with tacrolimus.

Zidovudine: Increased risk of haematological toxicity when NSAIDs are given with zidovudine. There is evidence of an increased risk of haemarthroses and haematoma in HIV(+) haemaophiliacs receiving concurrent treatment with zidovudine and ibuprofen.

4.6 Pregnancy and Lactation

Pregnancy: It is not recommended to take Mefenamic & Tranexamic acid (250/500 mg) Tablet during pregnancy since it might cause abnormalities in your developing foetus. If you take this medicine, it may delay labour and increase the risk of bleeding. Consult your doctor before taking this medicine if you are pregnant.
Breast-feeding: If you are breastfeeding, it is not recommended to take Mefenamic & Tranexamic (250/500 mg) Tablet as there is no sufficient data available to see if this medicine passes into your breastmilk. Hence, consult your doctor before taking this medicine if you are breastfeeding.

4.7 Effects on ability to drive and use machines

Menozip 250/500 mg has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Tranexamic acid 500mg

Immune system disorders

Very rare: Hypersensitivity reactions including anaphylaxis

Gastrointestinal disorders

Very rare: Digestive effects such as nausea, vomiting and diarrhoea my occur but disappear when the dosage is reduced

Nervous system disorders

Not known: Convulsions particularly in case of misuse (refer to sections 4.3 and 4.4)

Skin and subcutaneous tissue disorders

Rare: Allergic skin reactions.

Vascular disorders

Rare: thromboembolic events.

Very rare: Arterial or venous thrombosis at any sites

Eye disorders

Rare: impaired colour vision and other visual disturbances, retinal/artery occlusion

Mefenamic acid

The most frequently reported side effects associated with mefenamic acid involve the gastrointestinal tract.

Diarrhoea occasionally occurs following the use of mefenamic acid. Although this may occur soon after starting treatment, it may also occur after several months of continuous use. The diarrhoea has been investigated in some patients who have continued this drug in spite of its continued presence. These patients were found to have associated proctocolitis. If diarrhoea does develop the drug should be withdrawn immediately and this patient should not receive mefenamic acid again.

Frequencies are not known for the following adverse reactions:

Blood and the lymphatic system disorders

Haemolytic anaemia*, anaemia, hypoplasia bone marrow, haematocrit decreased, thrombocytopenic purpura, temporary lowering of the white blood cell count (leukopenia) with a risk of infection, sepsis, and disseminated intravascular coagulation.

Agranulocytosis, aplastic anaemia, eosinophilia, neutropenia, pancytopenia, thrombocytopenia.

reversible when mefenamic acid is stopped

Immune system disorders

Hypersensitivity reactions have been reported following treatment with NSAIDs. These may consist of (a) non-specific allergic reactions and anaphylaxis (b) respiratory tract reactivity comprising asthma, aggravated asthma, bronchospasm, or dyspnoea or (c) assorted skin disorders including rashes of various types, pruritus, urticaria, purpura, angioedema, and more rarely exfoliative or bullous dermatoses (including epidermal necrolysis and erythema multiforme).

Metabolism and nutrition disorders

Glucose intolerance in diabetic patients, hyponatraemia.

Psychiatric disorders

Confusion, depression, hallucinations, nervousness.

Nervous system disorders

Optic neuritis, headaches, paraesthesia, dizziness, drowsiness, reports of aseptic meningitis (especially in patients with existing auto-immune disorders, such as systemic lupus erythematosus, mixed connective tissue disease), with symptoms such as stiff neck, headache, nausea, vomiting, fever or disorientation (see section 4.4).

Blurred vision, convulsions, insomnia.

Eye disorders

Eye irritation, reversible loss of colour vision, visual disturbances.

Ear and labyrinth disorders

Ear pain, tinnitus, vertigo.

Cardiac / Vascular disorders

Oedema, hypertension and cardiac failure have been reported in association with NSAID treatment.

Clinical trial and epidemiological data suggest that use of some NSAIDs (particularly at high doses and in long term treatment) may be associated with an increased risk of arterial thrombotic events (for example myocardial infarction or stroke) (see section 4.4).

Palpitations.

Hypotension.

Respiratory, thoracic and mediastinal disorders

Asthma, dyspnoea.

Gastrointestinal disorders

The most commonly observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation or GI bleeding, sometimes fatal, particularly in the elderly, may occur (see section 4.4). Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease have been reported following administration. Less frequently, gastritis has been observed.

Elderly or debilitated patients seem to tolerate gastrointestinal ulceration or bleeding less well than other individuals and most spontaneous reports of fatal GI events are in this population.

Anorexia, colitis, enterocolitis, gastric ulceration with or without haemorrhage, pancreatitis, steatorrhea.

Hepatobiliary disorders

Borderline elevations of one or more liver function tests, cholestatic jaundice. Mild hepatotoxicity, hepatitis, hepatorenal syndrome.

Skin and subcutaneous tissue disorders

Angioedema, laryngeal oedema, erythema multiforme, face oedema, bullous reactions including Lyell's syndrome (toxic epidermal necrolysis) and Stevens-Johnson syndrome, perspiration, rash, photosensitivity reaction, pruritus and urticaria.

Renal and urinary disorders

Allergic glomerulonephritis, acute interstitial nephritis, dysuria, haematuria, nephrotic syndrome, non-oliguric renal failure (particularly in dehydration), proteinuria, renal failure including renal papillary necrosis.

General disorders and administration site conditions

Fatigue, malaise, multi-organ failure, pyrexia.

Investigations

A positive reaction in certain tests for bile in the urine of patients receiving mefenamic acid has been demonstrated to be due to the presence of the drug and its metabolites and not to the presence of bile.

Reporting of suspected adverse reactions

Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS)
https://pv.pharmacyboardkenya.org

4.9 Overdose

Missed Dose: Take the missed dose of Mefenamic & Tranexamic (250/500 mg) Tablet as soon as you remember. If your next dose is near, skip the missed dose. Do not double your dose to compensate for a missed one.

Overdose: Never take more than the prescribed dose. Seek emergency medical treatment or contact your doctor in case of an overdose with Mefenamic & Tranexamic (250/500 mg) Tablet.

5. Pharmacological properties

5.1 Pharmacodynamic properties

- **Tranexamic Acid**

Pharmacotherapeutic group: antifibrinolytic agent. ATC code: B02AA02

Tranexamic acid is an antifibrinolytic compound which is a potent competitive inhibitor of the activation of plasminogen to plasmin. At much higher concentrations it is a non-competitive inhibitor of plasmin. The inhibitory effect of tranexamic acid in plasminogen activation by urokinase has been reported to be 6-100 times and by streptokinase 6-40 times greater than that of aminocaproic acid. The antifibrinolytic activity of tranexamic acid is approximately ten times greater than that of aminocaproic acid.

- **Mefenamic acid**

Pharmacotherapeutic group: Anti-inflammatory and anti- rheumatic products, non-steroids, fenamates. ATC code: M01AG01.

Mechanism of action

Mefenamic acid is non-steroidal anti-inflammatory drug (NSAID) and has anti-inflammatory, analgesic and antipyretic properties.

Its anti-inflammatory effect was first established in the UV erythema model of inflammation. Further studies included inhibition of granulation tissue growth into subcutaneous cotton pellets in rats and carragheenin induced rat paw oedema tests.

Antipyretic activity was demonstrated in yeast-induced pyresis in rats. In this model its antipyretic activity was roughly equal to that of phenylbutazone and flufenamic acid, but less than that of indomethacin.

Analgesic activity was demonstrated in tests involving pain sensitivity of rats paws inflamed by brewers yeast. Mefenamic acid was less potent than flufenamic acid in this model.

Prostaglandins are implicated in a number of disease processes including inflammation, modulation of the pain response, dysmenorrhoea, menorrhagia and pyrexia.

In common with most NSAIDs mefenamic acid inhibits the action of prostaglandin synthetase (cyclo-oxygenase). This results in a reduction in the rate of prostaglandin synthesis and reduced prostaglandin levels.

The anti-inflammatory activity of NSAIDs in the rat paw oedema test has been correlated with their ability to inhibit prostaglandin synthetase. When mefenamic acid is ranked in both these tests it falls between indomethacin and phenylbutazone and it is probable that inhibition of prostaglandin synthesis contributes to the pharmacological activity and clinical efficacy of mefenamic acid.

There is also considerable evidence that the fenamates inhibit the action of prostaglandins after they have been formed. They therefore both inhibit the synthesis and response to prostaglandins. This double blockade may well be important in their mode of action.

5.2 Pharmacokinetic properties

Tranexamic Acid

Absorption: Peak plasma Tranexamic acid concentration is obtained immediately after intravenous administration (500mg). Then concentration decreases until the 6th hour. Elimination half-life is about 3 hours.

Distribution: Tranexamic acid administered parenterally is distributed in a two-compartment model. Tranexamic acid is delivered in the cell compartment and the cerebrospinal fluid with delay. The distribution volume is about 33% of the body mass.

Tranexamic acid crossed the placenta, and may reach one hundredth of the serum peak concentration in the milk of lactating women.

Elimination: Tranexamic acid is excreted in urine as unchanged compound. 90% of the administered dose is excreted by the kidney in the twelve first hours after administration (glomerular excretion without tubular reabsorption).

Following oral administration, 1.13% and 39% of the administered dose were recovered after 3 and 24 hours respectively.

Plasma concentrations are increased in patients with renal insufficiency.

Mefenamic acid

Absorption and Distribution: Mefenamic acid is absorbed from the gastro intestinal tract. Peak levels of 10 mg/l occur two hours after the administration of a 1g oral dose to adults.

Biotransformation: Mefenamic acid is predominantly metabolised by cytochrome P450 enzyme CYP2C9 in the liver, first to a 3 hydroxymethyl derivative (metabolite I) and then a 3-carboxyl derivative (metabolite II). Both metabolites undergo secondary conjugation to form glucuronides.

Therefore, in patients who are known or suspected to be poor CYP2C9 metabolisers based on previous history/experience with other CYP2C9

substrates, mefenamic acid should be administered with caution as they may have abnormally high plasma levels due to reduced metabolic clearance.

Elimination: Fifty two percent of a dose is recovered from the urine, 6% as mefenamic acid, 25% as metabolite I and 21% as metabolite II. Assay of stools over a 3-day period accounted for 10-20 % of the dose chiefly as unconjugated metabolite II.

The plasma levels of unconjugated mefenamic acid decline with a half-life of approximately two hours.

5.3 Preclinical safety data

There are no preclinical data of relevance to the prescriber which are additional to that already included in other sections of the Summary of Product Characteristics.

6. Pharmaceutical Particulars

6.1 List of Excipients

SR. NO.	INGREDIENTS	SPECIFICATION
1	Maize starch	BP
2	Microcrystalline Cellulose	USP
3	Sodium starch glycolate	BP
4	Lactose	BP
5	Sodium Methyl Paraben	BP
6	Povidone 30	BP
7	Colour Tartrazine supra	IH
8	Gelatine	BP
9	Magnesium Stearate	BP
10	Purified Talc	BP
11	Cross carmalose sodium	BP
12	Sodium Lauryl Sulphate	BP
13	Kyron T314	IH
14	Aerosil	BP

6.2 Incompatibilities

Not applicable.

6.3 Shelf-Life

36 months from date of manufacturing.

6.4 Special Precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and Content of container

10 tablets are packed in one Alu-Alu blister

6.6 Special precautions for disposal and other handling

This medicinal product does not require any special precautions for disposal and handling.

7. **Marketing Authorization Holder**
   NATIONAL PHARMACY LIMITED
8. **Marketing Authorization Number**
   CTD10249
9. **Date of first authorization/renewal of the authorization**
   28/03/2024
10. **Date of revision of the text**
    05/05/2025