For the use of a Registered Medical Practitioner or Hospital or a Laboratory only

XAMIC MF

1. Generic Name

Tranexamic Acid and Mefenamic Acid Tablets

2. Qualitative and quantitative composition

Each film coated tablet contains:
Tranexamic Acid I.P. 500 mg
Mefenamic Acid I.P. 250mg
Colour: Quinoline Yellow

The excipients used are Microcrystalline Cellulose, Starch, Polyvinyl Pyrrolidone, Colloidal Silicon Dixoide, Propylene Glycol, Sodium Lauryl Sulfate, Croscarmellose Sodium, Magnesium Stearate, Colour Coat FC4WQ260109 yellow .

3. Dosage form and strength

Dosage Form: Film-coated Tablets
Strength: Tranexamic Acid - 500 mg, Mefenamic Acid - 250mg.

4. Clinical particulars

4.1 Therapeutic indication

Xamic MF is used for the treatment of primary dysmenorrhoea and pain associated with menorrhagia in women.

4.2 Posology and method of administration

To be administered as directed by the physician.

4.3 Contraindications

- Hypersensitivity to the active substance or any of the excipients.
- Severe renal impairment because of risk of accumulation,
- Active thromboembolic disease.
- History of venous or arterial thrombosis
- Fibrinolytic conditions following consumption coagulopathy
- History of convulsions
- 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

Tranexamic Acid

In case of haematuria of renal origin (especially in haemophilia), there is a risk of mechanical anuria due to formation of a ureteral clot.

In the long-term treatment of patients with hereditary angioneurotic oedema, regular eye examinations (e.g. visual acuity, slit lamp, intraocular pressure, visual fields) and liver function tests should be performed.

Patients with irregular menstrual bleeding should not use Xamic MF until the cause of irregular bleeding has been established. If menstrual bleeding is not adequately reduced by Xamic MF, an alternative treatment should be considered.

Tranexamic acid should be administered with care in patients receiving oral contraceptives because of the increased risk of thrombosis.

Patients with a previous thromboembolic event and a family history of thromboembolic disease (patients with thrombophilia) should use Xamic MF only if there is a strong medical indication and under strict medical supervision.
The blood levels are increased in patients with renal insufficiency. Therefore, a dose reduction is recommended.

The use of tranexamic acid in cases of increased fibrinolysis due to disseminated intravascular coagulation is not recommended.

Patients who experience visual disturbance should be withdrawn from treatment.
Clinical experience with Xamic MF in menorrhagic children under 15 years of age is not available.

Mefenamic Acid

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see GI and cardiovascular risks below).

Patients on prolonged therapy 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.

Use with concomitant NSAIDs including cyclooxygenase 2 specific inhibitors.

Prolonged use of any type of painkiller for headaches can make them worse. If this situation is experienced or suspected, medical advice should be obtained and treatment should be discontinued. The diagnosis of 'Medication Overuse Headache' should be suspected in patients who have frequent or daily headaches despite (or because of) the regular use of headache medications.

Precaution should be taken in patients suffering from dehydration and renal disease, particularly the elderly.

Elderly: The elderly have an increased frequency of adverse reactions to NSAIDs especially gastrointestinal bleeding and perforation which may be.

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

Cardiovascular, Renal and Hepatic impairment: The administration of an NSAID may cause a dose dependant 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.

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.

Reported clinical trial and epidemiological data suggest that use of some NSAIDs (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 mefenamic acid.

Patients with uncontrolled hypertension, congestive heart failure, established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with mefenamic acid 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 can interfere with platelet function, they should be used in caution in patients with intracranial haemorrhage and bleeding diathesis.

Gastrointestinal bleeding, ulceration and perforation: GI bleeding, ulceration or perforation, which can be fatal, has been reported with all NSAIDs at any time during treatment, with or without warning symptoms or a previous history of serious GI events. Smoking and alcohol use are added risk factors.

The risk of GI bleeding, ulceration or perforation is higher with increasing NSAID doses, in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation, and in the elderly. Combination therapy with protective agents (e.g. misoprostol or proton pump inhibitors) should be considered for patients at risk of GI bleeding such as the elderly, and also for patients requiring concomitant low dose aspirin, or other drugs likely to increase gastrointestinal risk (see below and 4.5).

Patients with a history of GI toxicity, particularly when elderly, should report any unusual abdominal symptoms (especially GI bleeding) particularly in the initial stages of treatment.

Caution should be advised in patients receiving concomitant medications which could increase the risk of gastrotoxicity or bleeding such as corticosteroids, anticoagulants such as warfarin, selective serotonin reuptake inhibitors or anti-platelet agents such as aspirin.

When GI bleeding or ulceration occurs in patients receiving mefenamic acid the treatment should be withdrawn.

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. Patients appear to be at highest risk of these

reactions early in the course of therapy, the onset of the reaction occurring in the majority of cases within the first month of treatment. Mefenamic acid should be stopped at the first appearance of skin rash, mucosal lesions or any other sign of hypersensitivity.

Female fertility: The use of mefenamic acid 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 mefenamic acid should be considered.

In dysmenorrhoea and menorrhagia lack of response should alert the physician to investigate other causes.

Epilepsy: Caution should be exercised when treating patients suffering from epilepsy.

Sunset yellow may cause allergic-type reactions.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

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.

4.5 Drugs interactions

Tranexamic Acid will counteract the thrombolytic effect of fibrinolytic preparations.

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. 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 Ponstan 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.

Antidepressants: selective serotonin reuptake inhibitors (SSRIs): increased risk of gastrointestinal bleeding.

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.

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: increased the risk of gastrointestinal ulceration or bleeding.

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 Use in special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)

Tranexamic Acid

Pregnancy
Although there is no evidence from animal studies of a teratogenic effect, the usual caution with use of drugs in pregnancy should be observed.

Tranexamic acid crosses the placenta.

Lactation
Tranexamic acid passes into breast milk to a concentration of approximately one hundredth of the concentration in the maternal blood. An antifibrinolytic effect in the infant is unlikely.

Mefenamic Acid

Pregnancy
Congenital abnormalities have been reported in association with NSAID administration in man; however, these are low in frequency and do not appear to follow any discernible pattern. In view of the known effects of NSAIDs on the foetal cardiovascular system (risk of closure of the ductus arteriosus), use in the last trimester of pregnancy is contraindicated. The onset of labour may be delayed and the duration increased with an increased bleeding tendency in both mother and child. NSAIDs should not be used during the first two trimesters of pregnancy or labour unless the potential benefit to the patient outweighs the potential risk to the foetus.

Lactation
Trace amounts of mefenamic acid may be present in breast milk and transmitted to the nursing infant. Therefore, mefenamic acid should not be taken by nursing mothers.

See section Special warnings and precautions for use regarding female fertility

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. If affected, patients should not drive or operate machinery.

4.8 Undesirable effects

Tranexamic Acid
Adverse events are listed below by system organ class and frequency. Frequencies are defined as: very common (≥1/l0), common (≥1/100 and <1/10), uncommon (≥1/1000 and <1/100), rare (≥ 1/10,000 and <1/1000) and very rare (<1/10,000) including isolated reports, not known (cannot be estimated from the available data).

Immune system disorders
Very rare: Hypersensitivity reactions including anaphylaxis

Eye disorders
Rare: Colour vision disturbances, retinal/artery occlusion

Vascular disorders
Rare: Thromboembolic events
Very rare: Arterial or venous thrombosis at any sites

Gastro-intestinal disorders
Very rare: Digestive effects such as nausea, vomiting and diarrhoea, may occur but disappear when the dosage is reduced.

Skin and subcutaneous tissue disorders
Rare: Allergic skin reactions

Nervous system disorders
Frequency not known (cannot be estimated from the available data): Convulsions/Seizures, particularly in cases of misuse

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 nutritional disorders

Glucose intolerance in diabetic patients, hyponatraemia.

Pyschiatric 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.
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.

Reported 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.

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.

Hepato-bilary 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

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 side effects**
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at: http://www.torrentpharma.com/Index.php/site/info/adverse_event_reporting.

4.9 Overdose
It is important that the recommended dose is not exceeded and the regime adhered to

(a) Symptoms
Symptoms include headache, nausea, vomiting epigastric pain, gastrointestinal bleeding, rarely diarrhoea, orthostatic symptoms and/or hypotension, disorientation, excitation, coma, drowsiness, tinnitus, fainting, occasionally convulsions [Mefenamic acid has a

tendency to induce tonic-clonic (grand mal) convulsions in overdose]. In cases of significant poisoning acute renal failure and liver damage are possible.

(b) Therapeutic measure
Patients should be treated symptomatically as required.

Within one hour of ingestion of a potentially toxic amount activated charcoal should be considered. Alternatively, in adults gastric lavage should be considered within one hour of ingestion of a potentially life-threatening overdose.

Good urine output should be ensured

Renal and liver function should be closely monitored.
Patients should be observed for at least four hours after ingestion of potentially toxic amounts

Frequent or prolonged convulsions should be treated with intravenous diazepam.
Other measures may be indicated by the patient's clinical condition.

Haemodialysis is of little value since mefenamic acid and its metabolites are firmly bound to plasma proteins.

5. Pharmacological properties

5.1 Mechanism of Action

Tranexamic Acid
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.

Mefenamic Acid
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.

5.2 Pharmacodynamic properties

Tranexamic Acid
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
Mefenamic acid is non-steroidal anti-inflammatory drug (NSAID) with 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 carrageenin 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.

5.3 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 crosses 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.

Metabolism

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.

6. Nonclinical properties

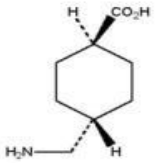
6.1 Animal Toxicology or Pharmacology

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.

7. Description

Tranexamic Acid

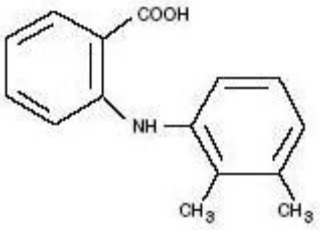
Tranexamic acid tablets are an antifibrinolytic drug. The chemical name is trans-4-aminomethyl-cyclohexanecarboxylic acid. The structural formula is:



Tranexamic acid is a white of almost white crystalline powder. It is freely soluble in water and in glacial acetic acid and is very slightly soluble in ethanol and practically insoluble in ether. The molecular formula is $C_8H_{15}NO_2$ and the molecular weight is 157.2.

Mefenamic Acid

Mefenamic Acid is a member of the fenamate group of nonsteroidal anti- inflammatory drugs (NSAIDs). The chemical name is N-(2,3-xylyl)anthranilic acid. The molecular weight is 241.3. Its molecular formula is $C_{15}H_{15}NO_2$ and the structural formula of mefenamic acid is:



Mefenamic acid is white to greyish white, microcrystalline powder. It is sparingly soluble in ether; slightly soluble in ethanol (95 percent) and in chloroform; practically insoluble in water.

Tranexamic Acid and Mefenamic Acid Tablets are yellow to light yellow colored smooth, capsule shaped film coated tablet with break line on one side and plain on other side. The excipients used are Microcrystalline Cellulose, Starch, Polyvinyl Pyrrolidone, Colloidal Silicon Dixoide, Propylene Glycol, Sodium Lauryl Sulfate, Croscarmellose Sodium, Magnesium Stearate, Colour Coat FC4WQ260109 yellow.

8. Pharmaceutical particulars

8.1 Incompatibilities

None known

8.2 Shelf-life

Do not use later than the date of expiry.

8.3 Packaging information

Xamic MF is available as strip pack of 10 tablets.

8.4 Storage and handing instructions

Store in a dry place at a temperature not exceeding 25°C. Protect from light.

9. Patient Counselling Information

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

• Keep this leaflet. You may need to read it again.

• If you have any further questions, ask your doctor or pharmacist.

• This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.

• If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 9.4.

What is in this leaflet:

9.1 What Xamic MF is and what it is used for

Xamic MF contains the active substance tranexamic acid which belongs to a group of medicines called anti-fibrinolytic drugs and Mefenamic acid belonging to the group of medicines called Non-steroidal Anti-inflammatory Drugs (NSAIDs). These are used For the treatment of primary dysmenorrhoea and pain associated with menorrhagia in women.

9.2 What you need to know before you use Xamic MF Tablets.

❖ **Do not take Xamic MF if:**

- You are allergic to tranexamic acid or Mefenamic acid or other non-steroidal anti-inflammatory drugs (aspirin, ibuprofen) or any of the other ingredients of this medicine
- You have serious problems with your kidneys (kidney failure)
- You have or have ever had a blood clot in your blood vessels (called a `thrombosis').
- You have a history of convulsions
- You are at risk of excessive bleeding as a result of a bleeding disorder called consumption coagulopathy
- You have or had a history of gastrointestinal bleeding or perforation or ulcer, related to previous NSAIDs therapy.
- You are in the last trimester of pregnancy
- You had coronary artery bypass graft (CABG) surgery.

If any of the above applies to you talk to your doctor or pharmacist.

Warnings and precautions
Talk to your doctor or pharmacist before taking Xamic MF if:
- You are already taking any type of painkiller
- You have blood in your urine
- You have ever had any uncontrollable bleeding
- You have disseminated intravascular coagulation (DIC), a disease where your blood starts to clot throughout your body
- You have been taking medicine to treat a hereditary disease called angioneurotic oedema (HANO) every day for a long time. If so, you may need to have regular eye tests and blood tests to check your liver is working properly
- You are a woman with irregular periods
- You are attempting to conceive or undergoing investigation for infertility.
- You or your family have a history of blood clots in your blood vessels (called a `thrombosis')
- Anyone in your family has suffered from blood clots in their blood vessels
- You have kidney, heart or liver disease.
- You have frequent or daily headaches despite (or because of) the regular use of headache medications.
- You are an elderly
- You are suffering from or have a history of bronchial asthma
- You have kidney, heart or liver diseases.
- You have a diseases which cause inflammation of connective tissues (called systemic lupus erythematosus), Steven Johnson Syndrome, toxic epidermal necrolysis
- You are or suspected to be poor CYP2C9 metaboliser.

Other medicines and Xamic MF
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, in particular the following:
- Fibrinolytic drugs (used to help dissolve blood clots), such as streptokinase. This is because Xamic MF will stop these drugs working
- Oral contraceptives. These may increase the risk of blood clots forming
- Anticoagulants (medicines that help prevent blood clots), Antiplatelet agents and Anti-depressants (medicines that help relieve the symptoms of depression). This may increase the risk of bleeding
- ACE inhibitors and angiotensin-II-receptor antagonists (medicines used to lower the blood pressure), Tacrolimus and Aminoglycosides (antibiotics) as it may not be good for your kidney
- Lithium
- Cardiac glycosides like Digoxin
- Corticosteroids (like bethamethasone, prednisone, prednisolone)
- Medicines for diabetes (high blood sugar)
- Methotrexate
- Mifepristone (used to bring about an abortion during pregnancy)
- Probenecid
- Quinolone antibiotics (like ciprofloxacin, ofloxacin, sparfloxacin)
- Zidovudine

Pregnancy, breast-feeding and fertility
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

9.3 How to use Xamic MF Tablets

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Important:
Your doctor will choose the dose that is right for you. Your dose will be shown clearly on the label that your pharmacist puts on your medicine. If it does not, or you are not sure, ask your doctor or pharmacist.

Remember: Your medicine should always be taken with a glass of water. The tablets should be swallowed whole. Do not crush or chew them.

If you take more Xamic MF than you should
If you accidentally take too much of your medicine, immediately tell your doctor or go to the nearest hospital casualty department.
Taking too much Xamic MF may make you feel sick, be sick or be dizzy or light-headed upon standing.

If you forget to take Xamic MF
Do not take a double dose to make up for a missed dose. Simply take the next dose as planned.

If you have any further questions about the use of this medicine, ask your doctor or pharmacist.

9.4 Possible Side Effects

Like all medicines Xamic MF can cause side effects, although not everybody gets them.

Eye disorders
– Problems with your eyesight, especially your colour vision
– A blood clot in your eye. This may cause bleeding in the eye, or a loss of vision

Immune system disorders
– this includes allergic reactions which cause difficulty in breathing or dizziness

Vascular disorders
– A blood clot in your blood vessels (called a `thrombosis')
– Fluid retention/build-up of fluid in the body (called as 'oedema')
– Fluctuations in blood pressure (called as 'hypertension' and 'hypotension')
– Heart Failure

Gastrointestinal disorders
– Feeling sick
– Being sick
– Diarrhoea
– Bleeding, perforation and peptic ulcers and dark sticky faeces (as a result of internal bleeding)
– Nausea and vomiting
– Flatulence
– Constipation
– Indigestion
– Abdominal Pain
– Inflamed pancrease

These are usually mild and pass very quickly, but if they continue, tell your doctor or pharmacist.

Hepato-biliary disorders
– Elevation of liver enzymes and other liver diseases
– Decrease in bile flow

Renal and urinary disorders

–Excretion of red blood cells and protein in the urine and burning sensation
–Kidney failure

Metabolism and nutritional disorders
Increased blood glucose and low level of sodium in the blood

Pyschiatric disorders
Confusion, depression, hallucinations, nervousness

Skin and subcutaneous tissue disorders
– Itchy, red or swollen skin

Nervous system disorders
– Convulsions, particularly in cases of misuse

Ear and labyrinth disorders
– Ear pain, tinnitus (ringing in ear), vertigo.

Respiratory, thoracic and mediastinal disorders
– Asthma or difficulty breathing.

- **Reporting of side effects**

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at: http://www.torrentpharma.com/Index.php/site/info/adverse_event_reporting.

9.5 How to store Xamic MF Tablets

Keep out of the sight and reach of children. Do not take this medicine after the expiry date shown on the strip and carton after EXP. The expiry date refers to the last day of that month. Store in a dry place at a temperature not exceeding 25°C. Protect from light. Medicines should not be disposed of via household wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help protect the environment.

9.6 Contents of the pack and other information

What Xamic MF Tablets contains:

The active substance in this product is Tranexamic Acid and Mefenamic Acid.

The other ingredients are Microcrystalline Cellulose, Starch, Polyvinyl Pyrrolidone, Colloidal Silicon Dixoide, Propylene Glycol, Sodium Lauryl Sulfate, Croscarmellose Sodium, Magnesium Stearate, Colour Coat FC4WQ260109 yellow.

10. Details of manufacturer

Manufactured by:
Acme Generics LLP.,
Plot No. 115, HPSIDC Industrial Area, Davni, P.O. Gurumajra,
Tehsil Nalagarh, Dist. Solan, Himachal Pradesh – 174 101.

11. Details of permission or licence number with date

Mfg Lic No. MNB/15/880 issued on 28.09.2015.

12. Date of revision

Aug 2019

MARKETED BY

TORRENT PHARMACEUTICALS LTD.

IN/XAMIC MF 500mg,250mg/Aug-2019/02/PI