Not to be sold by retail without the prescription of a Registered Medical Practitioner

Mefenamic Acid and Paracetamol Tablets
MEFTAL-FORTE® Tablets

Paracetamol: Box Warning About Its Liver Toxicity

Taking more than daily dose may cause serious liver damage or allergic reactions (e.g., swelling of the face, mouth and throat, difficulty in breathing, itching or rash). The risk of liver injury primarily occurs when patient take multiple products containing paracetamol/acetaminophen at one time and exceed the current maximum dose of 4,000 mg within a 24-hour period.

COMPOSITION
Each uncoated tablet contains:
Mefenamic Acid IP ……..… 500 mg.
Paracetamol IP ……..… 325 mg.

DOSAGE FORM
Tablets.

INDICATIONS
MEFTAL-FORTE Tablets are indicated for the symptomatic relief of mild to moderate pain in following conditions:

- Headache.
- Migraine.
- Dental pain.
- Post-operative pain.
- Post-partum pain.
- Pain associated with acute musculoskeletal disorders such as sprains and strains.
- Muscular and traumatic pain.
- Low back pain.

DOSE AND METHOD OF ADMINISTRATION
For Oral Administration in Adults and Adolescents: 1 tablet of MEFTAL-FORTE to be administered three times daily.
Therapy should not be given for longer than 7 days at a time. Do not exceed the stated dose.
MEFTAL-FORTE Tablets should be taken preferably with or after food.
Or, as prescribed by the physician.

USE IN SPECIAL POPULATIONS

Pregnant Women

Mefenamic Acid: Pregnancy Category C; Paracetamol: Pregnancy Category B.

For this combination product, there are no adequate or well controlled studies available in pregnant women. Epidemiological studies in human pregnancy have shown no ill effects due to paracetamol used in the recommended dosage. Congenital abnormalities have been reported with use of non-steroidal anti-inflammatory drugs (NSAIDs) in humans. NSAIDs are also known to produce effect on the foetal cardiovascular system (i.e., risk of premature closure of the ductus arteriosus). Thus, MEFTAL-FORTE Tablets are contraindicated for use in third trimester of pregnancy. When used during labour, the onset of labour may be delayed and the duration increased with an increased bleeding tendency in both mother and child. Thus, MEFTAL-FORTE Tablets should not be used during the first two trimesters of pregnancy or labour unless the potential benefit to the patient outweighs the possible risk to the fetus.

Lactating Women

Trace amounts of mefenamic acid may be present in breast milk and transmitted to the nursing infant. But, the risk to the infants seems to be limited. Paracetamol is excreted in breast milk, but not in clinically significant amounts. Available published data does not contraindicate use of paracetamol while breast-feeding. Thus, MEFTAL-FORTE Tablets are usually compatible with breast-feeding.

Paediatric Patients

MEFTAL-FORTE Tablets are not intended for use in children as there is no feasibility of dosage adjustments. Mefenamic acid is not recommended in children below 6 months of age. In recommended dosage, paracetamol is usually safe in children. It is advised that children under 12 years of age should use paediatric formulations of these drugs.

Geriatric Patients

The elderly patients have an increased frequency of adverse reactions to NSAIDs especially gastrointestinal (GI) bleeding and perforation which may be fatal. Thus, as like other NSAIDs, caution should be exercised while use of mefenamic acid in elderly population (> 65 years).

Elderly patients with normal renal function may be given the same dose as recommended for adults. Both, mefenamic acid and paracetamol are mainly excreted by the kidney, and the risk of toxic reactions to these drugs may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

Renal Impairment Patients

MEFTAL-FORTE Tablets should not be administered to patients with preexisting renal disease or in patients with significantly impaired renal function.

Hepatic Impairment Patients
MEFTAL-FORTE Tablets should not be administered in patients with severe hepatic impairment.

CONTRAINDICATIONS
MEFTAL-FORTE Tablets are contraindicated in the following:

- Known or suspected hypersensitivity to mefenamic acid or to paracetamol or to any component of this formulation.
- Pre-existing asthma and aspirin-sensitive asthma.
- Active ulceration/bleeding or chronic inflammation of upper or lower GI tract.
- Pre-existing renal disease/obstructive uropathy.
- Last trimester of pregnancy.
- Treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery.

WARNINGS AND PRECAUTIONS
Mefenamic Acid

Cardiovascular Thrombotic Events: Clinical trials of several COX-2 selective and nonselective NSAIDs of up to 3 years duration have shown an increased risk of serious cardiovascular (CV) thrombotic events, myocardial infarction (MI), and stroke, which can be fatal. All NSAIDs, both COX-2 selective and nonselective, may have a similar risk. Patients with known CV disease or risk factors for CV disease may be at greater risk. To minimize the potential risk for an adverse CV event in patients treated with an NSAID, the lowest effective dose should be used for the shortest duration possible. Physicians and patients should remain alert for the development of such events, even in the absence of previous CV symptoms. Patients should be informed about the signs and/or symptoms of serious CV events and the steps to take if they occur.

Hypertension: NSAIDs, including mefenamic acid, can lead to onset of new hypertension or worsening of pre-existing hypertension, either of which may contribute to the increased incidence of CV events. Patients taking thiazides or loop diuretics may have impaired response to these therapies when taking NSAIDs. NSAIDS, including mefenamic acid, should be used with caution in patients with hypertension. Blood pressure should be monitored closely during the initiation of NSAID treatment and throughout the course of therapy.

Congestive Heart Failure and Edema: Fluid retention and edema have been observed in some patients taking NSAIDs. Mefenamic acid should be used with caution in patients with fluid retention or heart failure.

Gastrointestinal Effects - Risk of Ulceration, Bleeding, and Perforation: NSAIDs, including mefenamic acid, can cause serious gastrointestinal (GI) adverse events including inflammation, bleeding, ulceration, and perforation of the stomach, small intestine, or large intestine, which can be fatal. These serious adverse events can occur at any time, with or without warning symptoms, in patients treated with NSAIDs. NSAIDs should be prescribed with extreme caution in those with a prior history of ulcer disease or GI bleeding. Patients with a prior history of peptic ulcer disease

and/or GI bleeding who use NSAIDs have a greater than 10-fold increased risk for developing a GI bleed compared to patients with neither of these risk factors. Other factors that increase the risk for GI bleeding in patients treated with NSAIDs include concomitant use of oral corticosteroids or anti-coagulants, longer duration of NSAID therapy, smoking, consuming alcohol, older age, and poor general health status. Most spontaneous reports of fatal GI events are in elderly or debilitated patients and therefore, special care should be taken in treating this population. To minimize the potential risk for an adverse GI event in patients treated with an NSAID, the lowest effective dose should be used for the shortest possible duration. Patients and physicians should remain alert for signs and symptoms of GI ulceration and bleeding during NSAID therapy and promptly initiate additional evaluation and treatment if a serious GI adverse event is suspected. This should include discontinuation of the NSAID until a serious GI adverse event is ruled out. For high risk patients, alternate therapies that do not involve NSAIDs should be considered.

Hepatic Effects: Borderline elevations of one or more liver tests may occur in up to 15% of patients taking NSAIDs, including mefenamic acid. These laboratory abnormalities may progress, may remain unchanged, or may be transient with continuing therapy. Notable elevations of ALT or AST (approximately 3 or more times the upper limit of normal - ULN) have been reported in approximately 1% of patients in clinical trials with NSAIDs. In addition, rare cases of severe hepatic reactions, including jaundice and fatal fulminant hepatitis, liver necrosis and hepatic failure, some of them with fatal outcomes have been reported. A patient with symptoms and/or signs suggesting liver dysfunction, or in whom an abnormal liver test has occurred, should be evaluated for evidence of the development of a more severe hepatic reaction while on therapy with mefenamic acid. If clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g., eosinophilia, rash, etc.), mefenamic acid should be discontinued.

Renal Effects: Long-term administration of NSAIDs has resulted in renal papillary necrosis and other renal injuries. Renal toxicity has also been seen in patients in whom renal prostaglandins have a compensatory role in the maintenance of renal perfusion. In these patients, administration of a NSAID may cause a dose-dependent reduction in prostaglandin formation and, secondarily, in renal blood flow, which may precipitate overt renal decompensation. Patients at greatest risk of this reaction are those with impaired renal function, heart failure, liver dysfunction, those taking diuretics and ACE inhibitors, and the elderly. Discontinuation of NSAID therapy is usually followed by recovery to the pretreatment state. No information is available for controlled studies regarding the use of mefenamic acid in patients with advanced renal disease. Therefore, treatment with mefenamic acid is not recommended in these patients with advanced renal disease.

Anaphylactoid Reactions: As with other NSAIDs, anaphylactoid reactions may occur in patients without known prior exposure to mefenamic acid. Mefenamic acid should not be given to patients with the aspirin triad. This symptom complex typically occurs in asthmatic patients who experience rhinitis with or without nasal polyps, or who exhibit severe, potentially fatal bronchospasm after taking aspirin or other NSAIDs. Emergency help should be sought in cases where an anaphylactoid reaction occurs.

Skin Reactions: NSAIDs, including mefenamic acid, can cause serious cutaneous adverse events such as exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, which can be fatal. These serious events may occur without warning. Patients should be informed about the signs and symptoms of serious skin manifestations and use of the drug should be discontinued at the first appearance of skin rash or any other sign of hypersensitivity.

Hematological Effects: Anemia is sometimes seen in patients receiving NSAIDs, including mefenamic acid. This may be due to fluid retention, GI blood loss, or an incompletely described effect upon erythropoiesis. Patients on long-term treatment with NSAIDs, including mefenamic acid, should have their hemoglobin or hematocrit checked if they exhibit any signs or symptoms of anemia. NSAIDs inhibit platelet aggregation and have been shown to prolong bleeding time in some patients. Unlike aspirin, their effect on platelet function is quantitatively less, of shorter duration, and reversible. Patients receiving mefenamic acid who may be adversely affected by alterations in platelet function, such as those with coagulation disorders or patients receiving anticoagulants, should be carefully monitored.

Preexisting Asthma: Patients with asthma may have aspirin-sensitive asthma. The use of aspirin in patients with aspirin-sensitive asthma has been associated with severe bronchospasm which can be fatal. Since cross reactivity, including bronchospasm, between aspirin and other NSAIDs has been reported in such aspirin-sensitive patients, mefenamic acid should not be administered to patients with this form of aspirin sensitivity and should be used with caution in patients with preexisting asthma.

Drug/Laboratory Test Interactions: Mefenamic acid may prolong prothrombin time. Therefore, when the drug is administered to patients receiving oral anticoagulant drugs, frequent monitoring of prothrombin time is necessary. A false-positive reaction for urinary bile, using the diazo tablet test, may result after mefenamic acid administration. If biliuria is suspected, other diagnostic procedures, such as the Harrison spot test, should be performed.

Effects on Ability to Drive and Use Machines: Undesirable effects such as dizziness, drowsiness, fatigue, and visual disturbances are possible after taking NSAIDs including mefenamic acid. If affected, patients should not drive or operate machinery.

Paracetamol

Significant overdosage of paracetamol can lead to hepatotoxicity in some patients. Thus, do not exceed the recommended dose. The hazards of overdose are greater in those with non-cirrhotic alcoholic liver disease.

Chronic heavy alcohol abusers may be at increased risk of liver toxicity from excessive paracetamol use, although rarely.

Do not take with any other paracetamol-containing products, so as to avoid the chances of overdosage.

Care is advised in the administration of paracetamol to patients with severe renal or severe hepatic impairment.

DRUG INTERACTIONS

Mefenamic Acid

A number of compounds are inhibitors of CYP2C9. Drug interactions studies of mefenamic acid and these compounds have not been conducted. The possibility of altered safety and efficacy should be considered when mefenamic acid is used concomitantly with these drugs.

ACE-Inhibitors: Reports suggest that NSAIDs may diminish the antihypertensive effect of angiotensin converting enzyme (ACE) inhibitors. This interaction should be given consideration in patients taking NSAIDs concomitantly with ACE-inhibitors.

Aspirin/NSAID: When mefenamic acid is administered with aspirin, its protein binding is reduced, although the clearance of free mefenamic acid is not altered. The clinical significance of this interaction is not known. However, as with other NSAIDs, concomitant administration of mefenamic acid and aspirin or any other NSAID is not generally recommended because of the potential of increased adverse effects.

Diuretics: Clinical studies, as well as observations during the post-approval period, have shown that mefenamic acid can reduce the natriuretic effect of furosemide and thiazides in some patients. This response has been attributed to inhibition of renal prostaglandin synthesis. During concomitant therapy of NSAIDs, the patient should be observed closely for signs of renal failure, as well as to assure diuretic efficacy.

Lithium: NSAIDs have produced an elevation of plasma lithium levels and a reduction in renal lithium clearance. The mean minimum lithium concentration increased 15% and the renal clearance decreased by approximately 20%. These effects have been attributed to inhibition of renal prostaglandin synthesis by the NSAID. Thus, when NSAIDs and lithium are administered concurrently, subjects should be observed carefully for signs of lithium toxicity.

Methotrexate: NSAIDs have been reported to competitively inhibit methotrexate accumulation in rabbit kidney slices. This may indicate that they could enhance the toxicity of methotrexate. Caution should be used when NSAIDs are administered concomitantly with methotrexate.

Warfarin: The effects of warfarin and NSAIDs on GI bleeding are synergistic, such that users of both drugs together have a risk of serious GI bleeding higher than users of either drug alone.

Antacids: In a single dose study, ingestion of an antacid containing 1.7 gram of magnesium hydroxide with 500 mg of mefenamic acid, resulted in the C_{max} and AUC of mefenamic acid increasing by 125% and 36%, respectively.

Aminoglycosides (Amikacin, Tobramycin, Gentamicin etc.): NSAIDs/mefenamic acid increases plasma concentration of aminoglycosides by decreasing its renal clearance. Also, reduction in renal function (in susceptible individuals) decreases elimination of aminoglycosides and increases its serum levels. Monitor serum aminoglycosides levels whenever mefenamic acid is used concomitantly.

Cardiac Glycosides (Digoxin): NSAIDs may exacerbate cardiac failure, reduces GFR and increases plasma cardiac glycoside levels. Further, concomitant use of mefenamic acid with digoxin has been reported to increase the serum concentration and prolong the half-life of digoxin. Thus, during concomitant use of mefenamic acid and digoxin, monitor serum digoxin levels.

Oral Hypoglycaemic Agents: NSAIDs may inhibit metabolism of sulfonylurea drugs, thereby prolongs half-life and increases risk of hypoglycaemia. Thus, caution should be exercised while administration of mefenamic acid and sulfonylurea drugs (such as glimepiride, gliclazide, glibenclamide etc.) concomitantly.

Antiplatelet Drugs: NSAIDs can interfere with platelet function; thus, administration of mefenamic acid with antiplatelet drugs (such as aspirin or clopidogrel) may increase risk of GI ulceration or bleeding. When GI bleeding or ulceration occurs, mefenamic acid therapy should be withdrawn.

Ciclosporin: Concomitant use of mefenamic acid and ciclosporin may increase risk of nephrotoxicity associated with ciclosporin. During concomitant use of mefenamic acid and ciclosporin, monitor patients for signs of worsening renal function.

Corticosteroids: Concomitant use of NSAIDs with corticosteroids increases risk of GI ulceration or bleeding. When GI bleeding or ulceration occurs, mefenamic acid therapy should be withdrawn immediately.

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

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: When NSAIDs are given with tacrolimus, risk of nephrotoxicity increases. Thus, when mefenamic acid and ciclosporin are used concomitantly, renal function should be monitored.

Zidovudine: There is 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.

Paracetamol

Cholestyramine: The speed of absorption of paracetamol is reduced by cholestyramine. Therefore, cholestyramine should not be taken within one hour, if maximal analgesia is required.

Metoclopramide and Domperidone: The absorption of paracetamol is increased by metoclopramide and domperidone. However, concurrent use need not be avoided.

Warfarin: The anti-coagulant effect of warfarin and other coumarins may be enhanced by prolonged regular use of paracetamol with increased risk of bleeding; occasional doses have no significant effect.

Chloramphenicol: Increased plasma concentration of chloramphenicol.

Alcohol, Anticonvulsants, and Isoniazid: Concomitant administration of alcohol, anticonvulsants, and isoniazid with paracetamol may increase risk of hepatotoxicity.

UNDESIRABLE EFFECTS

Mefenamic Acid

The most frequently reported side effects associated with mefenamic acid involve the gastrointestinal tract. Diarrhea occasionally occurs following the use of mefenamic acid.

Frequencies are not known for the following adverse reactions:

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. Nausea, vomiting, diarrhea, flatulence, constipation, dyspepsia, abdominal pain, malaena, hematemesis, 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 hemorrhage, pancreatitis, steatorrhea may occur.

Blood and Lymphatic System Disorders: Hemolytic anemia (reversible), hypoplastic bone marrow, decrease in hematocrit, thrombocytopenic purpura, temporary lowering of white blood cell count (leukopenia) with a risk of infection, sepsis, and disseminated intravascular coagulation. Agranulocytosis, aplastic anemia, eosinophilia, neutropenia, pancytopenia, thrombocytopenia may occur.

Immune System Disorders: Hypersensitivity reactions have been reported following treatment with NSAIDs. These may consist of non-specific allergic reactions and anaphylaxis; respiratory tract reactivity comprising asthma, aggravated asthma, bronchospasm, or dyspnea; or, 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 may occur.

Pyschiatric Disorders: Confusion, depression, hallucinations, nervousness can develop, *albeit* rarely.

Nervous System Disorders: Optic neuritis, headaches, paresthesia, 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 have been reported. Blurred vision, convulsions, insomnia may occur.

Eye Disorders: Eye irritation, reversible loss of color vision, visual disturbances may occur.

Ear and Labyrinth Disorders: Ear pain, tinnitus, vertigo may occur.

Cardiac/Vascular Disorders: Edema, 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 (e.g., myocardial infarction or stroke). Palpitations and hypotension may occur.

Respiratory, Thoracic, and Mediastinal Disorders: Asthma, dyspnea have been reported.

Hepato-Bilary Disorders: Borderline elevations of one or more liver function tests, cholestatic jaundice have been reported. Mild hepatotoxicity, hepatitis, hepatorenal syndrome may occur.

Skin and Subcutaneous Tissue Disorders: Angioedema, laryngeal edema, erythema multiforme, face edema, 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, hematuria, nephrotic syndrome, non-oliguric renal failure (particularly in dehydration), proteinuria, renal failure including renal papillary necrosis.
General Disorders: Fatigue, malaise, multi-organ failure, pyrexia may occur.
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.

Paracetamol
Adverse effects of paracetamol are rare. However, hypersensitivity including skin rash may occur. There have been reports of blood dyscrasias including thrombocytopenia purpura, methemoglobenemia and agranulocytosis, but these were not necessarily causality related to paracetamol.

OVERDOSE

Mefenamic Acid
Symptoms: Symptoms following acute NSAID overdose are usually limited to lethargy, drowsiness, nausea, vomiting, and epigastric pain, which are generally reversible with supportive care. Mefenamic acid has a tendency to induce tonic-clonic (grand mal) convulsions in overdose. Gastrointestinal bleeding, hypertension, acute renal failure, respiratory depression and coma may occur, but are rare. Anaphylactoid reactions have been reported with therapeutic ingestion of NSAIDs, and may occur following an overdose.
Treatment: Patients should be managed by symptomatic and supportive care following an NSAID overdose. There are no specific antidotes. Emesis and/or activated charcoal (60 to 100 g in adults, 1 to 2 g/kg in children) and/or osmotic cathartic may be indicated in patients seen within 4 hours of ingestion with symptoms or following a large overdose (5 to 10 times the usual dose). Forced diuresis, alkalinization of urine, hemodialysis, or hemoperfusion may not be useful due to high protein binding.

Paracetamol
Symptoms: Ingestion of 5 gram or more of paracetamol may lead to liver damage. Symptoms of paracetamol overdose in the first 24 hours are pallor, nausea, vomiting, anorexia and abdominal pain. Liver damage may become apparent 12 to 48 hours after ingestion. Abnormalities of glucose metabolism and metabolic acidosis may occur. In severe poisoning, hepatic failure may progress to encephalopathy, hemorrhage, hypoglycaemia, cerebral edema, and death. Acute renal failure with acute tubular necrosis, strongly suggested by loin pain, hematuria and proteinuria, may develop even in the absence of severe liver damage. Cardiac arrhythmias and pancreatitis have been reported.

Management: Immediate treatment is essential in the management of paracetamol overdose. Treatment with activated charcoal should be considered if the overdose has been taken within 1 hour. Plasma paracetamol concentration should be measured at 4 hours or later after ingestion (earlier concentrations are unreliable). Treatment with N-acetylcysteine (FDA approved antidote) may be used up to 24 hours after ingestion of paracetamol. However, the maximum protective effect is obtained up to 8 hours post ingestion.

PHARMACODYNAMICS

Mefenamic Acid

Mefenamic acid belongs to the NSAID category which exhibit anti-inflammatory, analgesic, and antipyretic activities. The mechanism of action of mefenamic acid is related to prostaglandin inhibition. Prostaglandins are implicated in a number of disease processes including inflammation, modulation of the pain response, dysmenorrhea, menorrhagia, and pyrexia. Like all other NSAIDs, mefenamic acid inhibits the enzyme cyclooxygenase (COX) which is responsible for formation of prostaglandins. This results in a reduction in the rate of prostaglandin synthesis and reduced prostaglandin levels. Additionally, mefenamic acid also blocks the prostaglandin receptors to prevent the effects of preformed prostaglandins. i.e., it inhibits binding of PGE_2 to its receptors. Mefenamic acid therefore inhibits both, the synthesis and response to prostaglandins. Mefenamic acid has analgesic and antipyretic properties acting by both central and peripheral mechanisms. This dual site, double blockade mode of action of mefenamic acid is important in its clinical efficacy.

Paracetamol

Analgesic Effect: The mechanism of analgesic action of paracetamol has not been fully determined. Paracetamol may act predominantly by inhibiting prostaglandin synthesis in the central nervous system (CNS) and to a lesser extent, through a peripheral action by blocking pain-impulse generation. The peripheral action may also be due to inhibition of prostaglandin synthesis or inhibition of the synthesis or actions of other substances that sensitise pain receptors to mechanical or chemical stimulation.

Antipyretic Effect: Paracetamol probably produces antipyretic effect by acting centrally on the hypothalamic heat-regulation center to produce peripheral vasodilation resulting in increased blood flow through the skin, sweating and heat loss. The central action probably involves inhibition of prostaglandin synthesis in the hypothalamus.

PHARMACOKINETICS

Mefenamic Acid

Mefenamic acid is rapidly absorbed after oral administration. Peak plasma levels are attained in 2 to 4 hours. More than 90% of mefenamic acid is bound to plasma proteins, mainly albumin. Mefenamic acid is metabolized by cytochrome P450 enzyme [CYP2C9] to 3-hydroxymethyl mefenamic acid. Approximately 52% of a mefenamic acid dose is excreted into the urine and up to 20% of the dose is excreted by fecal route. The elimination half-life of mefenamic acid is approximately 2 hours.

Because both renal and hepatic excretions are significant pathways of elimination, dosage adjustments in patients with renal or hepatic dysfunction may be necessary.

Paracetamol

Paracetamol is readily absorbed from the GI tract with peak plasma concentrations occurring about 30 minutes to 2 hours after ingestion. Paracetamol is metabolized in the liver and excreted in the urine mainly as the glucuronide and sulphate conjugates. Less than 5% is excreted as unchanged paracetamol. The elimination half-life varies from about 1 to 4 hours. Plasma-protein binding is negligible at usual therapeutic concentrations but increases with increasing concentrations.

INCOMPATIBILITIES

None known.

SHELF-LIFE

Expiry date as mentioned on the product pack.

PACKAGING INFORMATION

10 Tablets per strip.

STORAGE AND HANDLING INSTRUCTIONS

Store protected from light and moisture.
Keep out of reach of children.

Last updated: March 2020.