Mefpar Leaflet
Size A6

MEFPAR® CAPLETS

Composition
Each caplet contains:
Paracetamol BP …….500mg
Mefenamic acid BP ……...250 mg

Pharmacology
Paracetamol, a para-aminophenol derivative, has analgesic and antipyretic properties and weak anti-inflammatory activity. Paracetamol inhibits prostaglandin biosynthesis in the central nervous system but not (or hardly) in the peripheral tissues. In any case, paracetamol only has minimal anti-inflammatory action compared to non-steroidal anti-inflammatory agents.
Mefenamic acid, an anthranilic acid derivative, is a member of the fenamate group of nonsteroidal anti-inflammatory drugs (NSAIDs). It exhibits anti-inflammatory, analgesic, and antipyretic activities. Similar to other NSAIDs, mefenamic acid inhibits prostaglandin synthetase. Mefenamic acid binds the prostaglandin synthetase receptors COX-1 and COX-2, inhibiting the action of prostaglandin synthetase. As these receptors have a role as a major mediator of inflammation and/or a role for prostanoid signaling in activity-dependent plasticity, the symptoms of pain are temporarily reduced.

Pharmacokinetics
Paracetamol is readily absorbed from the gastrointestinal tract with peak plasma concentrations occurring about 10 to 60 minutes after oral doses. Paracetamol is distributed into most body tissues. It crosses the placenta and is present in breast milk. Plasma-protein binding is negligible at usual therapeutic concentrations but increases with increasing concentrations. The elimination half-life of paracetamol varies from about 1 to 3 hours. Paracetamol is metabolised mainly in the liver and excreted in the urine mainly as the glucuronide and sulfate conjugates. Less than 5% is excreted as unchanged paracetamol. A minor hydroxylated metabolite (N-acetyl-p-benzoquinoneimine) is usually produced in very small amounts by cytochrome P450 isoenzymes (mainly CYP2E1 and CYP3A4) in the liver and kidney. It is usually detoxified by conjugation with glutathione but may accumulate following paracetamol overdosage and cause tissue damage.
Mefenamic acid is absorbed from the gastrointestinal tract. Peak plasma concentrations occur about 2 to 4 hours after ingestion. The plasma elimination half-life is reported to be 2 to 4 hours. Mefenamic acid is extensively bound to plasma proteins. It is distributed into breast milk. Mefenamic acid is metabolised by the cytochrome P450 isoenzyme CYP2C9 to 3-hydroxymethyl mefenamic acid which may then be oxidised to 3-carboxymefenamic acid. Over 50% of a dose may be recovered in the urine, as unchanged drug or conjugates of mefenamic acid and its metabolites.

Indication
Mefpar® is given by mouth for mild to moderate pain and for fever. It is often the analgesic or antipyretic of choice, especially in the elderly and in patients in whom salicylates or other NSAIDs are contra-indicated. Such patients include asthmatics, those with a history of peptic ulcer, and children. Mefpar is used in mild to moderate pain including headache, dental pain, postoperative and postpartum pain, and dysmenorrhoea, in musculoskeletal and joint disorders such as osteoarthritis and rheumatoid arthritis, in menorrhagia, and in children with fever and juvenile idiopathic arthritis

Dosage
The usual dose of Mefpar® by mouth is 1 caplet every 8 hours up to a maximum of 4 caplets daily.
It is recommended that it should not be given for longer than 7 days at a time.

Side Effects
The commonest side-effects of Mefpar® are generally gastrointestinal disturbances, such as gastrointestinal discomfort, nausea, and diarrhoea; these are usually mild and reversible but in some patients peptic ulceration and severe gastrointestinal bleeding may occur. It is generally agreed that the gastrointestinal effects of NSAIDs are due to inhibition of cyclo-oxygenase-1 (COX-1); the selective inhibition of COX-2 improves gastrointestinal tolerance.
CNS-related side-effects include headache, vertigo, dizziness, nervousness, tinnitus, depression, drowsiness, and insomnia. Hypersensitivity reactions may occur occasionally and include fever, angioedema, bronchospasm, and rashes. Hepatotoxicity and aseptic meningitis, which occur rarely, may also be hypersensitivity reactions. Some patients may experience visual disturbances.
Haematological adverse effects of Mefpar® include anaemias, thrombocytopenia, neutropenia, eosinophilia, and agranulocytosis. Unlike aspirin, inhibition of platelet aggregation is reversible with other NSAIDs.
Some NSAIDs have been associated with nephrotoxicity such as interstitial nephritis and nephrotic syndrome; renal failure may be provoked by NSAIDs especially in patients with pre-existing renal impairment. Haematuria has also occurred. Fluid retention may occur, rarely precipitating heart failure in elderly patients. Long-term use or abuse of analgesics, including NSAIDs, has been associated with nephropathy. Other adverse effects include photosensitivity. Alveolitis, pulmonary eosinophilia, pancreatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis are other rare adverse effects. Induction or exacerbation of colitis has also been reported.

Precautions
Mefpar® should be given with care to patients with impaired kidney or liver function. It should also be given with care to patients with alcohol dependence. It is also contra-indicated in patients with active peptic ulceration.

Interactions
Interactions involving Mefpar® include enhancement of the effects of oral anticoagulants (especially by azapropazone and phenylbutazone) and increased plasma concentrations of lithium, methotrexate, and cardiac glycosides. The risk of nephrotoxicity may be increased if given with ACE inhibitors, ciclosporin, tacrolimus, or diuretics. Effects on renal function may lead to reduced excretion of some drugs. There may also be an increased risk of hyperkalaemia with ACE inhibitors and potassium-sparing diuretics. The antihypertensive effects of some antihypertensives including ACE inhibitors, beta blockers, and diuretics may be reduced. Convulsions may occur due to an interaction with quinolones. NSAIDs may enhance the effects of phenytoin and sulfonylurea antidiabetics.
The risk of gastrointestinal bleeding and ulceration associated with NSAIDs is increased when used with corticosteroids, the SSRIs, the antiplatelets clopidogrel and ticlopidine, or, possibly, alcohol, bisphosphonates, or pentoxifylline. There may be an increased risk of haematotoxicity during concomitant use of zidovudine and NSAIDs. Ritonavir may increase the plasma concentrations of NSAIDs. The manufacturer of mifepristone advises of a theoretical risk that prostaglandin synthetase inhibition by NSAIDs or aspirin may alter the efficacy of mifepristone. There have been occasional reports of increased adverse effects when NSAIDs were given with misoprostol although such combinations have sometimes been used to decrease the gastrointestinal toxicity of NSAIDs.

Presentation
10X10 caplets in blister pack.

Storage
Store in a dry place below 30^{o}C, protected from light.
Keep out of reach of children.

Manufactured by:

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