℞ Misoprostol Tablets IP 200 mcg

Miso-Kare

Each uncoated tablet contains:
Misoprostol IP.....200 mcg.
(As 1% Misoprostol Dispersion)
Excipients.....q.s.

PHARMACOLOGICAL CLASSIFICATION:
Prostaglandin (PGE1) analogue

PHARMACODYNAMICS/ PHARMACOKINETICS:

Pharmacodynamics:
Misoprostol is a prostaglandin E1 (PGE1) analogue used for the treatment and prevention of stomach ulcers. When administered, misoprostol stimulates increased secretion of the protective mucus that lines the gastrointestinal tract and increases mucosal blood flow, thereby increasing mucosal integrity. It is sometimes co-prescribed with non-steroidal anti-inflammatory drugs (NSAIDs) to prevent the occurrence of gastric ulceration, a common adverse effect of the NSAIDs.

Pharmacokinetics:
Misoprostol is rapidly absorbed following oral administration, with peak plasma levels of the active metabolite (misoprostol acid) occurring after about 30 minutes. The plasma elimination half-life of misoprostol acid is 20-40 minutes. No accumulation of misoprostol acid in plasma occurs after repeated dosing of 400 micrograms twice daily.

INDICATIONS:
Misoprostol Tablets are indicated for the healing of duodenal ulcer and gastric ulcer including those induced by nonsteroidal anti-inflammatory drugs (NSAID) in arthritic patients at risk, whilst continuing their NSAID therapy. In addition, Misoprostol Tablets can be used for the prophylaxis of NSAID-induced ulcers.

RECOMMENDED DOSE:

Adults

Healing of duodenal ulcer, gastric ulcer and NSAID-induced peptic ulcer: 800 micrograms daily in two or four divided doses taken with breakfast and / or each main meal and at bedtime. Treatment should be given initially for at least 4 weeks even if symptomatic relief has been achieved sooner. In most patients ulcers will be healed in 4 weeks but treatment may be continued for up to 8 weeks if required. If the ulcer relapses further treatment courses may be given.

Prophylaxis of NSAID-induced peptic ulcer: 200 micrograms twice daily, three times daily or four times daily. Treatment can be continued as required. Dosage should be individualised according to the clinical condition of each patient.

Elderly
The usual dosage may be used.

Renal impairment: Available evidence indicates that no adjustment of dosage is necessary in patients with renal impairment.

Hepatic impairment: Misoprostol Tablets are metabolised by fatty acid oxidising systems present in organs throughout the body. Its metabolism and plasma levels are therefore unlikely to be affected markedly in patients with hepatic impairment.

Children
Use of Misoprostol Tablets in children has not yet been evaluated in the treatment of peptic ulceration or NSAID-induced peptic ulcer disease.

MODE OF ADMINISTRATION: Tablets for Oral administration

CONTRAINDICATIONS:

Misoprostol is contraindicated:
- In women who are pregnant, or in whom pregnancy has not been excluded, or who are planning a pregnancy as misoprostol increases uterine tone and contractions in pregnancy which may cause partial or complete expulsion of the products of conception. Use in pregnancy has been associated with birth defects
- In patients with a known hypersensitivity to misoprostol or to any other component of the product, or to other prostaglandins

WARNINGS & PRECAUTIONS:

Women of childbearing potential should not be started on misoprostol until pregnancy is excluded, and should be fully counselled on the importance of adequate contraception while undergoing treatment. If pregnancy is suspected, use of the product should be discontinued.

In such patients it is advised that Misoprostol Tablets should only be used if the patient:
- takes effective contraceptive measures
- has been advised of the risks of taking Misoprostol Tablets if pregnant

Gastrointestinal bleeding, ulceration, and perforation have occurred in NSAID-treated patients receiving misoprostol. Physicians and patients should remain alert for ulceration, even in the absence of gastrointestinal symptoms, and, where appropriate, endoscopy and biopsy should be carried out before use to ensure that malignant disease is absent in the upper gastrointestinal tract. These investigations and any others considered necessary by the clinician should be repeated at appropriate intervals for follow-up purposes.

Symptomatic responses to misoprostol do not preclude the presence of gastric malignancy.

Misoprostol should be used with caution in patients with conditions that predispose them to diarrhoea, such as inflammatory bowel disease. To minimise the risk of diarrhoea, misoprostol should be taken with food, and magnesium-containing antacids should be avoided.

Misoprostol should be used with caution in patients in whom dehydration would be dangerous. These patients should be monitored carefully. The results of clinical studies indicate that Misoprostol Tablet does not produce hypotension at dosages effective in

promoting the healing of gastric and duodenal ulcers. Nevertheless, Misoprostol Tablets should be used with caution in the presence of disease states where hypotension might precipitate severe complications, e.g. cerebrovascular disease, coronary artery disease or severe peripheral vascular disease including hypertension. There is no evidence that Misoprostol Tablet has adverse effect on glucose metabolism in human volunteers or patients with diabetes mellitus.

INTERACTIONS WITH OTHER MEDICINES:

Concomitant administration of NSAIDs and misoprostol in rare cases can cause a transaminase increase and peripheral oedema.

Misoprostol is predominantly metabolised via fatty acid oxidising systems and has shown no adverse effect on the hepatic microsomal mixed function oxidase (P450) enzyme system. In specific studies no clinically significant pharmacokinetic interaction has been demonstrated with antipyrine, diazepam. A modest increase in propranolol concentrations (mean approximately 20% in AUC, 30% in Cmax) has been observed with multiple dosing of misoprostol. In extensive clinical studies no drug interactions have been attributed to Misoprostol. Additional evidence shows no clinically important pharmacokinetic or pharmacodynamic interaction with nonsteroidal anti-inflammatory drugs including aspirin, diclofenac, ibuprofen, piroxicam, aspirin, naproxen or indomethacin.

Magnesium-containing antacids should be avoided during treatment with misoprostol as this may worsen the misoprostol-induced diarrhoea.

PREGNANCY AND LACTATION:

Pregnancy:
Misoprostol is contraindicated in women who are pregnant because it increases uterine tone and contractions in pregnancy which may cause partial or complete expulsion of the products of conception. Misoprostol is associated with premature births. First trimester exposure to misoprostol is associated with a significantly increased risk of two birth defects; Möbius sequence, i.e., palsies of cranial nerves VI and VII, and terminal transverse limb defects. Other defects including arthrogryposis have been observed.

Lactation:
Misoprostol is rapidly metabolized in the mother to misoprostol acid, which is biologically active and is excreted in breast milk. Misoprostol should not be administered to nursing mothers because the excretion of misoprostol acid could cause undesirable effects such as diarrhoea in nursing infants.

UNDESIRABLE EFFECTS:

Very Common: Diarrhoea, Rashes

Common: Dizziness, Headache, Abdominal pain, Constipation, Flatulence, Nausea, Vomiting

Uncommon: Pyrexia

Not Known: Anaphylactic reactions, Birth Defects, Incomplete abortion, Premature birth

Syncope has been infrequently reported.

The pattern of adverse events associated with Misoprostol is similar when an NSAID is given concomitantly.

Special Populations:
There were no significant differences in the safety profile of misoprostol in patients who were 65 years of age or older, compared with younger patients. The use of misoprostol in children has not yet been evaluated. A number of side effects have been reported in clinical studies or in the literature following use of misoprostol for non-approved indications. These include abnormal uterine contractions, uterine haemorrhage, uterine rupture/perforation, retained placenta, amniotic fluid embolism, incomplete abortion, premature birth, foetal death, and birth defects.

OVERDOSAGE AND TREATMENT:
Signs and Symptoms of Overdose. The toxic dose of misoprostol in humans has not been determined. Clinical signs that may indicate an overdose are sedation, tremor, convulsions, dyspnea, abdominal pain, diarrhoea, fever, palpitations, hypotension, or bradycardia.

Treatment of Overdose
Because misoprostol is metabolized like a fatty acid, it is unlikely that dialysis would be appropriate treatment for overdosage. In cases of overdose, standard supportive measures should be adopted as required. In clinical trials patients have tolerated 1200 micrograms daily for three months without significant adverse effects.

STORAGE CONDITION:
Store in a cool, dry & dark place.
Keep out of reach of children.

DOSAGE FORMS AND PACKAGING AVAILABLE:
Dosage Forms: Uncoated Tablets
Packaging: 1x4's Alu-Alu Blister pack

SHELF LIFE: 24 months.

Manufactured in India by :
Synokem Pharmaceuticals Ltd.
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Ranipur (BHEL), Haridwar - 249 403 (Uttarakhand)

A Quality Product Of:
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