1.3 Product Information

1.3.1 Summary of products characteristics (SmPC):

Enclosed.

1.0 NAME OF THE MEDICINAL PRODUCT

1.1 Brand Name: MISO-FEM

1.2 Generic Name: Misoprostol Tablets

1.3 Strength: 200 mcg

1.4 Pharmaceutical Form: Tablets

2.0 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Uncoated Tablet Contains:
Misoprostol Dispersion USP ……. 20 mg
(As 1% HPMC Dispersion)
Eq. to Misoprostol USP ……. 200 mcg
Excipients …….. q.s.

For a full list of excipients, see section 6.1

3.0 PHARMACEUTICAL FORM & DESCRIPTION

Uncoated Tablets
White to off-white, round, biconvex, scored on one side, plain on other side & uncoated tablets.

4.0 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Medical termination of intrauterine pregnancy up to 49 days of pregnancy. For the healing of duodenal and gastric ulcers, including those induced by nonsteroidal anti-inflammatory drugs (NSAIDs) in arthritis patients at risk, while continuing their NSAID treatment. In addition, can be used for the prophylaxis of ulcers induced by NSAIDs.

4.2 DOSAGE AND ADMINISTRATION

Medical termination of intrauterine pregnancy
Day 1: Taking mifepristone
Three 200 mg (600 mg) tablets of mifepristone are taken as a single oral dose.
Day 3: Taking misoprostol
The patient takes two 200 mcg (400 mcg) tablets by mouth.

Adults
Healing of duodenal ulcer, gastric ulcer and peptic ulcer induced by NSAIDs: 800 micrograms per day 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 obtained earlier.
Prophylaxis of peptic ulcer disease induced by NSAIDs: 200 micrograms twice a day, three times a day or four times a day. Treatment can be continued as needed.
The elderly
The usual dosage can be used.

Renal impairment: Available data indicate that no dose adjustment is necessary in patients

with renal impairment.

Hepatic Insufficiency: Misoprostol is metabolized by oxidative fatty acid systems found in organs of the body. Its metabolism and plasma concentrations are therefore unlikely to be markedly affected in patients with hepatic impairment.

Children:
Use in children has not yet been evaluated in the treatment of peptic ulceration or peptic ulcer disease induced by NSAIDs.

4.3 CONTRAINDICATIONS

Misoprostol is contraindicated:

- In women who are pregnant, or in whom pregnancy has not been ruled out, or who are planning to become pregnant because misoprostol increases uterine tone and pregnancy contractions which may lead to partial or complete expulsion of the fruits of conception. Use during pregnancy has been associated with birth defects.
- In patients with known hypersensitivity to misoprostol or other prostaglandins.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Women of childbearing potential should not start taking misoprostol until pregnancy is ruled out and should be fully informed about the importance of adequate contraception during treatment. If pregnancy is suspected, the use of the product should be discontinued.

In these patients, it is advisable to use only if the patient:

- takes effective contraceptive measures
- has been advised of the risks associated with taking Misoprostol in pregnancy.

Gastrointestinal bleeding, ulcerations and perforations have occurred in patients treated with NSAIDs receiving misoprostol. Doctors and patients should remain vigilant for ulceration, even in the absence of gastrointestinal symptoms, and an appropriate endoscopy and biopsy should be performed before use to check for any malignant growth in the area.

Symptomatic reactions to misoprostol do not exclude the presence of gastric malignancy. Misoprostol should be used with caution in patients with conditions that predispose them to diarrhea, such as inflammatory bowel disease. To minimize the risk of diarrhea, misoprostol should be taken with food and antacids containing magnesium should be avoided.
Misoprostol should be used with caution in patients in whom dehydration would be dangerous. These patients should be closely monitored.
Results from clinical studies indicate that misoprostol does not produce hypotension at doses effective to promote healing of gastric and duodenal ulcers. Nevertheless, misoprostol should be used with caution in the presence of medical conditions where hypotension could precipitate serious complications, for example cerebrovascular disease, coronary artery disease or severe peripheral vascular disease including hypertension.

4.5 DRUG INTERACTIONS

Co-administration of NSAIDs and misoprostol in rare cases may lead to increased transaminases and peripheral edema.

Misoprostol is primarily metabolized via fatty acid oxidizing systems and has shown no adverse effects on the enzyme system of mixed liver microsomal oxidase (P450). In specific studies, no clinically significant pharmacokinetic interaction has been demonstrated with antipyrine or diazepam. A slight increase in propranolol concentrations has been observed with the administration of multiple doses of misoprostol. In extensive clinical studies, no drug interactions have been attributed to misoprostol. Drug interaction studies with misoprostol and several NSAIDs have revealed no clinically significant effect on the kinetics of ibuprofen, diclofenac, piroxicam, aspirin, naproxen or indomethacin.

Antacids containing magnesium should be avoided during treatment with misoprostol, as this may worsen the diarrhea caused by misoprostol.

4.6 PREGNANCY AND LACTATION

Pregnancy

Misoprostol is contraindicated in pregnant women because it causes uterine contractions and is associated with abortion, premature birth, fetal death, and birth defects. Exposure to misoprostol during the first trimester is associated with a significantly increased risk of two birth defects: Möbius sequence (cranial nerve palsy VI and VII) and terminal transverse limb abnormalities. Other defects, including arthrogryposis, have been observed.

The risk of uterine rupture increases with advanced gestational age and with previous uterine surgery, including cesarean section. High multiparity also seems to be a risk factor for uterine rupture.

Feeding with milk

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

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Misoprostol can cause dizziness. Patients should be cautioned against using machines and driving a vehicle.

4.8 UNDESIRABLE EFFECTS

Dizziness, Headache, Diarrhea, Abdominal pain, Constipation, Dyspepsia, Flatulence, Nausea, Vomiting, Rash, Pyrexia.

4.9 OVERDOSE

Signs and symptoms of overdose

The toxic dose of misoprostol in humans has not been determined. Clinical signs which may indicate overdose are sedation, tremors, convulsions, dyspnea, abdominal pain, diarrhea, fever, palpitations, hypotension or bradycardia.

Treatment of overdose

Since misoprostol is metabolized as a fatty acid, dialysis is unlikely to be an appropriate treatment for overdose. In case of overdose, standard supportive measures should be adopted as needed.

In clinical trials, patients tolerated 1200 micrograms per day for three months without significant side effects.

5. PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Misoprostol is a natural prostaglandin E1 analogue that promotes healing of peptic ulcers and relief of symptoms. Misoprostol protects the gastroduodenal mucosa by inhibiting basal secretion, stimulated and nocturnal acid secretion and reducing the volume of gastric secretions, the proteolytic activity of gastric fluid and by increasing that of bicarbonates and mucus.

Misoprostol has also been shown to increase the amplitude and frequency of uterine contractions during pregnancy by selectively binding to prostanoid EP-2 / EP-3 receptors.

5.2 PHARMACOKINETIC PROPERTIES

Misoprostol is widely absorbed and undergoes rapid deesterification to its free acid, which is responsible for its clinical activity and, unlike the parent compound, is detectable in plasma. The alpha side chain undergoes beta oxidation and the beta side chain undergoes omega oxidation followed by ketone reduction to give prostaglandin F analogs. The compound is a lipophilic pro methyl ester drug and is readily metabolized to free acid, which is the biologically active form. The plasma elimination half-life of misoprostol acid is 20 to 40 minutes. No accumulation of misoprostol acid in plasma occurs after repeated administration of 400 micrograms twice daily.

5.3 PRECLINICAL SAFETY DATA

The toxicological safety profile of Misoprostol has been established in animal and human experiments from extensive clinical experience. There are no new preclinical data relevant to the prescriber in addition to the data already presented in this summary of product characteristics.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Filleraa- Ceftas
Corn starch
Microcrystalline cellulose (PH-102)
Colloidal anhydrous silica
Purified talc
Magnesium stearate

6.2 INCOMPATIBILITIES

No effect noted to date.

6.3 SHELF LIFE

24 months

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 30°C away from direct sunlight.

6.5 NATURE AND CONTENTS OF CONTAINER

1x4's: 1 blister containing 4 tablets are packed in a carton along with packaging insert.
10x4's: 1 blister containing 4 tablets are packed in a monocarton along with pack insert. 10 such monocartons are packed in an outercarton.
3x4's: 3 blisters containing 4 tablets each are packed in monocarton along with pack insert.
6x12's: 3 blisters containing 4 tablets each are packed in monocarton along with pack insert. 6 such monocartons are packed in an outercarton.
100x4's: 100 alu-alu blisters containing 4 tablets each are packed in a carton along with pack insert.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING

No special requirements.

7. MARKETING AUTHORIZATION HOLDER:

DKT International Nigeria

8. NAME AND ADDRESS OF THE MANUFACTURER

AKUMS DRUGS & PHARMACEUTICALS LTD.
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District: Haridwar, Uttarakhand, INDIA