SUMMARY OF PRODUCT CHARACTERISTICS

1 – NAME OF THE MEDICINAL PRODUCT

OVOID
(Misoprostol Tablets 200 mcg)

2 – QUALITY AND QUANTITATIVE COMPOSITION

Each uncoated tablet contains:

Misoprostol Dispersion USP (As 1% HPMC Dispersion)	20 mg
Eq. to Misoprostol USP	200 mcg
Excipients	q.s.

3 – PHARMACEUTICAL FORM

Uncoated Tablets.

4. CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS:

For the medical termination of intrauterine pregnancy through 49 days pregnancy.
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, can be used for the prophylaxis of NSAID-induced ulcers.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION

For the medical termination of intrauterine pregnancy

Day One: Mifepristone administration
Three 200 mg tablets (600 mg) of mifepristone are taken in a single oral dose.
Day Three: Misoprostol administration
The patient takes two 200 mcg tablets (400 mcg) orally.
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.

Prophylaxis of NSAID-induced peptic ulcer: 200 micrograms twice daily, three times daily or four times daily. Treatment can be continued as required.

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 is 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 in children has not yet been evaluated in the treatment of peptic ulceration or NSAID-induced peptic ulcer disease.

4.3 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 other prostaglandins.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

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 should only be used if the patient:

- takes effective contraceptive measures
- has been advised of the risks of taking Misoprostol 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 appropriate endoscopy and biopsy

should be carried out before use to ensure that malignant disease is absent in the upper gastrointestinal tract.

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 does not produce hypotension at dosages effective in promoting the healing of gastric and duodenal ulcers. Nevertheless, Misoprostol 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.

4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTIONS

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 or diazepam. A modest increase in propranolol concentrations has been observed with multiple dosing of misoprostol. In extensive clinical studies no drug interactions have been attributed to Misoprostol. Drug interaction studies with misoprostol and several NSAIDs showed no clinically significant effect on the kinetics of ibuprofen, diclofenac, piroxicam, aspirin, naproxen or indomethacin.

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

4.6 PREGNANCY AND LACTATION

Pregnancy

Misoprostol is contraindicated in women who are pregnant because it induces uterine contractions and is associated with abortion, premature birth, foetal death and birth defects. 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.

The risk of uterine rupture increases with advancing gestational age and with prior uterine surgery, including Caesarean delivery. Grand multiparity also appears to be a risk factor for uterine rupture.

Lactation

Misoprostol is rapidly metabolised 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.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Misoprostol can cause dizziness. Patients should be cautioned about operating machinery and driving.

4.8 UNDESIRABLE EFFECTS

Dizziness, Headache, Diarrhoea, 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 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.

5 - PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Misoprostol is an analogue of naturally occurring prostaglandin E1 which promotes peptic ulcer healing and symptomatic relief.

Misoprostol protects the gastroduodenal mucosa by inhibiting basal, stimulated and nocturnal acid secretion and by reducing the volume of gastric secretions, the proteolytic activity of the gastric fluid, and increasing bicarbonate and mucus secretion.

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

5.2 PHARMACOKINETIC PROPERTIES

Misoprostol is extensively absorbed, and undergoes rapid de-esterification 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 reduction of the ketone to give prostaglandin F analogs. The compound is a lipophilic methyl ester prodrug and is readily metabolized to the free acid, which is the biologically active form. 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.

5.3 PRECLINICAL SAFETY DATA

The toxicological safety profile of Misoprostol has been established in animal experiments and in humans from extensive clinical experience. There are no new preclinical data of relevance to the prescriber which are additional to the data already presented in this Summary of Product Characteristics.

6. PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Filleraa- Ceftas IH
Maize Starch BP
Microcrystalline Cellulose (PH-102) BP
Colloidal Anhydrous Silica BP
Purified Talc BP
Magnesium Stearate BP

6.2 INCOMPATIBILITIES

Not applicable

6.3 SHELF LIFE

24 Months

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 30^0C, protected from light and moisture

6.5 NATURE AND CONTENTS OF CONTAINER

10 Tablets packed in an Alu-Alu blister, 3 such blisters packed in a printed carton with pack insert.

6.6 SPECIAL PRECAUTION FOR DISPOSAL AND HANDLING

None

7. MARKETING AUTHORIZATION HOLDER

Unosource Pharma Ltd
Unit: 503-504, 5^{th} floor,
Hubtown Solaris,
N.S. Phadke Marg, Andheri (East)
Mumbai – 400 069, INDIA

8. MARKETING AUTHORIZATION NUMBERS

Not Applicable

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION

Not applicable.

10. DATE OF REVISION OF THE TEXT

Not applicable