COMPOSITION :

Etron Tablets :
Each uncoated dispersible tablet contains:
Ondansetron hydrochloride IP
Equivalent to Ondansetron……..4mg.
Excipients……q.s. Colour: Tartrazine.

Etron Syrup :

Each 5ml contains:
Ondansetron hydrochloride IP
Equivalent to Ondansetron…….2mg.
In a flavoured syrupy base q.s.
Colour: Sunset Yellow FCF

Ondansetron Hydrochloride is a selective 5HT3 receptor antagonist used in the management of nausea and vomiting induced by cytotoxic chemotherapy and radiotherapy and also postoperative nausea and vomiting. Adverse effects include headache and a sensation of flushing or warmth.

The active ingredient in Etron tab. And syrup is Ondansetron hydrochloride as the dihydrate, the racemic form of Ondansetron and a selective blocking agent of the serotonin 5-HT3 receptor type.

MECHANISM OF ACTION :

It causes antiemetic effect by blocking 5-HT3 receptors in brain and periphery.The onset of action is within 30 minutes in the oral preparations and the duration of action is 8-10 hrs.

PHARMACOLOGY :

PHARMACOKINETICS :
Ondansetron is well absorbed from the gastrointestinal tract and undergoes some first pass metabolism. It has a systemic bioavailability of about 60 % in healthy subject. It is extensively metabolized and about 5 % of the dose is recovered in urine as parent compound.

The primary metabolic pathway is hydroxylation on the indole ring followed by subsequent glucuronide or sulphate conjugation. It is excreted as metabolites in the feces and urine. In- vitro studies have shown that Ondansetron is a substrate for human hepatic cytochrom P- 450 enzymes. Ondansetron elimination may be affected by cytochrom P-450 inducers. In patients with mild to moderate hepatic impairment, clearance is reduced two fold and mean half life is increased to 11.6 hrs compared to 5.7 hrs in normals.

PHARMACODYNAMICS:
Ondansetron is a selective 5 HT3 receptor antagonist. While its mechanism of action has not been fully characterized, Ondansetron is not a dopamine-receptor antagonist.Serotonin receptors of the 5 HT3 type are present both peripherally on vagal nerve terminals and centrally in the chemoreceptor trigger zone (CTZ) of the area postrema. It is not certain whether ondansetron's antiemetic action is mediated centrally, peripherally, or in both sites.

However, cytotoxic chemotherapy appears to be associated with release of Serotonin from the enterochromaffin cells of the small intestine. In human, urinary 5- HIIA(5- hydroxyindoleacetic acid) excretion increases after cisplatin administration in parallel with the onset of emesis. The released Serotonin may stimulate the vagal afferents through the 5- HT3 receptors and initiate the vomiting reflex.

In normal volunteers, single intravenous doses of 0.15mg/kg of ondansetron had no effect on esophageal motility, gastric motility, lower esophageal sphincter pressure, or small intestinal transit time. Multiday administration of ondansetron has been shown to slow colonic transit in normal volunteers. Ondansetron has no effect on plasma prolactin concentrations.

Ondansetron does not alter the respiratory depressant effects produced by alfentanil or the degree of neuromuscular blockade produced by atracurium. Interactions with general or local anesthetics have not been studied.

INDICATIONS :

- Prevention of nausea and vomiting associated with highly emetogenic cancer chemotherapy.
- Prevention of nausea and vomiting associated with moderately emetogenic cancer chemotherapy.
- Prevention of nausea and vomiting associated with radiotherapy, total body irradiation, single high dose fraction or daily fractions to abdomen.
- Post operative nausea and vomiting.

DOSAGE & ADMINISTRATION :

FOR TABLETS :

• Prevention of nausea and vomiting associated with highly emetogenic cancer chemotherapy- Adult :24 mg tab 30 minutes before start of therapy.
• Prevention of nausea and vomiting associated with moderately emetogenic cancer chemotherapy- Adult :8mg tab./ solution 30 minutes before start of therapy & 8 hour thereafter; 8mg bid for 1-2 days after therapy.
• Prevention of nausea and vomiting associated with radiotherapy, total body irradiation, single high dose fraction or daily fractions to abdomen- Adult : 8 mg tid.
• Post operative nausea and vomiting- Adilt : 16mg 1 hr before induction of anesthesia.

FOR SYRUP: 0.15 mg/kg/dose – administered 2-3 times a day depending upon severity.

Wt. (kg)	Dose (ml)/ 'tsp'
3-5	1.25 (1/4 tsp)
6-8	2.5 (1/2 tsp)
9-11	3.75 (3/4 tsp)
12-14	5 (1 tsp)
15-17	6.25 (1 +1/4 tsp)
18-20	7.5 (1 + ½ tsp)

NOTE :-
• 0.15 mg/kg dose of ondansetron is administered by IV in pediatric practice for prevention of chemotherapy-induced nausea and vomiting.
• 0.1 mg/kg dose of ondansetron is administered by IV in prevention of post operative nausea and vomiting.
• 0.15 mg/kg/dose is recommended for oral use. This is proper in view of about 60 % mean bioavailability.

CONTRAINDICATION :

Ondansetron is contraindicated for patients known to have hypersensitivity to the drug.

WARNING :

Hypersensitivity reactions have been reportedin patients who have exhibited hypersensitivity to other selective 5 HT3 receptor antagonists.

PRECAUTIONS :

Ondansetron is not a drug that stimulates gastric or intestinal peristalsis. It should not be used instead of nasogastric suction. The use of ondansetron in patients following abdominal surgery or in patients with chemotherapy induced nausea and vomiting may mask a progressive ileus and/or gastric distension.

DRUG INTERACTIONS :

Ondansetron does not itself appear to induce or inhibit the cytochrome P-450 drug- metabolizing enzyme system of the liver. Because ondansetron is metabolized by hepatic cytochrome P- 450 drug metabolizing enzymes, inducers or inhibitors of these enzymes may change the clearance and, hence, the half life of ondansetron. On the basis of available data, no dosage adjustment is recommended for patients on these drugs.

PREGNANCY :

It should be used in pregnancy only if clearly needed. This is because adequate studies are not available.

NURSING MOTHERS :

Caution should be exercised in nursing women although it is not known whether the drug is excreted in human milk.

PEDIATRIC USE :

Little information about dosage in pediatric patients 4 years of age or younger.

ADVERSE EFFECTS :

In chemotherapy / radiation-induced nausea and vomiting:- Headache, malaise/fatigue, constipation, diarrhea and dizziness in decreasing order.
Integumentary: Rash in about 1 % of the patients.
Others: Rarely anaphylaxis, bronchospasm, tachycardia, angina (chest pain), hypokalemia, ECG alterations, vascular occlusive events and grand mal epilepsy.
In postoperative nausea and vomiting: Headache,
General : Flushing,

Hepatobilliary: Liver enzyme abnormalities.
Lower respiratory: Hiccups
Skin: Urticaria .

PACKAGING INFORMATION :

ETRON 4mg Tablet : Available in a strip of 10 tablets.
ETRON SYRUP: Available in 30 ml bottle pack.