SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal product: EMITINO SYRUP

Ondansetron Oral Solution USP

2. Composition

Each 5ml contains

Ondansetron Hydrochloride USP

Equivalent to Ondansetron ..... 2 mg

S. No.	Name of Material	Specification	Label Claim	Qty. mg/5 ml	Function
1	Ondansetron HCl	USP	2.0 mg	2.5	Active Ingredient
2	Sucrose	BP	--	3.0 gm	Sweetening agent
3	Propylene Glycol	BP	--	250.0	Viscosity enhancer
4	Methyl Paraben	BP	--	9.0	Preservative
5	Propyl Paraben	BP	--	1.0	Preservative
6	Sodium Citrate	BP	--	0.68	pH Adjuster
7	Citric acid (Monohydrate)	BP	--	1.0	pH Adjuster
8	Colour Ponceau 4R	IH	--	0.250	Colouring agent
9	Flavour Fruit Mixed (Vital)	IH	--	0.005 ml	Flavouring agent
10	Purified Water	BP	--	Q.S.	Vehicle

3. Pharmaceutical form: Liquid Dosage form (Solution)

Pink colour clear liquid having sweet taste and pleasant flavor.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Ondansetron is a potent, highly selective 5HT 3 receptor antagonist. It is precise mode of action in the control of nausea and vomiting is not known. Chemotherapeutic agents and radiotherapy may cause release of 5HT in the small intestine initiating a vomiting reflex by activating vagal afferents via 5HT 3 receptors. Ondansetron blocks the initiation of this reflex. Activation vagal afferents may also cause a release of 5HT in the area postrema, located on the floor of the fourth ventricle and this may also promote emesis through a central mechanism. Thus, the effect of ondansetron in the management of nausea and vomiting induced by cytotoxic chemotherapy and radiotherapy is probably due to antagonism of 5HT 3 receptors or neurons located both in the peripheral and central

nervous system. The mechanisms of action in post-operative nausea and vomiting are not known but there may be common pathways with cytotoxic-induced nausea and vomiting.

4.2 Posology and method of administration

Chemotherapy and radiotherapy-

i) Children 4-11 year: 4 mg PO three times per day. The dosage schedule is the same as for adults. The first dose should be given 30minutes before the start of emetogenic chemotherapy, with two subsequent doses four hours and eight hours after the initial dose. Further doses may be given every 8 hours for 1-2 days after completion of chemotherapy. Dosage should be adjusted in hepatic impairment.

ii) Children < 4 years and BSA >1 m^2:4 mg PO three times per day.

Children < 4 years and BSA 0.6-1 m^2:3 mg PO three times per day. Children <

4 years and BSA 0.3.0.6 m^2: 2 mg PO1hree times per day. Children < 4 years

and BSA < 0.3 m^2:1 mg PO1hree times per day.

iii) Adults including the elderly, adolescents, and children >= 12 years: 8 mg PO three times per day

Nausea/vomiting associated with acute gastroenteritis:

NOTE: In children, only the first dose of PO Ondansetron was statistically significant in reducing the overall frequency of vomiting (vs. placebo).Vomiting in gastroenteritis usually peaks on the first day; determine if additional doses of Ondansetron are required based on the patient's clinical status. Ondansetron may cause diarrhea and then therefore worsen dehydration in gastroenteritis.

Children 4-12 years: 4 mg PO; may administer every 8 hours if needed. Children 1-3 years: 3.2 mg PO; may administer every 8 hours if needed. Infants 6 months-1 year: 1.6 mg PO; may administer every 8 hours if needed. Infants< 1 month: Safety and efficacy have not been established.

+ non-US FDA-approved indication.

4.3 Contraindications

Hypersensitivity to any components of the preparations.

4.4 Warnings and 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 distention.

4.5 Interaction with other medicinal products and other forms of interaction

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 (CYP3A4, CYP2D6, CYP1A2), inducers or inhibitors of these enzymes may change the clearance and, hence, the half-life of Ondansetron. On the basis of limited available data, no dosage adjustment is recommended for patients on these drugs.

Renal impairment

No alteration of daily dosage or frequency of dosing or route of administration is required.

Hepatic impairment

Clearance of ondansetron is significantly reduced and serum half-life significantly prolonged in subjects with moderate or severe impairment of hepatic function. In such patients a total daily dose of 8 mg should not be exceeded.

4.6 Pregnancy and Lactation:

Pregnancy

Category B. Emitino should be used during pregnancy only if clearly needed.

Lactation

It is not known whether Ondansetron is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Ondansetron is administered to a nursing woman.

Pediatric use

Little information is available about use of Emitino in children under 1 month of age for PONV.

Geriatric use

Dosage adjustment is not needed in patients over the age of 65 years.

4.7 Effects on ability to drive and use machines

Not known

4.8 Side effects

Ondansetron is known to increase large bowel transit time and may cause constipation in some patients. The following side effects can occur: headache, a sensation of flushing or warmth, and occasional transient asymptomatic increases in aminotransferase and possible extrapyramidal reactions.

There have been rare reports of immediate hypersensitivity reactions including anaphylaxis. Rare cases of Oculogyric crisis, transient visual disturbances (e.g. blurred vision) and dizziness have been reported during rapid intravenous administration of Ondansetron.

4.9 Over dosage

There is no specific antidote for Ondansetron overdose. Patients should be managed with appropriate supportive therapy. Individual doses as large as 150 mg and total daily dosages (three doses) as large as 252 mg have been administered intravenously without significant adverse events. These doses are more than 10 times the recommended daily dose.

In addition to the adverse events listed above, the following events have been described in the setting of Ondansetron

overdose: "Sudden blindness" (amaurosis) of 2 to 3 minutes' duration plus severe constipation occurred in one patient that was administered 72 mg of Ondansetron intravenously as a single dose. Hypotension (and faintness) occurred in another patient that took 48 mg of oral Ondansetron. Following infusion of 32 mg over only a 4-minute period, a vasovagal episode

with transient second-degree heart block was observed. In all instances, the events resolved completely.

5. Pharmacological properties

5.1 Pharmacodynamic properties

ATC code:- A04 Antiemetics and antinauseants

ATC group:- A04AA0 1 Serotonin (5HT3) antagonist

Ondansetron is a potent, highly selective 5HT 3 receptor antagonist. Its precise mode of action in the control of nausea and vomiting is not known. Chemotherapeutic agents and radiotherapy may cause release of 5HT in the small intestine initiating a vomiting reflex by activating vagal afferents via 5HT 3 receptors. Ondansetron blocks the initiation of this reflex. Activation of vagal afferents may also cause a release of 5HT in the area postrema, located on the floor of the fourth ventricle, and this may also promote emesis through a central mechanism. Thus, the effect of Ondansetron in the management of nausea and vomiting induced by cytotoxic chemotherapy and radiotherapy is probably due to antagonism of 5HT 3 receptors or neurons located both in the peripheral and central nervous system. The mechanisms of action in post-operative nausea and vomiting are not known but there may be common pathways with cytotoxic-induced nausea and vomiting.

5.2 Pharmacokinetic Properties

Following oral administration, Ondansetron is passively and completely absorbed from the gastrointestinal tract and undergoes first pass metabolism. Peak plasma concentrations of about 30ng/ml are attained approximately 1.5 hours after an 8mg dose. For doses above 8mg the increase in Ondansetron systemic exposure with dose is greater than proportional; this may reflect some reduction in first pass metabolism at higher oral doses. Bioavailability, following oral administration, is slightly enhanced by the presence of food but unaffected by antacids. Studies in healthy elderly volunteers have shown slight, but clinically insignificant, age-related increases in both oral bioavailability (65%) and half-life (five hours) of Ondansetron. Gender differences were shown in the disposition of Ondansetron, with females having a greater rate and extent of absorption following an oral dose and reduced systemic clearance and volume of distribution (adjusted for weight). The disposition of Ondansetron following oral, intramuscular (IM) and intravenous (IV) dosing is similar with a terminal half-life of about three hours and steady state volume of distribution of about 140L. Equivalent systemic exposure is achieved after IM and IV administration of Ondansetron.

Ondansetron is not highly protein bound (70-76%). Ondansetron is cleared from the systemic circulation predominantly by hepatic metabolism through multiple enzymatic pathways. Less

than 5% of the absorbed dose is excreted unchanged in the urine. The absence of the enzyme CYP2D6 (the debrisoquine polymorphism) has no effect on ondansetron's pharmacokinetics. The pharmacokinetic properties of Ondansetron are unchanged on repeat dosing.

Special Patient Populations

Children and Adolescents (aged 1 month to 17 years)

In pediatric patients aged 1 to 4 months (n=19) undergoing surgery, weight normalised clearance was approximately 30% slower than in patients aged 5 to 24 months (n=22) but comparable to the patients aged 3 to 12 years. The half-life in the patient population aged 1 to 4 month was reported to average 6.7 hours compared to 2.9 hours for patients in the 5 to 24 month and 3 to 12 year age range. The differences in pharmacokinetic parameters in the 1 to 4 month patient population can be explained in part by the higher percentage of total body water in neonates and infants and a higher volume of distribution for water soluble drugs like Ondansetron.

In pediatric patients aged 3 to 12 years undergoing elective surgery with general anaesthesia, the absolute values for both the clearance and volume of distribution of Ondansetron were reduced in comparison to values with adult patients. Both parameters increased in a linear fashion with weight and by 12 years of age, the values were approaching those of young adults.

5.3 Preclinical safety data

There are no pre-clinical data of relevance

6. Pharmaceutical particulars

6.1 List of excipients: Sucrose BP, Propylene Glycol BP, Methyl Paraben BP, Propyl Paraben BP, Sodium Citrate BP, Citric acid (Monohydrate) BP, Colour Ponceau 4R, Flavour Fruit Mixed (Vital), Purified Water BP.

6.2 Incompatibilities

Not Applicable

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store below 30°C. Protect from light.

Keep out of reach of children.

6.5 Nature and contents of container

30 ml/bottle

Primary Container: 30 ml in Amber coloured Pet Bottle sealed with 25 mm EPE WAD Cap

Secondary container: 10 ml transparent Measuring cups & Sticker Label as per text matter.

Such one bottle in a printed outer carton along with Pack insert.

6.6 Special precautions for disposal:

-Not Applicable

7. Marketing Authorization Holder and Manufacturing site address:

Cachet Pharmaceuticals Pvt. Ltd

415, Shah Nahar Industrial Estate,

Dr. E. Moses Road, Worli, Mumbai-400 018,

Maharashtra, India.

Manufacturer's Name and Address:

Cachet Pharmaceuticals PVT. LTD.

Village Thana, Baddi, Dist. Solan,

Himachal Pradesh – 173 205.

8. Marketing authorisation number(s):

Rwanda FDA-HMP-MA-0066

9. Date of first authorisation/renewal of the authorization:

01 June 2021

10. Date of revision of the text:

29.01.2024