SUMMARY OF PRODUCT CHARACTERISTICS (SPC)

1. Name of the medicinal product

EMITOSS 8 (ONDANSETRON ORALLY DISINTEGRATING TABLETS USP 8 MG)

2. Qualitative and quantitative composition

EMITOSS 8 (ONDANSETRON ORALLY DISINTEGRATING TABLETS USP 8 MG)

Each uncoated tablet contains:
Ondansetron USP … 8 mg
Sunset Yellow Lake (-)
--(--QS)

Sr. No.	Ingredients	Specification	Qty. mg/ Tablet	Function
1.	Ondansetron Hydrochloride Dihydrate equivalent to Ondansetron	USP	9.98	Active
2.	Mannitol DC (Pearlitol SD 200)	BP	96.4	Diluent
3.	Aspartame	USP	3.70	Sweetener
4.	Crospovidone XL 10	BP	10.0	Disintegrant
5.	Silicified Microcrystalline cellulose	USP	13.00	Binder
6.	Lake Sunset Yellow FCF	Inhouse	2.00	Colorant
Lubrication				
7.	Magnesium Stearate	BP	2.00	Lubricant
8.	Colloidal Anhydrous silica (Aerosil 200)	BP	4.00	Lubricant
9.	Strawberry Flavor	Inhouse	0.90	Flavoring agent
	Total		**140.00**	

(For full list of excipients see section 6.1)

3. Pharmaceutical form

Uncoated tablet
Orange coloured, circular shaped, biconvex, uncoated tablet, plain on both sides.

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4. Clinical particulars

4.1 Therapeutic indications

Adults:

Ondansetron is indicated in adults for the management of nausea and vomiting induced by cytotoxic chemotherapy and radiotherapy.
Ondansetron is indicated for the prevention of post-operative nausea and vomiting (PONV).

Paediatric Population:

Ondansetron is indicated in children aged ≥6 months for the management of chemotherapy-induced nausea and vomiting (CINV).
No studies have been conducted on the use of orally administered ondansetron in the prevention and treatment of PONV in children aged ≥1 month, administration by IV injection is recommended for this purpose.

4.2 Posology and method of administration

Place the Orally Disintegrating tablet on top of the tongue, where it will disperse within seconds, then swallow.

Chemotherapy and radiotherapy induced nausea and vomiting.

Adults:

The emetogenic potential of cancer treatment varies according to the doses and combinations of chemotherapy and radiotherapy regimens used. The selection of dose regimen should be determined by the severity of the emetogenic challenge.

Emetogenic chemotherapy and radiotherapy:

Ondansetron can be given either by rectal, oral (as an Orally Disintegrating tablet) intravenous or intramuscular administration.
For oral administration: 8 mg taken 1 to 2 hours before chemotherapy or radiation treatment, followed by 8 mg every 12 hours for a maximum of 5 days to protect against delayed or prolonged emesis.

For highly emetogenic chemotherapy:

A single dose of up to 24 mg Ondansetron taken with 12 mg oral dexamethasone sodium phosphate, 1 to 2 hours before chemotherapy, may be used.
To protect against delayed or prolonged emesis after the first 24 hours, treatment with Ondansetron may be continued for up to 5 days after a course of treatment.
The recommended dose is 8 mg to be taken twice daily.

Pediatric population:

CINV in children aged ≥ 6 months and adolescents.

The dose for CINV can be calculated based on body surface area (BSA) or weight – see below. In paediatric clinical studies, ondansetron was given by IV infusion diluted in 25 to 50 mL of saline or other compatible infusion fluid and infused over not less than 15 minutes. Weight-based dosing results in higher total daily doses compared to BSA-based dosing.

Elderly:

No alteration of oral dose or frequency of administration is required.

Post-operative nausea and vomiting (PONV)

Adults:

For the prevention of PONV: Ondansetron may be administered either orally (as an orodispersible tablet) or by intravenous or intramuscular injection.
For oral administration: 16mg taken one hour prior to anaesthesia.

For the treatment of established PONV: Intravenous or intramuscular administration is recommended.

Paediatric population:
PONV in children aged ≥ 1 month and adolescents.
Oral formulation:
No studies have been conducted on the use of orally administered ondansetron in the prevention or treatment of post-operative nausea and vomiting; slow IV injection (not less than 30 seconds) is recommended for this purpose.

Injection:
For prevention of PONV in paediatric patients having surgery performed under general anaesthesia, a single dose of ondansetron may be administered by slow intravenous injection (not less than 30 seconds) at a dose of 0.1mg/kg up to a maximum of 4mg either prior to, at or after induction of anaesthesia.
For the treatment of PONV after surgery in paediatric patients having surgery performed under general anaesthesia, a single dose of ondansetron may be administered by slow intravenous injection (not less than 30 seconds) at a dose of 0.1mg/kg up to a maximum of 4mg.
There are no data on the use of Ondansetron in the treatment of PONV in children below 2 years of age.

Elderly:
There is limited experience in the use of Ondansetron in the prevention and treatment of PONV in the elderly, however Ondansetron is well tolerated in patients over 65 years receiving chemotherapy.

For both indications
Patients with renal impairment:
No alteration of daily dosage or frequency of dosing, or route of administration are required.

Patients with 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 8mg should not be exceeded.

Patients with poor sparteine/debrisoquine metabolism:
The elimination half-life of ondansetron is not altered in subjects classified as poor metabolisers of sparteine and debrisoquine. Consequently, in such patients, repeat dosing will give drug exposure levels no different from those of the general population. No alteration of daily dosage or frequency of dosing is required.

4.3 Contraindications
Hypersensitivity to the active substance or to any of the excipients of the preparations.

4.4 Special warnings and precautions for use
Hypersensitivity reactions have been reported in patients who have exhibited hypersensitivity to other selective $5HT_3$ receptor antagonists. Respiratory events should be treated symptomatically, and clinicians should pay particular attention to them as precursors of hypersensitivity reactions.
Ondansetron prolongs the QT interval in a dose-dependent manner. In addition, post-marketing cases of Torsade de Pointes have been reported in patients using ondansetron. Avoid ondansetron in patients with congenital long QT syndrome. Ondansetron should be administered with caution to patients who have or may develop prolongation of QTc, including patients with electrolyte abnormalities, congestive heart failure, bradyarrhythmia or patients taking other medicinal products that lead to QT prolongation or electrolyte abnormalities.
Hypokalaemia and hypomagnesaemia should be corrected prior to Ondansetron administration.

As ondansetron is known to increase large bowel transit time, patients with signs of subacute intestinal obstruction should be monitored following administration.
In patients with adenotonsillar surgery prevention of nausea and vomiting with ondansetron may mask occult bleeding. Therefore, such patients should be followed carefully after ondansetron.
Ondansetron Oro dispersible tablets contain small amounts of sulphur dioxide that may rarely cause severe hypersensitivity reactions and bronchospasm.

Paediatric population:
Paediatric patients receiving Ondansetron with hepatotoxic chemotherapeutic agents should be monitored closely for impaired hepatic function.

CINV:
When calculating the dose on an mg/kg basis and administering three doses at 4-hour intervals, the total daily dose will be higher than if one single dose of 5mg/m2 followed by an oral dose is given. The comparative efficacy of these two different dosing regimens has not been investigated in clinical trials. Cross-trial comparison indicates similar efficacy for both regimens.

4.5 Interaction with other medicinal products and other forms of interaction

There is no evidence that ondansetron either induces or inhibits the metabolism of other drugs commonly co-administered with it. Specific studies have shown that there are no interactions when ondansetron is administered with alcohol, temazepam, furosemide, alfentanil, tramadol, morphine, lidocaine, thiopental or propofol.
Ondansetron is metabolised by multiple hepatic cytochrome P-450 enzymes: CYP3A4, CYP2D6 and CYP1A2. Due to the multiplicity of metabolic enzymes capable of metabolising ondansetron, enzyme inhibition or reduced activity of one enzyme (e.g. CYP2D6 genetic deficiency) is normally compensated by other enzymes and should result in little or no significant change in overall ondansetron clearance or dose requirement.
Caution should be exercised when ondansetron is co-administered with drugs that prolong the QT interval and/or cause electrolyte abnormalities.
Use of ondansetron with QT prolonging drugs may result in additional QT prolongation. Concomitant use of ondansetron with cardiotoxic drugs (e.g. anthracyclines (such as doxorubicin, daunorubicin) or trastuzumab), antibiotics (such as erythromycin), antifungals (such as ketoconazole), antiarrhythmics (such as amiodarone) and beta blockers (such as atenolol or timolol) may increase the risk of arrhythmias.

Serotonergic drugs (e.g. SSRIs and SNRIs):
There have been post-marketing reports describing patients with serotonin syndrome (including altered mental status, autonomic instability and neuromuscular abnormalities) following the concomitant use of ondansetron and other serotonergic drugs (including SSRIs and SNRIs).

Apomorphine:
Based on reports of profound hypotension and loss of consciousness when ondansetron was administered with apomorphine hydrochloride, concomitant use with apomorphine is contraindicated.

Phenytoin, Carbamazepine and Rifampicin:
In patients treated with potent inducers of CYP3A4 (i.e. phenytoin, carbamazepine, and rifampicin), the oral clearance of ondansetron was increased and ondansetron blood concentrations were decreased.

Tramadol:
Data from small studies indicate that ondansetron may reduce the analgesic effect of tramadol.

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4.6 Fertility, Pregnancy, and Lactation

Pregnancy

Based on human experience from epidemiological studies, ondansetron is suspected to cause orofacial malformations when administered during the first trimester of pregnancy.
In one cohort study including 1.8 million pregnancies, first trimester ondansetron use was associated with an increased risk of oral clefts.
The available epidemiological studies on cardiac malformations show conflicting results.
Animal studies does not indicate direct or indirect harmful effects with respect to reproductive toxicity.
Ondansetron should not be used during the first trimester of pregnancy.

Breast-feeding

Tests have shown that ondansetron passes into the milk of lactating animals. It is therefore recommended that mothers receiving Ondansetron should not breast-feed their babies.

Fertility

There is no information on the effects of ondansetron on human fertility.

4.7 Effects on ability to drive and use machines

In psychomotor testing, ondansetron does not impair performance nor cause sedation. No detrimental effects on such activities are predicted from the pharmacology of ondansetron.

4.8 Undesirable 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 Overdose

Symptoms and Signs

There is limited experience of ondansetron overdose. In the majority of cases, symptoms were similar to those already reported in patients receiving recommended doses. Manifestations that have been reported include visual disturbances, severe constipation, hypotension and a vasovagal episode with transient second-degree AV block.
Ondansetron prolongs the QT interval in a dose-dependent fashion. ECG monitoring is recommended in cases of overdose.
Cases consistent with serotonin syndrome have been reported in young children following oral overdose.

Treatment

There is no specific antidote for ondansetron, therefore in all cases of suspected overdose, symptomatic and supportive therapy should be given as appropriate.
Further management should be as clinically indicated or as recommended by the national poisons centre, where available.

The use of ipecacuanha to treat overdose with ondansetron is not recommended, as patients are unlikely to respond due to the anti-emetic action of ondansetron itself.

Paediatric population

Paediatric cases consistent with serotonin syndrome have been reported after inadvertent oral overdoses of ondansetron (exceeded estimated ingestion of 4mg/kg) in infants and children aged 12 months to 2 years.

SUMMARY OF PRODUCT CHARACTERISTICS (SPC)

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Serotonin (5HT3) antagonists, ATC code: A04AA01.

Mechanism of Action

Ondansetron is a potent, highly selective 5HT3 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 5HT3 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 the nausea and vomiting induced by cytotoxic chemotherapy and radiotherapy is probably due to antagonism of 5HT3 receptors on 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.
Ondansetron does not alter plasma prolactin concentrations.

5.2 Pharmacokinetic properties

Absorption

Following oral administration of ondansetron, absorption is rapid with maximum peak plasma concentrations of about 30ng/mL being attained and achieved in approximately 1.5 hours after an 8mg dose.

Distribution

The syrup and tablet formulations are bioequivalent and have an absolute oral bioavailability of 60%.

Elimination:

The disposition of ondansetron following oral, intravenous and intramuscular dosing is similar with a terminal elimination half-life of approximately 3 hours and a steady- state volume of distribution of about 140L. Ondansetron is not highly protein bound (70-76%) and 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 the pharmacokinetics of ondansetron. The pharmacokinetic properties of ondansetron are unchanged on repeat dosing.

Renal impairment

In patients with renal impairment (creatinine clearance 15-60mL/min), systemic clearance and volume of distribution are reduced, resulting in a slight, but clinically insignificant increase in elimination half-life (5.4 hours). A study in patients with severe renal impairment who required regular haemodialysis (studied between dialyses) showed ondansetron's pharmacokinetics to be essentially unchanged.

Hepatic impairment

In patients with severe hepatic impairment, systemic clearance is markedly reduced with prolonged elimination half-lives (15-32 hours) and an oral bioavailability approaching 100% because of reduced pre-systemic metabolism.

5.3 Preclinical safety data

No additional data of relevance.

SUMMARY OF PRODUCT CHARACTERISTICS (SPC)

6. Pharmaceutical particulars

6.1 List of excipients

Sr. No.	Ingredients	Specification
1.	Mannitol DC (Pearlitol SD 200)	BP
2.	Aspartame	USP
3.	Crospovidone XL 10	BP
4.	Silicified Microcrystalline cellulose	USP
5.	Lake Sunset Yellow FCF	Inhouse
6.	Magnesium Stearate	BP
7.	Colloidal Anhydrous silica (Aerosil 200)	BP
8.	Strawberry Flavor	Inhouse

6.2 Incompatibilities

None reported.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store below 30°C.
Protect from light and moisture.
Keep medicine out of reach of children.

6.5 Nature and contents of container

Alu-Alu blister pack of 1 x 10 tablets

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing authorisation holder

Galaxy Pharmaceuticals
P.O. Box 39107- 00623.
Nairobi, Kenya

8. Marketing authorisation number (s)

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9. Date of first authorisation/renewal of the authorisation

17 Oct 2020

10. Date of revision of the text

11/2023