SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Setofilm 8 mg Orodispersible Films

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Setofilm 8 mg Orodispersible Films:

Each film contains 8 mg of ondansetron (as base)

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Orodispersible Film.

Setofilm 8 mg Orodispersible Film:

White, rectangular (size 6 cm^2), orodispersible film.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Adults:

- Prophylaxis of acute nausea and vomiting induced by moderately emetogenic chemotherapy.
- Prophylaxis and treatment of delayed nausea and vomiting induced by moderately to highly emetogenic chemotherapy.
- Prophylaxis and treatment of acute and delayed nausea and vomiting induced by highly emetogenic radiotherapy.
- Prophylaxis and treatment of post-operative nausea and vomiting (PONV).

Paediatric Population:

- Management of chemotherapy-induced nausea and vomiting in children aged ≥6 months.
- Prophylaxis and treatment of post-operative nausea and vomiting (PONV) in children aged ≥4 years.

4.2 Posology and method of administration

SETOFILM is only indicated for oral use. Please refer to the relevant SmPC for other dosage forms of ondansetron.

SETOFILM may be recommended in patients with an enhanced risk of aspiration. It can be useful for patients that experience difficulties in swallowing, e.g., children or the elderly.

Method of administration:

- SETOFILM orodispersible film should be removed from each individual sachet taking care not to damage the film.
- Open the sachet only at the tear tag and tear this off slowly. Do not cut the sachet.
- Before use check the film for damage. Only undamaged films should be used.
- The patients' mouth should be empty and their fingers dry before placing SETOFILM orodispersible film on to the tongue.
- The film should disintegrate on the tongue without water in a few seconds (in saliva which should be subsequently swallowed).

Posology

4.2.1 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, intravenous or intramuscular administration.

SETOFILM is an oral formulation. The recommended oral dose is 8mg 1 to 2 hours before treatment, followed by 8mg orally 12 hours later.

To protect against delayed or prolonged emesis after the first 24 hours, oral treatment with SETOFILM should be continued for up to 5 days after a course of treatment. The recommended oral dosage is 8mg to be taken twice daily.

Highly emetogenic chemotherapy (e.g. high dose cisplatin)

Ondansetron can be given either by oral, rectal, intravenous or intramuscular administration.

SETOFILM is an oral formulation. The recommended oral dose is 24 mg taken together with oral dexamethasone sodium phosphate 12mg, 1 to 2 hours before treatment.

To protect against delayed or prolonged emesis after the first 24 hours, oral treatment with SETOFILM should be continued for up to 5 days after a course of treatment. The recommended oral dosage is 8mg to be taken twice daily.

Paediatric Population

Chemotherapy induced nausea and vomiting (CINV)
The dose for CINV can be calculated based on body surface area (BSA) or weight – see table 1 below. Weight – based dosing results in higher total daily doses compared to BSA based dosing. (See sections 4.4 and 5.1)

There are no data from controlled clinical trials on the use of ondansetron in the prevention of delayed or prolonged CINV or on the use of ondansetron for radiotherapy-induced nausea and vomiting (RINV) in children.

Ondansetron should be administered immediately before chemotherapy as a single intravenous dose. The intravenous dose must not exceed 8 mg.

Oral dosing can commence twelve hours later and may be continued for up to 5 days. See Table 1 below.

The total daily dose must not exceed adult dose of 32 mg.

Table 1: BSA and weight based dosing for Chemotherapy

BSA	**Day 1[a,b]**	**Day 2-6[b]**
$<0.6m^2$	5 mg/m^2 i.v*plus 2 mg** orally after 12 hrs	2 mg** orally every 12 hrs
$\geq 0.6m^2$	5 mg/m^2 i.v* plus 4 mg orally after 12 hrs	4 mg orally every 12 hrs
Weight	**Day 1[a,b]**	**Day 2-6[b]**
≤10 kg	Up to 3 i.v* doses of 0.15mg/kg every 4 hrs	2 mg** orally every 12 hrs
>10 kg	Up to 3 i.v* doses of 0.15mg/kg every 4 hrs	4 mg orally every 12 hrs

a The intravenous dose must not exceed 8 mg.
b The total daily dose must not exceed adult dose of 32 mg
*SETOFILM is an oral preparation only, and is not available in an intravenous formulation
**SETOFILM is only available in films of 4mg and 8mg. It is not possible to divide the film to obtain a 2mg dosage.

Elderly
Ondansetron is well tolerated by patients over 65 years and no alteration of dosage, dosing frequency or route of administration is required.

Prescribers intending to use ondansetron in the prevention of delayed nausea and vomiting associated with chemotherapy or radiotherapy in adults, adolescents or children should take into consideration current practice and appropriate guidelines.

4.2.2 Post-operative nausea and vomiting (PONV)

Adults

Prevention of Post-operative nausea and vomiting (PONV)
For the prevention of post-operative nausea and vomiting, the recommended oral dose is 16mg given 1 hour prior to anaesthesia.

Alternatively, use 8 mg one hour prior to anaesthesia followed by two further doses of 8 mg at eight hourly intervals.

Treatment of established Post-operative nausea and vomiting (PONV)
For the treatment of established PONV, intravenous or intramuscular administration by injection is recommended.

Paediatric population:

Post-operative nausea and vomiting
For the prevention and treatment of PONV, slow intravenous injection is recommended.

Alternatively, for administration in children weighing ≥ 40kg SETOFILM can be administered orally as a 4 mg dose, one hour prior to anaesthesia, followed by one further dose of 4 mg after 12 hours.

There are no data on the use of ondansetron for the treatment of PONV in children under 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.

Special populations – 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 ondansetron or to other selective 5-HT_3-receptor antagonists (e.g. granisetron, dolasetron) or to any of the excipients listed in section 6.1.
  Based on reports of profound hypotension and loss of consciousness when ondansetron was administered with apomorphine hydrochloride, concomitant use with apomorphine is contraindicated

4.4 Special warnings and precautions for use

Hypersensitivity reactions have been reported in patients who have exhibited hypersensitivity to other selective 5HT3 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 (see Clinical Pharmacology). 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, bradyarrhythmias or patients taking other medicinal products that lead to QT prolongation or electrolyte abnormalities.
Hypokalemia and hypomagnesemia should be corrected prior to ondansetron administration.
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 selective serotonin reuptake inhibitors (SSRI) and serotonin noradrenaline reuptake inhibitors (SNRIs)). If concomitant treatment with ondansetron and other serotonergic drugs is clinically warranted, appropriate observation of the patient is advised.

As ondansetron is known to increase large bowel transit time, patients with signs of sub-acute intestinal obstruction should therefore be monitored following administration.

In patients with adeno-tonsillar surgery prevention of nausea and vomiting with ondansetron may mask occult bleeding. Therefore, such patients should be followed carefully after ondansetron administration.

<u>Paediatric Population:</u>

Paediatric patients receiving ondansetron with hepatotoxic chemo-therapeutic agents should be monitored closely for impaired hepatic function.

***Chemotherapy-induced nausea and vomiting*:**
When calculating the dose on a mg/kg basis and administering three doses at 4 hourly intervals, the total daily dose will be higher than if one single dose of $5mg/m^2$ 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; refer to section 5.1.

4.5 Interaction with other medicinal products and other forms of interaction

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

There is no evidence that ondansetron either induces or inhibits the metabolism of other medicinal products 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, lignocaine, thiopental or propofol.

Ondansetron is metabolized 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 (eg, 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.

There have been post-marketing reports describing patients with serotonin syndrome a potentially life threatening condition, including altered mental status, autonomic instability, neuromuscular abnormalities and/or gastrointestinal symptoms, following the concomitant use of ondansetron and buprenorphine/opioids or other serotonergic drugs (including MAO inhibitors, tricyclic antidepressants, SSRIs and SNRIs). (See section 4.4).

Phenytoin, carbamazepine and rifampicin; in patients treated with potent inducers of CYP3A4, 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.

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), antifungal agents (such as ketoconazole), antiarrhythmics (such as amiodarone) and beta blockers (such as atenolol or timolol) may increase the risk of arrhythmias . (See section 4.4).

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

Women of childbearing potential should consider the use of contraception.

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 (3 additional cases per 10 000 women treated; adjusted relative risk, 1.24, (95% CI 1.03-1.48)).

The available epidemiological studies on cardiac malformations show conflicting results. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity.

Ondansetron should not be used during first trimester of pregnancy.

Breastfeeding

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

Ondansetron has no or negligible influence on the 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

Adverse events are listed below by system organ class and frequency. Frequencies are defined as: very common (≥ 1/10), common (≥ 1/100 and

<1/10), uncommon (≥ 1/1000 and <1/100), rare (≥ 1/10,000 and <1/1000) and very rare (<1/10,000). Very common, common and uncommon events were generally determined from clinical trial data. The incidence in placebo was taken into account. Rare and very rare events were generally determined from post marketing spontaneous data.

The following frequencies are estimated at the standard recommended doses of ondansetron according to indication and formulation.

Immune system disorders
Rare: Immediate hypersensitivity reactions sometimes severe, including anaphylaxis.

Nervous system disorders
Very common: Headache.
Uncommon: seizures, movement disorders including extrapyramidal reactions (such as dystonic reactions, oculogyric crisis and dyskinesia have been observed without definitive evidence of persistent clinical sequelae).
Rare: Dizziness during rapid intravenous administration.

Eye disorders
Rare: Transient visual disturbances (e.g. blurred vision) predominantly during intravenous administration.
Very rare: transient blindness predominantly during intravenous administration.

The majority of the blindness cases reported resolved within 20 minutes. Most patients had received chemotherapeutic agents, which included cisplatin. Some cases of transient blindness were reported as cortical in origin.

Cardiac disorders
Uncommon: Arrhythmias, chest pain with or without ST segment depression, bradycardia.
Rare: QTc prolongation (including Torsade de Pointes)

Vascular disorders
Common: Sensation of warmth or flushing.
Uncommon: Hypotension.

Respiratory, thoracic and mediastinal disorders
Uncommon: Hiccups.

Gastrointestinal disorders
Common: Constipation

Hepatobiliary disorders
Uncommon: Asymptomatic increases in liver function tests. These events were observed commonly in patients receiving chemotherapy with cisplatin.

Skin and subcutaneous tissue disorders

Very rare: Toxic skin eruption, including toxic epidermal necrolysis

Paediatric Population
The adverse event profile in children and adolescents was comparable to that seen in adults.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via Yellow Card Scheme: www.mhra.gov.uk/yellowcard.

4.9 Overdose

Little is known at present about over-dosage with ondansetron, however, a limited number of patients received overdoses. Manifestations that have been reported include visual disturbances, severe constipation, hypotension and vaso-vagal episodes with transient second degree AV block. In all instances, the events resolved completely.

Ondansetron prolongs QT interval in a dose-dependent manner. ECG monitoring is recommended in cases of overdose.

There is no specific antidote for ondansetron, therefore in all cases of suspected overdose, symptomatic and supportive therapy should be given as appropriate.

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 4 mg/kg) in infants and children aged 12 months to 2 years.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmaco-therapeutic group: Anti-emetics and anti-nauseants, Serotonin (5-HT_3) antagonists

ATC Code: A04AA01

Ondansetron is a potent, highly selective 5-HT_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 the nausea and vomiting induced by cytotoxic chemotherapy and radiotherapy is probably due to antagonism of $5HT_3$ 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.

The role of ondansetron in opiate-induced emesis is not yet established.

The effect of ondansetron on the QTc interval was evaluated in a double-blind, randomised, placebo and positive (moxifloxacin) controlled, crossover study in 58 healthy adult men and women. Ondansetron doses included 8 mg and 32 mg infused intravenously over 15 minutes. At the highest tested dose of 32 mg, the maximum mean (upper limit of 90% CI) difference in QTcF from placebo after baseline-correction was 19.6 (21.5) msec. At the lower tested dose of 8 mg, the maximum mean (upper limit of 90% CI) difference in QTcF from placebo after baseline correction was 5.8 (7.8) msec. In this study, there were no QTcF measurements greater than 480 msec and no QTcF prolongation was greater than 60 msec. No significant changes were seen in the measured electrocardiographic PR or QRS intervals.

<u>Paediatric Population</u>:

Chemotherapy-induced nausea and vomiting
The efficacy of ondansetron in the control of emesis and nausea induced by cancer chemotherapy was assessed in a double-blind randomised trial in 415 patients aged 1 to 18 years. On the days of chemotherapy, patients received either ondansetron 5 mg/m^2 intravenously + ondansetron 4 mg orally after 8-12 hrs; or ondansetron 0.45 mg/kg intravenous + placebo orally after 8-12 hrs. Post-chemotherapy both groups received 4 mg ondansetron orally twice daily for 3 days. Complete control of emesis on worst day of chemotherapy was 49% (5 mg/m^2 intravenously + ondansetron 4 mg orally) and 41% (0.45 mg/kg intravenously + placebo orally). Post-chemotherapy both groups received 4 mg ondansetron syrup twice daily for 3 days. There was no difference in the overall incidence or nature of adverse events between the two treatment groups.

A double-blind randomised placebo-controlled trial in 438 patients aged 1 to 17 years demonstrated complete control of emesis on the worst day of chemotherapy in:

• 73% of patients when ondansetron was administered intravenously at a dose of 5 mg/m^2 intravenous together with 2-4 mg dexamethasone orally

• 71% of patients when ondansetron was administered orally at a dose of 8 mg + 2 - 4 mg dexamethasone orally on the days of chemotherapy.

Post-chemotherapy both groups received 4 mg ondansetron orally twice daily for 2 days. There was no difference in the overall incidence or nature of adverse events between the two treatment groups.

The efficacy of ondansetron in 75 children aged 6 to 48 months was investigated in an open-label, non-comparative, single-arm study. All children received three 0.15 mg/kg doses of intravenous ondansetron, administered 30 minutes before the start of chemotherapy and then at four and eight hours after the first dose. Complete control of emesis was achieved in 56% of patients.

Another open-label, non-comparative, single-arm study investigated the efficacy of one intravenous dose of 0.15 mg/kg ondansetron followed by two oral ondansetron doses of 4 mg for children aged < 12 yrs and 8 mg for children aged ≥12 yrs (total number of children n= 28). Complete control of emesis was achieved in 42% of patients.

Prevention of post-operative nausea and vomiting
The efficacy of a single dose of ondansetron in the prevention of post-operative nausea and vomiting was investigated in a randomised, double-blind, placebo-controlled study in 670 children aged 1 to 24 months (post-conceptual age ≥44 weeks, weight ≥3 kg). Included subjects were scheduled to undergo elective surgery under general anaesthesia and had an ASA status ≤ III. A single dose of ondansetron 0.1 mg/kg was administered within five minutes following induction of anaesthesia. The proportion of subjects who experienced at least one emetic episode during the 24-hour assessment period (ITT) was greater for patients on placebo than those receiving ondansetron (28% vs. 11%, p <0.0001).

Four double-blind, placebo-controlled studies have been performed in 1469 male and female patients (2 to 12 years of age) undergoing general anaesthesia. Patients were randomised to either single intravenous doses of ondansetron (0.1 mg/kg for paediatric patients weighing 40 kg or less, 4 mg for paediatric patients weighing more than 40 kg; number of patients = 735) or placebo (number of patients = 734). Study drug was administered over at least 30 seconds, immediately prior to or following anaesthesic induction. Ondansetron was significantly more effective than placebo in preventing nausea and vomiting.

5.2 Pharmacokinetic properties

SETOFILM is an orodispersible film. Once in contact with saliva, it disintegrates in a few seconds.

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

Special Patient Populations

Children and Adolescents (aged 1 month to 17 years)
In paediatric 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 months 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 paediatric patients aged between 3 and 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. When clearance and volume of distribution values were normalized by body weight, the values for these parameters were similar between the different age group populations. Use of weight-based dosing compensates for age-related changes and is effective in normalizing systemic exposure in paediatric patients.

Population pharmacokinetic analysis was performed on 428 subjects (cancer patients, surgery patients and healthy volunteers) aged 1 month to 44 years following intravenous administration of ondansetron. Based on this analysis, systemic exposure (AUC) of ondansetron following oral or IV dosing in children and adolescents was comparable to adults, with the exception of infants aged 1 to 4 months. Volume was related to age and was lower in adults than in infants and children. Clearance was related to weight but not to age with the exception of infants aged 1 to 4 months. It is difficult to conclude whether there was an additional reduction in clearance related to age in infants 1 to 4 months or simply inherent variability due to the low number of subjects studied in this age group. Since patients less than 6 months of age will only

receive a single dose in PONV a decreased clearance is not likely to be clinically relevant.

Elderly
Studies in healthy elderly volunteers have shown a slight but clinically insignificant, age-related increases in both oral bioavailability (65%) and half-life (5h) 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).

Renal impairment
In patients with renal impairment (creatinine clearance >15 ml/min), systemic clearance and volume of distribution are reduced, resulting in a slight, but clinically insignificant increase in elimination half-life (5.4h). 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 (15-32h) and an oral bioavailability approaching 100% because of reduced pre-systemic metabolism.

5.3 Preclinical safety data

Preclinical data revealed no special hazard for humans based on conventional studies of repeated dose toxicity, genotoxicity and carcinogenic potential.

Ondansetron and its metabolites accumulate in the milk of rats, milk/plasma-ratio was 5.2:1. A study in cloned human cardiac ion channels has shown ondansetron has the potential to affect cardiac repolarisation via blockade of HERG potassium channels.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Poly (vinyl alcohol)
Macrogol 1000
Acesulfame potassium E950
Glycerol E422
Titanium dioxide E171
Rice starch

Levomenthol
Polysorbate 80 E433

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Keep the sachet tightly closed in order to protect from moisture.

6.5 Nature and contents of container

The primary packaging material is a sachet, which will be opened and removed before application. The material is a composite foil composed of kraft paper (outer layer), LDPE, aluminium foil and Surlyn (inner layer).

Pack size of 2, 4, 6, 10, 30 and 50.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

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

7. MARKETING AUTHORISATION HOLDER

Norgine Pharmaceuticals Limited
ARC Uxbridge, Building 01,
Sanderson Road,
Uxbridge,
UB8 1DH, UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 20011/0042

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

11/05/2010

10. DATE OF REVISION OF THE TEXT

13/04/2025