Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Galantax XL 24mg Prolonged-release Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 24 mg capsule contains 24 mg galantamine (as hydrobromide).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Prolonged release capsule, hard

Opaque orange size 2 hard gelatine capsules containing three round biconvex tablets

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Galantax XL is indicated for the symptomatic treatment of mild to moderately severe dementia of the Alzheimer type.

4.2 Posology and method of administration

Adults/Elderly

Before start of treatment

The diagnosis of probable Alzheimer type of dementia should be adequately confirmed according to current clinical guidelines (see section 4.4).

Starting dose

The recommended starting dose is 8 mg/day for 4 weeks.

Maintenance dose

- The tolerance and dosing of Galantax XL should be reassessed on a regular basis, preferably within three months after start of treatment. Thereafter, the clinical benefit of Galantax XL and the patient's tolerance of treatment should be reassessed on a regular basis according to current clinical guidelines. Maintenance treatment can be continued for as long as therapeutic benefit is favourable and the patient tolerates treatment with Galantax XL. Discontinuation of Galantax XL should be considered when evidence of a therapeutic effect is no longer present or if the patient does not tolerate treatment.
- The initial maintenance dose is 16 mg/day and patients should be maintained on 16 mg/day for at least 4 weeks.
- An increase to the maintenance dose of 24 mg/day should be considered on an individual basis after appropriate assessment including evaluation of clinical benefit and tolerability.
- In individual patients not showing an increased response or not tolerating 24 mg/day, a dose reduction to 16 mg/day should be considered.

- There is no rebound effect after abrupt discontinuation of treatment (e.g. in preparation for surgery).

Switching to Galantax XL prolonged release capsules from immediate release tablets or oral solution

It is recommended that the same total daily dose of galantamine is administered to patients. Patients switching to the once-daily regimen should take their last dose of immediate release tablets or oral solution in the evening and start Galantax XL prolonged release capsules once daily the following morning.

Concomitant treatment

In patients treated with potent CYP2D6 or CYP3A4 inhibitors, dose reductions can be considered (see section 4.5).

Hepatic and renal impairment

Galantamine plasma levels may be increased in patients with moderate to severe hepatic or renal impairment. In patients with moderately impaired hepatic function, based on pharmacokinetic modelling, it is recommended that dosing should begin with 8 mg prolonged release capsule once every other day, preferably taken in the morning, for one week. Thereafter, patients should proceed with 8 mg once daily for four weeks. In these patients, daily doses should not exceed 16 mg. In patients with severe hepatic impairment (Child-Pugh score greater than 9), the use of galantamine is contraindicated (see section 4.3). No dosage adjustment is required for patients with mild hepatic impairment.

For patients with a creatinine clearance greater than 9 ml/min no dosage adjustment is required. In patients with severe renal impairment (creatinine clearance less than 9 ml/min), the use of galantamine is contraindicated (see section 4.3).

Paediatric population

Galantax XL is not recommended for use in children due to a lack of data on safety and efficacy.

Method of administration

Galantax XL prolonged release capsules should be administered once daily in the morning, preferably with food. The capsules should be swallowed whole together with some liquid. The capsules must not be chewed or crushed.

Adequate fluid intake during treatment should be ensured (see section 4.8).

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Since no data are available on the use of galantamine in patients with severe hepatic (Child-Pugh score greater than 9) and severe renal (creatinine clearance less than 9 ml/min) impairment, galantamine is contraindicated in these populations. Galantamine is contraindicated in patients who have both significant renal and hepatic dysfunction.

4.4 Special warnings and precautions for use

Galantax XL is indicated for a patient with mild to moderately severe dementia of the Alzheimer type. The benefit of galantamine in patients with other types of dementia or other types of memory impairment has not been demonstrated. In 2 clinical trials of two years duration in individuals with so called mild cognitive impairment (milder types of memory impairment not fulfilling the criteria of Alzheimer dementia), galantamine therapy failed to demonstrate any benefit either in slowing cognitive decline or reducing the clinical conversion to dementia. The mortality rate in the galantamine group was significantly higher than in the placebo group, 14/1026 (1.4%) patients on galantamine and 3 /1022 (0.3%) patients on placebo. The deaths were due to various causes. About half of the galantamine deaths appeared to result from various vascular causes (myocardial infarction, stroke, and sudden death). The relevance of this finding for the treatment of patients with Alzheimer dementia is unknown. In Alzheimer dementia, placebo-controlled studies of only 6 months duration have been conducted. In these studies no increased mortality in the galantamine groups appeared.

A diagnosis of Alzheimer's dementia should be made according to current guidelines by an experienced physician. Therapy with galantamine should occur under the supervision of a physician and should only be initiated if a caregiver is available who will regularly monitor medicinal product intake by the patient.

Patients with Alzheimer's disease lose weight. Treatment with cholinesterase inhibitors, including galantamine, has been associated with weight loss in these patients. During therapy, patient's weight should be monitored.

As with other cholinomimetics, Galantamine should be given with caution in the following conditions:

Cardiac disorders

Because of their pharmacological action, cholinomimetics may have vagotonic effects on heart rate (e.g. bradycardia). The potential for this action may be particularly important to patients with 'sick sinus syndrome' or other supraventricular cardiac conduction disturbances or in those who use medicinal products that significantly reduce heart rate concomitantly, such as digoxin and beta blockers or for patients with an uncorrected electrolyte disturbance (e.g. hyperkalaemia, hypokalaemia).

Caution should therefore be exercised when administering galantamine to patients with cardiovascular diseases, e.g. immediate post-myocardial infarction period, new-onset atrial fibrillation, second degree heart block or greater, unstable angina pectoris, or congestive heart failure, especially NYHA group III – IV.

In a pooled analysis of placebo-controlled studies in patients with Alzheimer dementia treated with galantamine an increased incidence of certain cardiovascular adverse events were observed (see section 4.8).

Gastrointestinal disorders

Patients at increased risk of developing peptic ulcers, e.g. those with a history of ulcer disease or those predisposed to these conditions, including those receiving concurrent non-steroidal anti-inflammatory drugs (NSAIDs), should be monitored for symptoms. The use of galantamine is not recommended in patients with gastrointestinal obstruction or recovering from gastrointestinal surgery.

Nervous system disorders

Although cholinomimetics are believed to have some potential to cause seizures, seizure activity may also be a manifestation of Alzheimer's disease. In rare cases an increase in cholinergic tone may worsen Parkinsonian symptoms.

In a pooled analysis of placebo-controlled studies in patients with Alzheimer's dementia treated with galantamine cerebrovascular events were uncommonly observed (see section 4.8). This should be considered when administering galantamine to patients with cerebrovascular disease.

Respiratory, thoracic and mediastinal disorders

Cholinomimetics should be prescribed with care for patients with a history of severe asthma or obstructive pulmonary disease or active pulmonary infections (e.g. pneumonia).

Renal and urinary disorders

The use of galantamine is not recommended in patients with urinary outflow obstruction or recovering from bladder

surgery.

Surgical and medical procedures

Galantamine, as a cholinomimetic is likely to exaggerate succinylcholine-type muscle relaxation during anaesthesia, especially in cases of pseudocholinesterase deficiency.

4.5 Interaction with other medicinal products and other forms of interaction

Because of its mechanism of action, galantamine should not be given concomitantly with other cholinomimetics (such as ambenonium, donepezil, neostigmine, pyridostigmine, rivastigmine or systemically administered pilocarpine). Galantamine has the potential to antagonise the effect of anticholinergic medication. Should anticholinergic medicinal products such as atropine be abruptly stopped there is a potential risk that galantamine's effect could be exacerbated. As expected with cholinomimetics, a pharmacodynamic interaction is possible with medicinal products that significantly reduce the heart rate such as digoxin, beta-blockers, certain calcium-channel blocking agents and amiodarone. Caution should be taken with medicinal products that have potential to cause torsades de pointes. In such cases an ECG should be considered.

Galantamine, as a cholinomimetic, is likely to exaggerate succinylcholine-type muscle relaxation during anaesthesia, especially in cases of pseudocholinesterase deficiency.

Pharmacokinetic interactions

Multiple metabolic pathways and renal excretion are involved in the elimination of galantamine. The possibility of clinically relevant interactions is low. However, the occurrence of significant interactions may be clinically relevant in individual cases.

Concomitant administration with food slows the absorption rate of galantamine but does not affect the extent of absorption. It is recommended that Galantamine be taken with food in order to minimise cholinergic side effects.

Other medicinal products affecting the metabolism of galantamine

Formal drug interaction studies showed an increase in galantamine bioavailability of about 40% during co-administration of paroxetine (a potent CYP2D6 inhibitor) and of 30% and 12% during co-treatment with ketoconazole and erythromycin (both CYP3A4 inhibitors). Therefore, during initiation of treatment with potent inhibitors of CYP2D6 (e.g. quinidine, paroxetine or fluoxetine) or CYP3A4 (e.g. ketoconazole or ritonavir) patients may experience an increased incidence of cholinergic adverse reactions, predominantly nausea and vomiting. Under these circumstances, based on tolerability, a reduction of the galantamine maintenance dose can be considered (see section 4.2).

Memantine, an N-methyl-D-aspartate (NMDA) receptor antagonist, at a dose of 10 mg once a day for 2 days followed by 10 mg twice a day for 12 days, had no effect on the pharmacokinetics of galantamine (as Galantax XL prolonged-release capsules 16 mg once a day) at steady state.

Effect of galantamine on the metabolism of other medicinal products

Therapeutic doses of galantamine 24 mg/day had no effect on the kinetics of digoxin, although pharmacodynamic interactions may occur (see also pharmacodynamic interactions).

Therapeutic doses of galantamine 24 mg/day had no effect on the kinetics and prothrombin time of warfarin.

4.6 Fertility, pregnancy and lactation

Pregnancy

For galantamine no clinical data on exposed pregnancies are available. Studies in animals have shown reproductive toxicity (see section 5.3). Caution should be exercised when prescribing to pregnant women.

Breastfeeding

It is not known whether galantamine is excreted in human breast milk and there are no studies in lactating women. Therefore, women on galantamine should not breast-feed.

4.7 Effects on ability to drive and use machines

Galantamine has minor or moderate influence on the ability to drive and use machines. Symptoms include dizziness and somnolence, especially during the first weeks after initiation of treatment.

4.8 Undesirable effects

The table below reflects data obtained with in seven placebo-controlled, double-blind clinical trials (N=4457), five open-label clinical trials (N=1454), and from postmarketing spontaneous reports. The most commonly reported adverse drug reactions were nausea (25%) and vomiting (13%). They occurred mainly during titration periods, lasted less than a week in most cases and the majority of patients had one episode. Prescription of anti-emetics and ensuring adequate fluid intake may be useful in these instances.

In a randomised, double-blind, placebo-controlled clinical trial, the safety profile of once-daily treatment with Galantamine prolonged-release capsules was similar in frequency and nature to that seen with immediate release tablets.

Frequency estimate: very common (≥1/10); common (≥1/100 to < 1/10); uncommon (≥1/1000 to < 1/100); rare (≥1/10,000 to <1/1000); and very rare (<1/10,000).

System Organ Class	**Adverse Drug Reaction Frequency**				
	Very common	Common	Uncommon	Rare	Very rare
Immune system disorders			Hypersensitivity		
Metabolism and nutrition disorders		Decreased appetite; Anorexia	Dehydration		
Psychiatric disorders		Hallucination; Depression	Hallucination visual; Hallucination auditory		
Nervous system disorders		Syncope; Dizziness; Tremor; Headache; Somnolence; Lethargy	Paraesthesia; Dysgeusia; Hypersomnia Seizures*		
Eye disorders			Vision blurred		

Ear and labyrinth disorders			Tinnitus	
Cardiac disorders		Bradycardia	Supraventricular extrasystoles; Atrioventricular block first degree; Sinus bradycardia; Palpitations	
Vascular disorders		Hypertension	Hypotension; Flushing	
Gastrointestinal disorders	Vomiting; Nausea	Abdominal pain; Abdominal pain upper; Diarrhoea; Dyspepsia; Stomach discomfort; Abdominal discomfort	Retching	
Hepatobiliary disorders				Hepatitis
Skin and subcutaneous tissue disorders		Hyperhidrosis		
Musculoskeletal and connective tissue disorders		Muscle spasms	Muscular weakness	
General disorders and administration site conditions		Fatigue; Asthenia; Malaise		
Investigations		Weight decreased	Hepatic enzyme increased	
Injury, poisoning and procedural complications		Fall		

* Class-related effects reported with acetylcholinesterase-inhibitor antidementia drugs include convulsions/seizures (see 4.4 Nervous system disorders)

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 Pharmacovigilance Section, Irish Medicines Board, Kevin O'Malley House, Earlsfort Centre, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517; Website: www.imb.ie; e-mail: imbpharmacovigilance@imb.ie

4.9 Overdose

Symptoms

Signs and symptoms of significant overdosing of galantamine are predicted to be similar to those of overdosing of other cholinomimetics. These effects generally involve the central nervous system, the parasympathetic nervous system, and the neuromuscular junction. In addition to muscle weakness or fasciculations, some or all of the signs of a cholinergic crisis may develop: severe nausea, vomiting, gastrointestinal cramping, salivation, lacrimation, urination, defecation, sweating, bradycardia, hypotension, collapse and convulsions. Increasing muscle weakness together with tracheal hypersecretions and bronchospasm, may lead to vital airway compromise.

There have been post-marketing reports of torsade de pointes, QT prolongation, bradycardia, ventricular tachycardia and brief loss of consciousness in association with inadvertent overdoses of galantamine. In one case where the dose was known, eight galantamine 4 mg tablets (32 mg total) were ingested on a single day.

Two additional cases of accidental ingestion of 32 mg (nausea, vomiting, and dry mouth; nausea, vomiting, and substernal chest pain) and one of 40 mg (vomiting) resulted in brief hospitalisations for observation with full recovery. One patient, who was prescribed 24 mg/day and had a history of hallucinations over the previous two years, mistakenly received 24 mg twice daily for 34 days and developed hallucinations requiring hospitalisation. Another patient, who was prescribed 16 mg/day of oral solution, inadvertently ingested 160 mg (40 ml) and experienced sweating, vomiting, bradycardia, and near-syncope one hour later, which necessitated hospital treatment. His symptoms resolved within 24 hours.

Treatment

As in any case of overdose, general supportive measures should be used. In severe cases, anticholinergics such as atropine can be used as a general antidote for cholinomimetics. An initial dose of 0.5 to 1.0 mg i.v. is recommended, with subsequent doses based on the clinical response.

Because strategies for the management of overdose are continually evolving, it is advisable to contact a poison control centre to determine the latest recommendations for the management of an overdose.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anti-dementia drugs

ATC-code: N06DA04

Galantamine, a tertiary alkaloid is a selective, competitive and reversible inhibitor of acetylcholinesterase. In addition, galantamine enhances the intrinsic action of acetylcholine on nicotinic receptors, probably through binding to an allosteric site of the receptor. As a consequence, an increased activity in the cholinergic system associated with improved cognitive function can be achieved in patients with dementia of the Alzheimer type.

Clinical studies

Galantamine was originally developed in the form of immediate-release tablets for twice-daily administration. The dosages of galantamine effective in these placebo-controlled clinical trials with a duration of 5 to 6 months were 16, 24 and 32 mg/day. Of these doses 16 and 24 mg/day were determined to have the best benefit/risk relationship and are the recommended maintenance doses. The efficacy of galantamine has been shown using outcome measures which evaluate the three major symptom complexes of the disease and a global scale: the ADAS-cog/11 (a performance based measure of cognition), DAD and ADCS-ADL-Inventory (measurements of basic and instrumental Activities of Daily

Living), the Neuropsychiatric Inventory (a scale that measures behavioural disturbances) and the CIBIC-plus (a global assessment by an independent physician based on a clinical interview with the patient and caregiver).

Composite Responder Analysis Based on at Least 4 Points Improvement in ADAS-cog/11 Compared to Baseline and CIBIC-plus Unchanged + Improved (1-4), and DAD/ADL Score Unchanged + Improved. See Table below.

At least 4 points improvement from baseline in ADAS-cog/11 and CIBIC-plus Unchanged + Improved								
Treatment	Change in DAD ≥ 0 GAL-USA-1 and GAL-INT-1(Month 6)				Change in ADCS/ADL-Inventory ≥ 0 GAL-USA-10 (Month 5)			
	n	n (%) of responder	Comparison with placebo		n	n (%) of responder	Comparison with placebo	
			Diff (95% CI)	p-value†			Diff (95% CI)	p-value†
Classical ITT#								
Placebo	422	21 (5.0)	–	–	273	18 (6.6)	–	–
Galantamine 16 mg/day	–	–	–	–	266	39 (14.7)	8.1 (3, 13)	0.003
Galantamine 24 mg/day	424	60 (14.2)	9.2 (5, 13)	<0.001	262	40 (15.3)	8.7 (3, 14)	0.002
*Traditional LOCF**								
Placebo	412	23 (5.6)	–	–	261	17 (6.5)	–	–
Galantamine 16 mg/day	–	–	–	–	253	36 (14.2)	7.7 (2, 13)	0.005
Galantamine 24 mg/day	399	58 (14.5)	8.9 (5, 13)	<0.001	253	40 (15.8)	9.3 (4, 15)	0.001

ITT: Intent To Treat

† CMH test of difference from placebo.

* LOCF: Last Observation Carried Forward.

The efficacy of Galantamine prolonged release capsules was studied in a randomised, double-blind, placebo-controlled trial, GAL-INT-10, using a 4-week dose escalation, flexible dosing regimen of 16 or 24 mg/day for a treatment duration of 6 months. Galantamine immediate-release tablets (Gal-IR) were added as a positive control arm. Efficacy was evaluated using the ADAS-cog/11 and the CIBIC-plus scores as co-primary efficacy criteria, and ADCS-ADL and NPI scores as secondary end-points. Galantamine prolonged release capsules (Gal-PR) demonstrated statistically significant improvements in the ADAS-cog/11 score compared to placebo, but were not statistically different in the CIBIC-plus score compared to placebo. The results of the ADCS-ADL score were statistically significantly better compared to placebo at week 26.

Composite Responder Analysis at Week 26 Based on at Least 4 Points Improvement from Baseline in ADAS-

cog/11, Total ADL Score Unchanged + Improved (≥0) and No Worsening in CIBIC-plus Score (1-4). See Table below.

GAL-INT-10	Placebo	Gal-IR†	Gal-PR*	p-value (Gal-PR* vs. Placebo)
	(n = 245)	(n = 225)	(n = 238)	
Composite Response: n (%)	20 (8.2)	43 (19.1)	38 (16.0)	0.008
† Immediate release tablets * Prolonged release capsules				

The results of a 26-week double-blind placebo-controlled trial, in which patients with vascular dementia and patients with Alzheimer's disease and concomitant cerebrovascular disease (“mixed dementia”) were included, indicate that the symptomatic effect of galantamine is maintained in patients with Alzheimer's disease and concomitant cerebrovascular disease (see section 4.4, Nervous system disorders). In a post-hoc subgroup analysis, no statistically significant effect was observed in the subgroup of patients with vascular dementia alone.

In a second 26-week placebo-controlled trial in patients with probable vascular dementia, no clinical benefit of galantamine treatment was demonstrated.

5.2 Pharmacokinetic properties

Galantamine is an alkalinic compound with one ionisation constant (pKa 8.2). It is slightly lipophilic and has a partition coefficient (Log P) between n-octanol/buffer solution (pH 12) of 1.09. The solubility in water (pH 6) is 31 mg/ml. Galantamine has three chiral centres. The S, R, S-form is the naturally occurring form. Galantamine is partially metabolised by various cytochromes, mainly CYP2D6 and CYP3A4. Some of the metabolites formed during the degradation of galantamine have been shown to be active *in vitro* but are of no importance *in vivo*.

General characteristics of galantamine

Absorption

The absolute bioavailability of galantamine is high, 88.5 ± 5.4%. Galantamine prolonged release capsules are bioequivalent to the twice-daily immediate-release tablets with respect to AUC_{24h} and C_{min}. The C_{max} value is reached after 4.4 hours and is about 24% lower than that of the tablet. Food has no significant effect on AUC of the prolonged release capsules. C_{max} was increased by about 12% and T_{max} increased by about 30 minutes when the capsule was given after food. However, these changes are unlikely to be clinically significant.

Distribution

The mean volume of distribution is 175 l. Plasma protein binding is low, 18%.

Metabolism

Up to 75% of galantamine dosed is eliminated via metabolism. *In vitro* studies indicate that CYP2D6 is involved in the formation of O-desmethylgalantamine and CYP3A4 is involved in the formation of N-oxide-galantamine. The levels of

excretion of total radioactivity in urine and faeces were not different between poor and extensive CYP2D6 metabolisers. In plasma from poor and extensive metabolisers, unchanged galantamine and its glucuronide accounted for most of the sample radioactivity. None of the active metabolites of galantamine (norgalantamine, O-desmethylgalantamine and O-desmethyl-norgalantamine) could be detected in their unconjugated form in plasma from poor and extensive metabolisers after single dosing. Norgalantamine was detectable in plasma from patients after multiple dosing, but did not represent more than 10% of the galantamine levels. *In vitro* studies indicated that the inhibition potential of galantamine with respect to the major forms of human cytochrome P450 is very low.

Elimination

Galantamine plasma concentration declines bi-exponentially, with a terminal half-life around 8-10 hours in healthy subjects. Typical oral clearance in the target population is about 200 ml/min with intersubject variability of 30% as derived from the population analysis of immediate-release tablets. Seven days after a single oral dose of 4 mg ^{3}H-galantamine, 90-97% of the radioactivity is recovered in urine and 2.2-6.3% in faeces. After i.v. infusion and oral administration, 18-22% of the dose was excreted as unchanged galantamine in the urine in 24 hours, with a renal clearance of 68.4 ±22.0 ml/min, which represents 20-25% of the total plasma clearance.

Dose-linearity

Galantamine pharmacokinetics of Galantamine prolonged release capsules are dose proportional within the studied dose range of 8 mg to 24 mg once-daily in elderly and young age groups.

Characteristics in patients

Data from clinical trials in patients indicate that the plasma concentrations of galantamine in patients with Alzheimer's disease are 30% to 40% higher than in healthy young subjects primarily due to the advanced age and reduced kidney function. Based upon the population pharmacokinetic analysis, clearance in female subjects is 20% lower as compared to males. The galantamine clearance in poor metabolisers of CYP2D6 is about 25% lower than in extensive metabolisers, but no bimodality in the population is observed. Therefore, the metabolic status of the patient is not considered to be of clinical relevance in the overall population.

The pharmacokinetics of galantamine in subjects with mild hepatic impairment (Child-Pugh score of 5 to 6) were comparable to those in healthy subjects. In patients with moderate hepatic impairment (Child-Pugh score of 7 to 9), AUC and half-life of galantamine were increased by about 30% (see section 4.2).

Elimination of galantamine decreases with decreasing creatinine clearance as observed in a study with renally impaired subjects. Compared to Alzheimer patients, peak and trough plasma concentrations are not increased in patients with a creatinine clearance of $\geq$ 9 ml/min. Therefore, no increase in adverse events is expected and no dosage adjustments are needed (see section 4.2).

Pharmacokinetic/pharmacodynamic relationship

No apparent correlation between average plasma concentrations and efficacy parameters (i.e. change in ADAS-cog/11 and CIBIC-plus at month 6) were observed in the large Phase III trials with a dose-regimen of 12 and 16 mg twice-daily.

Plasma concentrations in patients experiencing syncope were within the same range as in the other patients at the same dose.

The occurrence of nausea is shown to correlate with higher peak plasma concentrations (see section 4.5).

5.3 Preclinical safety data

Non-clinical data suggest no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and carcinogenic potential.

Reproduction toxicity studies showed a slight delay in development in rats and rabbits, at doses that are below the threshold of toxicity in the pregnant females.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule contents

Cellulose microcrystalline

Hypromellose

Ethylcellulose

Magnesium stearate

Capsule shell

Gelatin
Titanium dioxide (E171)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Transparent PVC/PE/PvdC-Aluminium blister.

pack sizes:
10, 28, 30, 84, 90, 100, 300 prolonged release capsules

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Clonmel Healthcare Ltd
Waterford Road,
Clonmel,

Co. Tipperary,
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0126/222/003

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of First Authorisation: 1st March 2013

10 DATE OF REVISION OF THE TEXT

December 2015