SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Selegiline Hydrochloride 10mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 10mg of selegiline hydrochloride

Excipients with known effect: Each tablet contains 105.6mg of lactose

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Tablet

A white, round shaped tablets with an approximate diameter of 8mm, embossed "SEL10" on one side and break line on the other side

The score line is not intended for breaking the tablet

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Selegiline is indicated for the treatment of Parkinson's disease or symptomatic parkinsonism which is being treated with levodopa alone or levodopa and peripheral decarboxylase inhibitor.
Selegiline, in conjunction with maximal levodopa treatment, is indicated particularly in patients during maximal levodopa treatment who develop fluctuations in their condition such as ‘end-dose’ type fluctuations, ‘on-off’ symptoms or other dyskinesias.

4.2 Posology and method of administration

Posology
Dosage (dose and interval) and duration

When used as an adjunct to established Levodopa therapy, the initial dose of Selegiline is 5mg in the morning.
If symptoms are very severe e.g. on/off symptoms and little response is achieved with 5mg Selegiline daily, the dose of Selegiline can be increased to 10mg in the morning.

When selegiline is added to a levodopa regimen it is possible to reduce the levodopa dosage by an average of 10-30%. Reduction of levodopa dose should be gradual in steps of 10% every 3 to 4 days.

Dosage adjustment in renal or liver insufficiency, dialysis, concomitant disease
No dosage adjustment is indicated

Maximum tolerated daily dose and the maximum dose for an entire course of therapy
The maximum recommended daily dose is 10mg, although no problems have been reported with overdosage (due to the low toxicity of Selegiline hydrochloride).

Monitoring advice
No special monitoring required.

Special Populations
Patients with hepatic impairment
No data are known on dose adjustment in patients with mild hepatic impairment.

Patients with renal impairment
No data are known on dose adjustment in patients with mild renal impairment.

4.3 Contraindications

Selegiline is contra-indicated

- In patients with known hypersensitivity (including severe dizziness or hypotension) to selegiline or to any of the excipients listed in section 6.1.
- In patients receiving treatment with serotonin-agonists (e.g. sumatriptan, naratriptan, zolmitriptan and rizatriptan).
- For concomitant use with pethidine and other opioids (see section 4.5).
- In patients who are being treated with antidepressant drugs including MAO inhibitors tricyclic antidepressants, selective serotonin reuptake inhibitors (SSRI) (e.g citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline) and serotonin noradrenaline reuptake inhibitor (SNRI) (venlafaxine) (see section 4.5).
- with other drugs which are also monoamine oxidase inhibitors, e.g. linezolid.
- In combination with sympathomimetics (see section 4.5).
- Selegiline should not be used in patients with active duodenal or gastric ulcer.
- Selegiline should not be used in patients with other extrapyramidal disorders not related to dopamine deficiency.
- When selegiline is prescribed in combination with levodopa, the contraindications which apply to levodopa must be taken into account. Selegiline in combination with levodopa is contra-indicated in severe cardiovascular disease, arterial hypertension, hyperthyroidism, phaeochromocytoma, narrow-angle glaucoma, prostatic adenoma with appearance of residual urine, tachycardia, arrhythmias, severe angina pectoris, psychoses, advanced dementia and thyrotoxicosis.

4.4 Special warnings and precautions for use

The precise dose at which selegiline becomes a non-selective inhibitor of all MAO has not been determined, but with doses higher than 10 mg/day there is a theoretical risk of hypertension after ingestion of tyramine-rich food.

Concomitant treatment with medicines which inhibit MAO-A, (or non-selective MAO inhibitors) can cause hypotensive reactions. Hypotension, sometimes sudden in onset, has been reported with conventional selegiline.

Selegiline should be administered cautiously to patients with history of or who have peptic or duodenal ulceration, labile hypertension, cardiac arrhythmias, severe angina pectoris, or psychosis as aggravation of these conditions may occur during treatment.

Although serious hepatic toxicity has not been observed, caution is recommended in patients with a history of hepatic dysfunction. Transient or continuing abnormalities with a tendency for elevated plasma concentrations of liver enzymes have been described during long-term therapy with conventional tablets of selegiline.

Selegiline should be used with caution in severe liver or kidney dysfunction.

In higher doses (higher than recommended one, 10 mg) the selectivity of selegiline begins to diminish resulting in loss of its MAO-B selectivity and increased inhibition of MAO-A. Thus in higher doses there is a risk of hypertension.

Since the selegiline potentiates the effect of levodopa, the side effects of levodopa may be more pronounced, especially if patients are receiving levodopa therapy with high doses. These patients should be monitored. The addition of selegiline to maximum tolerated dose of levodopa therapy may cause creation of involuntary movements and/or agitation. These undesirable effects disappear after levodopa doses reduction. Dosage of levodopa could be reduced to about 30 % in combination with selegiline. Levodopa should be reduced by about 10 to 30% when selegiline is added to the treatment (see section 4.2). When an optimum dose of levodopa is reached, adverse effects from the combination are less than those observed with levodopa on its own.

Some studies concluded in an increased risk of mortality in patients receiving selegiline and levodopa compared to those receiving levodopa only. However, it is noteworthy that multiple methodological bias were identified in these studies and that a meta analysis and large cohort studies concluded that there was no significant difference in mortality in patients treated with selegiline to those treated with comparators or with the association selegiline/levodopa.

Studies have related the risk of an increased hypotensive response to concomitant administration of selegiline and levodopa, in patients with cardiovascular risk.

The addition of selegiline to levodopa may not be beneficial in those patients who experience fluctuations in response which are not dose dependent.

Caution should be exercised in patients receiving MAO inhibitors during general anaesthesia in surgery. MAO inhibitors, including selegiline, may potentiate the effects of CNS depressants used for general anaesthesia.

Transient respiratory and cardiovascular depression, hypotension and coma have been reported (see section 4.5).

Caution is advised when selegiline is taken in combination with other centrally acting medicinal products and substances. The concomitant intake of alcohol should be avoided.

Parkinson's disease patients treated with dopamine agonists and other dopaminergic treatments have been reported as exhibiting impulse control disorders and compulsions like pathological gambling, increased libido, hypersexuality, binge eating, shopping and different kinds of compulsive /repetitive activities (punding). These may also be possible with selegiline but very few cases have been reported to date.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Serotonin agonists

Selegiline should not be used in combination with serotonin agonists (e.g. sumatriptan, naratriptan, zolmitriptan, rizatriptan, lasmiditan) due to the risk of severe interactions (potentially leading to serotonin syndrome).

Association contra-indicated (*see section 4.3*)

Sympathomimetics

Because of the risk of hypertension, co-administration of selegiline and sympathomimetics is contraindicated.

Selegiline should not be administered with any type of antidepressant.

Pethidine and other opioids

Interactions between non-selective MAO-inhibitors and pethidine as well as selegiline and pethidine have been described. The mechanism of this interaction is not fully understood. The concomitant administration of the selective MAO-B inhibitor selegiline and pethidine and other opioids are contraindicated. (see section 4.3).

Tricyclic antidepressants

Severe central nervous system toxicity (serotonin syndrome), sometimes associated with hypertension, hypotension, diaphoresis has been occasionally reported in patients with the combination of tricyclic antidepressants and selegiline.

In one patient receiving amitriptyline and selegiline this included hyperpyrexia and death, and another patient receiving protriptyline and selegiline experienced tremor, agitation, and restlessness followed by unresponsiveness and death two weeks after selegiline was added.

Other adverse reactions occasionally reported in patients receiving a combination of selegiline with various tricyclic antidepressants include hyper/hypotension, dizziness, diaphoresis, tremor, seizures and changes in behavioural and mental status. Therefore, the concomitant use of selegiline and tricyclic antidepressants is contraindicated.

Selective serotonin reuptake inhibitors (SSRIs) and serotonin noradrenaline reuptake inhibitors (SNRIs)

When selegiline is used at its recommended dose, it selectively inhibits MAO-B. The combined use of the SSRI, fluoxetine and Selegiline, should only be used under clinical supervision.

Serious reactions with signs and symptoms that may include diaphoresis, flushing, ataxia, tremor, hyperthermia, hyper/hypotension, seizures, palpitation, dizziness and mental changes that include agitation, confusion and hallucinations progressing to delirium and coma have been reported in some patients receiving a combination of selegiline and fluoxetine. Similar experience has been reported in patients receiving selegiline and two other serotonin reuptake inhibitors, sertraline and paroxetine. There is a potential risk of interaction with fluvoxamine and venlafaxine.

Because of the risk of confusion, hypomania, hallucination and manic episodes, agitation, myoclonus, hyperreflexia, incoordination, shivering, tremor, convulsion, ataxia, diaphoresis, diarrhea, fever, hypertension, which can be part of the serotonine syndrome,

concomitant administration of selegiline and SSRIs or SNRIs is contraindicated.

Use of selegiline beyond the recommended dose could lead to non-selectivity and serious adverse effects.

Death has been reported to occur following the initiation of therapy with nonselective MAO inhibitors shortly after discontinuation of fluoxetine. Fluoxetine should not be used less than 14 days after discontinuation of selegiline. Since fluoxetine and its active metabolite have long elimination half-lives, at least 5 weeks should be allowed after stopping/discontinuation of fluoxetine and before starting selegiline.

Selegiline should not be started until 2 weeks after stopping sertraline. For all other serotonin reuptake inhibitors, a time interval of 1 week is recommended between discontinuation of the serotonin reuptake inhibitor and initiation of selegiline. In general, selegiline should not be introduced after a drug that is known to interact with selegiline, until after 5 half lives of that drug have elapsed.

At least 14 days should lapse between the discontinuation of selegiline and initiation of treatment with any drug known to interact with selegiline.

A time interval of 24 hours is recommended between the discontinuation of selegiline and initiation of serotonin agonists.

Patients being treated with selegiline currently or within the past 2 weeks should receive dopamine only after careful risk-benefit assessment, as this combination enhances the risk of hypertensive reactions.

Selegiline should not be given in conjunction with non-specific MAO inhibitors, e.g.
linezolid.

MAO inhibitors

Concomitant administration of selegiline and MAO inhibitors may cause central nervous and cardiovascular system disorders *(*see section 4.4*).*

Associations not recommended

MAO inhibitors

Concomitant administration of selegiline and MAO inhibitors may cause severe hypotension *(see section 4.4).*

Oral contraceptives

The combination of selegiline and oral contraceptives or drugs for hormone replacement therapy, should be avoided, as this combination may increase the bioavailability of selegiline.

In view of the high degree of binding to plasma proteins by selegiline particular attention must be given to patients who are being concomitantly treated with medicines with a narrow therapeutic margin/index such as digitalis and/or anticoagulants, requires caution and careful monitoring.

Concomitant use of nasal decongestants, hypertensive agents, antihypertensives, psychostimulants, central suppressant drugs (sedatives, hypnotics) and alcohol should be avoided.

Concomitant administration of amantadine and anticholinergic drugs can lead to an increased occurrence of side-effects.

Four patients receiving altretamine and a monamine oxidase inhibitor experienced symptomatic hypotension after four to seven days of concomitant therapy.

Food interactions

As selegiline is a specific MAO-B inhibitor, foods containing tyramine have not been reported to induce hypertensive reactions during selegiline treatment at recommended dosage (i.e., it does not cause the so-called “cheese-effect”). Therefore, no dietary restrictions are required. However, in case of combination of selegiline and conventional MAO inhibitors or MAO-A, dietary restrictions (i.e.

avoidance of food with large amounts of tyramine such as aged cheese and yeast products) are recommended.

4.6 Fertility, pregnancy and lactation

Selegiline is indicated for the treatment of Parkinson's disease which, in most cases, is a disease occurring after childbearing age.

Pregnancy

Very limited data on pregnant patients are available.

The available safety data concerning the use during pregnancy and lactation is insufficient to justify the use of selegiline in these patient groups.

Studies in animals have shown reproductive toxicity only at high multiple of human doses.

As a precautionary measure, it is preferable to avoid the use of selegiline in pregnancy.

Breast-feeding

It is unknown whether selegiline is excreted in human breast milk. The excretion of selegiline in milk has not been studied in animals. Physico-chemical data on selegiline point to excretion in breast milk and a risk to the suckling child cannot be excluded. Selegiline should not be used during breast-feeding.

4.7 Effects on ability to drive and use machines

As even when used correctly, this medicine may cause dizziness, or can affect reaction capacity to the extent that driving or operating machinery is affected and therefore patients should be advised not to drive or use machines if they experience these adverse reactions during treatment.

This medicine can impair cognitive function and can affect a patient's ability to drive safely. This class of medicine is in the list of drugs included in regulations under 5a of the Road Traffic Act 1988. When prescribing this medicine, patients should be told:

- The medicine is likely to affect your ability to drive
- Do not drive until you know how the medicine affects you
- It is an offence to drive while under the influence of this medicine
- However, you would not be committing an offence (called 'statutory defence') if:
  - The medicine has been prescribed to treat a medical or dental problem and

- You have taken it according to the instructions given by the prescriber and in the information provided with the medicine and
- It was not affecting your ability to drive safely

4.8 Undesirable effects

In monotherapy, selegiline has been found to be well tolerated. Dry mouth, transient rise of serum alanine aminotransferase (ALAT) values and sleeping disorders have been reported more frequently than in patients receiving placebo. Because selegiline potentiates the effects of levodopa, the adverse reactions/side effects of levodopa, e.g. restlessness, hyperkinesis, abnormal movements **(**such as dyskinesias), nausea, agitation, confusion, hallucinations, headache, postural hypotension, cardiac arrhythmias and vertigo, may be enhanced in combination therapy (levodopa should be given in association with a peripheral decarboxylase inhibitor), particularly if the dose of levodopa is too high. Such adverse reactions usually disappear when the levodopa dosage is decreased. Levodopa dosage can be reduced by an average of 30% when selegiline is added to the treatment. Once the optimum levodopa dose level has been established, the side-effects produced by the combination will usually be less than those caused by the levodopa therapy on its own.

Micturition difficulties and skin reactions have also been reported during selegiline treatment. Follow-up of these possible adverse reactions is important.

Hypersexuality has been very rarely reported in association with selegiline use, either as monotherapy or in combination with other dopaminergic antiparkinsonian medication.

A summary of the undesirable effects in terms of frequency of occurrence is shown below. The following undesirable effects have been reported with selegiline during clinical trials and/or post-marketing use. They are listed below as MedDRA preferred term by system organ class and frequency.Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness. Very common (≥ 1/10); Common (≥ 1/100 to <1/10); Uncommon (≥ 1/1,000 to <1/100); Rare (≥ 1/10,000 to <1/1,000); Very rare (<1/10,000), Not known (cannot be established from the available data).

System Organ Class	Frequency	Undesirable effects
Infections and infestations	Uncommon	Pharyngitis

Blood and lymphatic system disorders	Uncommon	Leucocytopenia, thrombocytopenia
Metabolism and nutrition disorders	Uncommon	Loss of appetite
Psychiatric disorders	Common	Sleeping disorders, confusion, hallucinations, depression
	Uncommon	Mood change, abnormal dreams, agitation, anxiety, psychoses.
	Not known	Impulse control disorders and compulsions*
Nervous system disorders	Common	Abnormal movements (such as dyskinesias), akinesia, bradykinesia dizziness , headache, impaired balance, tremor
	Uncommon	Mild transient sleep disorder
Eye disorders	Uncommon	Blurred vision
Ear and labyrinth disorders	Common	Vertigo
Cardiac disorders	Common	Bradycardia
	Uncommon	Supraventricular tachycardia, cardiac arrhythmia, palpitations, angina pectoris
Vascular disorders	Common	hypotension, hypertension
	Uncommon	Orthostatic hypotension
	Rare	Postural hypotension
Respiratory, thoracic and mediastinal disorders	Common	Nasal congestion, sore throat
	Uncommon	Dyspnoea
Gastrointestinal disorders	Very common	Stomatitis

	Common	Nausea, constipation, diarrhoea, mouth ulceration
	Uncommon	Dry mouth
Hepato-biliary disorders	Common	Transient rise of serum alanine aminotransferase (ALAT)
Skin and subcutaneous tissue	Common	Sweating increased
	Uncommon	Hair loss, skin eruptions
	Rare	Skin reactions
Musculoskeletal and lymphatic system disorders	Common	Arthralgia, back pain, muscle cramps
	Uncommon	Myopathy
Renal and urinary disorders	Uncommon	Micturition disorders
	Not known	Urinary retention
General disorders and administration site conditions	Common	Fatigue
	Uncommon	Chest pain, irritability, ankle oedema
Injury, poisoning and procedural complications	Common	Fall
Investigations	Common	Mild hepatic enzymes increased

*****Parkinson's disease patients treated with dopamine agonists and other dopaminergic treatments have been reported as exhibiting impulse control disorders and compulsions like pathological gambling, increased libido, hypersexuality, compulsive spending or buying, binge eating and complusive eating, and different kinds of compulsive/repetitive activities (punding). These may also be possible with selegiline but very few cases have been reported to date.

In combination with levodopa

As selegiline potentiates the effects of levodopa (levodopa should be usually given in association with a peripheral decarboxylase inhibitor), the side effects of levodopa may be emphasised unless the dosage of levodopa is reduced. Selegiline combination therapy may permit further reduction of levodopa dose (even by 30%). The most common undesirable effect reported for conventional tablets is dyskinesia (4% of patients) other side effects include restlessness,

hyperkinesis, abnormal movements, agitation, confusion, hallucination, postural hypotension, cardiac arrhythmias. Once the optimum dose level has been established, the side effects produced by the combination will be less than those caused by the levodopa therapy on its own.

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 at: www.mhra.gov.uk/yellowcard.

4.9 Overdose

No over dosage problems have been reported, due to the low toxicity of Selegiline hydrochloride and its rapid metabolism to, and excretion of, the metabolites. If overdosage is suspected, the patient should be monitored for 24-48 hours.

Overdoses have no specific clinical picture. No overdosage cases are known. Since the selective inhibition of MAO-B by selegiline is achieved only at doses recommended for the treatment of Parkinson's disease (5 to 10 mg/day). However, experience gained during selegiline's development reveals that some individuals exposed to doses of 600 mg/day selegiline suffered severe hypotension and psychomotor agitation.

Theoretically, the overdosage causes significant inhibition of both MAO-A and MAO-B and thus symptoms of overdosage may resemble those observed with non-selective MAO-inhibitors which can progress over 24 hours to include, such as different central nervous and cardiovascular system disorders (e.g. drowsiness, dizziness, faintness, irritability, hyperactivity, agitation, severe headache, hallucination, tremor, alternating hypertension and hypotension, vascular collapse, rapid and irregular pulse, precordial pain, respiratory depression and failure, severe muscle spasms, hyperpyrexia, diaphoresis, coma and convulsions). There is no specific antidote and the treatment is symptomatic.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Selective monoamine oxidase type B (MAO-B) inhibitor.
ATC Code: N04BD

Mechanism of action
Selegiline hydrochloride inhibits the MAO-B induced metabolism of dopamine in the brain, and inhibits re-uptake at the pre-synaptic dopamine receptor. These effects potentiate dopaminergic function in the brain and help to even out and prolong the effect of exogenous and endogenous dopamine. Thus selegiline potentiates and prolongs the effect of levodopa in the treatment of Parkinsonism. Since it does not interfere with the breakdown of 5 hydroxytryptamine (serotonin) or noradrenaline, it does not cause any hypertensive crises or changes in the plasma or urinary metabolites of these monoamines. Although dietary restrictions are not necessary during selegiline treatment, inhibition of MAO B in blood platelets can lead to a slight potentiation of the circulatory effects of any tyramine not broken down by gastrointestinal MAO A during absorption.

Pharmacodynamic effects
The magnitude of increase in the urinary excretion of β phenylethylamine over 24 hours is simply related to the area under the selegiline plasma-concentration-time curve after any selegiline product. Urinary β phenylethylamine increase reflects the degree of inhibition of MAO B.

Clinical efficacy and safety
Double-blind studies on early phase parkinsonian patients showed that patients receiving selegiline monotherapy manage significantly longer without levodopa therapy than controls receiving placebo. These patients could also maintain their ability to work longer.

The addition of selegiline to levodopa (with or without decarboxylase inhibitor) therapy helps to alleviate dose related fluctuations and end of dose deterioration.

When selegiline is added to such a regimen it is possible to reduce the levodopa dosage by an average of 30%. Unlike conventional MAO-inhibitors, which inhibit both the MAO-A and MAO-B enzymes, selegiline is a specific MAO-B inhibitor and can be given safely with levodopa.

Selegiline hydrochloride does not cause the so called “cheese effect” either when used alone as monotherapy, or when used with other drugs, except for moclobemide or nonselective MAO-inhibitors.

Selegiline administration has been associated with isolated reports of hypotension and nausea. Confusion or psychosis have also been reported.

5.2 Pharmacokinetic properties

Absorption
Selegiline hydrochloride is rapidly ($t_{½}$ of absorption 0.39hours) and completely absorbed from the gastro-intestinal tract and crosses the blood-brain barrier. The maximal concentrations are reached in 0.5-0.75h after oral administration in fasting state. The bioavailability is low; 10% (on the average; interindividual variations is large) of unchanged selegiline can reach the systemic circulation

Distribution
Selegiline is lipophilic, slightly basic compound which quickly penetrates into tissues, also into brain. The drug is rapidly distributed throughout the body and 75-85% of selegiline is bound to plasma proteins at therapeutic concentrations.. Selegiline hydrochloride crosses the blood-brain barrier. The apparent volume of distribution being 500L after an intravenous 10mg dose. Selegiline hydrochloride inhibits enzyme MAO-B irreversibly and enzyme activity only increases again after new enzyme is synthesized. The strong inhibitory effect platelet enzyme MAO-B activity after single 10mg dose lasts over 24 hour and the platelet enzyme MAO-B activity returns to normal level approximately after 2 weeks.

BiotransformationSelegiline hydrochloride is rapidly metabolised, mainly in the liver, into active metabolites l-amphetamine, l-methylamphetamine and to desmethylselegiline derivatives with elimination half-life of 17.7 hour, 20.5 hour and 2.1 hour respectively. *In-vitro* studies indicate that CYP2B6 is the main hepatic cytochrome P450(CYP) enzyme involved in the metabolism of selegiline with a possible contribution of CYP3A4 and CYP2A6.

Selegiline AUC and desmethylselegiline AUC increase 2.7 fold and 1.5 fold respectively from day 1 to day 8 on dosing 10mg od. However, the half-lives of selegiline (range, 1.5-3.5 hour) and desmethylselegiline (range, 3.4-5.3 hour) were found to be relatively short. Accordingly, the short half-lives of these compounds failed to predict the apparent accumulation.

The most likely explanation for the significant increase in selegiline and desmethylselegiline concentrations in serum which was observed during the 8-day multiple dose administration of selegiline hydrochloride is saturation of MAO-B binding sites in tissues, as the rapid elimination of both selegiline and desmethylselegiline cannot explain the apparent accumulation observed. However,

decrease in the first pass metabolism of selegiline on the multiple dosing cannot be ruled out.

Elimination
In humans three metabolites have been identified in the plasma and urine after single and multiple doses of selegiline. An average of 52% of the dose is excreted in the urine in 24 hours and 73% in 72 hours, mostly as the metabolites methylamphetamine and amphetamine. The mean elimination half-life is 1.5-3.5 hour for selegiline. The total body clearance of selegiline is about 240 L/hour. The metabolites of selegiline are excreted mainly via urine with only 15% is excreted in faeces.

5.3 Preclinical safety data

Selegiline has not been sufficiently tested for reproductive toxicity. Studies with selegiline revealed no evidence of mutagenic or carcinogenic effects. The only safety concerns for human use derived from animal studies were effects associated with an exaggerated pharmacological action (see section 4.6).

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose
Maize Starch
Povidone K-30
Citric Acid Monohydrate
Purified Water
Magnesium Stearate

6.2 Incompatibilities

None known

6.3 Shelf life

Shelf life of the product as packaged for sale
2 years

Shelf life after dilution or reconstitution according to directions
Not applicable

Shelf life after first opening the container
Not applicable

6.4 Special precautions for storage

Store in a dry place, below 25ºC. Store in the original package in order to protect from light.

6.5 Nature and contents of container

Tablets are packed in either HDPE (tubular) tablet containers with HDPE caps and tamper-evident tear strip (7, 14, 21, 28, 30, 50, 56, 60, 84, 90, 100, 112 & 120 tablets)
Or
In strips (Aluminium lidding foil and polyamide/Aluminium/PVC base), or PVdC coated PVC/Aluminium blisters (60g/m^2 PVdC on 250µm PVC/20µm Al) containing 7, 14, 21, 28, 30, 50, 56, 60, 84, 90, 100, 112 & 120 tablets.

Not all packs sizes or pack types may be marketed.

6.6 Special precautions for disposal

No special requirements for disposal. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Activase Pharmaceuticals Limited

11 Boumpoulinas

Nicosia

1060

Cyprus

8 MARKETING AUTHORISATION NUMBER(S)

PL 28444/0215

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

10/04/2026