Summary of Product Characteristics (SPC)

1. Name of medicinal product

1.1. Product name

SPORA-DERM CAPSULE

1.2 Strength

100 mg

1.3. Pharmaceutical dosage form

Hard capsule

2. Quality & Quantitative Composition

2.1. Qualitative declaration

Itraconazole 100 mg

2.2. Quantitative declaration

Each hard capsule contains Itraconazole 100 mg

3. Pharmaceutical form

Each hard capsule, with milk-white blue-colored cap and pink-colored body, is filled with white to pale yellow granules.

4. Clinical Particulars

4.1. Therapeutic indications

1. Vulvovaginal candidiasis.
2. Pityriasis versicolor.
3. Dermatophytoses caused by organisms susceptible to itraconazole (Trichophyton spp., Microsporum spp., Epidermophyton floccosum) e.g. tinaea pedis, tinea cruris, tinea corporis, tinea manuum.
4. Oropharyngeal candidiasis.
5. Mycotic keratitis
6. Onychomycosis caused by dermatophytes and/or yeasts.
7. Systemic mycoses, such as candidiasis, aspergillosis, cryptococcosis, histoplasmosis, and paracoccidioidomycosis

4.2. Posology and method of a administration

Itraconazole is for oral administration and must be taken immediately after a meal for maximal absorption.

Short term administration;

Itraconazole remains substantially longer in the skin than in the blood. Optimal healing is thus achieved 2-4 weeks after withdrawing Itraconazole in case of mycoses of the skin.

1) Vulvovaginal candidiasis : 200 mg twice daily for 1 day, or 200 mg once daily for 3 days

2) Pityriasis versicolor : 200 mg once daily for 7 days

3) Tinea corporis, Tinea cruris : 100 mg once daily for 15 days

4) Tinea pedis (interdigital), Tinea manuum (interdigital): 100 mg once daily for 15 days

5) Tinea pedis (soles), Tinea manuum (palms) : 100 mg once daily for 30 days or 200 mg twice daily for 7 days

6) Oropharyngeal candidiasis : 100 mg once daily for 15 days

7) Mycotic keratitis : 200 mg once daily for 21 days

Onychomycosis;

1) Pulse treatment (see table below):

Pulse itraconazole treatment consists of taking two capsules twice a day (200 mg b.i.d.) for one week.

For fingernail infections two pulse treatments are recommended, and for toenail infections, three. Each pulse should be separated by a period of three weeks with no treatment. Clinical response can be seen by in the form of nail growth when the treatment is ended.

Location of onychomycoses	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 9
Toenails with or without fingernail involvement	First pulse cycle	No itraconazole therapy			Second pulse cycle	No itraconazole therapy			Third pulse cycle
Finger nails only	First pulse cycle	No itraconazole therapy			Second pulse cycle				

2) Continuous treatment:

200 mg a day for three months. Effect of treatment lasts for 3 months in fingernails and 6 months in toenails.

3) Systemic mycoses

In some patients with compromised immune systems, such as neutropenic, AIDS or transplant patients, the bioavailability of oral itraconazole may be diminished. In these cases the dose may have to be doubled.

INDICATIONS	DOSE	AVERAGE DURATION	COMMENTS
Aspergillosis	200 mg o.d.	2-5 months	Increase dose to 200 mg b.i.d. in the case of widespread infection
Candidiasis	100-200 mg o.d.	3 weeks-7 months	
Non-meningeal cryptococcosis	200 mg o.d.	10 weeks	Maintenance therapy (meningeal cases): 200 mg o.d.
Cryptococcal meningitis	200 mg b.i.d.	2 months – 6 months	
Histoplasmosis	200 mg o.d.	8 months	
	200 mg b.i.d.		

4.3. Contraindications

SPORA-DERM should not be administered in the following cases:

1) Patients who have shown hypersensitivity to the drug or its excipients.

2) Patients with evidence of ventricular dysfunction such as congestive heart failure (CHF) or patients with a history of CHF should not use Itraconazole for the treatment of onychomycosis

3) Concomitant administration with CYP3A4 inducing agents. The use of itraconazole with these drugs may lead to subtherapeutic plasma levels of itraconazole and thus treatment failure. Co-administration may result in increased plasma concentrations of these substrates, which can lead to QT prolongation and rare occurrences of torsade de pointes. Detailed list of drugs are written in "DRUG INTERACTIONS" section.

4) Pregnant women or women of childbearing potential, and lactating women.

4.4. Special warning and precaution for use

WARNING

Itraconazole should not be administered in patients with evidence of ventricular dysfunction such as congestive heart failure (CHF) or in patients with a history of CHF for the treatment of onychomycosis in patients. If signs or symptoms congestive heart failure occur during treatment, Itraconazole should be discontinued. Myocardial contractility reduction was observed when Itraconazole was intravenously administered to healthy volunteers and dogs.

SPECIAL PRECAUTIONS

Itraconazole should be administered with caution in the following cases:

1) Patients with hepatic impairment or has a history of hepatic toxicity from other medications: Use Itraconazole only if benefits outweigh the risks because Itraconazole is usually metabolized in the liver, and in this case, liver function should be monitored.)

2) Patients with evidence of ventricular dysfunction such as congestive heart failure

(CHF) or patients with a history of CHF.
3) Patients with renal impairment (consider dosage adjustment as bioavailability is reduced)
4) Patients who have developed neuralgia from Itraconazole
5) Patients with compromised immune systems, such as neutropenic, AIDS or transplant patients, the bioavailability of oral itraconazole may be diminished. In these cases the dose may have to be adjusted.
6) For initial treatment of life-threatening systemic fungal infections
7) Patients with a history of hypersensitivity to other azole agents.

GENERAL PRECAUTIONS

1) Cardiac effects
In a healthy volunteer study with intravenous itraconazole, a transient asymptomatic decrease of the left ventricular ejection fraction was observed; this resolved before the next infusion. The clinical relevance of these findings to the oral formulations is unknown.
Itraconazole has been shown to have a negative inotropic effect and has been associated with reports of congestive heart failure. Heart failure was more frequently reported among spontaneous reports of 400 mg total daily dose than among those of lower total daily doses, suggesting that the risk of heart failure might increase with the total daily dose of itraconazole.
Itraconazole should not be used in patients with congestive heart failure or with a history of congestive heart failure unless the benefit clearly outweighs the risk. This individual benefit/risk assessment should take into consideration factors such as the severity of the indication, the dosing regimen (e.g., total daily dose), and individual risk factors for congestive heart failure. These risk factors include cardiac disease, such as ischemic and valvular disease; significant pulmonary disease, such as chronic obstructive pulmonary disease; and renal failure and other edematous disorders. Such patients should be informed of the signs and symptoms of congestive heart failure, should be treated with caution, and should be monitored for signs and symptoms of congestive heart failure during treatment; if such signs or symptoms do occur during treatment, itraconazole should be discontinued.
Calcium channel blockers can have negative inotropic effects which may be additive to those of itraconazole. In addition, itraconazole can inhibit the metabolisms of calcium channel blockers.Therefore, concurrent administration of itraconazole and calcium channel blockers should be carried out with caution (see section 4.5).
2) Hepatic effects
Very rare cases of serious hepatotoxicity, including some cases of fatal acute liver failure, have occurred with the use of itraconazole. Most of these cases involved

patients who, had pre-existing liver disease, were treated for systemic indications, had significant other medical conditions and/or were taking other hepatotoxic drugs. Some patients had no obvious risk factors for liver disease. Some of these cases were observed within the first month of treatment, including some within the first week. Liver function monitoring should be considered in patients receiving itraconazole treatment. Patients should be instructed to promptly report to their physician signs and symptoms suggestive of hepatitis such as anorexia, nausea, vomiting, fatigue, abdominal pain or dark urine. In these patients treatment should be stopped immediately and liver function testing should be conducted. In patients with raised liver enzymes or active liver disease, or who have experienced liver toxicity with other drugs, treatment should not be started unless the expected benefit exceeds the risk of hepatic injury. In such cases close liver enzyme monitoring is necessary.

3) Decreased gastric acidity : Absorption of itraconazole is impaired when gastric acidity is decreased. In patients also receiving acid neutralizing medicines (e.g. aluminium hydroxide), these should be administered at least 2 hours after the intake of Itraconazole. In patients with achlorhydria, such as certain AIDS patients and patients on acid secretion supressors (e.g. H_2-antagonists, proton-pump inhibitors), it is advisable to administer Itraconazole with a cola beverage.

4) Rarely cases of hepatitis and cholestatic jaundice have been reported, mainly in patients treated fro longer than one month. It is therefore advisable to monitor liver function in patients receiving continuous treatment of more than one month’s duration. If during treatment patients develop symptoms suggestive of hepatitis such as anorexia, nausea, vomiting, fatigue, abdominal pain or dark urine, liver enzymes should be monitored promptly. If these are abnormal, treatment should be stopped. In patients with raised liver enzymes or active liver disease, or who have experienced liver toxicity with other drugs, treatment should not be started unless the expected benefit exceeds the risk of hepatic injury. In such cases, liver enzyme monitoring is necessary.

5) Hepatic impairment : Itraconazole is predominantly metabolized in the liver. A slight decrease in oral bioavailability in cirrhotic patients has been observed, although this was not of statistical significance. The terminal half-life was however significantly increased. The dose should be adapted if necessary.

6) Renal impairment : The oral bioavailability of Itraconazole may be lower in patients with renal insufficiency. Dose adaptation may be considered.

7) If neuropathy occurs which may be attributable to Itraconazole, treament should be discontinued.

8) There is no information regarding cross hypersensitivity between Itraconazole and other azole antifungal agents. Caution should be used in prescribing Itraconazole to patients with hypersensitivity to other azoles.

9) In systemic candidiasis, if fluconazole-resistant strains of Candida species are

suspected, it cannot be assumed that these are sensitive to itraconazole, hence their sensitivity should be tested before the start of Itraconazole therapy.
10) Hearing loss: Transient or permanent hearing loss has been reported in patients receiving treatment with itraconazole. Several of these reports included concurrent administration of quinidine which is contraindicated. The hearing loss usually resolves when treatment is stopped, but can persist in some patients

4.5. Interaction with other medicinal products and other forms of interactions

Itraconazole is mainly metabolised through CYP3A4. Other substances that either share this metabolic pathway or modify CYP3A4 activity may influence the pharmacokinetics of itraconazole. Similarly, itraconazole may modify the pharmacokinetics of other substances that share this metabolic pathway. Itraconazole is a potent CYP3A4 inhibitor and a P-glycoprotein inhibitor. When using concomitant medication, it is recommended that the corresponding label be consulted for information on the route of metabolism and the possible need to adjust dosages.

1) Medicinal products that may decrease itraconazole plasma concentrations
Medicinal products that reduce the gastric acidity (e.g. acid neutralising medicines such as aluminum hydroxide, or acid secretion suppressors such as H2-receptor antagonists and proton pump inhibitors) impair the absorption of itraconazole from itraconazole capsules. It is recommended that these medicinal products be used with caution when coadministered with itraconazole capsules.
It is recommended that itraconazole be administered with an acidic beverage (such as non-diet cola) upon co-treatment with medicinal products reducing gastric acidity.
It is recommended that acid neutralising medicines (e.g. aluminum hydroxide) be administered at least 1 hour before or 2 hours after the intake of itraconazole capsules.
Upon coadministration, it is recommended that the antifungal activity be monitored and the itraconazole dose increased as deemed necessary.
Coadministration of itraconazole with potent enzyme inducers of CYP3A4 may decrease the bioavailability of itraconazole and hydroxy-itraconazole to such an extent that efficacy may be largely reduced. Examples include:
Antibacterials: isoniazid, rifabutin (see also under section “Medicinal products that may have their plasma concentrations increased by itraconazole”), rifampicin.
Anticonvulsants: carbamazepine, (see also under section “Medicinal products that may have their plasma concentrations increased by itraconazole”), phenobarbital, phenytoin.
Antivirals: efavirenz, nevirapine.
Therefore, administration of potent enzyme inducers of CYP3A4 with itraconazole is not recommended. It is recommended that the use of these medicinal produts be

avoided from 2 weeks before and during treatment with itraconazole, unless the benefits outweigh the risk of potentially reduced itraconazole efficacy.
Upon coadministration, it is recommended that the antifungal activity be monitored and the itraconazole dose increased as deemed necessary.

2) Medicinal products that may increase itraconazole plasma concentrations
Potent inhibitors of CYP3A4 may increase the bioavailability of itraconazole.
Examples include:
Antibacterials: ciprofloxacin, clarithromycin, erythromycin
Antivirals: ritonavir-boosted darunavir, ritonavir-boosted fosamprenavir, indinavir (see also under section “Medicinal products that may have their plasma concentrations increased by itraconazole”), ritonavir (see also under section “Medicinal products that may have their plasma concentrations increased by itraconazole”).
It is recommended that these medicinal products be used with caution when coadministered with itraconazole capsules. It is recommended that patients who must take itraconazole concomitantly with potent inhibitors of CYP3A4 be monitored closely for signs or symptoms of increased or prolonged pharmacologic effects of itraconazole, and the itraconazole dose be decreased as deemed necessary. When appropriate, it is recommended that itraconazole plasma concentrations be measured.

3) Medicinal products that may have their plasma concentrations increased by itraconazole
Itraconazole and its major metabolite, hydroxy-itraconazole, can inhibit the metabolism of active ingredients metabolised by CYP3A4 and can inhibit the transport of active ingredients by P-glycoprotein, which may result in increased plasma concentrations of these active ingredients and/or their active metabolite(s) when they are administered with itraconazole. These elevated plasma concentrations may increase or prolong both therapeutic and adverse effects of these medicinal products. CYP3A4-metabolised active ingredients known to prolong the QT interval may be contraindicated with itraconazole, since the combination may lead to ventricular tachyarrhythmias including occurrences of torsade de pointes, a potentially fatal arrhythmia. Once treatment is stopped, itraconazole plasma concentrations decrease to an almost undetectable concentration within 7 to 14 days, depending on the dose and duration of treatment. In patients with hepatic cirrhosis or in subjects receiving CYP3A4 inhibitors, the decline in plasma concentrations may be even more gradual. This is particularly important when initiating therapy with active ingredients whose metabolism is affected by itraconazole.

The interacting medicinal products are categorized as follows:

- 'Contraindicated': Under no circumstances is the medicinal product to be coadministered with itraconazole, and up to two weeks after discontinuation of treatment with itraconazole.
- 'Not recommended': It is recommended that the use of the medicinal product be avoided during and up to two weeks after discontinuation of treatment with itraconazole, unless the benefits outweigh the potentially increased risks of side effects. If coadministration cannot be avoided, clinical monitoring for signs or symptoms of increased or prolonged effects or side effects of the interacting medicinal product is recommended, and its dosage be reduced or interrupted as deemed necessary. When appropriate, it is recommended that plasma concentrations be measured.
- 'Use with caution': Careful monitoring is recommended when the medicinal product is coadministered with itraconazole. Upon coadministration, it is recommended that patients be monitored closely for signs or symptoms of increased or prolonged effects or side effects of the interacting medicinal product, and its dosage be reduced as deemed necessary. When appropriate, it is recommended that plasma concentrations be measured.

Examples of active ingredients that may have their plasma concentrations increased by itraconazole presented by class of active ingredient with advice regarding coadministration with itraconazole:

Class of active ingredient	**Contraindicated**	**Not recommended**	**Use with caution**
Alpha Blockers		tamsulosin	
Analgesics	levacetylmethadol (levomethadyl), methadone	fentanyl	alfentanil, buprenorphine IV and sublingual, oxycodone
Antiarrhythmics	disopyramide, dofetilide, dronedarone, quinidine		digoxin
Antibacterials		rifabutin[a]	
Anticoagulants and antiplatelet medicinal products		rivaroxaban	coumarins, cilostazol, dabigatran
Anticonvulsants		carbamazepine[a]	
Antidiabetics			repaglinide, saxagliptin
Antihelmintics and antiprotozoals	halofantrine		praziquantel

Antihistamines	astemizole, mizolastine, terfenadine		ebastine
Antimigraine medicinal products	ergot alkaloids, such as dihydroergotamine, ergometrine (ergonovine), ergotamine, methylergometrine (methylergonovine)		eletriptan
Antineoplastics	irinotecan	dasatinib, nilotinib, trabectedin	bortezomib, busulphan, docetaxel, erlotinib, ixabepilone, lapatinib, trimetrexate, vinca alkaloids
Antipsychotics, anxiolytics and hypnotics	lurasidone, oral midazolam, pimozide, sertindole, triazolam		alprazolam, aripiprazole, brotizolam, buspirone, haloperidol, midazolam IV, perospirone, quetiapine, ramelteon, risperidone
Antivirals			maraviroc, indinavir[b], ritonavir[b], saquinavir
Beta Blockers			nadolol
Calcium Channel Blockers	bepridil, felodipine, lercanidipine, nisoldipine		other dihydropyridines, including verapamil
Cardiovascular medicinal products, miscellaneous	ivabradine, ranolazine	aliskiren	
Diuretics	eplerenone		
Gastrointestinal medicinal products	cisapride		aprepitant, domperidone
Immunosuppressants		everolimus	budesonide, ciclesonide, ciclosporin, dexamethasone, fluticasone, methylprednisolone, rapamycin (also known as sirolimus), tacrolimus, temsirolimus
Lipid regulating medicinal products	lovastatin, simvastatin		atorvastatin
Respiratory medicinal products		salmeterol	
SSRIs, tricyclics and related antidepressants			reboxetine

Urological medicinal products		vardenafil	fesoterodine. imidafenacin, sildenafil, solifenacin, tadalafil, tolterodine
Other	colchicine, in subjects with renal or hepatic impairment	colchicine	alitretinoin (oral formulation), cinacalcet, mozavaptan, tolvaptan
[a] See also under section "Medicinal products that may decrease itraconazole plasma concentrations" [b] See also under section "Medicinal products that may increase itraconazole plasma concentrations"			

4) Medicinal products that may have their plasma concentrations decreased by itraconazole

Coadministration of itraconazole with the NSAID meloxicam may decrease the plasma concentrations of meloxicam. It is recommended that meloxicam be used with caution when coadministered with itraconazole, and its effects or side effects be monitored. It is recommended that the dosage of meloxicam, if coadministered with itraconazole, be adapted if necessary.

4.6. Pregnancy and lactation

Pregnancy: When administered at high doses to pregnant rats (40 mg/kg/day or higher) and mice (80 mg/kg/day or higher), itraconazole was shown to increase the incidence of foetal abnormalities and did produce adverse effects on the embryo. Studies of the use of itraconazole in pregnant women are not available. Therefore, Itraconazole should only be given in life-threatening cases of systemic mycosis and when in these cases the potential benefit outweighs the potential harm to the foetus.
Lactation: A very small amount of Itraconazole is excreted in human milk. The expected benefits of Itraconazole therapy should be weighed against the risks of breast feeding. In case of doubt, the patient should not breast feed.

4.7. Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. When driving vehicles and operating machinery the possibility of adverse reactions such as dizziness, visual disturbances and hearing loss, which may occur in some instances, must be taken into account.

4.8. Undesirable effects

The ADRs in the table below were derived from open-label and double-blind clinical trials with itraconazole capsules involving 8499 patients in the treatment of dermatomycoses or onychomycosis, and from spontaneous reporting. The table lists

adverse events reported by at least 1% of patients.

The table below presents ADRs by System Organ Class. Within each System Organ Class, the ADRs are presented by incidence, using the following convention:

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 estimated from the available data)

System Organ Class	**Common** ≥ 1/100 to < 1/10	**Uncommon** ≥ 1/1000 to < 1/100	**Rare** ≥ 1/10 000 to < 1/1000
Infections and infestations		Sinusitis, upper respiratory tract infection, rhinitis	
Blood and lymphatic system disorders			Leukopenia
Immune system disorders		Hypersensitivity*	Serum sickness, angioneurotic oedema, anaphylactic reaction
Metabolism and nutrition disorders			Hypertriglyceridemia
Nervous system disorders	Headache		Hypoaesthesia, paraesthesia, dysgeusia
Eye disorders			Visual disturbance (including diplopia and blurred vision)
Ear and labyrinth disorders			Transient or permanent hearing loss*, tinnitus
Cardiac disorders			Congestive heart failure*
Respiratory, thoracic and mediastinal disorders			Dyspnoe
Gastrointestinal disorders	Abdominal pain, nausea	Vomiting, diarrhoea, constipation, dyspepsia, flatulence	Pancreatitis
Hepatobiliary disorders		Hepatic function abnormal	Serious hepatotoxicity (including some cases of fatal acute liver failure)*, hyperbilirubinaemia
Skin and subcutaneous tissue disorders		Urticaria, rash, pruritus	Toxic epidermal necrolysis, Stevens-Johnson Syndrome, acute generalised exanthematous pustulosis, erythema multiforme, exfoliative dermatitis, leukocytoclastic vasculitis, alopecia, photosensitivity

Renal and urinary disorders			Pollakiuria
Reproductive system and breast disorders		Menstrual disorder	Erectile dysfunction
General disorders and administration site conditions			Oedema
Investigations			Blood creatine phosphokinase increased

Paediatric population

The safety of itraconazole was evaluated in 165 paediatric patients aged 1 year to 17 years. These patients received at least one dose of itraconazole oral solution for prophylaxis of fungal infections or for treatment of oral thrush or systemic fungal infections and provided safety data. Based on pooled safety data from these clinical trials, the very common reported ADRs in paediatric patients were headache (3.0%), vomiting (3.0%), abdominal pain (2.4%), diarrhoea (2.4%), nausea (1.2%), and rash (1.2%). The nature of ADRs in paediatric patients is similar to that observed in adult subjects, but the incidence is higher in the paediatric patients.

Description of selected adverse reactions

The following is a list of ADRs associated with itraconazole that have been reported in clinical trials of itraconazole oral solution and intravenous itraconazole, excluding the ADR term “Injection site inflammation”, which is specific to the injection route of administration.

Blood and lymphatic system disorders	Granulocytopenia, thrombocytopenia
Immune system disorders	Anaphylactoid reaction
Metabolism and nutrition disorders	Hyperglycaemia, hyperkalaemia, hypokalaemia, hypomagnesaemia
Psychiatric disorders	Confusional state
Nervous system disorders	Peripheral neuropathy*, dizziness, somnolence, tremor
Cardiac disorders	Cardiac failure, left ventricular failure, tachycardia
Vascular disorders	Hypertension, hypotension
Respiratory, thoracic and mediastinal disorders	Pulmonary oedema, dysphonia, cough
Gastrointestinal disorders	Gastrointestinal disorder
Hepatobiliary disorders	Hepatic failure*, hepatitis, jaundice
Skin and subcutaneous tissue disorders	Rash erythematous, hyperhidrosis
Musculoskeletal and connective tissue disorders	Myalgia, arthralgia
Renal and urinary disorders	Renal impairment, urinary incontinence
General disorders and	Generalised oedema, face oedema, chest pain, pyrexia,

administration site conditions	pain, fatigue, chills
Investigations	Alanine aminotransferase increased, aspartate aminotransferase increased, blood alkaline phosphatase increased, blood lactate dehydrogenase increased, blood urea increased, gamma-glutamyltransferase increased, hepatic enzyme increased, urine analysis abnormal

4.9. Overdose

In the event of overdosage, patients should be treated symptomatically with supportive measures. Within the first hour after ingestion, gastric lavage may be performed. Activated charcoal may be given if considered appropriate. No specific antidote is available. Itraconazole cannot be removed by haemodialysis.

5. Pharmacological Properties

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Antimycotics for systemic use, triazole derivatives.
Itraconazole inhibits fungal 14α-demethylase, resulting in a depletion of ergosterol and disruption of membrane synthesis by fungi.

5.2. Pharmacokinetic properties

The pharmacokinetics of itraconazole has been investigated in healthy subjects, special populations and patients after single and multiple dosing.
Itraconazole is rapidly absorbed after oral administration. Peak plasma concentrations of the unchanged drug are reached within 2 to 5 hours following an oral dose. The observed absolute bioavailability of itraconazole is about 55%. Oral bioavailability is maximal when the capsules are taken immediately after a full meal.

6. Pharmaceutical Particulars

6.1. Incompatibilities

Not applicable

6.2. Shelf life

36 months

6.3. Special precautions for storage

Preserve in dry and well-closed containers.
Store at room temperature not exceeding 30℃.

6.4. Nature and contents of container

10 Capsules/Box (10 Capsule/PTP x1)

6.5. Special precautions for disposal and other handling

Keep out of reach of children.

Do not preserve in other containers in order to maintain quality of the drug and avoid misuse.

7. Marketing Authorization Holder

Korea United Pharm. Inc.

25-23, Nojanggongdan-gil, Jeondong-myeon, Sejong-si, Korea

8. Marketing Authorization Numbers

823 (Korea Registration Number)

9. Date of First Authorization/Renewal of The Authorization

March 20, 2003

10. Date of Revision of The Text

August 09, 2017