IRISH MEDICINES BOARD ACTS 1995 AND 2006

MEDICINAL PRODUCTS(CONTROL OF PLACING ON THE MARKET)REGULATIONS,2007

(S.I. No.540 of 2007)

PPA1151/119/001
Case No: 2066045

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

Imbat Limited

Unit L2, **North Ring Business Park**, **Santry**, **Dublin 9**

an authorisation, subject to the provisions of the said Regulations, in respect of the product

Clorom 500mg Film-Coated Tablets

The particulars of which are set out in Part I and Part II of the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **25/09/2009**.

Signed on behalf of the Irish Medicines Board this

_____

A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Clorom 500mg Film-Coated Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Clarithromycin 500mg
Excipients-Contains Lactose Monohydrate
For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-Coated tablet

Product imported from Germany:
White, oblong, convex, scored on both faces

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Clorom 500 mg Film-Coated Tablets are indicated for the treatment of the following acute and chronical bacterial infections, when caused by clarithromycin-susceptible bacteria:

- Infections of the lower respiratory tract such as acute exacerbation of chronic bronchitis and community acquired pneumonia.
- Infections of the upper respiratory tract such as sinusitis and pharyngitis.
- Skin infections and soft tissue infections of mild to moderate severity.

In appropriate combination with antibacterial therapeutic regimes and an appropriate ulcer healing agent for the eradication of Helicobacter pylori in patients with Helicobacter pylori associated ulcers (see section 4.2).

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and method of administration

The dosage of clarithromycin depends on the clinical condition of the patient and has to be defined in any case by the physician.

Adults and adolescents
The usual dosage is 250 mg twice daily.
In severe infections, dosage can be increased to 500 mg twice daily.

Children
Clorom 500mg Film-Coated Tablets are not suitable for childeren up to 12 years with weight less than 30 kg.
For these patients other pharmaceutical forms are available.

Elderly: As for adults

Elimination of Helicobacter pylori in adults:
In patients with gastro-duodenal ulcers due to H. pylori infection clarithromycin can be used in a dose of 500 mg twice daily during the eradication therapy in combination with amoxicillin 1000 mg twice daily and omeprazole 20 mg twice daily.

Dosage in renal impairment: Dosage adjustments are not usually required except in patients with severe renal impairmei (creatinine clearance <30 ml/min). If adjustment is necessary, the total daily dosage should be reduced by half, e.g. 250 mg once daily or 250 mg twice daily in more severe infections. Treatment should not be continued beyond 14 days in these patients.

Duration of therapy:
The duration of therapy with clarithromycin depends on the clinical condition of the patient and has to be determined in any case by the physician.

- The usual duration of treatment is 7 to 14 days.
- Therapy should be continued at least for 2 days after symptoms have subsided.
- In *Streptococcus pyogenes* (group A beta-haemolytic streptococcus) infections the duration of therapy should be at least 10 days.
- Combination therapy for the eradication of H. pylori infection, e.g. clarithromycin 500 mg (two 250 mg tablets or one 500 mg tablet) twice daily in combination with amoxicillin 1000 mg twice daily and omeprazole 20 mg twice daily should be continued for 7 days.

Method of administration
Clorom 500 mg Film-Coated Tablets can be taken irrespective of food intake (see section 5.2).

4.3 Contraindications

- Clarithromycin is contraindicated in patients with known hypersensitivity to the active substance clarithromycin, to other macrolides or to any of the excipients of the tablets.
- Clarithromycin and ergot derivatives should not be co-administered.
- Concomitant administration of clarithromycin and any of the following active substances is contraindicated: cisapride, pimozide and terfenadine. Elevated cisapride, pimozide and terfenadine levels have been reported in patients receiving either of these active substances and clarithromycin concomitantly. This may result in QT prolongation and cardiac arrhythmias including ventricular tachycardia, ventricular fibrillation and Torsade de Pointes. Similar effects have been observed with concomitant administration of astemizole and other macrolides (see section 4.5).
- Clarithromycin should not be administered to hypokalemic patients (risk of prolongation of QT-time).

4.4 Special warnings and precautions for use

- Clarithromycin is mainly excreted by the liver. Therefore, caution should be taken in administering clarithromycin to patients with impaired hepatic function.
- As with other antibiotics when renal function is poor, dosage of Clarithromycin should be suitably reduced depending on the degree of the impairment (see section 4.2). In elderly patients, the possibility of renal impairment should be considered.
- Clarithromycin therapy for H. pylori may select for drug-resistant organisms.
- Patients who are hypersensitive to lincomycin or clindamycin may also be hypersensitive to clarithromycin. Therefore, caution is required when prescribing clarithromycin for such patients.
- Prolonged or repeated use of clarithromycin may result in superinfections with insusceptible organisms. In case of superinfection, clarithromycin therapy should be stopped.
- Pseudomembranous colitis has been reported with the use of broad-spectrum antibiotics. Therefore, it is important to consider its diagnosis in patients who develop severe diarrhoea during or after therapy with clarithromycin.

- Due to a risk of increased QT-interval, clarithromycin should be used with caution in patients with a coronary vessel disease, a history of ventricular arrhythmia, severe cardiac insufficiency, non-compensated hypokalemia and/or hypomagnesemia, bradycardia (< 50 bpm), or when co-administered with other medicinal products with a QT-prolonging effect. Clarithromycin should not be used in patients with congenital or documented acquired QT prolongation (see section 4.5).
- Clarithromycin should be used with caution whenever indicated for use in patients receiving treatment with an inducer of CYP3A4 (see section 4.5).
- Clarithromycin is an inhibitor of CYP3A4, and concomitant use with other medicinal products that are metabolised to a large extent by this enzyme should be restricted to situations where it is clearly indicated (see section 4.5).
- Clarithromycin inhibits the metabolism of some HMG-CoA reductase inhibitors, which results in increased plasma concentrations of these medicinal products (see section 4.5).

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

Contraindicated combinations
Concomitant administration of clarithromycin and terfenadine, cisapride, pimozide and ergot alkaloids is contraindicated.

The effect of other medicinal products on Clarithromycin tablets
Clarithromycin is metabolised by the enzyme CYP3A4. Hence, strong inhibitors of this enzyme may inhibit the metabolism of clarithromycin, resulting in increased plasma concentrations of clarithromycin.

Although the plasma concentrations of clarithromycin and omeprazole may be increased when they are administered concurrently, no adjustment to the dosage is necessary. Increased plasma concentrations of clarithromycin may also occur when it is co-administered with antacids or ranitidine. No adjustment to the dosage is necessary.

Ritonavir (200 mg t.i.d) have been shown to inhibit the metabolism of clarithromycin (500 mg b.i.d.), with an increase in Cmax, Cmin and AUC of 31, 182 and 77%, respectively, when co-administered with ritonavir. Formation of the active 14-OH-hydroxy metabolite was almost completely inhibited. A general dose reduction is probably not required in patients with normal renal function, but the daily dose of clarithromycin should not exceed 1 g. Dose reduction should be considered in patients with renal impairment. For patients with a creatinine clearance of 30 to 60 ml/min, the clarithromycin dose should be reduced with 50%, and at a creatinine clearance of < 30 ml/min the dose should be reduced with 75%.

Products that are inducers of CYP3A4 (e.g. rifampicin, phenytoin, carbamazepin, phenobarbital, St. Johns Wort) may induce the metabolism of clarithromycin. This may result in sub-therapeutic levels of clarithromycin leading to a reduced efficacy. When clarithromycin is clearly indicated it might be necessary to increase the dose of clarithromycin and monitor the efficacy and safety of clarithromycin carefully. Furthermore monitoring the plasma levels of the CYP3A4 inducer might be necessary because the latter could be increased owing to the inhibition of CYP3A4 by clarithromycin (see also the relevant product information for the CYP3A4 inducer administered).

Concomitant administration of rifabutin and clarithromycin resulted in an increase and decrease, respectively, in serum levels, followed by an increased risk of uveitis.

A 39% reduction in AUC for clarithromycin and a 34% increase in AUC for the active 14-OH-hydroxy metabolite have been seen when clarithromycin was used concomitantly with the CYP3A4 inducer efavirenz.

The effect of Clarithromycin tablets on other medicinal products
Clarithromycin is an inhibitor of the metabolising enzyme CYP3A4 and the transport protein P-glycoprotein. The degree of inhibition with different CYP3A4 substrates is difficult to predict. Hence, clarithromycin should not be used during treatment with other medicinal products that are substrates for CYP3A4, unless plasma levels, therapeutic effect or adverse events of the CYP3A4 substrate can be closely monitored.

A dose reduction may be necessary for medicinal products that are substrates for CYP3A4 if co-administered with clarithromycin. Alternatively, treatment with these products may be interrupted during clarithromycin treatment.

Medicinal products with a potential to prolong QT-interval
Clarithromycin has been reported to inhibit the metabolism of cisapride and terfenadine, with a 2 to 3-fold increase in plasma levels reported for terfenadine. This has been associated with QT-prolongation and cardiac arrhythmias including ventricular tachycardia, ventricular fibrilation and torsades de pointes. Similar symptoms have been described for patients treated with pimozide when combined with clarithromycin. Concomitant administration of clarithromycin and terfenadine, cisapride or pimozide is contraindicated (see section 4.3)

Cases with torsades de pointes has been reported in patients where clarithromycin has been co-administered with quinidine or disopyramid. These combinations should therefore be avoided, or plasma levels of quinidine or disopyramid closely monitored to allow dose adjustment.

Caution is warranted when clarithromyin is administered to patients treated taking other medicinal products with the potential to prolong QT (see section 4.4).

HMG-CoA reductase inhibitors
Clarithromycin inhibits the metabolism of some HMG-CoA reductse inhibitors, which results in increased plasma concentrations of these medicinal products. Rhabdomyolysis in association with increased plasma concentrations have in rare cases been reported in patients treated with clarithromycin and simvastatin or lovastatin. Clarithromycin may produce a similar interaction with atorvastatin and a lesser interaction with cerivastatin. When treatment with clarithromycin is indicated in patients receiving treatment with either simvastatin or lovastatin or atorvastatin or cerivastatin patients should be monitored for signs and symptoms of myopathy.

Ergot vasoconstrictors (e.g. dihydroergotamine, ergotamine)
Cases of ergotism due to increased plasma levels of ergot alkaloids have been reported when these products have been co-administered with macrolides. The combination is contraindicated (see section 4.3).

Benzodiazepines
When midazolam was co-administered with clarithromycin tablets (250 mg b.i.d.), midazolam AUC was increased 2.7-fold after intravenous administration of midazolam and 7-fold after oral administration. Concomitant administration of oral midazolam and clarithromycin should be avoided. If intravenous midazolam is co-administered with clarithromycin, the patient must be closely monitored to allow dose adjustment. The same precautions should also apply to other benzodiazepines that are metabolised by CYP3A4, especially triazolam but also alprazolam. Forbenzodiazepines which are not metabolised by CYP3A4 (temazepam, nitrazepam, lorazepam) an interaction with clarithromycin is unlikely.

Cyclosporin, tacrolimus and sirolimus
Concomitant use of oral clarithromycin and cyclosporin or tacrolimus have resulted in more than a 2-fold increase of the Cmin-levels of both cyclosporin and tacrolimus. Similar effects are also expected for sirolimus. When initiating treatment with clarithromycin in patients already receiving any of these immunosuppressive agents, cyclosporin, tacrolimus or sirolimus plasma levels must be closely monitored and their doses decreased as necessary. When clarithromycin is discontinued in these patients, close monitoring of plasma levels of cyclosporin, tacrolimus or sirolimus, is again necessary to guide dose adjustment.

Digoxin
The concentration of digoxin may be increased when co-administered with clarithromycin. Monitoring of plasma levels of digoxin should be considered when co-treatment with clarithromycin is initiated or terminated since a dose adjustment may be warranted.

Theophylline
The administration of clarithromycin to patients who are receiving theophylline has been associated with an increase in serum theophylline levels and potential theophylline toxicity.

Warfarin
The use of clarithromycin in patients receiving warfarin may result in potentiation of the effects of warfarin. Prothrombin time should be frequently monitored in these patients.

Zidovudine
Simultaneous oral administration of clarithromycin tablets and zidovudine to HIV infected adult patients may result in decreased steady-state zidovudine levels. This can be largely avoided by staggering the doses of clarithromycin and zidovudine by 1-2 hours. No such reaction has been reported in children.

4.6 Pregnancy and lactation

Pregnancy
Data on the use of clarithromycin during the first trimester of more than 200 pregnancies show no clear evidence of teratogenic effects, or of adverse effects or on the health of the neonate. Data from a limited number of pregnant women exposed in the first trimester indicate a possible increased risk of abortions. To date no other relevant epidemiological data are available.
Data from animal studies have shown reproductive toxicity (see section 5.3). The risk for humans is unknown. Clarithromycin should only be given to pregnant women after a careful benefit/risk assessment.

Lactation
Clarithromycin and its active metabolite are excreted in breast milk. Therefore, diarrhoea and fungus infection of the mucous membranes could occur in the breast-fed infant, so that nursing might have to be discontinued. The possibility of sensitisation should be borne in mind. The benefit of treatment of the mother should be weighed against the potential risk for the infant.

4.7 Effects on ability to drive and use machines

There are no data available on the effect of clarithromycin on the ability to drive or use machines. When performing these activities the possible occurrence of the adverse reactions dizziness, vertigo, confusion and disorientation should be taken into account.

4.8 Undesirable effects

In this section undesirable effects are defined as follows:
Very common (> 1/10), common (> 1/100, < 1/10), uncommon (> 1/1000, < 1/100), rare (> 1/10000, < 1/1000), very rare (< 1/10000).

Infections and infestations
Common: Oral monilia
As with other antibiotics, prolonged use may result in the overgrowth of non-susceptible organisms.

Blood and the lymphatic system disorders
Uncommon: Decreased leucocyte levels
Very rare: Thrombocytopenia

Immune system disorders
Uncommon: Allergic reactions ranging from urticaria and mild skin eruptions to anaphylaxis.

Psychiatric disorders
Very rare: Anxiety, insomnia, hallucinations, psychosis, disorientation, depersonalisation, bad dreams and confusion.

Nervous system disorders
Common: Headache, smell alteration
Very rare: Dizziness, vertigo, paraesthesia, convulsions.

Ear and labyrinth disorders
Rare: Tinnitus
Very rare: Reversible hearing loss

Cardiac disorders
Very rare: QT prolongation, ventricular tachycardia and Torsades de Pointes.

Gastrointestinal disorders
Common: Nausea, diarrhoea, vomiting, abdominal pain, dyspepsia, stomatitis, glossitis, reversible tooth and tongue discolouration, and taste perversion, i.e. metallic or bitter taste.
Very rare: Pancreatitis. Pseudomembranous colitis has been reported very rarely with clarithromycin, and may range in severity from mild to life threatening.

Hepato-biliary disorders
Uncommon: Hepatic dysfunction, which is usually transient and reversible, hepatitis and cholestasis with or without jaundice.
Very rare: Fatal hepatic failure has been reported particularly in patients with pre-existing liver disease or taking other hepatotoxic medicinal products.

Skin and subcutaneous tissue disorders
Very rare: Stevens-Johnson syndrome and toxic epidermal necrolysis

Musculoskeletal, connective tissue and bone disorders
Uncommon: Arthralgia, myalgia.

Renal and urinary disorders
Very rare: Interstitial nephritis, renal failure.

Investigations
Common: Elevated BUN
Uncommon: Prolongation of prothrombin time, elevated serum creatinine, altered liver function tests (increased transaminase levels).
Very rare: Hypoglycaemia has been observed especially after concomitant administration with antidiabetic medicinal products and insulin.

4.9 Overdose

Symptoms of intoxication:
Reports indicate that the ingestion of large amounts of clarithromycin can be expected to produce gastrointestinal symptoms. Symptoms of overdose may largely correspond to the profile of adverse reactions. One patient who had a history of bipolar disorder ingested 8 grams of clarithromycin and showed altered mental status, paranoid behaviour, hypokaliaemia and hypoxaemia.

Therapy of intoxication:
There is no specific antidote on overdose. Serum levels of clarithromycin cannot be reduced by haemodialysis or peritoneal dialysis.

Adverse reactions accompanying overdosage should be treated by gastric lavage and supportive measures. Severe acute allergic reactions may be seen very rarely, e.g. anaphylactic shock. At first signs of hypersensitivity reactions therapy with clarithromycin must be discontinued and the required measures should be initiated immediately.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

General properties
Pharmacotherapeutic group: Macroldies

ATC code: J01FA09

Mode of action:

Clarithromycin is a semi-synthetic derivative of erythromycin A. It exerts its antibacterial action by binding to the 50s ribosomal sub-unit of susceptible bacteria and suppresses protein synthesis.

It is highly potent against a wide variety of aerobic and anaerobic gram-positive and gram-negative organisms. The minimum inhibitory concentrations (MICs) of clarithromycin are generally two-fold lower than the MICs of erythromycin.

The 14-hydroxy metabolite of clarithromycin also has antimicrobial activity. The MICs of this metabolite are equal or two-fold higher than the MICs of the parent compound, except for *H. influenzae* where the 14-hydroxy metabolite is two-fold more active than the parent compound.

Mechanisms of resistance:
Resistance mechanisms against macrolide antibiotics include alteration of the target site of the antibiotic or are based on modification and/or the active efflux of the antibiotic.
Resistance development can be mediated via chromosomes or plasmids, be induced or exist constitutively. Macrolide-resistant bacteria generate enzymes which lead to methylation of residual adenine at ribosomal RNA and consequently to inhibition of the antibiotic binding to the ribosome. Macrolide-resistant organisms are generally cross-resistant to lincosamides and streptogramine B based on methylation of the ribosomal binding site. Clarithromycin ranks among the strong inducers of this enzyme as well. Furthermore, macrolides have a bacteriostatic action by inhibiting the peptidyl transferase of ribosomes.
A complete cross-resistance exists among clarithromycin, erythromycin and azithromycin.
Methicillin-resistant staphylococci and penicillin-resistant Streptococcus pneumoniae are resistant to macrolides such as clarithromycin.

Breakpoints
According to the NCCLS (US National Committee on Clinical Laboratory Standards) in 2003 the following breakpoints have been defined for clarithromycin:
- *Staphylococcus* spp.: ≤ 2 µg/ml susceptible, ≥ 8 µg/ml resistant
- *Haemophilus* spp.: ≤ 8 µg/ml susceptible
- *Streptococcus* spp. including *S. pneumoniae:* ≤ 0.25 µg/ml susceptible, ≥ 1 µg/ml resistant

Susceptibility
The prevalence of acquired resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.

Commonly susceptible species (i.e. resistance < 10% in all EU Member States)
Aerobic Gram-positive microorganisms
Streptococcus group A
Streptococcus group B
Streptococcus group C, F, G

Aerobic Gram-negative microorganisms
Moraxella catarrhalis
Passteurella multocida
Legionella spp.
Anaerobic microorganisms
Bacteroides spp.
Peptococcus/Peptostreptococcus spp.
Clostridium spp. other than C. difficile
Fusobacterium spp.
Other microorganisms
Mycoplasma pneumoniae
Chlamydia trachomatis
Chlamydia pneumoniae

Species for which acquired resistance may be a problem (i.e. resistance ≥ 10% in at least one EU Member State)
Aerobic Gram-positive microorganisms
Staphylococcus aureus .....Methicillin-susceptible
*Streptococcus pneumoniae**
Aerobic Gram-negative microorganisms
Haemophilus influenzae
Helicobacter pylori
Inherently resistant organisms
Aerobic Gram-positive microorganisms
Enterococcus spp.
Staphylococcus aureus .....Methicillin-resistant or Erythromycin resistant
Other microorganisms
Mycobacterium tuberculosis

*comments regarding resistance see “Mechanisms of resistance”

5.2 Pharmacokinetic properties

Absorption:
Clarithromycin is rapidly and well absorbed from the gastrointestinal tract – primarily in the jejunum – but undergoes extensive first-pass metabolism after oral administration. The absolute bioavailability of a 250-mg clarithromycin tablet is approximately 50%. Food slightly delays the absorption but does not affect the extent of bioavailability. Therefore, clarithromycin tablets may be given without regard to food. Due to its chemical structure (6-O-Methylerythromycin) clarithromycin is quite resistant to degradation by stomach acid. Peak plasma levels of 1 – 2 µg/ml clarithromycin were observed in adults after oral administration of 250 mg twice daily. After administration of 500 mg clarithromycin twice daily the peak plasma level was 2,8 µg/ml.

After administration of 250 mg clarithromycin twice daily the microbiologically active 14-hydroxy metabolite attains peak plasma concentrations of 0,6 µg/ml. Steady state is attained within 2 days of dosing.

Distribution:
Clarithromycin penetrates well into different compartments, with an estimated volume of distribution of 200-400 l Clarithromycin provides concentrations in some tissues that are several times higher than the circulating drug levels. Increased levels have been found in both tonsils and lung tissue. Clarithromycin also penetrates the gastric mucus.

Clarithromycin is approximately 80% bound to plasma proteins at therapeutic levels.

Biotransformation and elimination:
Clarithromycin is rapidly and extensively metabolised in the liver. Metabolism involves mainly N-dealkylation, oxidation and stereospecific hydroxylation at position C 14.

The pharmacokinetics of clarithromycin is non-linear due to saturation of hepatic metabolism at high doses. Elimination half-life increased from 2-4 hours following administration of 250 mg clarithromycin twice daily to 5 hours following administration of 500 mg clarithromycin twice daily. The half-life of the active 14-hydroxy metabolite ranges between 5 to 6 hours following administration of 250 mg clarithromycin twice daily.

After oral administration of radioactive clarithromycin 70 - 80% of the radioactivity was found in the faeces. Approximately 20 -30% of clarithromycin is collected as the unchanged active substance in the urine. This proportion is increased when the dose is increased. Renal insufficiency increases clarithromycin levels in plasma, if the dose is not decreased.
Total plasma clearance has been estimated to approximately 700 ml/min, with a renal clearance of approximately 170 ml/min.

Special populations
Renal impairment: Reduced renal insufficiency function results in increased plasma levels of clarithromycin and the active metabolite levels in plasma.

5.3 Preclinical safety data

In 4-week-studies in animals, toxicity of clarithromycin was found to be related to the dose and to the duration of the treatment. In all species, the first signs of toxicity were observed in the liver, in which lesions were seen within 14 days in dogs and monkeys. The systemic levels of exposure, related to this toxicity, are not known in detail, but toxic doses were clearly higher than the therapeutic doses recommended for humans. Cardiovascular malformations were observed in rats treated with doses of 150 mg/kg/d. No mutagenic effects were found in *in vitro*- and *in vivo* -studies with clarithromycin. Studies on reproduction toxicity showed that administration of clarithromycin at doses 2x the clinical dose in rabbit (iv) and x10 the clinical dose in monkey (po) resulted in an increased incidence of spontaneous abortions. These doses were related to maternal toxicity. No embryotoxicity or teratogenicity was noted in rat studies. In mouse at doses x70 the clinical dose cleft palate occurred at varying incidence (3-30%).

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core:
Microcrystalline Cellulose
Croscarmellose Sodium
Magnesium Stearate
Powdered Cellulose
Colloidal Anhydrous Silica

Coat (Opadry White OY-L-28900):
Hypromellose
Lactose Monohydrate
Titanium Dioxide (E171)
Macrogol 4000

6.2 Incompatibilities

Not applicable

6.3 Shelf Life

The shelf life expiry date of this product is the date shown on the blister strips and outer carton of the product as marketed in the country of origin.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions

6.5 Nature and contents of container

Over-labelled carton containing blister strips
Pack size: 14

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements

7 Parallel Product Authorisation Holder

Imbat Ltd
Unit L2
North Ring Business Park
Santry
Dublin 9

8 Parallel Product Authorisation Number

PPA 1151/119/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 25th September 2009

10 DATE OF REVISION OF THE TEXT