SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Co-Careldopa 10 mg/100 mg Tablets
Co-Careldopa 12.5 mg/50 mg Tablets
Co-Careldopa 25 mg/100 mg Tablets
Co-Careldopa 25 mg/250 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 10.8 mg carbidopa monohydrate (equivalent to 10 mg of anhydrous carbidopa) and 100 mg levodopa.

Each tablet contains 13.5 mg carbidopa monohydrate (equivalent to 12.5 mg of anhydrous carbidopa) and 50 mg levodopa.

Each tablet contains 27.0 mg carbidopa monohydrate (equivalent to 25 mg of anhydrous carbidopa) and 100 mg levodopa.

Each tablet contains 27.0 mg carbidopa monohydrate (equivalent to 25 mg of anhydrous carbidopa) and 250 mg levodopa.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet

Round shaped, light blue coloured tablet, with “C” on one side and “18” on other side of tablet. The tablet dimensions are 8.00 ± 0.2 mm.

Light yellow coloured, oval shaped tablet with “C” on one side and “17” on other side. The tablet dimensions are 9.65 mm x 5.00 mm ± 0.20 mm.

Round shaped, light yellow coloured tablet, with “C” on one side and “19” on other side of tablet. The tablet dimensions are 8.00 ± 0.2 mm.

Round shaped, light blue coloured tablet, with “C” on one side and “20” on other side of tablet. The tablet dimensions are 10.40 ± 0.2 mm.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For treatment of Parkinson's disease.

4.2 Posology and method of administration

Posology
The optimum daily dosage of Co-Careldopa must be determined by careful titration in each patient.

Co-Careldopa Tablets are available in a ratio of 1:4 or 1:10 of carbidopa to levodopa to provide facility for fine dosage titration for each patient.

General Considerations
Studies show that the peripheral dopa-decarboxylase is fully inhibited (saturated) by carbidopa at doses between 70 and 100 mg a day. Patients receiving less than this amount of carbidopa are more likely to experience nausea and vomiting.

Standard antiparkinsonian drugs, other than levodopa alone, may be continued while Co-Careldopa is being administered, although their dosage may have to be adjusted.

Because both therapeutic and adverse effects are seen more rapidly with Co-Careldopa than with levodopa, patients should be carefully monitored during the dosage adjustment period. Involuntary movements, particularly blepharospasm, are a useful early sign of excess dosage in some patients.

Patients not receiving levodopa
Dosage may be best initiated with one tablet of Co-Careldopa 25 mg/100 mg three times a day. This dosage schedule provides 75 mg of carbidopa per day. Dosage may be increased by one tablet of Co-Careldopa 12.5 mg/50 mg or Co-Careldopa 25 mg/100 mg' every day or every other day, as necessary, until a dosage equivalent of eight tablets of Co-Careldopa 25 mg/100 mg a day is reached.

If Co-Careldopa10 mg/100 mg Tablets or Co-Careldopa 12.5 mg/50 mg Tablets are used, dosage may be initiated with one tablet three or four times a day. Titration upward may be required in some patients to achieve optimum dosage of carbidopa. The dosage may be increased by one tablet every day or every other day until a total of eight tablets (two tablets q.d.s.) is reached.

For patients starting with Co-Careldopa 25 mg/250 mg Tablets', the initial dose is one-half tablet taken once or twice daily. However, this may not provide the optimal amount of carbidopa needed by many patients. If necessary, add one-half tablet every day or every other day until optimal response is reached.

Response has been observed in one day, and sometimes after one dose. Fully effective doses usually are reached within seven days as compared to weeks or months with levodopa alone.

Co-Careldopa 12.5 mg/50 mg Tablets' or Co-Careldopa 10 mg/100 mg Tablets' may be used to facilitate dosage titration according to the needs of the individual patient.

Patients receiving levodopa
Discontinue levodopa at least 12 hours (24 hours for slow-release preparations) before starting therapy with Co-Careldopa. The easiest way to do this is to give Co-Careldopa as the first morning dose after a night without any levodopa. The dose of Co-Careldopa should be approximately 20% of the previous daily dosage of levodopa.

Patients taking less than 1,500 mg levodopa a day should be started on one tablet of Co-Careldopa 25 mg/100 mg three or four times a day dependent on patient need. The suggested starting dose for most patients taking more than 1,500 mg levodopa a day is one tablet of Co-Careldopa 25 mg/250 mg' three or four times a day.

Maintenance
Therapy with Co-Careldopa should be individualised and adjusted gradually according to response. When a greater proportion of carbidopa is required, each tablet of Co-Careldopa10 mg/100 mg may be replaced with a tablet of Co-Careldopa 25 mg/100 mg or Co-Careldopa 12.5 mg/50 mg'.

When more levodopa is required, Co-Careldopa 25 mg/250 mg tablets should be substituted at a dosage of one tablet three or four times a day. If necessary, the dosage of Co-Careldopa 25 mg/250 mg tablets' may be increased by one tablet every day or every other day to a maximum of eight tablets a day. Experience with a total daily dosage greater than 200 mg carbidopa is limited.

Patients receiving levodopa with another decarboxylase inhibitor
When transferring a patient to Co-Careldopa from levodopa combined with another decarboxylase inhibitor, discontinue dosage at least 12 hours before Co-Careldopa is started. Begin with a dosage of Co-Careldopa that will

provide the same amount of levodopa as contained in the other levodopa/decarboxylase inhibitor combination.

Use in children
The safety of Co-Careldopa in patients under 18 years of age has not been established and its use in patients below the age of 18 is not recommended.

Use in the elderly
There is wide experience in the use of this product in elderly patients. The recommendations set out above reflect the clinical data derived from this experience.

Patients receiving other antiparkinsonian agents
Current evidence indicates that other antiparkinsonian agents may be continued when Co-careldopa is introduced, although dosage may have to be adjusted in line with manufacturers recommendations.

Method of administration
To be taken orally

4.3 Contraindications

- Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1.
- Non-selective monoamine oxidase (MAO) inhibitors are contraindicated for use with Co-Careldopa. These inhibitors must be discontinued at least two weeks before starting Co-Careldopa Co-Careldopa. may be administered concomitantly with the manufacturer's recommended dose of an MAO inhibitor with selectivity for MAO type B (e.g. selegiline hydrochloride). (See 4.5 'Interaction with other medicinal products and other forms of interaction'.)
- Co-Careldopa is contraindicated in patients with narrow-angle glaucoma
- Since levodopa may activate a malignant melanoma, it should not be used in patients with suspicious undiagnosed skin lesions or a history of melanoma.
- Use in patients with severe psychoses. (See also 4.6 ‘Pregnancy and lactation’).

4.4 Special warnings and precautions for use

Co-Careldopa is not recommended for the treatment of drug-induced extrapyramidal reactions or Huntington’s chorea.

Co-Careldopa should be administered cautiously to patients with severe cardiovascular or pulmonary disease, bronchial asthma, renal, hepatic or endocrine disease, or history of peptic ulcer disease (because of the possibility of upper gastro-intestinal haemorrhage).

Care should be exercised when Co-Careldopa is administered to patients with a history of myocardial infarction who have residual atrial nodal, or ventricular arrhythmias. Cardiac function should be monitored with particular care in such patients during the period of initial dosage adjustment.
Levodopa has been associated with somnolence and episodes of sudden sleep onset. Sudden onset of sleep during daily activities, in some cases without awareness or warning signs, has been reported very rarely. Patients must be informed of this and advised to exercise caution while driving or operating machines during treatment with levodopa. Patients who have experienced somnolence and/or an episode of sudden sleep onset must refrain from driving or operating machines. Furthermore, a reduction of dosage or termination of therapy may be considered.

All patients should be monitored carefully for the development of mental changes, depression with suicidal tendencies, and other serious antisocial behaviour. Patients with current psychoses should be treated with caution.
Dyskinesias may occur in patients previously treated with levodopa alone because carbidopa permits more levodopa to reach the brain and, thus, more dopamine to be formed. The occurrence of dyskinesias may require dosage reduction.

As with levodopa, Co-Careldopa may cause involuntary movements and mental disturbances. Patients with a history of severe involuntary movements or psychotic episodes when treated with levodopa alone should be observed carefully when Co-Careldopa is substituted. These reactions are thought to be due to increased brain dopamine following administration of levodopa, and use of Co-Careldopa may cause a recurrence. A syndrome resembling the neuroleptic malignant syndrome including muscular rigidity, elevated body temperature, mental changes and increased serum creatine phosphokinase has been reported with the abrupt withdrawal of antiparkinsonian agents.
Therefore, any abrupt dosage reduction or withdrawal of Co-Careldopa should be carefully observed, particularly in patients who are also receiving neuroleptics.

Concomitant administration of psycho-active drugs such as phenothiazines or butyrophenones should be carried out with caution, and the patient carefully observed for loss of antiparkinsonian effect. Patients with a history of convulsions should be treated with caution.

As with levodopa, periodic evaluation of hepatic, haematopoetic, cardiovascular and renal function are recommended during extended therapy.
Patients with chronic wide-angle glaucoma may be treated cautiously with Co-Careldopa, provided the intra-ocular pressure is well controlled and the patient monitored carefully for changes in intra-ocular pressure during therapy.
If general anaesthesia is required, therapy with Co-Careldopa may be continued for as long as the patient is permitted to take fluids and medication by mouth. If therapy has to be stopped temporarily, Co-Careldopa may be restarted as soon as oral medication can be taken at the same daily dosage as before.

Epidemiological studies have shown that patients with Parkinson's disease have a higher risk of developing melanoma than the general population (approximately 2-6 fold higher). It is unclear whether the increased risk observed was due to Parkinson's disease, or other factors such as drugs used to treat Parkinson's disease. Therefore patients and providers are advised to monitor for melanomas on a regular basis when using Co-Careldopa for any indication. Ideally, periodic skin examinations should be performed by appropriately qualified individuals (e.g., dermatologists).

Treatment with carbidopa/levodopa can lead to vitamin B6 deficiency, which may increase the risk of seizures, particularly in patients receiving higher doses, and/or those with poor nutritional status. Monitoring of pyridoxine (vitamin B6) levels and vitamin B6 supplementation should be considered in patients receiving high-dose carbidopa/levodopa and those presenting with clinical manifestations suggestive of vitamin B6 deficiency.

Impulse control disorders
Patients should be regularly monitored for the development of impulse control disorders. Patients and carers should be made aware that behavioural symptoms of impulse control disorders including pathological gambling, increased libido, hypersexuality, compulsive spending or buying, binge eating and compulsive eating can occur in patients treated with dopamine agonists and/or other dopaminergic treatments containing levodopa including Co-Careldopa. Review of treatment is recommended if such symptoms develop.

Laboratory Tests
Commonly, levels of blood urea nitrogen, creatinine, and uric acid are lower during administration of Co-Careldopa than with levodopa. Transient abnormalities include elevated levels of blood urea, AST (SGOT), ALT (SGPT), LDH, bilirubin, and alkaline phosphatase.

Decreased haemoglobin, haematocrit, elevated serum glucose and white blood cells, bacteria and blood in the urine have been reported.

Positive Coombs' tests have been reported, both with Co-Careldopa and levodopa alone.

Co-Careldopa may cause a false positive result when a dipstick is used to test for urinary ketone; and this reaction is not altered by boiling the urine. The use of glucose oxidase methods may give false negative results for glycosuria. Dopamine Dysregulation Syndrome (DDS) is an addictive disorder resulting in excessive use of the product seen in some patients treated with carbidopa/ levodopa. Before initiation of treatment, patients and caregivers should be warned of the potential risk of developing DDS (see also section 4.8).

4.5 Interaction with other medicinal products and other forms of interaction

Caution should be exercised when the following drugs are administered concomitantly with Co-Careldopa.

Antihypertensive agents
Postural hypotension can occur when Co-Careldopa is added to the treatment of patients already receiving antihypertensive drugs. Dosage adjustment of the antihypertensive agent may be required.

Antidepressants
Rarely, reactions including hypertension and dyskinesia have been reported with the concomitant use of tricyclic antidepressants. (See section4.3 'Contraindications' for patients receiving MAOIs).

Anticholinergics
Anticholinergics may act synergistically with levodopa to decrease tremor; however, they can exacerbate abnormal involuntary movements. They may also in high dosage diminish the beneficial effects of levodopa by delaying its absorption thus increasing gastric metabolism of the drug. An adjustment of the dose of Levodopa/Carbidopa may be needed.

Iron
Studies demonstrate a decrease in the bioavailability of carbidopa and/or levodopa when it is ingested with ferrous sulphate or ferrous gluconate. When given concomitantly a 30%-50% reduction of the AUC of levodopa have been observed and a 75% reduction in AUC of carbidopa.

Other drugs
To date there has been no indication of interactions that would preclude concurrent use of standard antiparkinsonian drugs.

Dopamine D_2 receptor antagonists (e.g. phenothiazines, butyrophenones, and risperidone) and isoniazid, may reduce the therapeutic effects of levodopa. The beneficial effects of levodopa in Parkinson's disease have been reported to be reversed by phenytoin and papaverine. Patients taking these drugs with Co-Careldopa should be carefully observed for loss of therapeutic response.
Use of Co-careldopa with dopamine-depleting agents (e.g., tetrabenazine) or other drugs known to deplete monoamine stores is not recommended.
Concomitant therapy with selegiline and carbidopa-levodopa may be associated with severe orthostatic hypotension not attributable to carbidopa-levodopa alone (See section 4.3 Contraindication). Since levodopa competes with certain amino acids, the absorption of Co-Careldopa may be impaired in some patients on a high protein diet. The effect of simultaneous administration of antacids with Co-Careldopa on the bioavailability of levodopa has not been studied. Co-Careldopa may be given to patients with Parkinson's disease and syndrome who are taking vitamin preparations that contain pyridoxine hydrochloride (Vitamin B6).

4.6 Fertility, pregnancy and lactation

Pregnancy
Although the effects of Co-Careldopa on human pregnancy are unknown, both levodopa and combinations of carbidopa and levodopa have caused visceral and skeletal malformations in rabbits. Therefore, the use of Co-Careldopa in women of childbearing potential requires that the anticipated benefits of the drug be weighed against possible hazards should pregnancy occur.

Breast-feeding
It is not known whether carbidopa is excreted in human milk. In a study of one nursing mother with Parkinson's disease, excretion of levodopa in human breast milk was reported. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in infants, a decision should be made whether to discontinue breast-feeding or discontinue the use of Co-careldopa, taking into account the importance of the drug to the mother.

Fertility
No adverse reactions on fertility were observed in preclinical studies with carbidopa or levodopa alone. Fertility studies in animals have not been conducted with the combination of levodopa and carbidopa.

4.7 Effects on ability to drive and use machines

Individual responses to medication may vary and certain side effects that have been reported with Co-Careldopa may affect some patients' ability to drive or operate machinery. Patients treated with levodopa and presenting with somnolence and/or sudden sleep episodes must be informed to refrain from

driving or engaging in activities where impaired alertness may put themselves or others at risk of serious injury or death (e.g. operating machines), until such recurrent episodes and somnolence have resolved (see also section 4.4 Special warnings and precautions for use).

4.8 Undesirable effects

Side effects that occur frequently with Co-Careldopa are those due to the central neuropharmacological activity of dopamine. These reactions can usually be diminished by dosage reduction. The most common are dyskinesias including choreiform, dystonic and other involuntary movements and nausea. Muscle twitching and blepharospasm may be taken as early signs to consider dosage reduction.

Other side effects reported in clinical trials or in post-marketing experience include:

Infections and Infestations:
Very common- Urinary tract infections

***General disorders and administration site conditions*:**
syncope, chest pain, anorexia.

Cardiac disorders:
cardiac irregularities and/or palpitations, orthostatic effects including hypotensive episodes, hypertension, phlebitis.

***Gastro-intestinal disorders*:**
vomiting, gastro-intestinal bleeding, development of duodenal ulcer, diarrhoea, dark saliva.

Blood and lymphatic system disorders:
leucopenia, haemolytic and non-haemolytic anaemia, thrombocytopenia, agranulocytosis.

Immune system disorders:
angioedema, urticaria, pruritus, Henoch-Schonlein purpura.

Nervous system disorders:
neuroleptic malignant syndrome (see section 4.4), bradykinetic episodes (the "on-off" phenomenon), dizziness, paraesthesia, psychotic episodes including delusions, hallucinations and paranoid ideation, depression with or without development of suicidal tendencies, dementia, dream abnormalities, agitation, confusion, increased libido. Levodopa is associated with somnolence and has

been associated very rarely with excessive daytime somnolence and sudden sleep onset episodes.

***Respiratory, thoracic and mediastinal disorders*:**
dyspnoea.

Skin and subcutaneous tissue disorders*:*
alopecia, rash, dark sweat.

Renal and urinary disorders:
dark urine.

Psychiatric disorders: Dopamine dysregulation syndrome (Unknown frequency)
Rarely convulsions have occurred; however, a causal relationship with Co-Careldopa has not been established.

Other side effects that have been reported with levodopa or levodopa/ carbidopa combinations and may be potential side effects include:

Gastrointestinal disorders:
dyspepsia, dry mouth, bitter taste, sialorrhoea, dysphagia, bruxism, hiccups, abdominal pain and distress, constipation, flatulence, burning sensation of the tongue.

Metabolism and nutrition disorders:
weight gain or loss, oedema.
Common*:* Vitamin B6 deficiency

Nervous system disorders:
asthenia, decreased mental acuity, disorientation, ataxia, numbness, increased hand tremor, muscle cramp, trismus, activation of latent Horner's syndrome, insomnia, anxiety, euphoria, falling and gait abnormalities and Dopamine Dysregulation Syndrome.

Impulse control disorders
Pathological gambling, increased libido, hypersexuality, compulsive spending or buying, binge eating and compulsive eating can occur in patients treated with dopamine agonists and/or other dopaminergic treatments containing levodopa including Co-Careldopa (see section 4.4 ‘Special warnings and precautions for use’.)

Skin and subcutaneous tissue disorders:
flushing, increased sweating.

Special senses: diplopia, blurred vision, dilated pupils, oculogyric crises.
Renal and urinary disorders:
urinary retention, urinary incontinence, priapism.

General disorders and administration site conditions:
weakness, faintness, fatigue, headache, hoarseness, malaise, hot flushes, sense of stimulation, bizarre breathing patterns, malignant melanoma (see section 4.3 Contraindications).

Description of selected adverse reactions
Dopamine Dysregulation Syndrome (DDS) is an addictive disorder seen in some patients treated with carbidopa/ levodopa. Affected patients show a compulsive pattern of dopaminergic drug misuse above doses adequate to control motor symptoms, which may in some cases result in severe dyskinesias (see also section 4.4).

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 the Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Management of acute over dosage with Co-Careldopa is basically the same as management of acute over dosage with levodopa; however, pyridoxine is not effective in reversing the actions of Co-Careldopa. ECG monitoring should be instituted, and the patient carefully observed for the possible development of arrhythmias; if required, appropriate anti-arrhythmic therapy should be given. The possibility that the patient may have taken other drugs as well as Co-Careldopa should be taken into consideration. To date, no experience has been reported with dialysis, and hence its value in the treatment of over dosage is not known.

The terminal half-life of levodopa is about two hours in the presence of carbidopa.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: levodopa-dopaminergics; carbidopa-dopadecarboxylase inhibitor
ATC Code: N04B A02

Levodopa is a precursor of dopamine, and is given as replacement therapy in Parkinson's disease.

Carbidopa is a peripheral dopa decarboxylase inhibitor. It prevents metabolism of levodopa to dopamine in the peripheral circulation, ensuring that a higher proportion of the dose reaches the brain, where dopamine acts. A lower dose of levodopa can be used, reducing the incidence and severity of side effects. Co-Careldopa is useful in relieving many of the symptoms of parkinsonism, particularly rigidity and bradykinesia. It is frequently helpful in the management of tremor, dysphagia, sialorrhoea, and postural instability associated with Parkinson's disease and syndrome.

When response to levodopa alone is irregular, and signs and symptoms of Parkinson's disease are not controlled evenly throughout the day, substitution of Co-Careldopa usually reduces fluctuations in response. By reducing some of the adverse reactions produced by levodopa alone, Co-Careldopa permits more patients to obtain adequate relief from the symptoms of Parkinson's disease.

5.2 Pharmacokinetic properties

Following oral dosing levodopa, in the absence of decarboxylase inhibitor, is rapidly but variably absorbed from the gastro-intestinal tract. It has a plasma half-life of about 1 hour and is mainly converted by decarboxylation to dopamine, a proportion of which is converted to noradrenaline. Up to 30 % is converted to 3-O-methyldopa which has a half-life of 9 to 22 hours. About 80 % of levodopa is excreted in the urine within 24 hours mainly as homovanillic acid and dihydroxyphenylactic acid. Less than 1% is excreted unchanged. Once in the circulation it competes with other neutral amino acids for transport across the blood brain barrier. Once it has entered the striatal neurones it is decarboxylated to dopamine, stored and released from presynaptic neurones. Because levodopa is so rapidly decarboxylated in the gastro-intestinal tract and the liver, very little unchanged drug is available for transport into the brain. The peripheral decarboxylation reduces the therapeutic effectiveness of levodopa but is responsible for many of its side effects. For this reason

levodopa is usually administered together with a peripheral decarboxylase inhibitor such as carbidopa, so that lower doses may be given to achieve the same therapeutic effect.

Carbidopa in the absence of levodopa, is rapidly but incompletely absorbed from the gastrointestinal tract following oral dosing. Following an oral dose approximately 50% is recorded in the urine, with about 30% of this as unchanged drug. It does not cross the blood brain barrier but crosses the placenta and is excreted in breast milk. Turnover of the drug is rapid and virtually all unchanged drug appears in the urine within 7 hours.
Carbidopa inhibits the peripheral decarboxylation of levodopa to dopamine but as it does not cross the blood brain barrier, effective brain levels of dopamine get produced with lower levels of levodopa therapy reducing the peripheral side effects, noticeably nausea and vomiting and cardiac arrhythmias.

5.3 Preclinical safety data

Animal studies with regard to the pharmacological safety and toxicity after repeated administration, mutagenicity studies and carcinogenicity investigations showed no particular risk for humans. In reproductive toxicity studies both levodopa and the combination of carbidopa/levodopa have caused visceral and skeletal malformations in rabbits.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

PL 17907/0470
Crospovidone (E1202)
Indigo carmine lake (E132)
Magnesium stearate (E572)
Microcrystalline cellulose (E460)
Pre gelatinised starch (maize)

PL 17907/0471
Crospovidone (E1202)
Quinoline Yellow lake (E104)
Magnesium stearate (E572)
Microcrystalline cellulose (E460)
Pre gelatinised starch (maize)

PL 17907/0472
Crospovidone (E1202)

Quinoline Yellow lake (E104)
Magnesium stearate (E572)
Microcrystalline cellulose (E460)
Pre gelatinised starch (maize)

PL 17907/0473
Crospovidone (E1202)
Indigo carmine lake (E132)
Magnesium stearate (E572)
Microcrystalline cellulose (E460)
Pre gelatinised starch (maize)

6.2 Incompatibilities
Not applicable

6.3 Shelf life
3 years

6.4 Special precautions for storage
Store below 25°C

6.5 Nature and contents of container

PL 17907/0470 - Alu-Alu blister packs of 90 and100 tablets
PL 17907/0471 - Alu-Alu blister packs of 30, 50, 90 and 100 tablets
PL 17907/0472 - Alu-Alu blister packs of 30, 50, 56, 60, 90, 98, 100, 196 and 200 tablets
PL 17907/0473 - Alu-Alu blister packs of 30, 50, 60, 90, 98, 100, 120, 196 and 200 tablets

Not all pack sizes may be marketed.

6.6 Special precautions for disposal
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER
Bristol Laboratories Ltd,
Unit 3, Canalside,
Northbridge Road, Berkhamsted,
Herts, HP4 1EG, UK

8 MARKETING AUTHORISATION NUMBER(S)
PL 17907/0470

PL 17907/0471
PL 17907/0472
PL 17907/0473

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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