SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Carbidopa/Levodopa Fair-Med 12.5 mg/50 mg tablets
Carbidopa/Levodopa Fair-Med 10 mg/100 mg tablets
Carbidopa/Levodopa Fair-Med 25 mg/100 mg tablets
Carbidopa/Levodopa Fair-Med 25 mg/250 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet of Carbidopa/Levodopa Fair-Med contains 13.5 mg carbidopa monohydrate (equivalent to 12.5 mg of anhydrous carbidopa) and 50 mg levodopa.
Each tablet of Carbidopa/Levodopa Fair-Med contains 10.8 mg carbidopa monohydrate (equivalent to 10 mg of anhydrous carbidopa) and 100 mg levodopa.
Each tablet of Carbidopa/Levodopa Fair-Med contains 27.0 mg carbidopa monohydrate (equivalent to 25 mg of anhydrous carbidopa) and 100 mg levodopa.
Each tablet of Carbidopa/Levodopa Fair-Med 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.

Carbidopa/Levodopa Fair-Med 12.5 mg/50 mg tablets are light yellow colored, round shaped, with a diameter of 6 mm, with “C” on one side and “17” on other side of tablet.
Carbidopa/Levodopa Fair-Med 10 mg/100 mg tablets are light blue colored, round shaped, with a diameter of 8 mm, with “C” on one side and “18” on other side of tablet.
Carbidopa/Levodopa Fair-Med 25 mg/100 mg tablets are light yellow colored, round shaped, with a diameter of 8 mm, with “C” on one side and “19” on other side of tablet.
Carbidopa/Levodopa Fair-Med 25 mg/250 mg tablets are light blue colored, round shaped, with a diameter of 10.40 mm, with “C” on one side and “20” on other side of tablet.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Antiparkinsonian agent.

For treatment of Parkinson's disease and syndrome.

4.2 Posology and method of administration

Posology

The optimum daily dosage of carbidopa/levodopa must be determined by careful titration in each patient.
Carbidopa/Levodopa Fair-Med 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.
For doses not realisable/practicable with this medicinal product, other medicinal products are available.

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 carbidopa/levodopa is being administered, although their dosage may have to be adjusted.

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.

Dosage may be best initiated with one tablet of Carbidopa/Levodopa Fair-Med 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 Carbidopa/Levodopa Fair-Med 12.5 mg/50 mg or Carbidopa/Levodopa Fair-Med 25 mg/100 mg every day or every other day, as necessary, until a dosage equivalent of eight tablets of Carbidopa/Levodopa Fair-Med 25 mg/100 mg a day is reached.

If Carbidopa/Levodopa Fair-Med 10 mg/100 mg Tablets or Carbidopa/Levodopa Fair-Med 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.

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.

Carbidopa/Levodopa Fair-Med 12.5 mg/50 mg Tablets or Carbidopa/Levodopa Fair-Med 10 mg/100 mg Tablets may be used to facilitate dosage titration according to the needs of the individual patient.

Maintenance
Therapy with Carbidopa/Levodopa Fair-Med should be individualised and adjusted gradually according to response. When a greater proportion of carbidopa is required, each tablet of Carbidopa/Levodopa Fair-Med 10 mg/100 mg may be replaced with a tablet of Carbidopa/Levodopa Fair-Med 25 mg/100 mg or Carbidopa/Levodopa Fair-Med 12.5 mg/50 mg.

When more levodopa is required, Carbidopa/Levodopa Fair-Med 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 Carbidopa/Levodopa Fair-Med 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
Begin with a dosage of Carbidopa/Levodopa Fair-Med that will provide the same amount of levodopa as contained in the other levodopa/decarboxylase inhibitor combination.

Patients receiving other antiparkinsonian agents
Current evidence indicates that other antiparkinsonian agents may be continued when carbidopa/levodopa is introduced, although dosage may have to be adjusted in line with manufacturer’s recommendations.

Paediatric population
The safety of carbidopa/levodopa in patients under 18 years of age has not been established and its use in patients below the age of 18 is not recommended.

Patients with hepatic impairment
Carbidopa/ Levodopa Fair-Med should be administered cautiously to patients with hepatic impairment. The dose should be titrated individually.

Patients with renal impairment

Impact of renal function on levodopa/carbidopa clearance is limited. Carbidopa/ Levodopa Fair-Med should be administered cautiously to patients with renal impairment. The dose should be titrated individually.

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.

Method of administration
To be taken orally.

4.3 Contraindications

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

Non-selective monoamine oxidase (MAO) inhibitors and selective MAO type A inhibitors are contraindicated for use with Carbidopa/Levodopa Fair-Med.
These inhibitors must be discontinued at least two weeks before starting therapy with Carbidopa/Levodopa Fair-Med. Carbidopa/Levodopa Fair-Med 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 section 4.5 'Interaction with other medicinal products and other forms of interaction'.)

Carbidopa/Levodopa Fair-Med 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.

Conditions in which adrenergics are contraindicated, e.g. pheochromocytoma, hyperthyroidism, Cushing's syndrome, severe cardiovascular diseases.

4.4 Special warnings and precautions for use

Carbidopa/Levodopa Fair-Med is not recommended for the treatment of drug-induced extrapyramidal reactions.

Carbidopa/Levodopa Fair-Med 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 Carbidopa/Levodopa Fair-Med 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.

Carbidopa/Levodopa Fair-Med may induce orthostatic hypotension. Therefore Carbidopa/Levodopa Fair-Med should be given cautiously to patients who are taking other medicinal products which may cause orthostatic hypotension.

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, Carbidopa/Levodopa Fair-Med 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 Carbidopa/Levodopa Fair-Med is substituted. These reactions are thought to be due to increased brain dopamine following administration of levodopa, and use of Carbidopa/Levodopa Fair-Med 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 carbidopa/levodopa should be carefully observed, particularly in patients who are also receiving neuroleptics.

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).

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 Carbidopa/Levodopa Fair-Med. Review of treatment is recommended if such symptoms develop.

Concomitant administration of antipsychotics with dopamine receptor blocking properties, particularly D2 receptor antagonists should be carried out with caution, and the patient carefully observed for loss of antiparkinsonian effect or worsening of parkinsonian symptoms.

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 Carbidopa/Levodopa Fair-Med, 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 Carbidopa/Levodopa Fair-Med 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, carbidopa/levodopa 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 Carbidopa/Levodopa Fair-Med for any indication. Ideally, periodic skin examinations should be performed by appropriately qualified individuals (e.g., dermatologists).

Laboratory Tests
Commonly, levels of blood urea nitrogen, creatinine, and uric acid are lower during administration of carbidopa/levodopa 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 carbidopa/levodopa and levodopa alone.
Carbidopa/Levodopa Fair-Med 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.

4.5 Interaction with other medicinal products and other forms of interaction

Caution should be exercised when the following drugs are administered concomitantly with carbidopa/levodopa.

Antihypertensive agents
Postural hypotension can occur when carbidopa/levodopa 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 first paragraph of section 4.3 'Contraindications' for patients receiving MAOIs).

Anticholinergics
.
Anticholinergics may act synergistically with levodopa to decrease tremor. However, combined use may exacerbate abnormal involuntary movements. Anticholinergics may decrease the effects of levodopa by delaying its absorption. An adjustment of the dose of Carbidopa/Levodopa Fair-Med may be needed.

COMT inhibitors (tolcapone, entacapone)
Concomitant use of COMT (Catechol-O-Methyl Transferase) inhibitors and Carbidopa/Levodopa Fair-Med can increase the bioavailability of levodopa. The dose of Carbidopa/Levodopa Fair-Med may need adjustment**.**

Iron
Studies demonstrate a decrease in the bioavailability of carbidopa and/or levodopa when it is ingested with ferrous sulphate or ferrous gluconate. Therefore administration of Carbidopa/Levodopa Fair-Med and iron preparations should be separated by the longest possible interval in time.

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

Dopamine D2 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 carbidopa/levodopa should be carefully observed for loss of therapeutic response.

Concomitant therapy with selegiline and carbidopa-levodopa may be associated with severe orthostatic hypotension not attributable to carbidopa-levodopa alone (see section 4.3 'Contraindications').

Since levodopa competes with certain amino acids, the absorption of levodopa may be impaired in some patients on a high protein diet.

The effect of simultaneous administration of antacids with carbidopa/levodopa on the bioavailability of levodopa has not been studied.

Carbidopa/levodopa may be given to patients with Parkinson's disease and syndrome who are taking vitamin preparations that contain pyridoxine hydrochloride (Vitamin B6).

Amantadine has synergic effect with levodopa and may increase levodopa related adverse events. An adjustment of the dose of Carbidopa/Levodopa Fair-Med may be needed.

Sympathicomimetics may increase cardiovascular adverse events related to levodopa.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no or limited amount of data from the use of carbidopa/levodopa in pregnant women. Studies in animals have shown reproductive toxicity (see section 5.3). Carbidopa/Levodopa Fair-Med is not recommended during pregnancy or in women of childbearing potential not using contraception unless the benefits for the mother outweigh the possible risk to the fetus.

Breast-feeding
It is not known whether carbidopa or its metabolites are excreted in human milk. Animal studies have shown excretion of carbidopa in breast milk. Levodopa and possibly levodopa metabolites are excreted in human milk. There is insufficient information on the effects of carbidopa/levodopa or their metabolites in newborns/infants. Breastfeeding should be discontinued during treatment with Carbidopa/Levodopa Fair-Med.

Fertility
There are no data on the effects of carbidopa/levodopa on human fertility. No adverse effect on fertility has been observed in animal studies with levodopa alone. Fertility studies in animals have not been conducted with the combination of carbidopa and levodopa.

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 carbidopa/levodopa 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

Summary of the safety profile

Side effects that occur frequently with carbidopa/levodopa 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.

Description of selected adverse reactions

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 Carbidopa/ Levodopa (see section 4.4 “Special warning and precautions for use”).

Tabulated list of adverse reactions

MedDRA System Organ Class	**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)**
Infections and Infestations	Urinary tract infections					
Blood and lymphatic system disorders				Leukopenia, haemolytic and non-haemolytic anaemia, thrombocytopenia	Agranulocytosis	
Metabolism and nutrition disorders		Anorexia	Weight gain or loss			
Psychiatric disorders		Hallucinations, confusion, dizziness, nightmares, sleepiness, fatigue, insomnia, depression with very rare suicide attempts, euphoria, dementia, feeling of stimulation, dream abnormalities		Agitation, fear, reduced thinking capacity, disorientation, headache, increased libido, numbness and convulsions, psychotic episodes including delusions and paranoid ideation		Dopamine dysregulation syndrome
Nervous system disorders		Dyskinesia, chorea, dystonia, extrapyramidal and movement disorders, bradykinetic episodes (the “on-off” phenomenon) may appear some months to years after the beginning of treatment with levodopa and is probably related to the progression of the disease. The adaptation of dose schedule and dose intervals may be required.	Ataxia, increased hand tremor	Malignant neuroleptic syndrome, paraesthesia, falling, walking defects, trismus	Levodopa/carbidopa is associated with somnolence and has been associated very rarely with excessive daytime somnolence and sudden sleep onset episodes.	Muscle twitching
Eye disorders				Blurred vision, blepharospasm, activation of a latent Horner's syndrome, diplopia, dilated pupils, and oculogyric crises. Blepharospasm can be an early sign of overdosage.		
Cardiac disorders		Palpitations, irregular heartbeat				

MedDRA System Organ Class	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)
Vascular disorders		Orthostatic hypotension, inclination to faint, syncope	Hypertension	Phlebitis		
Respiratory, thoracic and mediastinal disorders			Hoarseness, chest pain	Dyspnoea, abnormal breathing pattern		
Gastrointestinal disorders		Nausea, vomiting, dry mouth, bitter taste	Constipation, diarrhoea, sialorrhoea, dysphagia, flatulence	Dyspepsia, gastrointestinal pain, dark saliva, bruxism, hiccups, gastrointestinal bleeding, burning sensation of the tongue, duodenal ulceration		
Skin and subcutaneous tissue disorders			Oedema	Angioedema, urticaria, pruritus, facial redness, hair loss, rash, increased sweating, dark sweat and Henoch-Schonlein purpura		
Musculoskeletal and connective tissue disorders			Muscle spasms			
Renal and urinary disorders			Dark urine	Urinary retention, urinary incontinence, priapism		
General disorders and administration site conditions			Asthenia, weakness, malaise, hot flushes			

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 national reporting system <to be completed nationally>

4.9 Overdose

Treatment

Management of acute overdosage with Carbidopa/Levodopa Fair-Med is basically the same as management of acute overdosage with levodopa; however pyridoxine is not effective in reversing the actions of Carbidopa/Levodopa Fair-Med. 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 Carbidopa/Levodopa Fair-Med should be taken into consideration. To date, no experience has been reported with dialysis, and hence its value in the treatment of overdosage 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: Anti-Parkison drugs, dopaminergic agents, ATC code: N04BA02

Mechanism of action
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.

Pharmacodynamic effects
Carbidopa/levodopa 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.

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

5.2 Pharmacokinetic properties

Absorption
Levodopa is rapidly and completely absorbed but undergoes extensive first pass metabolism. The bioavailability of levodopa is approximately 30% without co-administration of carbidopa. Maximal plasma concentrations of levodopa occur approximately 45 minutes after dose administration. Levodopa is co-administered with carbidopa, a decarboxylase inhibitor, which increases the bioavailability and decreases clearance for levodopa.

Distribution
Volume of distribution for levodopa is 0.9-1.6 l/kg, when given together with a decarboxylase inhibitor. The partitioning ratio for levodopa between erythrocytes and plasma is approximately 1. The protein binding of levodopa in plasma is negligible (about 10%-30%). Levodopa is transported into the brain by the carrier mechanism for large neutral amino acids.

Carbidopa is approximately 36% bound to plasma protein. Carbidopa does not cross the blood-brain barrier.

Biotransformation and elimination
Levodopa is eliminated completely through metabolism and the metabolites formed are excreted mainly in the urine. Four metabolic pathways are known, but levodopa is mainly eliminated via metabolism by the aromatic amino acid decarboxylase (AAAD) and the catechol-O-methyl-transferase (COMT) enzymes. Other routes of metabolism are transamination and oxidation. The decarboxylation of levodopa to dopamine by AAAD is the major enzymatic pathway when no enzyme inhibitor is co-administered. When levodopa is co-administered

with carbidopa, the decarboxylase enzyme is inhibited, so that metabolism via catechol-O-methyl-transferase (COMT) becomes the dominant metabolic pathway. O-methylation of levodopa by COMT forms 3-O-methyldopa. Clearance for levodopa is 0.3 l/hour/kg, when given together with a decarboxylase inhibitor. When administered with carbidopa, the elimination half-life for levodopa is approximately 1.5 hours.

Carbidopa is metabolized to two main metabolites (α-methyl-3-methoxy-4-hydroxyphenylpropionic acid and α-methyl-3,4-dihydroxyphenylpropionic acid). These 2 metabolites are primarily eliminated in the urine unchanged or as glucuronide conjugates. Unchanged carbidopa accounts for 30% of the total urinary excretion. The elimination half-life of carbidopa is approximately 2 hours.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeat-dose toxicity, genotoxicity and carcinogenic potential. In reproductive toxicity studies both levodopa and the combination of carbidopa and levodopa have caused visceral and skeletal malformations in rabbits.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

10 mg/100 mg and 25 mg/250 mg:
Crospovidone
Indigo carmine lake (E132)
Magnesium stearate
Cellulose microcrystalline
Starch, pregelatinised

12.5mg/50 mg and 25 mg/100 mg:
Crospovidone
Quinoline yellow lake (E104)
Magnesium stearate
Cellulose microcrystalline
Starch, pregelatinised

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Tablets are packed in Alu-Alu blisters.

Packs containing:
12.5 mg/50 mg and 10 mg /100mg: 30, 50, 90, 100 tablets
25 mg /100mg: blister packs of 20, 30, 50, 60, 90, 100, 120, 180, 200 tablets
25 mg /250mg: blister packs of 20, 30, 50, 60, 90, 100, 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

<To be completed nationally>

8. MARKETING AUTHORISATION NUMBER(S)

<To be completed nationally>

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

<To be completed nationally>

10. DATE OF REVISION OF THE TEXT

2024-01-30