ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Corbilta 50 mg/12.5 mg/200 mg film-coated tablets
Corbilta 75 mg/18.75 mg/200 mg film-coated tablets
Corbilta 100 mg/25 mg/200 mg film-coated tablets
Corbilta 125 mg/31.25 mg/200 mg film-coated tablets
Corbilta 150 mg/37.5 mg/200 mg film-coated tablets
Corbilta 175 mg/43.75 mg/200 mg film-coated tablets
Corbilta 200 mg/50 mg/200 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

50 mg/12.5 mg/200 mg
Each tablet contains 50 mg of levodopa, 12.5 mg of carbidopa and 200 mg of entacapone.

Excipient with known effect:
Each tablet contains 1.2 mg of sucrose.

75 mg/18.75 mg/200 mg
Each tablet contains 75 mg of levodopa, 18.75 mg of carbidopa and 200 mg of entacapone.

Excipient with known effect:
Each tablet contains 1.4 mg of sucrose.

100 mg/25 mg/200 mg
Each tablet contains 100 mg of levodopa, 25 mg of carbidopa and 200 mg of entacapone.

Excipient with known effect:
Each tablet contains 1.6 mg of sucrose.

125 mg/31.25 mg/200 mg
Each tablet contains 125 mg of levodopa, 31.25 mg of carbidopa and 200 mg of entacapone.

Excipient with known effect:
Each tablet contains 1.6 mg of sucrose.

150 mg/37.5 mg/200 mg
Each tablet contains 150 mg of levodopa, 37.5 mg of carbidopa and 200 mg of entacapone.

Excipients with known effect:
Each tablet contains 1.9 mg of sucrose and 2.6 mg sodium as a constituent of an excipient.

175 mg/43.75 mg/200 mg
Each tablet contains 175 mg of levodopa, 43.75 mg of carbidopa and 200 mg of entacapone.

Excipient with known effect:
Each tablet contains 1.89 mg of sucrose.

200 mg/50 mg/200 mg
Each tablet contains 200 mg of levodopa, 50 mg of carbidopa and 200 mg of entacapone.

Excipient with known effect:
Each tablet contains 2.3 mg of sucrose.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet (tablet)

50 mg/12.5 mg/200 mg
Brownish or greyish red, round, convex, unscored film-coated tablets marked with “LCE 50” on one side.

75 mg/18.75 mg/200 mg
Light brownish red, oval film-coated tablets marked with “LCE 75” on one side.

100 mg/25 mg/200 mg
Brownish or greyish red, oval, unscored film-coated tablets marked with “LCE 100” on one side.

125 mg/31.25 mg/200 mg
Light brownish red, oval film-coated tablets marked with “LCE 125” on one side.

150 mg/37.5 mg/200 mg
Brownish or greyish red, elongated-ellipse shaped, unscored film-coated tablets marked with “LCE 150” on one side.

175 mg/43.75 mg/200 mg
Light brownish red, oval, unscored film-coated tablets marked with “LCE 175” on one side.

200 mg/50 mg/200 mg
Dark brownish red, oval, unscored film-coated tablets marked with “LCE 200” on one side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Corbilta is indicated for the treatment of adult patients with Parkinson’s disease and end-of-dose motor fluctuations not stabilised on levodopa/dopa decarboxylase (DDC) inhibitor treatment.

4.2 Posology and method of administration

Posology

The optimum daily dose must be determined by careful titration of levodopa in each patient. The daily dose should be preferably optimised using one of the seven available tablet strengths (50 mg/12.5 mg/200 mg, 75 mg/18.75 mg/200 mg, 100 mg/25 mg/200 mg, 125 mg/31.25 mg/200 mg, 150 mg/37.5 mg/200 mg, 175 mg/43.75 mg/200 mg or 200 mg/50 mg/200 mg levodopa/carbidopa/entacapone).

Patients should be instructed to take only one Corbilta tablet per dose administration. Patients receiving less than 70–100 mg carbidopa a day are more likely to experience nausea and vomiting. While the experience with total daily dose greater than 200 mg carbidopa is limited, the maximum recommended daily dose of entacapone is 2 000 mg and therefore the maximum dose is 10 tablets per day for the Corbilta strengths of 50 mg/12.5 mg/200 mg, 75 mg/18.75 mg/200 mg, 100 mg/25 mg/200 mg, 125 mg/31.25 mg/200 mg and 150 mg/37.5 mg/200 mg. Ten tablets of Corbilta 150 mg/37.5 mg/200 mg equals 375 mg of carbidopa a day. According to this daily carbidopa dose, the maximum recommended daily dose of Corbilta 175 mg/43.75 mg/200 mg is 8 tablets per day and Corbilta 200 mg/50 mg/200 mg dose is 7 tablets per day.

Usually Corbilta is to be used in patients who are currently treated with corresponding doses of standard release levodopa/DDC inhibitor and entacapone.

How to transfer patients taking levodopa/DDC inhibitor (carbidopa or benserazide) preparations and entacapone tablets to Corbilta

a. Patients who are currently treated with entacapone and with standard release levodopa/carbidopa in doses equal to Corbilta tablet strengths can be directly transferred to corresponding Corbilta tablets. For example, a patient taking one tablet of 50 mg/12.5 mg of levodopa/carbidopa with one tablet of entacapone 200 mg four times daily can take one 50 mg/12.5 mg/200 mg Corbilta tablet four times daily in place of their usual levodopa/carbidopa and entacapone doses.

b. When initiating Corbilta therapy for patients currently treated with entacapone and levodopa/carbidopa in doses not equal to Corbilta tablets (50 mg/12.5 mg/200 mg or 75 mg/18.75 mg/200 mg or 100 mg/25 mg/200 mg or 125 mg/31.25 mg/200 mg or 150 mg/37.5 mg/200 mg or 175 mg/43.75 mg/200 mg or 200 mg/50 mg/200 mg), Corbilta dosing should be carefully titrated for optimal clinical response. At the initiation, Corbilta should be adjusted to correspond as closely as possible to the total daily dose of levodopa currently used.

c. When initiating Corbilta in patients currently treated with entacapone and levodopa/benserazide in a standard release formulation, the dosing of levodopa/benserazide should be discontinued in the previous night, and Corbilta should be started in the next morning. The starting dose of Corbilta should provide either the same amount of levodopa or slightly (5–10%) more.

How to transfer patients not currently treated with entacapone to Corbilta

Initiation of Corbilta may be considered at corresponding doses to current treatment in some patients with Parkinson's disease and end-of-dose motor fluctuations, who are not stabilised on their current standard release levodopa/DDC inhibitor treatment. However, a direct switch from levodopa/DDC inhibitor to Corbilta is not recommended for patients who have dyskinesias or whose daily levodopa dose is above 800 mg. In such patients it is advisable to introduce entacapone treatment as a separate treatment (entacapone tablets) and adjust the levodopa dose if necessary, before switching to Corbilta.

Entacapone enhances the effects of levodopa. It may therefore be necessary, particularly in patients with dyskinesia, to reduce levodopa dose by 10–30% within the first days to first weeks after initiating Corbilta treatment. The daily dose of levodopa can be reduced by extending the dosing intervals and/or by reducing the amount of levodopa per dose, according to the clinical condition of the patient.

Dose adjustment during the course of the treatment

When more levodopa is required, an increase in the frequency of doses and/or the use of an alternative strength of Corbilta should be considered, within the dose recommendations.

When less levodopa is required, the total daily dose of Corbilta should be reduced either by decreasing the frequency of administration by extending the time between doses, or by decreasing the strength of Corbilta at an administration.

If other levodopa products are used concomitantly with a Corbilta tablet, the maximum dose recommendations should be followed.

Discontinuation of Corbilta therapy: If Corbilta treatment (levodopa/carbidopa/entacapone) is discontinued and the patient is transferred to levodopa/DDC inhibitor therapy without entacapone, it is necessary to adjust the dosing of other antiparkinsonian treatments, especially levodopa, to achieve a sufficient level of control of the parkinsonian symptoms.

Paediatric population: The safety and efficacy of Corbilta in children aged below 18 years have not been established. No data are available.

Elderly: No dose adjustment of Corbilta is required for elderly.

Hepatic impairment: It is advised that Corbilta should be administered cautiously to patients with mild to moderate hepatic impairment. Dose reduction may be needed (see section 5.2). For severe hepatic impairment see section 4.3.

Renal impairment: Renal impairment does not affect the pharmacokinetics of entacapone. No particular studies are reported on the pharmacokinetics of levodopa and carbidopa in patients with renal insufficiency, therefore Corbilta therapy should be administered cautiously to patients in severe renal impairment including those receiving dialysis therapy (see section 5.2).

Method of administration

Each tablet is to be taken orally either with or without food (see section 5.2). One tablet contains one treatment dose and the tablet may only be administered as whole tablets.

4.3 Contraindications

- Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.
- Severe hepatic impairment.
- Narrow-angle glaucoma.
- Pheochromocytoma.
- Coadministration of Corbilta with non-selective monoamine oxidase (MAO-A and MAO-B) inhibitors (e.g. phenelzine, tranylcypromine).
- Coadministration with a selective MAO-A inhibitor and a selective MAO-B inhibitor (see section 4.5).
- A previous history of Neuroleptic Malignant Syndrome (NMS) and/or non-traumatic rhabdomyolysis.

4.4 Special warnings and precautions for use

- Corbilta is not recommended for the treatment of drug-induced extrapyramidal reactions.
- Corbilta therapy should be administered cautiously to patients with ischemic heart disease, severe cardiovascular or pulmonary disease, bronchial asthma, renal or endocrine disease, history of peptic ulcer disease or history of convulsions.
- In patients with a history of myocardial infarction who have residual atrial nodal or ventricular arrhythmias; cardiac function should be monitored with particular care during the period of initial dose adjustments.
- All patients treated with Corbilta should be monitored carefully for the development of mental changes, depression with suicidal tendencies, and other serious antisocial behaviour. Patients with past or current psychosis should be treated with caution.
- Concomitant administration of antipsychotics with dopamine receptor-blocking properties, particularly D_2 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 chronic wide-angle glaucoma may be treated with Corbilta with caution, provided the intra-ocular pressure is well controlled and the patient is monitored carefully for changes in intra-ocular pressure.
- Corbilta may induce orthostatic hypotension. Therefore Corbilta should be given cautiously to patients who are taking other medicinal products which may cause orthostatic hypotension.
- Entacapone in association with levodopa has been associated with somnolence and episodes of sudden sleep onset in patients with Parkinson's disease and caution should therefore be exercised when driving or operating machines (see section 4.7).

- In clinical studies, dopaminergic adverse reactions, e.g. dyskinesia, were more common in patients who received entacapone and dopamine agonists (such as bromocriptine), selegiline or amantadine compared to those who received placebo with this combination. The doses of other antiparkinsonian medicinal products may need to be adjusted when Corbilta treatment is substituted for a patient currently not treated with entacapone.
- Rhabdomyolysis secondary to severe dyskinesias or neuroleptic malignant syndrome (NMS) has been observed rarely in patients with Parkinson's disease. Therefore, any abrupt dose reduction or withdrawal of levodopa should be carefully observed, particularly in patients who are also receiving neuroleptics. NMS, including rhabdomyolysis and hyperthermia, is characterised by motor symptoms (rigidity, myoclonus, tremor), mental status changes (e.g., agitation, confusion, coma), hyperthermia, autonomic dysfunction (tachycardia, labile blood pressure) and elevated serum creatine phosphokinase. In individual cases, only some of these symptoms and/or findings may be evident. The early diagnosis is important for the appropriate management of NMS. 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. Neither NMS nor rhabdomyolysis have been reported in association with entacapone treatment from controlled trials in which entacapone was discontinued abruptly. Since the introduction of entacapone into the market, isolated cases of NMS have been reported, especially following abrupt reduction or discontinuation of entacapone and other concomitant dopaminergic medicinal products. When considered necessary, the replacement of Corbilta with levodopa and DDC inhibitor without entacapone or other dopaminergic treatment should proceed slowly and an increase in levodopa dose may be necessary.
- If general anaesthesia is required, therapy with Corbilta may be continued for as long as the patient is permitted to take fluids and medicinal products by mouth. If therapy has to be stopped temporarily, Corbilta may be restarted as soon as oral medicinal products can be taken at the same daily dose as before.
- Periodic evaluation of hepatic, haematopoietic, cardiovascular and renal function is recommended during extended therapy with Corbilta.
- For patients experiencing diarrhoea, a follow-up of weight is recommended in order to avoid potential excessive weight decrease. Prolonged or persistent diarrhoea appearing during use of entacapone may be a sign of colitis. In the event of prolonged or persistent diarrhoea, the drug should be discontinued and appropriate medical therapy and investigations considered.
- 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 Corbilta. Review of treatment is recommended if such symptoms develop.
- 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).
- For patients who experience progressive anorexia, asthenia and weight decrease within a relatively short period of time, a general medical evaluation including liver function should be considered.
- Levodopa/carbidopa may cause false positive result when a dipstick is used to test for urinary ketone and this reaction is not altered by boiling the urine sample. The use of glucose oxidase methods may give false negative results for glycosuria.
- Corbilta contains sucrose, and therefore patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.
- Corbilta 150 mg/37.5 mg/200 mg contains 2.6 mg sodium per tablet. The maximum recommended daily dose (10 tablets) contains 26 mg sodium, equivalent to 1.3% of the WHO recommended maximum daily intake of 2 g sodium for an adult.
- Corbilta 50 mg/12.5 mg/200 mg, 75 mg/18.75 mg/200 mg, 100 mg/25 mg/200 mg,

125 mg/31.25 mg/200 mg, 175 mg/43.75 mg/200 mg and 200 mg/50 mg/200 mg film-coated tablets contain less than 1 mmol (23 mg) sodium per maximum recommended daily dose, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Other antiparkinsonian medicinal products: To date there has been no indication of interactions that would preclude concurrent use of standard antiparkinsonian medicinal products with Corbilta therapy. Entacapone in high doses may affect the absorption of carbidopa. However, no interaction with carbidopa has been observed with the recommended treatment schedule (200 mg of entacapone up to 10 times daily). Interactions between entacapone and selegiline have been investigated in repeated dose studies in Parkinson's disease patients treated with levodopa/DDC inhibitor and no interaction was observed. When used with Corbilta, the daily dose of selegiline should not exceed 10 mg.

Caution should be exercised when the following active substances are administered concomitantly with levodopa therapy.

Antihypertensives: Symptomatic postural hypotension may occur when levodopa is added to the treatment of patients already receiving antihypertensives. Dose 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 and levodopa/carbidopa. Interactions between entacapone and imipramine and between entacapone and moclobemide have been investigated in single dose studies in healthy volunteers. No pharmacodynamic interactions were observed. A significant number of Parkinson's disease patients have been treated with the combination of levodopa, carbidopa and entacapone with several active substances including MAO-A inhibitors, tricyclic antidepressants, noradrenaline reuptake inhibitors such as desipramine, maprotiline and venlafaxine and medicinal products that are metabolised by COMT (e.g. catechol-structured compounds, paroxetine). No pharmacodynamic interactions have been observed. However, caution should be exercised when these medicinal products are used concomitantly with Corbilta (see sections 4.3 and 4.4).

Other active substances: Dopamine receptor antagonists (e.g. some antipsychotics and antiemetics), phenytoin and papaverine may reduce the therapeutic effect of levodopa. Patients taking these medicinal products with Corbilta should be carefully observed for loss of therapeutic response.

Due to entacapone's affinity to cytochrome P450 2C9 *in vitro* (see section 5.2), Corbilta may potentially interfere with active substances whose metabolism is dependent on this isoenzyme, such as S-warfarin. However, in an interaction study with healthy volunteers, entacapone did not change the plasma levels of S-warfarin, while the AUC for R-warfarin increased on average by 18% [CI_{90} 11–26%]. The INR values increased on average by 13% [CI_{90} 6–19%]. Thus, a control of INR is recommended when Corbilta is initiated for patients receiving warfarin.

Other forms of interactions: Since levodopa competes with certain amino acids, the absorption of Corbilta may be impaired in some patients on high protein diet.

Levodopa and entacapone may form chelates with iron in the gastrointestinal tract. Therefore, Corbilta and iron preparations should be taken at least 2–3 hours apart (see section 4.8).

In vitro data: Entacapone binds to human albumin binding site II which also binds several other medicinal products, including diazepam and ibuprofen. According to *in vitro* studies, significant displacement is not anticipated at therapeutic concentrations of the medicinal products. Accordingly, to date there has been no indication of such interactions.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no adequate data from the use of the combination of levodopa/carbidopa/entacapone in pregnant women. Studies in animals have shown reproductive toxicity of the separate compounds (see section 5.3). The potential risk for humans is unknown. Corbilta should not be used during pregnancy unless the benefits for the mother outweigh the possible risks to the foetus.

Breast-feeding
Levodopa is excreted in human breast milk. There is evidence that breast-feeding is suppressed during treatment with levodopa. Carbidopa and entacapone were excreted in milk in animals but is not known whether they are excreted in human breast milk. The safety of levodopa, carbidopa or entacapone in the infant is not known. Women should not breast-feed during treatment with Corbilta.

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

4.7 Effects on ability to drive and use machines

Corbilta may have a major influence on the ability to drive and use machines. Levodopa, carbidopa and entacapone together may cause dizziness and symptomatic orthostatism. Therefore, caution should be exercised when driving or using machines.

Patients being treated with Corbilta and presenting with somnolence and/or sudden sleep onset episodes must be instructed 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 have resolved (see section 4.4).

4.8 Undesirable effects

a. Summary of the safety profile

The most frequently reported adverse reactions with Corbilta are dyskinesias occurring in approximately 19% of patients; gastrointestinal symptoms including nausea and diarrhoea occurring in approximately 15% and 12% of patients, respectively; muscle, musculoskeletal and connective tissue pain occurring in approximately 12% of patients; and harmless reddish-brown discolouration of urine (chromaturia) occurring in approximately 10% of patients. Serious events of gastrointestinal haemorrhage (uncommon) and angioedema (rare) have been identified from the clinical trials with Corbilta or entacapone combined with levodopa/DDC inhibitor. Serious hepatitis with mainly cholestatic features, rhabdomyolysis and neuroleptic malignant syndrome may occur with Corbilta although no cases have been identified from the clinical trial data.

b. Tabulated list of adverse reactions

The following adverse reactions, listed in Table 1, have been accumulated both from a pooled data of eleven double-blind clinical trials consisting of 3 230 patients (1 810 treated with Corbilta or entacapone combined with levodopa/DDC inhibitor, and 1 420 treated with placebo combined with levodopa/DDC inhibitor or cabergoline combined with levodopa/ DDC inhibitor), and from the post-marketing data since the introduction of entacapone into the market for the combination use of entacapone with levodopa/DDC inhibitor.

Adverse reactions are ranked under headings of frequency, the most frequent first, 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, since no valid estimate can be derived from clinical trials or epidemiological studies).

Table 1. Adverse reactions

Blood and lymphatic system disorders

Common:	Anaemia
Uncommon:	Thrombocytopenia

Metabolism and nutrition disorders

Common:	Weight decreased*, decreased appetite*

Psychiatric disorders

Common:	Depression, hallucination, confusional state*, abnormal dreams*, anxiety, insomnia
Uncommon:	Psychosis, agitation*
Not known:	Suicidal behaviour, Dopamine dysregulation syndrome

Nervous system disorders

Very common:	Dyskinesia*
Common:	Parkinsonism aggravated (e.g. bradykinesia)*, tremor, on and off phenomenon, dystonia, mental impairment (e.g. memory impairment, dementia), somnolence, dizziness*, headache
Not known:	Neuroleptic malignant syndrome*

Eye disorders

Common:	Blurred vision

Cardiac disorders

Common:	Ischemic heart disease events other than myocardial infarction (e.g. angina pectoris)**, irregular heart rhythm
Uncommon:	Myocardial infarction**

Vascular disorders

Common:	Orthostatic hypotension, hypertension
Uncommon:	Gastrointestinal haemorrhage

Respiratory, thoracic and mediastinal disorders

Common:	Dyspnoea

Gastrointestinal disorders

Very common:	Diarrhoea*, nausea*
Common:	Constipation*, vomiting*, dyspepsia, abdominal pain and discomfort*, dry mouth*
Uncommon:	Colitis*, dysphagia

Hepatobiliary disorders

Uncommon:	Hepatic function test abnormal*
Not known:	Hepatitis with mainly cholestatic features (see section 4.4)*

Skin and subcutaneous tissue disorders

Common:	Rash*, hyperhidrosis
Uncommon:	Discolourations other than urine (e.g. skin, nail, hair, sweat)*
Rare:	Angioedema
Not known:	Urticaria*

Musculoskeletal and connective tissue disorders

Very common:	Muscle, musculoskeletal and connective tissue pain*
Common:	Muscle spasms, arthralgia
Not known:	Rhabdomyolysis*

Renal and urinary disorders
Very common: Chromaturia*
Common: Urinary tract infection
Uncommon: Urinary retention

General disorders and administration site conditions
Common: Chest pain, peripheral oedema, fall, gait disturbance, asthenia, fatigue
Uncommon: Malaise

*Adverse reactions that are mainly attributable to entacapone or are more frequent (by the frequency difference of at least 1% in the clinical trial data) with entacapone than levodopa/DDC inhibitor alone. See section c.

**The incidence rates of myocardial infarction and other ischemic heart disease events (0.43% and 1.54%, respectively) are derived from an analysis of 13 double-blind studies involving 2 082 patients with end-of-dose motor fluctuations receiving entacapone.

c. Description of selected adverse reactions

Adverse reactions that are mainly attributable to entacapone or are more frequent with entacapone than levodopa/DDC inhibitor alone are indicated with an asterisk in Table 1, section 4.8b. Some of these adverse reactions relate to the increased dopaminergic activity (e.g. dyskinesia, nausea and vomiting) and occur most commonly at the beginning of the treatment. Reduction of levodopa dose decreases the severity and frequency of these dopaminergic reactions. Few adverse reactions are known to be directly attributable to the active substance entacapone including diarrhoea and reddish-brown discolouration of urine. Entacapone may in some cases cause also discolouration of e.g. skin, nail, hair and sweat. Other adverse reactions with an asterisk in Table 1, section 4.8b are marked based on either their more frequent occurring (by the frequency difference of at least 1%) in the clinical trial data with entacapone than levodopa/DDCI alone or the individual case safety reports received after the introduction of entacapone into the market.

Convulsions have occurred rarely with levodopa/carbidopa; however a causal relationship to levodopa/carbidopa therapy has not been established.

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 Corbilta (see section 4.4).

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).

Entacapone in association with levodopa has been associated with isolated cases of excessive daytime somnolence and sudden sleep onset episodes.

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 listed in Appendix V.

4.9 Overdose

The post-marketing data includes isolated cases of overdose in which the reported highest daily doses of levodopa and entacapone have been at least 10 000 mg and 40 000 mg, respectively. The acute symptoms and signs in these cases of overdose included agitation, confusional state, coma, bradycardia, ventricular tachycardia, Cheyne-Stokes respiration, discolourations of skin, tongue and conjunctiva, and chromaturia. Management of acute overdose with Corbilta therapy is similar to acute overdose with levodopa. Pyridoxine, however, is not effective in reversing the actions of Corbilta. Hospitalisation is advised and general supportive measures should be employed with immediate gastric lavage and repeated doses of charcoal over time. This may hasten the elimination of entacapone in particular by decreasing its absorption/reabsorption from the GI tract. The adequacy of the respiratory, circulatory and renal systems should be carefully monitored and appropriate supportive measures employed. ECG monitoring should be started and the patient carefully monitored for the possible development of arrhythmias. If required, appropriate anti-arrhythmic therapy should be given. The possibility that the patient has taken other active substances in addition to Corbilta should be taken into consideration. The value of dialysis in the treatment of overdose is not known.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: anti-parkinson drugs, dopa and dopa derivatives, ATC code: N04BA03

According to the current understanding, the symptoms of Parkinson's disease are related to depletion of dopamine in the corpus striatum. Dopamine does not cross the blood-brain barrier. Levodopa, the precursor of dopamine, crosses the blood brain barrier and relieves the symptoms of the disease. As levodopa is extensively metabolised in the periphery, only a small portion of a given dose reaches the central nervous system when levodopa is administered without metabolic enzyme inhibitors.

Carbidopa and benserazide are peripheral DDC inhibitors which reduce the peripheral metabolism of levodopa to dopamine, and thus, more levodopa is available to the brain. When decarboxylation of levodopa is reduced with the co-administration of a DDC inhibitor, a lower dose of levodopa can be used and the incidence of adverse reactionssuch as nausea is reduced.

With inhibition of the decarboxylase by a DDC inhibitor, catechol-*O*-methyltransferase (COMT) becomes the major peripheral metabolic pathway catalyzing the conversion of levodopa to 3-O-methyldopa (3-OMD), a potentially harmful metabolite of levodopa. Entacapone is a reversible, specific and mainly peripherally acting COMT inhibitor designed for concomitant administration with levodopa. Entacapone slows the clearance of levodopa from the bloodstream resulting in an increased area under the curve (AUC) in the pharmacokinetic profile of levodopa. Consequently the clinical response to each dose of levodopa is enhanced and prolonged.

The evidence of the therapeutic effects of Corbilta is based on two phase III double-blind studies, in which 376 Parkinson's disease patients with end-of-dose motor fluctuations received either entacapone or placebo with each levodopa/DDC inhibitor dose. Daily ON time with and without entacapone was recorded in home-diaries by patients. In the first study, entacapone increased the mean daily ON time by 1 h 20 min ($CI_{95\%}$ 45 min, 1 h 56 min) from baseline. This corresponded to an 8.3% increase in the proportion of daily ON time. Correspondingly, the decrease in daily OFF time was 24% in the entacapone group and 0% in the placebo group. In the second study, the mean proportion of daily ON time increased by 4.5% ($CI_{95\%}$ 0.93%, 7.97%) from baseline. This is translated to a mean increase of 35 min in the daily ON time. Correspondingly, the daily OFF time decreased by 18% on entacapone and by 5% on placebo. Because the effects of Corbilta tablets are equivalent with entacapone 200 mg tablet administered concomitantly with the commercially available standard release carbidopa/levodopa preparations in corresponding doses these results are applicable to describe the effects of Corbilta as well.

5.2 Pharmacokinetic properties

General characteristics of the active substances

Absorption/distribution: There are substantial inter- and intra-individual variations in the absorption of levodopa, carbidopa and entacapone. Both levodopa and entacapone are rapidly absorbed and eliminated. Carbidopa is absorbed and eliminated slightly slower compared with levodopa. When given separately without the two other active substances, the bioavailability for levodopa is 15–33%, for carbidopa 40–70% and for entacapone 35% after a 200 mg oral dose. Meals rich in large neutral amino acids may delay and reduce the absorption of levodopa. Food does not significantly affect the absorption of entacapone. The distribution volume of both levodopa (Vd 0.36–1.6 l/kg) and entacapone (Vd_{ss} 0.27 l/kg) is moderately small while no data for carbidopa are available.

Levodopa is bound to plasma protein only to a minor extent of about 10–30% and carbidopa is bound approximately 36%, while entacapone is extensively bound to plasma proteins (about 98%) –mainly to serum albumin. At therapeutic concentrations, entacapone does not displace other extensively bound active substances (e.g. warfarin, salicylic acid, phenylbutazone, or diazepam), nor is it displaced to any significant extent by any of these substances at therapeutic or higher concentrations.

Biotransformation and elimination: Levodopa is extensively metabolised to various metabolites: decarboxylation by dopa decarboxylase (DDC) and O-methylation by catechol-O-methyltransferase (COMT) being the most important pathways.

Carbidopa is metabolized to two main metabolites which are excreted in the urine as glucuronides and unconjugated compounds. Unchanged carbidopa accounts for 30% of the total urinary excretion.

Entacapone is almost completely metabolized prior to excretion via urine (10 to 20%) and bile/faeces (80 to 90%). The main metabolic pathway is glucuronidation of entacapone and its active metabolite, the cis-isomer, which accounts for about 5% of plasma total amount.

Total clearance for levodopa is in the range of 0.55–1.38 l/kg/h and for entacapone is in the range of 0.70 l/kg/h. The elimination-half life is ($t_{1/2}$) is 0.6–1.3 hours for levodopa, 2–3 hours for carbidopa and 0.4–0.7 hours for entacapone, each given separately.

Due to short elimination half-lives, no true accumulation of levodopa or entacapone occurs on repeated administration.

Data from *in vitro* studies using human liver microsomal preparations indicate that entacapone inhibits cytochrome P450 2C9 (IC50 ~ 4 μM). Entacapone showed little or no inhibition of other types of P450 isoenzymes (CYP1A2, CYP2A6, CYP2D6, CYP2E1, CYP3A and CYP2C19); see section 4.5.

Characteristics in patients

Elderly: When given without carbidopa and entacapone, the absorption of levodopa is greater and elimination is slower in elderly than in young people. However, after combination of carbidopa with levodopa, the absorption of levodopa is similar between the elderly and the young people, but the AUC is still 1.5 fold greater in the elderly due to decreased DDC activity and lower clearance by aging. There are no significant differences in the AUC of carbidopa or entacapone between younger (45–64 years) and elderly (65–75 years).

Gender: Bioavailability of levodopa is significantly higher in women than in men. In the pharmacokinetic studies with Corbilta the bioavailability of levodopa is higher in women than in men, primarily due to the difference in body weight, while there is no gender difference with carbidopa and entacapone.

Hepatic impairment: The metabolism of entacapone is slowed in patients with mild to moderate

hepatic impairment (Child-Pugh Class A and B) leading to an increased plasma concentration of entacapone both in the absorption and elimination phases (see sections 4.2 and 4.3). No particular studies on the pharmacokinetics of carbidopa and levodopa in patients with hepatic impairment are reported, however, it is advised that Corbilta should be administered cautiously to patients with mild or moderate hepatic impairment.

Renal impairment: Renal impairment does not affect the pharmacokinetics of entacapone. No particular studies are reported on the pharmacokinetics of levodopa and carbidopa in patients with renal impairment. However, a longer dosing interval of Corbilta may be considered for patients who are receiving dialysis therapy (see section 4.2).

5.3 Preclinical safety data

Preclinical data of levodopa, carbidopa and entacapone, tested alone or in combination, revealed no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, and carcinogenic potential. In repeated dose toxicity studies with entacapone, anaemia most likely due to iron chelating properties of entacapone was observed. Regarding reproduction toxicity of entacapone, decreased foetal weight and a slightly delayed bone development were noticed in rabbits treated at systemic exposure levels in the therapeutic range. Both levodopa and combinations of carbidopa and levodopa have caused visceral and skeletal malformations in rabbits.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:
Croscarmellose sodium
Magnesium stearate
Maize starch
Mannitol (E421)
Povidone K 30 (E1201)

Film-coating of 50/12.5/200 mg, 100/25/200 mg and 150/37.5/200 mg:
Glycerol (85 per cent) (E422)
Hypromellose
Magnesium stearate
Polysorbate 80
Red iron oxide (E172)
Sucrose
Titanium dioxide (E171)
Yellow iron oxide (E172)

Film-coating of 75/18.75/200 mg, 125/31.25/200 mg, 175/43.75/200 mg and 200/50/200 mg:
Glycerol (85 per cent) (E422)
Hypromellose
Magnesium stearate
Polysorbate 80
Red iron oxide (E172)
Sucrose
Titanium dioxide (E171)

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

HDPE bottle with a child resistant PP-closure.

Pack sizes of 50/12.5/200 mg, 100/25/200 mg and 150/37.5/200 mg:
10, 30, 100, 130, 175 and 250 tablets.

Pack sizes of 75/18.75/200 mg, 125/31.25/200 mg, 175/43.75/200 mg and 200/50/200 mg:
10, 30, 100, 130 and 175 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

Orion Corporation
Orionintie 1
FI-02200 Espoo
Finland

8. MARKETING AUTHORISATION NUMBERS

50 mg/12.5 mg/200 mg
EU/1/13/859/001-006

75 mg/18.75 mg/200 mg
EU/1/13/859/007-011

100 mg/25 mg/200 mg
EU/1/13/859/012-017

125 mg/31.25 mg/200 mg
EU/1/13/859/018-022

150 mg/37.5 mg/200 mg
EU/1/13/859/023-028

175 mg/43.75 mg/200 mg
EU/1/13/859/029-033

200 mg/50 mg/200 mg
EU/1/13/859/034-038

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 11 November 2013
Date of latest renewal: 6 July 2018

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of European Medicines Agency http://www.ema.europa.eu.

ANNEX II

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

Orion Corporation Orion Pharma
Joensuunkatu 7
FI-24100 Salo
Finland

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

BOTTLE LABEL AND OUTER CARTON TEXT

1. NAME OF THE MEDICINAL PRODUCT

Corbilta 50 mg/12.5 mg/200 mg film-coated tablets
levodopa/carbidopa/entacapone

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each film-coated tablet contains 50 mg of levodopa, 12.5 mg of carbidopa and 200 mg of entacapone.

3. LIST OF EXCIPIENTS

Contains sucrose.

4. PHARMACEUTICAL FORM AND CONTENTS

Carton
10 film-coated tablets
30 film-coated tablets
100 film-coated tablets
130 film-coated tablets
175 film-coated tablets
250 film-coated tablets

Label
10 tablets
30 tablets
100 tablets
130 tablets
175 tablets
250 tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Carton
Orion Corporation
Orionintie 1
FI-02200 Espoo
Finland

Label
Orion Corporation

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/13/859/001 10 film-coated tablets
EU/1/13/859/002 30 film-coated tablets
EU/1/13/859/003 100 film-coated tablets
EU/1/13/859/004 130 film-coated tablets
EU/1/13/859/005 175 film-coated tablets
EU/1/13/859/006 250 film-coated tablets

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

corbilta 50/12.5/200 mg *[carton only]*

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included *[carton only]*

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

[carton only]:

PC {number}
SN {number}
<NN {number}>

PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

BOTTLE LABEL AND OUTER CARTON TEXT

1. NAME OF THE MEDICINAL PRODUCT

Corbilta 75 mg/18.75 mg/200 mg film-coated tablets
levodopa/carbidopa/entacapone

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each film-coated tablet contains 75 mg of levodopa, 18.75 mg of carbidopa and 200 mg of entacapone.

3. LIST OF EXCIPIENTS

Contains sucrose.

4. PHARMACEUTICAL FORM AND CONTENTS

Carton
10 film-coated tablets
30 film-coated tablets
100 film-coated tablets
130 film-coated tablets
175 film-coated tablets

Label
10 tablets
30 tablets
100 tablets
130 tablets
175 tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Carton
Orion Corporation
Orionintie 1
FI-02200 Espoo
Finland

Label
Orion Corporation

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/13/859/007 10 film-coated tablets
EU/1/13/859/008 30 film-coated tablets
EU/1/13/859/009 100 film-coated tablets
EU/1/13/859/010 130 film-coated tablets
EU/1/13/859/011 175 film-coated tablets

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

corbilta 75/18.75/200 mg *[carton only]*

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included *[carton only]*

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

[carton only]:

PC {number}
SN {number}
<NN {number}>

PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

BOTTLE LABEL AND OUTER CARTON TEXT

1. NAME OF THE MEDICINAL PRODUCT

Corbilta 100 mg/25 mg/200 mg film-coated tablets
levodopa/carbidopa/entacapone

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each film-coated tablet contains 100 mg of levodopa, 25 mg of carbidopa and 200 mg of entacapone.

3. LIST OF EXCIPIENTS

Contains sucrose.

4. PHARMACEUTICAL FORM AND CONTENTS

Carton
10 film-coated tablets
30 film-coated tablets
100 film-coated tablets
130 film-coated tablets
175 film-coated tablets
250 film-coated tablets

Label
10 tablets
30 tablets
100 tablets
130 tablets
175 tablets
250 tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Carton
Orion Corporation
Orionintie 1
FI-02200 Espoo
Finland

Label
Orion Corporation

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/13/859/012 10 film-coated tablets
EU/1/13/859/013 30 film-coated tablets
EU/1/13/859/014 100 film-coated tablets
EU/1/13/859/015 130 film-coated tablets
EU/1/13/859/016 175 film-coated tablets
EU/1/13/859/017 250 film-coated tablets

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

corbilta 100/25/200 mg *[carton only]*

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included *[carton only]*

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

[carton only]:

PC {number}
SN {number}
<NN {number}>

PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

BOTTLE LABEL AND OUTER CARTON TEXT

1. NAME OF THE MEDICINAL PRODUCT

Corbilta 125 mg/31.25 mg/200 mg film-coated tablets
levodopa/carbidopa/entacapone

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each film-coated tablet contains 125 mg of levodopa, 31.25 mg of carbidopa and 200 mg of entacapone.

3. LIST OF EXCIPIENTS

Contains sucrose.

4. PHARMACEUTICAL FORM AND CONTENTS

Carton
10 film-coated tablets
30 film-coated tablets
100 film-coated tablets
130 film-coated tablets
175 film-coated tablets

Label
10 tablets
30 tablets
100 tablets
130 tablets
175 tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Carton
Orion Corporation
Orionintie 1
FI-02200 Espoo
Finland

Label
Orion Corporation

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/13/859/018 10 film-coated tablets
EU/1/13/859/019 30 film-coated tablets
EU/1/13/859/020 100 film-coated tablets
EU/1/13/859/021 130 film-coated tablets
EU/1/13/859/022 175 film-coated tablets

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

corbilta 125/31.25/200 mg *[carton only]*

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included *[carton only]*

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

[carton only]:

PC {number}
SN {number}
<NN {number}>

PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

BOTTLE LABEL AND OUTER CARTON TEXT

1. NAME OF THE MEDICINAL PRODUCT

Corbilta 150 mg/37.5 mg/200 mg film-coated tablets
levodopa/carbidopa/entacapone

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each film-coated tablet contains 150 mg of levodopa, 37.5 mg of carbidopa and 200 mg of entacapone.

3. LIST OF EXCIPIENTS

Contains sucrose and sodium.

4. PHARMACEUTICAL FORM AND CONTENTS

Carton
10 film-coated tablets
30 film-coated tablets
100 film-coated tablets
130 film-coated tablets
175 film-coated tablets
250 film-coated tablets

Label
10 tablets
30 tablets
100 tablets
130 tablets
175 tablets
250 tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Carton
Orion Corporation
Orionintie 1
FI-02200 Espoo
Finland

Label
Orion Corporation

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/13/859/023 10 film-coated tablets
EU/1/13/859/024 30 film-coated tablets
EU/1/13/859/025 100 film-coated tablets
EU/1/13/859/026 130 film-coated tablets
EU/1/13/859/027 175 film-coated tablets
EU/1/13/859/028 250 film-coated tablets

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

corbilta 150/37.5/200 mg *[carton only]*

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included *[carton only]*

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

[carton only]:

PC {number}
SN {number}
<NN {number}>

PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

BOTTLE LABEL AND OUTER CARTON TEXT

1. NAME OF THE MEDICINAL PRODUCT

Corbilta 175 mg/43.75 mg/200 mg film-coated tablets
levodopa/carbidopa/entacapone

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each film-coated tablet contains 175 mg of levodopa, 43.75 mg of carbidopa and 200 mg of entacapone.

3. LIST OF EXCIPIENTS

Contains sucrose.

4. PHARMACEUTICAL FORM AND CONTENTS

Carton
10 film-coated tablets
30 film-coated tablets
100 film-coated tablets
130 film-coated tablets
175 film-coated tablets

Label
10 tablets
30 tablets
100 tablets
130 tablets
175 tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Carton
Orion Corporation
Orionintie 1
FI-02200 Espoo
Finland

Label
Orion Corporation

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/13/859/029 10 film-coated tablets
EU/1/13/859/030 30 film-coated tablets
EU/1/13/859/031 100 film-coated tablets
EU/1/13/859/032 130 film-coated tablets
EU/1/13/859/033 175 film-coated tablets

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

corbilta 175/43.75/200 mg *[carton only]*

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included [*carton only*]

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

[*carton only*]:

PC {number}
SN {number}
<NN {number}>

PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

BOTTLE LABEL AND OUTER CARTON TEXT

1. NAME OF THE MEDICINAL PRODUCT

Corbilta 200 mg/50 mg/200 mg film-coated tablets
levodopa/carbidopa/entacapone

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each film-coated tablet contains 200 mg of levodopa, 50 mg of carbidopa and 200 mg of entacapone.

3. LIST OF EXCIPIENTS

Contains sucrose.

4. PHARMACEUTICAL FORM AND CONTENTS

Carton
10 film-coated tablets
30 film-coated tablets
100 film-coated tablets
130 film-coated tablets
175 film-coated tablets

Label
10 tablets
30 tablets
100 tablets
130 tablets
175 tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Carton
Orion Corporation
Orionintie 1
FI-02200 Espoo
Finland

Label
Orion Corporation

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/13/859/034 10 film-coated tablets
EU/1/13/859/035 30 film-coated tablets
EU/1/13/859/036 100 film-coated tablets
EU/1/13/859/037 130 film-coated tablets
EU/1/13/859/038 175 film-coated tablets

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

corbilta 200/50/200 mg *[carton only]*

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included [*carton only*]

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

[carton only]:

PC {number}
SN {number}
<NN {number}>

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Corbilta 50 mg/12.5 mg/200 mg film-coated tablets
levodopa/carbidopa/entacapone

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Corbilta is and what it is used for

Corbilta contains three active substances (levodopa, carbidopa and entacapone) in one film-coated tablet. Corbilta is used for the treatment of Parkinson's disease.

Parkinson's disease is caused by low levels of a substance called dopamine in the brain. Levodopa increases the amount of dopamine and hence reduces the symptoms of Parkinson's disease. Carbidopa and entacapone improve the antiparkinson effects of levodopa.

2. What you need to know before you take Corbilta

Do not take Corbilta if you:

- are allergic to levodopa, carbidopa or entacapone, or any of the other ingredients of this medicine (listed in section 6)
- have narrow-angle glaucoma (an eye disorder)
- have a tumour of the adrenal gland
- are taking certain medicines for treating depression (combinations of selective MAO-A and MAO-B inhibitors, or non-selective MAO-inhibitors)
- have ever had neuroleptic malignant syndrome (NMS – this is a rare reaction to medicines used to treat severe mental disorders)
- have ever had non-traumatic rhabdomyolysis (a rare muscle disorder)
- have a severe liver disease.

Warnings and precautions

Talk to your doctor or pharmacist before taking Corbilta if you have or have ever had:
- a heart attack or any other diseases of the heart including cardiac arrhythmias, or of the blood vessels
- asthma or any other disease of the lungs
- a liver problem, because your dose may need to be adjusted
- kidney or hormone-related diseases

- stomach ulcers or convulsions
- if you experience prolonged diarrhoea consult your doctor as it may be a sign of inflammation of the colon
- any form of severe mental disorder like psychosis
- chronic wide-angle glaucoma, because your dose may need to be adjusted and the pressure in your eyes may need to be monitored.

Consult your doctor if you are currently taking:
- antipsychotics (medicines used to treat psychosis)
- a medicine which may cause low blood pressure when rising from a chair or bed. You should be aware that Corbilta may make these reactions worse.

Consult your doctor if during the treatment with Corbilta you:
- notice that your muscles get very rigid or jerk violently, or if you get tremors, agitation, confusion, fever, rapid pulse, or wide fluctuations in your blood pressure. If any of this happens, **contact your doctor immediately.**
- feel depressed, have suicidal thoughts, or notice unusual changes in your behaviour
- find yourself suddenly falling asleep, or if you feel very drowsy. If this happens, you should not drive or use any tools or machines (see also section "Driving and using machines").
- notice that uncontrolled movements begin or get worse after you started to take Corbilta. If this happens, your doctor may need to change the dose of your antiparkinson medicine.
- experience diarrhoea: monitoring of your weight is recommended in order to avoid potentially excessive weight loss
- experience progressive anorexia, asthenia (weakness, exhaustion) and weight decrease within a relatively short period of time. If this happens, a general medical evaluation including liver function should be considered.
- feel the need to stop using Corbilta, see section "If you stop taking Corbilta".

Tell your doctor if you or your family/carer notices you are developing addiction-like symptoms leading to craving for large doses of Corbilta and other medicines used to treat Parkinson's disease.

Tell your doctor if you or your family/carer notices you are developing urges or cravings to behave in ways that are unusual for you or you cannot resist the impulse, drive or temptation to carry out certain activities that could harm yourself or others. These behaviours are called impulse control disorders and can include addictive gambling, excessive eating or spending, an abnormally high sex drive or a preoccupation with an increase in sexual thoughts or feelings. Your doctor may need to review your treatments.

Your doctor may take some regular laboratory tests during a long term treatment with Corbilta.

If you must undergo surgery, please tell your doctor that you are using Corbilta.

Corbilta is not recommended to be used for treatment of extrapyramidal symptoms (e.g. involuntary movements, shaking, muscle rigidity and muscle contractions) caused by other medicines.

Children and adolescents

Experience with Corbilta in patients under 18 years is limited. Therefore, the use of Corbilta in children or adolescents is not recommended.

Other medicines and Corbilta

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Do not take Corbilta if you are taking certain medicines for treating depression (combinations of selective MAO-A and MAO-B inhibitors, or non-selective MAO inhibitors).

Corbilta may increase the effects and side effects of certain medicines. These include:
- medicines used to treat depression such as moclobemide, amitriptyline, desipramine, maprotiline, venlafaxine and paroxetine
- rimiterole and isoprenaline, used to treat respiratory diseases
- adrenaline, used for severe allergic reactions
- noradrenaline, dopamine and dobutamine, used to treat heart diseases and low blood pressure
- alpha-methyldopa, used to treat high blood pressure
- apomorphine, which is used to treat Parkinson's disease.

The effects of Corbilta may be weakened by certain medicines. These include:
- dopamine antagonists used to treat mental disorders, nausea and vomiting
- phenytoin, used to prevent convulsions
- papaverine used to relax the muscles.

Corbilta may make it harder for you to digest iron. Therefore, do not take Corbilta and iron supplements at the same time. After taking one of them, wait at least 2 to 3 hours before taking the other.

Corbilta with food and drink

Corbilta may be taken with or without food. For some patients, Corbilta may not be well absorbed if it is taken with, or shortly after eating protein-rich food (such as meats, fish, dairy products, seeds and nuts). Consult your doctor if you think this applies to you.

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

You should not breast-feed during treatment with Corbilta.

Driving and using machines

Corbilta may lower your blood pressure, which may make you feel light-headed or dizzy. Therefore, be particularly careful when you drive or when you use any tools or machines.

If you feel very drowsy, or if you sometimes find yourself suddenly falling asleep, wait until you feel fully awake again before driving or doing anything else that requires you to be alert. Otherwise, you may put yourself and others at risk of serious injury or death.

Corbilta contains sucrose

Corbilta contains sucrose (1.2 mg/tablet). If you have been told by your doctor that you have intolerance to some sugars, contact your doctor before taking this medicine.

This medicine contains less than 1 mmol (23 mg) sodium per maximum recommended daily dose, that is to say essentially 'sodium-free'.

3. How to take Corbilta

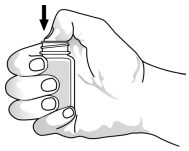
Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

For adults and elderly:
- Your doctor will tell you exactly how many tablets of Corbilta to take each day.
- The tablets are not intended to be split or broken into smaller pieces.
- You should take only one tablet each time.
- Depending on how you respond to treatment, your doctor may suggest a higher or lower dose.
- If you are taking Corbilta 50 mg/12.5 mg/200 mg, 75 mg/18.75 mg/200 mg, 100 mg/25 mg/200 mg, 125 mg/31.25 mg/200 mg or 150 mg/37.5 mg/200 mg tablets, do not take more than 10 tablets per day.

Talk to your doctor or pharmacist if you think the effect of Corbilta is too strong or too weak, or if you experience possible side effects.

To open the bottle for the first time: open the closure, and then press with your thumb on the seal until it breaks. See picture 1.

Picture 1



If you take more Corbilta than you should

If you have accidentally taken more Corbilta tablets than you should, talk to your doctor or pharmacist immediately. In case of an overdose you may feel confused or agitated, your heart rate may be slower or faster than normal or the colour of your skin, tongue, eyes or urine may change.

If you forget to take Corbilta

Do not take a double dose to make up for a forgotten tablet.

If it is more than 1 hour until your next dose:
Take one tablet as soon as you remember, and the next tablet at the normal time.

If it is less than 1 hour until your next dose:
Take a tablet as soon as you remember, wait 1 hour, then take another tablet. After that carry on as normal.

Always leave at least an hour between Corbilta tablets, to avoid possible side effects.

If you stop taking Corbilta

Do not stop taking Corbilta unless your doctor tells you to. In such a case your doctor may need to adjust your other antiparkinson medicines, especially levodopa, to give sufficient control of your symptoms. If you suddenly stop taking Corbilta and other antiparkinsonian medicines it may result in unwanted side effects.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Many of the side effects can be relieved by adjusting the dose.

If you during the treatment with Corbilta experience the following symptoms, **contact your doctor immediately**:

- Your muscles get very rigid or jerk violently, you get tremors, agitation, confusion, fever, rapid pulse, or wide fluctuations in your blood pressure. These can be symptoms of neuroleptic malignant syndrome (NMS, a rare severe reaction to medicines used to treat disorders of the central nervous system) or rhabdomyolysis (a rare severe muscle disorder).
- Allergic reaction, the signs may include hives (nettle rash), itching, rash, swelling of your face, lips, tongue or throat. This may cause difficulties in breathing or swallowing.

Very common (*may affect more than 1 in 10 people*):
- uncontrolled movements (dyskinesias)
- feeling sick (nausea)
- harmless reddish-brown discolouration of urine
- muscle pain
- diarrhoea.

Common (*may affect up to 1 in 10 people*):
- light-headedness or fainting due to low blood pressure, high blood pressure
- worsening of Parkinson`s symptoms, dizziness, drowsiness
- vomiting, abdominal pain and discomfort, heartburn, dry mouth, constipation
- inability to sleep, hallucinations, confusion, abnormal dreams (including nightmares), tiredness
- mental changes – including problems with memory, anxiety and depression (possibly with thoughts of suicide)
- heart or artery disease events (e.g. chest pain), irregular heart rate or rhythm
- more frequent falling
- shortness of breath
- increased sweating, rashes
- muscle cramps, swelling of legs
- blurred vision
- anaemia
- decreased appetite, decreased weight
- headache, joint pain
- urinary tract infection.

Uncommon (*may affect up to 1 in 100 people*):
- heart attack
- bleeding in the gut
- changes in the blood cell count which may result in bleeding, abnormal liver function tests
- convulsions
- feeling agitated
- psychotic symptoms
- colitis (inflammation of the colon)
- discolourations other than urine (e.g. skin, nail, hair, sweat)
- swallowing difficulties
- inability to urinate.

Not known (*frequency cannot be estimated from the available data*):
Craving for large doses of Corbilta in excess of that required to control motor symptoms, known as dopamine dysregulation syndrome. Some patients experience severe abnormal involuntary movements (dyskinesias), mood swings or other side effects after taking large doses of Corbilta.

The following side effects have also been reported:
- hepatitis (inflammation of the liver)
- itching.

You may experience the following side effects:
- Inability to resist the impulse to perform an action that could be harmful, which may include:
  - strong impulse to gamble excessively despite serious personal or family consequences

- altered or increased sexual interest and behaviour of significant concern to you or to others, for example, an increased sexual drive
- uncontrollable excessive shopping or spending
- binge eating (eating large amounts of food in a short time period) or compulsive eating (eating more food than normal and more than is needed to satisfy your hunger).

Tell your doctor if you experience any of these behaviours; they will discuss ways of managing or reducing the symptoms.

Reporting of side effects
If you get any side effects talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Corbilta

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the bottle and the carton. The expiry date refers to the last day of that month.

This medicinal product does not require any special storage conditions.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What Corbilta contains

- The active substances of Corbilta are levodopa, carbidopa and entacapone.
- Each Corbilta 50 mg/12.5 mg/200 mg tablet contains 50 mg of levodopa, 12.5 mg of carbidopa and 200 mg of entacapone.
- The other ingredients in the tablet core are croscarmellose sodium, magnesium stearate, maize starch, mannitol (E421) and povidone (E1201).
- The ingredients in the film-coating are glycerol (85 per cent) (E422), hypromellose, magnesium stearate, polysorbate 80, red iron oxide (E172), sucrose, titanium dioxide (E171), and yellow iron oxide (E172).

What Corbilta looks like and contents of the pack

Corbilta 50 mg/12.5 mg/200 mg: brownish or greyish red, round, convex unscored film-coated tablets marked with “LCE 50” on one side.

Corbilta comes in six different pack sizes (10, 30, 100, 130, 175 or 250 tablets). Not all pack sizes may be marketed.

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Finland

Manufacturer
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For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder.

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This leaflet was last revised in.

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

Package leaflet: Information for the user
Corbilta 75 mg/18.75 mg/200 mg film-coated tablets
levodopa/carbidopa/entacapone

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Corbilta is and what it is used for

Corbilta contains three active substances (levodopa, carbidopa and entacapone) in one film-coated tablet. Corbilta is used for the treatment of Parkinson's disease.

Parkinson's disease is caused by low levels of a substance called dopamine in the brain. Levodopa increases the amount of dopamine and hence reduces the symptoms of Parkinson's disease. Carbidopa and entacapone improve the antiparkinson effects of levodopa.

2. What you need to know before you take Corbilta

Do not take Corbilta if you:

- are allergic to levodopa, carbidopa or entacapone, or any of the other ingredients of this medicine (listed in section 6)
- have narrow-angle glaucoma (an eye disorder)
- have a tumour of the adrenal gland
- are taking certain medicines for treating depression (combinations of selective MAO-A and MAO-B inhibitors, or non-selective MAO-inhibitors)
- have ever had neuroleptic malignant syndrome (NMS – this is a rare reaction to medicines used to treat severe mental disorders)
- have ever had non-traumatic rhabdomyolysis (a rare muscle disorder)
- have a severe liver disease.

Warnings and precautions

Talk to your doctor or pharmacist before taking Corbilta if you have or have ever had:
- a heart attack or any other diseases of the heart including cardiac arrhythmias, or of the blood vessels
- asthma or any other disease of the lungs
- a liver problem, because your dose may need to be adjusted
- kidney or hormone-related diseases

- stomach ulcers or convulsions
- if you experience prolonged diarrhoea consult your doctor as it may be a sign of inflammation of the colon
- any form of severe mental disorder like psychosis
- chronic wide-angle glaucoma, because your dose may need to be adjusted and the pressure in your eyes may need to be monitored.

Consult your doctor if you are currently taking:
- antipsychotics (medicines used to treat psychosis)
- a medicine which may cause low blood pressure when rising from a chair or bed. You should be aware that Corbilta may make these reactions worse.

Consult your doctor if during the treatment with Corbilta you:
- notice that your muscles get very rigid or jerk violently, or if you get tremors, agitation, confusion, fever, rapid pulse, or wide fluctuations in your blood pressure. If any of this happens, **contact your doctor immediately.**
- feel depressed, have suicidal thoughts, or notice unusual changes in your behaviour
- find yourself suddenly falling asleep, or if you feel very drowsy. If this happens, you should not drive or use any tools or machines (see also section "Driving and using machines").
- notice that uncontrolled movements begin or get worse after you started to take Corbilta. If this happens, your doctor may need to change the dose of your antiparkinson medicine.
- experience diarrhoea: monitoring of your weight is recommended in order to avoid potentially excessive weight loss
- experience progressive anorexia, asthenia (weakness, exhaustion) and weight decrease within a relatively short period of time. If this happens, a general medical evaluation including liver function should be considered.
- feel the need to stop using Corbilta, see section "If you stop taking Corbilta".

Tell your doctor if you or your family/carer notices you are developing addiction-like symptoms leading to craving for large doses of Corbilta and other medicines used to treat Parkinson's disease.

Tell your doctor if you or your family/carer notices you are developing urges or cravings to behave in ways that are unusual for you or you cannot resist the impulse, drive or temptation to carry out certain activities that could harm yourself or others. These behaviours are called impulse control disorders and can include addictive gambling, excessive eating or spending, an abnormally high sex drive or a preoccupation with an increase in sexual thoughts or feelings. Your doctor may need to review your treatments.

Your doctor may take some regular laboratory tests during a long term treatment with Corbilta.

If you must undergo surgery, please tell your doctor that you are using Corbilta.

Corbilta is not recommended to be used for treatment of extrapyramidal symptoms (e.g. involuntary movements, shaking, muscle rigidity and muscle contractions) caused by other medicines.

Children and adolescents

Experience with Corbilta in patients under 18 years is limited. Therefore, the use of Corbilta in children or adolescents is not recommended.

Other medicines and Corbilta

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

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Corbilta may increase the effects and side effects of certain medicines. These include:
- medicines used to treat depression such as moclobemide, amitriptyline, desipramine, maprotiline, venlafaxine and paroxetine
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- alpha-methyldopa, used to treat high blood pressure
- apomorphine, which is used to treat Parkinson's disease.

The effects of Corbilta may be weakened by certain medicines. These include:
- dopamine antagonists used to treat mental disorders, nausea and vomiting
- phenytoin, used to prevent convulsions
- papaverine used to relax the muscles.

Corbilta may make it harder for you to digest iron. Therefore, do not take Corbilta and iron supplements at the same time. After taking one of them, wait at least 2 to 3 hours before taking the other.

Corbilta with food and drink

Corbilta may be taken with or without food. For some patients, Corbilta may not be well absorbed if it is taken with, or shortly after eating protein-rich food (such as meats, fish, dairy products, seeds and nuts). Consult your doctor if you think this applies to you.

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

You should not breast-feed during treatment with Corbilta.

Driving and using machines

Corbilta may lower your blood pressure, which may make you feel light-headed or dizzy. Therefore, be particularly careful when you drive or when you use any tools or machines.

If you feel very drowsy, or if you sometimes find yourself suddenly falling asleep, wait until you feel fully awake again before driving or doing anything else that requires you to be alert. Otherwise, you may put yourself and others at risk of serious injury or death.

Corbilta contains sucrose

Corbilta contains sucrose (1.4 mg/tablet). If you have been told by your doctor that you have intolerance to some sugars, contact your doctor before taking this medicine.

This medicine contains less than 1 mmol (23 mg) sodium per maximum recommended daily dose, that is to say essentially 'sodium-free'.

3. How to take Corbilta

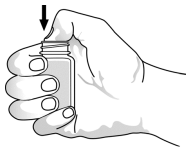
Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

For adults and elderly:
- Your doctor will tell you exactly how many tablets of Corbilta to take each day.
- The tablets are not intended to be split or broken into smaller pieces.
- You should take only one tablet each time.
- Depending on how you respond to treatment, your doctor may suggest a higher or lower dose.
- If you are taking Corbilta 50 mg/12.5 mg/200 mg, 75 mg/18.75 mg/200 mg, 100 mg/25 mg/200 mg, 125 mg/31.25 mg/200 mg or 150 mg/37.5 mg/200 mg tablets, do not take more than 10 tablets per day.

Talk to your doctor or pharmacist if you think the effect of Corbilta is too strong or too weak, or if you experience possible side effects.

To open the bottle for the first time: open the closure, and then press with your thumb on the seal until it breaks. See picture 1.

Picture 1



If you take more Corbilta than you should

If you have accidentally taken more Corbilta tablets than you should, talk to your doctor or pharmacist immediately. In case of an overdose you may feel confused or agitated, your heart rate may be slower or faster than normal or the colour of your skin, tongue, eyes or urine may change.

If you forget to take Corbilta

Do not take a double dose to make up for a forgotten tablet.

If it is more than 1 hour until your next dose:
Take one tablet as soon as you remember, and the next tablet at the normal time.

If it is less than 1 hour until your next dose:
Take a tablet as soon as you remember, wait 1 hour, then take another tablet. After that carry on as normal.

Always leave at least an hour between Corbilta tablets, to avoid possible side effects.

If you stop taking Corbilta

Do not stop taking Corbilta unless your doctor tells you to. In such a case your doctor may need to adjust your other antiparkinson medicines, especially levodopa, to give sufficient control of your symptoms. If you suddenly stop taking Corbilta and other antiparkinsonian medicines it may result in unwanted side effects.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

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Like all medicines, this medicine can cause side effects, although not everybody gets them. Many of the side effects can be relieved by adjusting the dose.

If you during the treatment with Corbilta experience the following symptoms, **contact your doctor immediately**:

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- Allergic reaction, the signs may include hives (nettle rash), itching, rash, swelling of your face, lips, tongue or throat. This may cause difficulties in breathing or swallowing.

Very common (*may affect more than 1 in 10 people*):
- uncontrolled movements (dyskinesias)
- feeling sick (nausea)
- harmless reddish-brown discolouration of urine
- muscle pain
- diarrhoea.

Common (*may affect up to 1 in 10 people*):
- light-headedness or fainting due to low blood pressure, high blood pressure
- worsening of Parkinson's symptoms, dizziness, drowsiness
- vomiting, abdominal pain and discomfort, heartburn, dry mouth, constipation
- inability to sleep, hallucinations, confusion, abnormal dreams (including nightmares), tiredness
- mental changes – including problems with memory, anxiety and depression (possibly with thoughts of suicide)
- heart or artery disease events (e.g. chest pain), irregular heart rate or rhythm
- more frequent falling
- shortness of breath
- increased sweating, rashes
- muscle cramps, swelling of legs
- blurred vision
- anaemia
- decreased appetite, decreased weight
- headache, joint pain
- urinary tract infection.

Uncommon (*may affect up to 1 in 100 people*):
- heart attack
- bleeding in the gut
- changes in the blood cell count which may result in bleeding, abnormal liver function tests
- convulsions
- feeling agitated
- psychotic symptoms
- colitis (inflammation of the colon)
- discolourations other than urine (e.g. skin, nail, hair, sweat)
- swallowing difficulties
- inability to urinate.

Not known (*frequency cannot be estimated from the available data*):
Craving for large doses of Corbilta in excess of that required to control motor symptoms, known as dopamine dysregulation syndrome. Some patients experience severe abnormal involuntary movements (dyskinesias), mood swings or other side effects after taking large doses of Corbilta.

The following side effects have also been reported:
- hepatitis (inflammation of the liver)
- itching.

You may experience the following side effects:
- Inability to resist the impulse to perform an action that could be harmful, which may include:
  - strong impulse to gamble excessively despite serious personal or family consequences

- altered or increased sexual interest and behaviour of significant concern to you or to others for example, an increased sexual drive
- uncontrollable excessive shopping or spending
- binge eating (eating large amounts of food in a short time period) or compulsive eating (eating more food than normal and more than is needed to satisfy your hunger).

Tell your doctor if you experience any of these behaviours; they will discuss ways of managing or reducing the symptoms.

Reporting of side effects
If you get any side effects talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Corbilta

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the bottle and the carton. The expiry date refers to the last day of that month.

This medicinal product does not require any special storage conditions.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What Corbilta contains

- The active substances of Corbilta are levodopa, carbidopa and entacapone.
- Each Corbilta 75 mg/18.75 mg/200 mg tablet contains 75 mg of levodopa, 18.75 mg of carbidopa and 200 mg of entacapone.
- The other ingredients in the tablet core are croscarmellose sodium, magnesium stearate, maize starch, mannitol (E421) and povidone (E1201).
- The ingredients in the film-coating are glycerol (85 per cent) (E422), hypromellose, magnesium stearate, polysorbate 80, red iron oxide (E172), sucrose, and titanium dioxide (E171).

What Corbilta looks like and contents of the pack

Corbilta 75 mg/18.75 mg/200 mg: light brownish red, oval film-coated tablets marked with “LCE 75” on one side.

Corbilta 75 mg/18.75 mg/200 mg tablet comes in five different pack sizes (10, 30, 100, 130 or 175 tablets). Not all pack sizes may be marketed.

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Orion Corporation
Orionintie 1
FI-02200 Espoo
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Manufacturer

Orion Corporation Orion Pharma
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For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder.

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This leaflet was last revised in.

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

Package leaflet: Information for the user

Corbilta 100 mg/25 mg/200 mg film-coated tablets
levodopa/carbidopa/entacapone

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Corbilta is and what it is used for

Corbilta contains three active substances (levodopa, carbidopa and entacapone) in one film-coated tablet. Corbilta is used for the treatment of Parkinson's disease.

Parkinson's disease is caused by low levels of a substance called dopamine in the brain. Levodopa increases the amount of dopamine and hence reduces the symptoms of Parkinson's disease. Carbidopa and entacapone improve the antiparkinson effects of levodopa.

2. What you need to know before you take Corbilta

Do not take Corbilta if you:

- are allergic to levodopa, carbidopa or entacapone, or any of the other ingredients of this medicine (listed in section 6)
- have narrow-angle glaucoma (an eye disorder)
- have a tumour of the adrenal gland
- are taking certain medicines for treating depression (combinations of selective MAO-A and MAO-B inhibitors, or non-selective MAO-inhibitors)
- have ever had neuroleptic malignant syndrome (NMS – this is a rare reaction to medicines used to treat severe mental disorders)
- have ever had non-traumatic rhabdomyolysis (a rare muscle disorder)
- have a severe liver disease.

Warnings and precautions

Talk to your doctor or pharmacist before taking Corbilta if you have or have ever had:
- a heart attack or any other diseases of the heart including cardiac arrhythmias, or of the blood vessels
- asthma or any other disease of the lungs
- a liver problem, because your dose may need to be adjusted
- kidney or hormone-related diseases

- stomach ulcers or convulsions
- if you experience prolonged diarrhoea consult your doctor as it may be a sign of inflammation of the colon
- any form of severe mental disorder like psychosis
- chronic wide-angle glaucoma, because your dose may need to be adjusted and the pressure in your eyes may need to be monitored.

Consult your doctor if you are currently taking:
- antipsychotics (medicines used to treat psychosis)
- a medicine which may cause low blood pressure when rising from a chair or bed. You should be aware that Corbilta may make these reactions worse.

Consult your doctor if during the treatment with Corbilta you:
- notice that your muscles get very rigid or jerk violently, or if you get tremors, agitation, confusion, fever, rapid pulse, or wide fluctuations in your blood pressure. If any of this happens, **contact your doctor immediately.**
- feel depressed, have suicidal thoughts, or notice unusual changes in your behaviour
- find yourself suddenly falling asleep, or if you feel very drowsy. If this happens, you should not drive or use any tools or machines (see also section "Driving and using machines").
- notice that uncontrolled movements begin or get worse after you started to take Corbilta. If this happens, your doctor may need to change the dose of your antiparkinson medicine.
- experience diarrhoea: monitoring of your weight is recommended in order to avoid potentially excessive weight loss
- experience progressive anorexia, asthenia (weakness, exhaustion) and weight decrease within a relatively short period of time. If this happens, a general medical evaluation including liver function should be considered.
- feel the need to stop using Corbilta, see section "If you stop taking Corbilta".

Tell your doctor if you or your family/carer notices you are developing addiction-like symptoms leading to craving for large doses of Corbilta and other medicines used to treat Parkinson's disease.

Tell your doctor if you or your family/carer notices you are developing urges or cravings to behave in ways that are unusual for you or you cannot resist the impulse, drive or temptation to carry out certain activities that could harm yourself or others. These behaviours are called impulse control disorders and can include addictive gambling, excessive eating or spending, an abnormally high sex drive or a preoccupation with an increase in sexual thoughts or feelings. Your doctor may need to review your treatments.

Your doctor may take some regular laboratory tests during a long term treatment with Corbilta.

If you must undergo surgery, please tell your doctor that you are using Corbilta.

Corbilta is not recommended to be used for treatment of extrapyramidal symptoms (e.g. involuntary movements, shaking, muscle rigidity and muscle contractions) caused by other medicines.

Children and adolescents

Experience with Corbilta in patients under 18 years is limited. Therefore, the use of Corbilta in children or adolescents is not recommended.

Other medicines and Corbilta

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Do not take Corbilta if you are taking certain medicines for treating depression (combinations of selective MAO-A and MAO-B inhibitors, or non-selective MAO inhibitors).

Corbilta may increase the effects and side effects of certain medicines. These include:
- medicines used to treat depression such as moclobemide, amitriptyline, desipramine, maprotiline, venlafaxine and paroxetine
- rimiterole and isoprenaline, used to treat respiratory diseases
- adrenaline, used for severe allergic reactions
- noradrenaline, dopamine and dobutamine, used to treat heart diseases and low blood pressure
- alpha-methyldopa, used to treat high blood pressure
- apomorphine, which is used to treat Parkinson's disease.

The effects of Corbilta may be weakened by certain medicines. These include:
- dopamine antagonists used to treat mental disorders, nausea and vomiting
- phenytoin, used to prevent convulsions
- papaverine used to relax the muscles.

Corbilta may make it harder for you to digest iron. Therefore, do not take Corbilta and iron supplements at the same time. After taking one of them, wait at least 2 to 3 hours before taking the other.

Corbilta with food and drink

Corbilta may be taken with or without food. For some patients, Corbilta may not be well absorbed if it is taken with, or shortly after eating protein-rich food (such as meats, fish, dairy products, seeds and nuts). Consult your doctor if you think this applies to you.

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

You should not breast-feed during treatment with Corbilta.

Driving and using machines

Corbilta may lower your blood pressure, which may make you feel light-headed or dizzy. Therefore, be particularly careful when you drive or when you use any tools or machines.

If you feel very drowsy, or if you sometimes find yourself suddenly falling asleep, wait until you feel fully awake again before driving or doing anything else that requires you to be alert. Otherwise, you may put yourself and others at risk of serious injury or death.

Corbilta contains sucrose

Corbilta contains sucrose (1.6 mg/tablet). If you have been told by your doctor that you have intolerance to some sugars, contact your doctor before taking this medicine.

This medicine contains less than 1 mmol (23 mg) sodium per maximum recommended daily dose, that is to say essentially 'sodium-free'.

3. How to take Corbilta

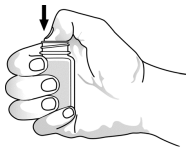
Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

For adults and elderly:
- Your doctor will tell you exactly how many tablets of Corbilta to take each day.
- The tablets are not intended to be split or broken into smaller pieces.
- You should take only one tablet each time.
- Depending on how you respond to treatment, your doctor may suggest a higher or lower dose.
- If you are taking Corbilta 50 mg/12.5 mg/200 mg, 75 mg/18.75 mg/200 mg, 100 mg/25 mg/200 mg, 125 mg/31.25 mg/200 mg or 150 mg/37.5 mg/200 mg tablets, do not take more than 10 tablets per day.

Talk to your doctor or pharmacist if you think the effect of Corbilta is too strong or too weak, or if you experience possible side effects.

To open the bottle for the first time: open the closure, and then press with your thumb on the seal until it breaks. See picture 1.

Picture 1



If you take more Corbilta than you should

If you have accidentally taken more Corbilta tablets than you should, talk to your doctor or pharmacist immediately. In case of an overdose you may feel confused or agitated, your heart rate may be slower or faster than normal or the colour of your skin, tongue, eyes or urine may change.

If you forget to take Corbilta

Do not take a double dose to make up for a forgotten tablet.

If it is more than 1 hour until your next dose:
Take one tablet as soon as you remember, and the next tablet at the normal time.

If it is less than 1 hour until your next dose:
Take a tablet as soon as you remember, wait 1 hour, then take another tablet. After that carry on as normal.

Always leave at least an hour between Corbilta tablets, to avoid possible side effects.

If you stop taking Corbilta

Do not stop taking Corbilta unless your doctor tells you to. In such a case your doctor may need to adjust your other antiparkinson medicines, especially levodopa, to give sufficient control of your symptoms. If you suddenly stop taking Corbilta and other antiparkinsonian medicines it may result in unwanted side effects.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Many of the side effects can be relieved by adjusting the dose.

If you during the treatment with Corbilta experience the following symptoms, **contact your doctor immediately**:

- Your muscles get very rigid or jerk violently, you get tremors, agitation, confusion, fever, rapid pulse, or wide fluctuations in your blood pressure. These can be symptoms of neuroleptic malignant syndrome (NMS, a rare severe reaction to medicines used to treat disorders of the central nervous system) or rhabdomyolysis (a rare severe muscle disorder).
- Allergic reaction, the signs may include hives (nettle rash), itching, rash, swelling of your face, lips, tongue or throat. This may cause difficulties in breathing or swallowing.

Very common (*may affect more than 1 in 10 people*):
- uncontrolled movements (dyskinesias)
- feeling sick (nausea)
- harmless reddish-brown discolouration of urine
- muscle pain
- diarrhoea.

Common (*may affect up to 1 in 10 people*):
- light-headedness or fainting due to low blood pressure, high blood pressure
- worsening of Parkinson's symptoms, dizziness, drowsiness
- vomiting, abdominal pain and discomfort, heartburn, dry mouth, constipation
- inability to sleep, hallucinations, confusion, abnormal dreams (including nightmares), tiredness
- mental changes – including problems with memory, anxiety and depression (possibly with thoughts of suicide)
- heart or artery disease events (e.g. chest pain), irregular heart rate or rhythm
- more frequent falling
- shortness of breath
- increased sweating, rashes
- muscle cramps, swelling of legs
- blurred vision
- anaemia
- decreased appetite, decreased weight
- headache, joint pain
- urinary tract infection.

Uncommon (*may affect up to 1 in 100 people*):
- heart attack
- bleeding in the gut
- changes in the blood cell count which may result in bleeding, abnormal liver function tests
- convulsions
- feeling agitated
- psychotic symptoms
- colitis (inflammation of the colon)
- discolourations other than urine (e.g. skin, nail, hair, sweat)
- swallowing difficulties
- inability to urinate.

Not known (*frequency cannot be estimated from the available data*):
Craving for large doses of Corbilta in excess of that required to control motor symptoms, known as dopamine dysregulation syndrome. Some patients experience severe abnormal involuntary movements (dyskinesias), mood swings or other side effects after taking large doses of Corbilta.

The following side effects have also been reported:
- hepatitis (inflammation of the liver)
- itching.

You may experience the following side effects:
- Inability to resist the impulse to perform an action that could be harmful, which may include:
  - strong impulse to gamble excessively despite serious personal or family consequences

- altered or increased sexual interest and behaviour of significant concern to you or to others, for example, an increased sexual drive
- uncontrollable excessive shopping or spending
- binge eating (eating large amounts of food in a short time period) or compulsive eating (eating more food than normal and more than is needed to satisfy your hunger).

Tell your doctor if you experience any of these behaviours; they will discuss ways of managing or reducing the symptoms.

Reporting of side effects
If you get any side effects talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Corbilta

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the bottle and the carton. The expiry date refers to the last day of that month.

This medicinal product does not require any special storage conditions.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What Corbilta contains

- The active substances of Corbilta are levodopa, carbidopa and entacapone.
- Each Corbilta 100 mg/25 mg/200 mg tablet contains 100 mg of levodopa, 25 mg of carbidopa and 200 mg of entacapone.
- The other ingredients in the tablet core are croscarmellose sodium, magnesium stearate, maize starch, mannitol (E421) and povidone (E1201).
- The ingredients in the film-coating are glycerol (85 per cent) (E422), hypromellose, magnesium stearate, polysorbate 80, red iron oxide (E172), sucrose, titanium dioxide (E171), and yellow iron oxide (E172).

What Corbilta looks like and contents of the pack

Corbilta 100 mg/25 mg/200 mg: brownish or greyish red, oval, unscored film-coated tablets marked with “LCE 100” on one side.

Corbilta comes in six different pack sizes (10, 30, 100, 130, 175 or 250 tablets). Not all pack sizes may be marketed.

Marketing Authorisation Holder
Orion Corporation
Orionintie 1
FI-02200 Espoo
Finland

Manufacturer
Orion Corporation Orion Pharma
Joensuunkatu 7
FI-24100 Salo
Finland

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder.

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This leaflet was last revised in.

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

Package leaflet: Information for the user

Corbilta 125 mg/31.25 mg/200 mg film-coated tablets
levodopa/carbidopa/entacapone

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What is in this leaflet:

1. What Corbilta is and what it is used for

Corbilta contains three active substances (levodopa, carbidopa and entacapone) in one film-coated tablet. Corbilta is used for the treatment of Parkinson's disease.

Parkinson's disease is caused by low levels of a substance called dopamine in the brain. Levodopa increases the amount of dopamine and hence reduces the symptoms of Parkinson's disease. Carbidopa and entacapone improve the antiparkinson effects of levodopa.

2. What you need to know before you take Corbilta

Do not take Corbilta if you:

- are allergic to levodopa, carbidopa or entacapone, or any of the other ingredients of this medicine (listed in section 6)
- have narrow-angle glaucoma (an eye disorder)
- have a tumour of the adrenal gland
- are taking certain medicines for treating depression (combinations of selective MAO-A and MAO-B inhibitors, or non-selective MAO-inhibitors)
- have ever had neuroleptic malignant syndrome (NMS – this is a rare reaction to medicines used to treat severe mental disorders)
- have ever had non-traumatic rhabdomyolysis (a rare muscle disorder)
- have a severe liver disease.

Warnings and precautions

Talk to your doctor or pharmacist before taking Corbilta if you have or have ever had:
- a heart attack or any other diseases of the heart including cardiac arrhythmias, or of the blood vessels
- asthma or any other disease of the lungs
- a liver problem, because your dose may need to be adjusted
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- stomach ulcers or convulsions
- if you experience prolonged diarrhoea consult your doctor as it may be a sign of inflammation of the colon
- any form of severe mental disorder like psychosis
- chronic wide-angle glaucoma, because your dose may need to be adjusted and the pressure in your eyes may need to be monitored.

Consult your doctor if you are currently taking:
- antipsychotics (medicines used to treat psychosis)
- a medicine which may cause low blood pressure when rising from a chair or bed. You should be aware that Corbilta may make these reactions worse.

Consult your doctor if during the treatment with Corbilta you:
- notice that your muscles get very rigid or jerk violently, or if you get tremors, agitation, confusion, fever, rapid pulse, or wide fluctuations in your blood pressure. If any of this happens, **contact your doctor immediately.**
- feel depressed, have suicidal thoughts, or notice unusual changes in your behaviour
- find yourself suddenly falling asleep, or if you feel very drowsy. If this happens, you should not drive or use any tools or machines (see also section "Driving and using machines").
- notice that uncontrolled movements begin or get worse after you started to take Corbilta. If this happens, your doctor may need to change the dose of your antiparkinson medicine.
- experience diarrhoea: monitoring of your weight is recommended in order to avoid potentially excessive weight loss
- experience progressive anorexia, asthenia (weakness, exhaustion) and weight decrease within a relatively short period of time. If this happens, a general medical evaluation including liver function should be considered.
- feel the need to stop using Corbilta, see section "If you stop taking Corbilta".

Tell your doctor if you or your family/carer notices you are developing addiction-like symptoms leading to craving for large doses of Corbilta and other medicines used to treat Parkinson's disease.

Tell your doctor if you or your family/carer notices you are developing urges or cravings to behave in ways that are unusual for you or you cannot resist the impulse, drive or temptation to carry out certain activities that could harm yourself or others. These behaviours are called impulse control disorders and can include addictive gambling, excessive eating or spending, an abnormally high sex drive or a preoccupation with an increase in sexual thoughts or feelings. Your doctor may need to review your treatments.

Your doctor may take some regular laboratory tests during a long term treatment with Corbilta.

If you must undergo surgery, please tell your doctor that you are using Corbilta.

Corbilta is not recommended to be used for treatment of extrapyramidal symptoms (e.g. involuntary movements, shaking, muscle rigidity and muscle contractions) caused by other medicines.

Children and adolescents

Experience with Corbilta in patients under 18 years is limited. Therefore, the use of Corbilta in children or adolescents is not recommended.

Other medicines and Corbilta

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Corbilta may increase the effects and side effects of certain medicines. These include:
- medicines used to treat depression such as moclobemide, amitriptyline, desipramine, maprotiline, venlafaxine and paroxetine
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- dopamine antagonists used to treat mental disorders, nausea and vomiting
- phenytoin, used to prevent convulsions
- papaverine used to relax the muscles.

Corbilta may make it harder for you to digest iron. Therefore, do not take Corbilta and iron supplements at the same time. After taking one of them, wait at least 2 to 3 hours before taking the other.

Corbilta with food and drink

Corbilta may be taken with or without food. For some patients, Corbilta may not be well absorbed if it is taken with, or shortly after eating protein-rich food (such as meats, fish, dairy products, seeds and nuts). Consult your doctor if you think this applies to you.

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

You should not breast-feed during treatment with Corbilta.

Driving and using machines

Corbilta may lower your blood pressure, which may make you feel light-headed or dizzy. Therefore, be particularly careful when you drive or when you use any tools or machines.

If you feel very drowsy, or if you sometimes find yourself suddenly falling asleep, wait until you feel fully awake again before driving or doing anything else that requires you to be alert. Otherwise, you may put yourself and others at risk of serious injury or death.

Corbilta contains sucrose

Corbilta contains sucrose (1.6 mg/tablet). If you have been told by your doctor that you have intolerance to some sugars, contact your doctor before taking this medicine.

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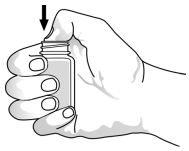
Talk to your doctor or pharmacist if you think the effect of Corbilta is too strong or too weak, or if you experience possible side effects.

To open the bottle for the first time: open the closure, and then press with your thumb on the seal until it breaks. See picture 1.

Picture 1



If you take more Corbilta than you should

If you have accidentally taken more Corbilta tablets than you should, talk to your doctor or pharmacist immediately. In case of an overdose you may feel confused or agitated, your heart rate may be slower or faster than normal or the colour of your skin, tongue, eyes or urine may change.

If you forget to take Corbilta

Do not take a double dose to make up for a forgotten tablet.

If it is more than 1 hour until your next dose:
Take one tablet as soon as you remember, and the next tablet at the normal time.

If it is less than 1 hour until your next dose:
Take a tablet as soon as you remember, wait 1 hour, then take another tablet. After that carry on as normal.

Always leave at least an hour between Corbilta tablets, to avoid possible side effects.

If you stop taking Corbilta

Do not stop taking Corbilta unless your doctor tells you to. In such a case your doctor may need to adjust your other antiparkinson medicines, especially levodopa, to give sufficient control of your symptoms. If you suddenly stop taking Corbilta and other antiparkinsonian medicines it may result in unwanted side effects.

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Like all medicines, this medicine can cause side effects, although not everybody gets them. Many of the side effects can be relieved by adjusting the dose.

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Very common (*may affect more than 1 in 10 people*):
- uncontrolled movements (dyskinesias)
- feeling sick (nausea)
- harmless reddish-brown discolouration of urine
- muscle pain
- diarrhoea.

Common (*may affect up to 1 in 10 people*):
- light-headedness or fainting due to low blood pressure, high blood pressure
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- vomiting, abdominal pain and discomfort, heartburn, dry mouth, constipation
- inability to sleep, hallucinations, confusion, abnormal dreams (including nightmares), tiredness
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- more frequent falling
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- blurred vision
- anaemia
- decreased appetite, decreased weight
- headache, joint pain
- urinary tract infection.

Uncommon (*may affect up to 1 in 100 people*):
- heart attack
- bleeding in the gut
- changes in the blood cell count which may result in bleeding, abnormal liver function tests
- convulsions
- feeling agitated
- psychotic symptoms
- colitis (inflammation of the colon)
- discolourations other than urine (e.g. skin, nail, hair, sweat)
- swallowing difficulties
- inability to urinate.

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Craving for large doses of Corbilta in excess of that required to control motor symptoms, known as dopamine dysregulation syndrome. Some patients experience severe abnormal involuntary movements (dyskinesias), mood swings or other side effects after taking large doses of Corbilta.

The following side effects have also been reported:
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6. Contents of the pack and other information

What Corbilta contains

- The active substances of Corbilta are levodopa, carbidopa and entacapone.
- Each Corbilta 125 mg/31.25 mg/200 mg tablet contains 125 mg of levodopa, 31.25 mg of carbidopa and 200 mg of entacapone.
- The other ingredients in the tablet core are croscarmellose sodium, magnesium stearate, maize starch, mannitol (E421) and povidone (E1201).
- The ingredients in the film-coating are glycerol (85 per cent) (E422), hypromellose, magnesium stearate, polysorbate 80, red iron oxide (E172), sucrose, and titanium dioxide (E171).

What Corbilta looks like and contents of the pack

Corbilta 125 mg/31.25 mg/200 mg: light brownish red, oval film-coated tablets marked with “LCE 125” on one side.

Corbilta 125 mg/31.25 mg/200 mg tablet comes in five different pack sizes (10, 30, 100, 130 or 175 tablets). Not all pack sizes may be marketed.

Marketing Authorisation Holder
Orion Corporation
Orionintie 1
FI-02200 Espoo
Finland

Manufacturer

Orion Corporation Orion Pharma
Joensuunkatu 7
FI-24100 Salo
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For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder.

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This leaflet was last revised in.

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

Package leaflet: Information for the user

Corbilta 150 mg/37.5 mg/200 mg film-coated tablets
levodopa/carbidopa/entacapone

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Corbilta is and what it is used for

Corbilta contains three active substances (levodopa, carbidopa and entacapone) in one film-coated tablet. Corbilta is used for the treatment of Parkinson's disease.

Parkinson's disease is caused by low levels of a substance called dopamine in the brain. Levodopa increases the amount of dopamine and hence reduces the symptoms of Parkinson's disease. Carbidopa and entacapone improve the antiparkinson effects of levodopa.

2. What you need to know before you take Corbilta

Do not take Corbilta if you:

- are allergic to levodopa, carbidopa or entacapone, or any of the other ingredients of this medicine (listed in section 6)
- have narrow-angle glaucoma (an eye disorder)
- have a tumour of the adrenal gland
- are taking certain medicines for treating depression (combinations of selective MAO-A and MAO-B inhibitors, or non-selective MAO-inhibitors)
- have ever had neuroleptic malignant syndrome (NMS – this is a rare reaction to medicines used to treat severe mental disorders)
- have ever had non-traumatic rhabdomyolysis (a rare muscle disorder)
- have a severe liver disease.

Warnings and precautions

Talk to your doctor or pharmacist before taking Corbilta if you have or have ever had:
- a heart attack or any other diseases of the heart including cardiac arrhythmias, or of the blood vessels
- asthma or any other disease of the lungs
- a liver problem, because your dose may need to be adjusted
- kidney or hormone-related diseases

- stomach ulcers or convulsions
- if you experience prolonged diarrhoea consult your doctor as it may be a sign of inflammation of the colon
- any form of severe mental disorder like psychosis
- chronic wide-angle glaucoma, because your dose may need to be adjusted and the pressure in your eyes may need to be monitored.

Consult your doctor if you are currently taking:
- antipsychotics (medicines used to treat psychosis)
- a medicine which may cause low blood pressure when rising from a chair or bed. You should be aware that Corbilta may make these reactions worse.

Consult your doctor if during the treatment with Corbilta you:
- notice that your muscles get very rigid or jerk violently, or if you get tremors, agitation, confusion, fever, rapid pulse, or wide fluctuations in your blood pressure. If any of this happens, **contact your doctor immediately.**
- feel depressed, have suicidal thoughts, or notice unusual changes in your behaviour
- find yourself suddenly falling asleep, or if you feel very drowsy. If this happens, you should not drive or use any tools or machines (see also section "Driving and using machines").
- notice that uncontrolled movements begin or get worse after you started to take Corbilta. If this happens, your doctor may need to change the dose of your antiparkinson medicine.
- experience diarrhoea: monitoring of your weight is recommended in order to avoid potentially excessive weight loss
- experience progressive anorexia, asthenia (weakness, exhaustion) and weight decrease within a relatively short period of time. If this happens, a general medical evaluation including liver function should be considered.
- feel the need to stop using Corbilta, see section "If you stop taking Corbilta".

Tell your doctor if you or your family/carer notices you are developing addiction-like symptoms leading to craving for large doses of Corbilta and other medicines used to treat Parkinson's disease.

Tell your doctor if you or your family/carer notices you are developing urges or cravings to behave in ways that are unusual for you or you cannot resist the impulse, drive or temptation to carry out certain activities that could harm yourself or others. These behaviours are called impulse control disorders and can include addictive gambling, excessive eating or spending, an abnormally high sex drive or a preoccupation with an increase in sexual thoughts or feelings. Your doctor may need to review your treatments.

Your doctor may take some regular laboratory tests during a long term treatment with Corbilta.

If you must undergo surgery, please tell your doctor that you are using Corbilta.

Corbilta is not recommended to be used for treatment of extrapyramidal symptoms (e.g. involuntary movements, shaking, muscle rigidity and muscle contractions) caused by other medicines.

Children and adolescents

Experience with Corbilta in patients under 18 years is limited. Therefore, the use of Corbilta in children or adolescents is not recommended.

Other medicines and Corbilta

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Do not take Corbilta if you are taking certain medicines for treating depression (combinations of selective MAO-A and MAO-B inhibitors, or non-selective MAO inhibitors).

Corbilta may increase the effects and side effects of certain medicines. These include:
- medicines used to treat depression such as moclobemide, amitriptyline, desipramine, maprotiline, venlafaxine and paroxetine
- rimiterole and isoprenaline, used to treat respiratory diseases
- adrenaline, used for severe allergic reactions
- noradrenaline, dopamine and dobutamine, used to treat heart diseases and low blood pressure
- alpha-methyldopa, used to treat high blood pressure
- apomorphine, which is used to treat Parkinson's disease.

The effects of Corbilta may be weakened by certain medicines. These include:
- dopamine antagonists used to treat mental disorders, nausea and vomiting
- phenytoin, used to prevent convulsions
- papaverine used to relax the muscles.

Corbilta may make it harder for you to digest iron. Therefore, do not take Corbilta and iron supplements at the same time. After taking one of them, wait at least 2 to 3 hours before taking the other.

Corbilta with food and drink

Corbilta may be taken with or without food. For some patients, Corbilta may not be well absorbed if it is taken with, or shortly after eating protein-rich food (such as meats, fish, dairy products, seeds and nuts). Consult your doctor if you think this applies to you.

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

You should not breast-feed during treatment with Corbilta.

Driving and using machines

Corbilta may lower your blood pressure, which may make you feel light-headed or dizzy. Therefore, be particularly careful when you drive or when you use any tools or machines.

If you feel very drowsy, or if you sometimes find yourself suddenly falling asleep, wait until you feel fully awake again before driving or doing anything else that requires you to be alert. Otherwise, you may put yourself and others at risk of serious injury or death.

Corbilta contains sucrose and sodium

Corbilta contains sucrose (1.9 mg/tablet). If you have been told by your doctor that you have intolerance to some sugars, contact your doctor before taking this medicine.

This medicine contains 2.6 mg sodium (main component of cooking/table salt) in each tablet. The maximum recommended daily dose (10 tablets) contains 26 mg of sodium. This is equivalent to 1.3% of the recommended maximum daily dietary intake of sodium for an adult.

3. How to take Corbilta

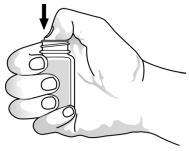
Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

For adults and elderly:
- Your doctor will tell you exactly how many tablets of Corbilta to take each day.
- The tablets are not intended to be split or broken into smaller pieces.
- You should take only one tablet each time.
- Depending on how you respond to treatment, your doctor may suggest a higher or lower dose.
- If you are taking Corbilta 50 mg/12.5 mg/200 mg, 75 mg/18.75 mg/200 mg, 100 mg/25 mg/200 mg, 125 mg/31.25 mg/200 mg or 150 mg/37.5 mg/200 mg tablets, do not take more than 10 tablets per day.

Talk to your doctor or pharmacist if you think the effect of Corbilta is too strong or too weak, or if you experience possible side effects.

To open the bottle for the first time: open the closure, and then press with your thumb on the seal until it breaks. See picture 1.

Picture 1



If you take more Corbilta than you should

If you have accidentally taken more Corbilta tablets than you should, talk to your doctor or pharmacist immediately. In case of an overdose you may feel confused or agitated, your heart rate may be slower or faster than normal or the colour of your skin, tongue, eyes or urine may change.

If you forget to take Corbilta

Do not take a double dose to make up for a forgotten tablet.

If it is more than 1 hour until your next dose:
Take one tablet as soon as you remember, and the next tablet at the normal time.

If it is less than 1 hour until your next dose:
Take a tablet as soon as you remember, wait 1 hour, then take another tablet. After that carry on as normal.

Always leave at least an hour between Corbilta tablets, to avoid possible side effects.

If you stop taking Corbilta

Do not stop taking Corbilta unless your doctor tells you to. In such a case your doctor may need to adjust your other antiparkinson medicines, especially levodopa, to give sufficient control of your symptoms. If you suddenly stop taking Corbilta and other antiparkinsonian medicines it may result in unwanted side effects.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Many of the side effects can be relieved by adjusting the dose.

If you during the treatment with Corbilta experience the following symptoms, **contact your doctor immediately**:
- Your muscles get very rigid or jerk violently, you get tremors, agitation, confusion, fever, rapid pulse, or wide fluctuations in your blood pressure. These can be symptoms of neuroleptic malignant syndrome (NMS, a rare severe reaction to medicines used to treat disorders of the central nervous system) or rhabdomyolysis (a rare severe muscle disorder).
- Allergic reaction, the signs may include hives (nettle rash), itching, rash, swelling of your face, lips, tongue or throat. This may cause difficulties in breathing or swallowing.

Very common (*may affect more than 1 in 10 people*):
- uncontrolled movements (dyskinesias)
- feeling sick (nausea)
- harmless reddish-brown discolouration of urine
- muscle pain
- diarrhoea.

Common (*may affect up to 1 in 10 people*):
- light-headedness or fainting due to low blood pressure, high blood pressure
- worsening of Parkinson's symptoms, dizziness, drowsiness
- vomiting, abdominal pain and discomfort, heartburn, dry mouth, constipation
- inability to sleep, hallucinations, confusion, abnormal dreams (including nightmares), tiredness
- mental changes – including problems with memory, anxiety and depression (possibly with thoughts of suicide)
- heart or artery disease events (e.g. chest pain), irregular heart rate or rhythm
- more frequent falling
- shortness of breath
- increased sweating, rashes
- muscle cramps, swelling of legs
- blurred vision
- anaemia
- decreased appetite, decreased weight
- headache, joint pain
- urinary tract infection.

Uncommon (*may affect up to 1 in 100 people*):
- heart attack
- bleeding in the gut
- changes in the blood cell count which may result in bleeding, abnormal liver function tests
- convulsions
- feeling agitated
- psychotic symptoms
- colitis (inflammation of the colon)
- discolourations other than urine (e.g. skin, nail, hair, sweat)
- swallowing difficulties
- inability to urinate.

Not known (*frequency cannot be estimated from the available data*):
Craving for large doses of Corbilta in excess of that required to control motor symptoms, known as dopamine dysregulation syndrome. Some patients experience severe abnormal involuntary movements (dyskinesias), mood swings or other side effects after taking large doses of Corbilta.

The following side effects have also been reported:
- hepatitis (inflammation of the liver)
- itching.

You may experience the following side effects:

- Inability to resist the impulse to perform an action that could be harmful, which may include:
  - strong impulse to gamble excessively despite serious personal or family consequences
  - altered or increased sexual interest and behaviour of significant concern to you or to others, for example, an increased sexual drive
  - uncontrollable excessive shopping or spending
  - binge eating (eating large amounts of food in a short time period) or compulsive eating (eating more food than normal and more than is needed to satisfy your hunger).

Tell your doctor if you experience any of these behaviours; they will discuss ways of managing or reducing the symptoms.

Reporting of side effects
If you get any side effects talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Corbilta

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the bottle and the carton. The expiry date refers to the last day of that month.

This medicinal product does not require any special storage conditions.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What Corbilta contains

- The active substances of Corbilta are levodopa, carbidopa and entacapone.
- Each Corbilta 150 mg/37.5 mg/200 mg tablet contains 150 mg of levodopa, 37.5 mg of carbidopa and 200 mg of entacapone.
- The other ingredients in the tablet core are croscarmellose sodium, magnesium stearate, maize starch, mannitol (E421) and povidone (E1201).
- The ingredients in the film-coating are glycerol (85 per cent) (E422), hypromellose, magnesium stearate, polysorbate 80, red iron oxide (E172), sucrose, titanium dioxide (E171), and yellow iron oxide (E172).

What Corbilta looks like and contents of the pack

Corbilta 150 mg/37.5 mg/200 mg: brownish or greyish red, elongated-ellipse shaped, unscored film-coated tablets marked with “LCE 150” on one side.

Corbilta comes in six different pack sizes (10, 30, 100, 130, 175 or 250 tablets). Not all pack sizes may be marketed.

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Finland

Manufacturer
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This leaflet was last revised in.

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

Package leaflet: Information for the user

Corbilta 175 mg/43.75 mg/200 mg film-coated tablets
levodopa/carbidopa/entacapone

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Corbilta is and what it is used for

Corbilta contains three active substances (levodopa, carbidopa and entacapone) in one film-coated tablet. Corbilta is used for the treatment of Parkinson's disease.

Parkinson's disease is caused by low levels of a substance called dopamine in the brain. Levodopa increases the amount of dopamine and hence reduces the symptoms of Parkinson's disease. Carbidopa and entacapone improve the antiparkinson effects of levodopa.

2. What you need to know before you take Corbilta

Do not take Corbilta if you:
- are allergic to levodopa, carbidopa or entacapone, or any of the other ingredients of this medicine (listed in section 6)
- have narrow-angle glaucoma (an eye disorder)
- have a tumour of the adrenal gland
- are taking certain medicines for treating depression (combinations of selective MAO-A and MAO-B inhibitors, or non-selective MAO-inhibitors)
- have ever had neuroleptic malignant syndrome (NMS – this is a rare reaction to medicines used to treat severe mental disorders)
- have ever had non-traumatic rhabdomyolysis (a rare muscle disorder)
- have a severe liver disease.

Warnings and precautions

Talk to your doctor or pharmacist before taking Corbilta if you have or have ever had:
- a heart attack or any other diseases of the heart including cardiac arrhythmias, or of the blood vessels
- asthma or any other disease of the lungs
- a liver problem, because your dose may need to be adjusted
- kidney or hormone-related diseases
- stomach ulcers or convulsions

- if you experience prolonged diarrhoea consult your doctor as it may be a sign of inflammation of the colon
- any form of severe mental disorder like psychosis
- chronic wide-angle glaucoma, because your dose may need to be adjusted and the pressure in your eyes may need to be monitored.

Consult your doctor if you are currently taking:
- antipsychotics (medicines used to treat psychosis)
- a medicine which may cause low blood pressure when rising from a chair or bed. You should be aware that Corbilta may make these reactions worse.

Consult your doctor if during the treatment with Corbilta you:
- notice that your muscles get very rigid or jerk violently, or if you get tremors, agitation, confusion, fever, rapid pulse, or wide fluctuations in your blood pressure. If any of this happens, **contact your doctor immediately.**
- feel depressed, have suicidal thoughts, or notice unusual changes in your behaviour
- find yourself suddenly falling asleep, or if you feel very drowsy. If this happens, you should not drive or use any tools or machines (see also section "Driving and using machines").
- notice that uncontrolled movements begin or get worse after you started to take Corbilta. If this happens, your doctor may need to change the dose of your antiparkinson medicine.
- experience diarrhoea: monitoring of your weight is recommended in order to avoid potentially excessive weight loss
- experience progressive anorexia, asthenia (weakness, exhaustion) and weight decrease within a relatively short period of time. If this happens, a general medical evaluation including liver function should be considered.
- feel the need to stop using Corbilta, see section "If you stop taking Corbilta".

Tell your doctor if you or your family/carer notices you are developing addiction-like symptoms leading to craving for large doses of Corbilta and other medicines used to treat Parkinson's disease.

Tell your doctor if you or your family/carer notices you are developing urges or cravings to behave in ways that are unusual for you or you cannot resist the impulse, drive or temptation to carry out certain activities that could harm yourself or others. These behaviours are called impulse control disorders and can include addictive gambling, excessive eating or spending, an abnormally high sex drive or a preoccupation with an increase in sexual thoughts or feelings. Your doctor may need to review your treatments.

Your doctor may take some regular laboratory tests during a long term treatment with Corbilta.

If you must undergo surgery, please tell your doctor that you are using Corbilta.

Corbilta is not recommended to be used for treatment of extrapyramidal symptoms (e.g. involuntary movements, shaking, muscle rigidity and muscle contractions) caused by other medicines.

Children and adolescents

Experience with Corbilta in patients under 18 years is limited. Therefore, the use of Corbilta in children or adolescents is not recommended.

Other medicines and Corbilta

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Do not take Corbilta if you are taking certain medicines for treating depression (combinations of selective MAO-A and MAO-B inhibitors, or non-selective MAO inhibitors).

Corbilta may increase the effects and side effects of certain medicines. These include:
- medicines used to treat depression such as moclobemide, amitriptyline, desipramine, maprotiline, venlafaxine and paroxetine
- rimiterole and isoprenaline, used to treat respiratory diseases
- adrenaline, used for severe allergic reactions
- noradrenaline, dopamine and dobutamine, used to treat heart diseases and low blood pressure
- alpha-methyldopa, used to treat high blood pressure
- apomorphine, which is used to treat Parkinson's disease.

The effects of Corbilta may be weakened by certain medicines. These include:
- dopamine antagonists used to treat mental disorders, nausea and vomiting
- phenytoin, used to prevent convulsions
- papaverine used to relax the muscles.

Corbilta may make it harder for you to digest iron. Therefore, do not take Corbilta and iron supplements at the same time. After taking one of them, wait at least 2 to 3 hours before taking the other.

Corbilta with food and drink

Corbilta may be taken with or without food. For some patients, Corbilta may not be well absorbed if it is taken with, or shortly after eating protein-rich food (such as meats, fish, dairy products, seeds and nuts). Consult your doctor if you think this applies to you.

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

You should not breast-feed during treatment with Corbilta.

Driving and using machines

Corbilta may lower your blood pressure, which may make you feel light-headed or dizzy. Therefore, be particularly careful when you drive or when you use any tools or machines.

If you feel very drowsy, or if you sometimes find yourself suddenly falling asleep, wait until you feel fully awake again before driving or doing anything else that requires you to be alert. Otherwise, you may put yourself and others at risk of serious injury or death.

Corbilta contains sucrose

Corbilta contains sucrose (1.89 mg/tablet). If you have been told by your doctor that you have intolerance to some sugars, contact your doctor before taking this medicine.

This medicine contains less than 1 mmol (23 mg) sodium per maximum recommended daily dose, that is to say essentially 'sodium-free'.

3. How to take Corbilta

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

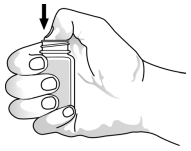
<u>For adults and elderly</u>:

- Your doctor will tell you exactly how many tablets of Corbilta to take each day.
- The tablets are not intended to be split or broken into smaller pieces.
- You should take only one tablet each time.
- Depending on how you respond to treatment, your doctor may suggest a higher or lower dose.
- If you are taking Corbilta 175 mg/43.75 mg/200 mg tablets, do not take more than 8 tablets of this strength per day.

Talk to your doctor or pharmacist if you think the effect of Corbilta is too strong or too weak, or if you experience possible side effects.

To open the bottle for the first time: open the closure, and then press with your thumb on the seal until it breaks. See picture 1.

Picture 1



If you take more Corbilta than you should

If you have accidentally taken more Corbilta tablets than you should, talk to your doctor or pharmacist immediately. In case of an overdose you may feel confused or agitated, your heart rate may be slower or faster than normal or the colour of your skin, tongue, eyes or urine may change.

If you forget to take Corbilta

Do not take a double dose to make up for a forgotten tablet.

If it is more than 1 hour until your next dose:
Take one tablet as soon as you remember, and the next tablet at the normal time.

If it is less than 1 hour until your next dose:
Take a tablet as soon as you remember, wait 1 hour, then take another tablet. After that carry on as normal.

Always leave at least an hour between Corbilta tablets, to avoid possible side effects.

If you stop taking Corbilta

Do not stop taking Corbilta unless your doctor tells you to. In such a case your doctor may need to adjust your other antiparkinson medicines, especially levodopa, to give sufficient control of your symptoms. If you suddenly stop taking Corbilta and other antiparkinsonian medicines it may result in unwanted side effects.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Many of the side effects can be relieved by adjusting the dose.

If you during the treatment with Corbilta experience the following symptoms, **contact your doctor immediately**:
- Your muscles get very rigid or jerk violently, you get tremors, agitation, confusion, fever, rapid pulse, or wide fluctuations in your blood pressure. These can be symptoms of neuroleptic malignant syndrome (NMS, a rare severe reaction to medicines used to treat disorders of the central nervous system) or rhabdomyolysis (a rare severe muscle disorder).

- Allergic reaction, the signs may include hives (nettle rash), itching, rash, swelling of your face, lips, tongue or throat. This may cause difficulties in breathing or swallowing.

Very common (*may affect more than 1 in 10 people*):
- uncontrolled movements (dyskinesias)
- feeling sick (nausea)
- harmless reddish-brown discolouration of urine
- muscle pain
- diarrhoea.

Common (*may affect up to 1 in 10 people*):
- light-headedness or fainting due to low blood pressure, high blood pressure
- worsening of Parkinson's symptoms, dizziness, drowsiness
- vomiting, abdominal pain and discomfort, heartburn, dry mouth, constipation
- inability to sleep, hallucinations, confusion, abnormal dreams (including nightmares), tiredness
- mental changes – including problems with memory, anxiety and depression (possibly with thoughts of suicide)
- heart or artery disease events (e.g. chest pain), irregular heart rate or rhythm
- more frequent falling
- shortness of breath
- increased sweating, rashes
- muscle cramps, swelling of legs
- blurred vision
- anaemia
- decreased appetite, decreased weight
- headache, joint pain
- urinary tract infection.

Uncommon (*may affect up to 1 in 100 people*):
- heart attack
- bleeding in the gut
- changes in the blood cell count which may result in bleeding, abnormal liver function tests
- convulsions
- feeling agitated
- psychotic symptoms
- colitis (inflammation of the colon)
- discolourations other than urine (e.g. skin, nail, hair, sweat)
- swallowing difficulties
- inability to urinate.

Not known (*frequency cannot be estimated from the available data*):
Craving for large doses of Corbilta in excess of that required to control motor symptoms, known as dopamine dysregulation syndrome. Some patients experience severe abnormal involuntary movements (dyskinesias), mood swings or other side effects after taking large doses of Corbilta.

The following side effects have also been reported:
- hepatitis (inflammation of the liver)
- itching.

You may experience the following side effects:
- Inability to resist the impulse to perform an action that could be harmful, which may include:
  - strong impulse to gamble excessively despite serious personal or family consequences
  - altered or increased sexual interest and behaviour of significant concern to you or to others, for example, an increased sexual drive
  - uncontrollable excessive shopping or spending
  - binge eating (eating large amounts of food in a short time period) or compulsive eating

(eating more food than normal and more than is needed to satisfy your hunger).

Tell your doctor if you experience any of these behaviors; they will discuss ways of managing or reducing the symptoms.

Reporting of side effects
If you get any side effects talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Corbilta

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the bottle and the carton. The expiry date refers to the last day of that month.

This medicinal product does not require any special storage conditions.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What Corbilta contains

- The active substances of Corbilta are levodopa, carbidopa and entacapone.
- Each Corbilta 175 mg/43.75 mg/200 mg tablet contains 175 mg of levodopa, 43.75 mg of carbidopa and 200 mg of entacapone.
- The other ingredients in the tablet core are croscarmellose sodium, magnesium stearate, maize starch, mannitol (E421) and povidone (E1201).
- The ingredients in the film-coating are glycerol (85 per cent) (E422), hypromellose, magnesium stearate, polysorbate 80, red iron oxide (E172), sucrose, and titanium dioxide (E171).

What Corbilta looks like and contents of the pack

Corbilta 175 mg/43.75 mg/200 mg: light brownish red, oval, unscored film-coated tablets marked with "LCE 175" on one side.

Corbilta 175 mg/43.75 mg/200 mg tablet comes in five different pack sizes (10, 30, 100, 130 or 175 tablets). Not all pack sizes may be marketed.

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This leaflet was last revised in.

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

Package leaflet: Information for the user

Corbilta 200 mg/50 mg/200 mg film-coated tablets
levodopa/carbidopa/entacapone

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Corbilta is and what it is used for

Corbilta contains three active substances (levodopa, carbidopa and entacapone) in one film-coated tablet. Corbilta is used for the treatment of Parkinson's disease.

Parkinson's disease is caused by low levels of a substance called dopamine in the brain. Levodopa increases the amount of dopamine and hence reduces the symptoms of Parkinson's disease. Carbidopa and entacapone improve the antiparkinson effects of levodopa.

2. What you need to know before you take Corbilta

Do not take Corbilta if you
- are allergic to levodopa, carbidopa or entacapone, or any of the other ingredients of this medicine (listed in section 6)
- have narrow-angle glaucoma (an eye disorder)
- have a tumour of the adrenal gland
- are taking certain medicines for treating depression (combinations of selective MAO-A and MAO-B inhibitors, or non-selective MAO-inhibitors)
- have ever had neuroleptic malignant syndrome (NMS – this is a rare reaction to medicines used to treat severe mental disorders)
- have ever had non-traumatic rhabdomyolysis (a rare muscle disorder)
- have a severe liver disease.

Warnings and precautions

Talk to your doctor or pharmacist before taking Corbilta if you have or have ever had:
- a heart attack or any other diseases of the heart including cardiac arrhythmias, or of the blood vessels
- asthma or any other disease of the lungs
- a liver problem, because your dose may need to be adjusted
- kidney or hormone-related diseases
- stomach ulcers or convulsions

- if you experience prolonged diarrhoea consult your doctor as it may be a sign of inflammation of the colon
- any form of severe mental disorder like psychosis
- chronic wide-angle glaucoma, because your dose may need to be adjusted and the pressure in your eyes may need to be monitored.

Consult your doctor if you are currently taking:
- antipsychotics (medicines used to treat psychosis)
- a medicine which may cause low blood pressure when rising from a chair or bed. You should be aware that Corbilta may make these reactions worse.

Consult your doctor if during the treatment with Corbilta you:
- notice that your muscles get very rigid or jerk violently, or if you get tremors, agitation, confusion, fever, rapid pulse, or wide fluctuations in your blood pressure. If any of this happens, **contact your doctor immediately.**
- feel depressed, have suicidal thoughts, or notice unusual changes in your behaviour
- find yourself suddenly falling asleep, or if you feel very drowsy. If this happens, you should not drive or use any tools or machines (see also section "Driving and using machines").
- notice that uncontrolled movements begin or get worse after you started to take Corbilta. If this happens, your doctor may need to change the dose of your antiparkinson medicine.
- experience diarrhoea: monitoring of your weight is recommended in order to avoid potentially excessive weight loss
- experience progressive anorexia, asthenia (weakness, exhaustion) and weight decrease within a relatively short period of time. If this happens, a general medical evaluation including liver function should be considered.
- feel the need to stop using Corbilta, see section "If you stop taking Corbilta".

Tell your doctor if you or your family/carer notices you are developing addiction-like symptoms leading to craving for large doses of Corbilta and other medicines used to treat Parkinson's disease.

Tell your doctor if you or your family/carer notices you are developing urges or cravings to behave in ways that are unusual for you or you cannot resist the impulse, drive or temptation to carry out certain activities that could harm yourself or others. These behaviours are called impulse control disorders and can include addictive gambling, excessive eating or spending, an abnormally high sex drive or a preoccupation with an increase in sexual thoughts or feelings. Your doctor may need to review your treatments.

Your doctor may take some regular laboratory tests during a long term treatment with Corbilta.

If you must undergo surgery, please tell your doctor that you are using Corbilta.

Corbilta is not recommended to be used for treatment of extrapyramidal symptoms (e.g. involuntary movements, shaking, muscle rigidity and muscle contractions) caused by other medicines.

Children and adolescents

Experience with Corbilta in patients under 18 years is limited. Therefore, the use of Corbilta in children or adolescents is not recommended.

Other medicines and Corbilta

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Do not take Corbilta if you are taking certain medicines for treating depression (combinations of selective MAO-A and MAO-B inhibitors, or non-selective MAO inhibitors).

Corbilta may increase the effects and side effects of certain medicines. These include:
- medicines used to treat depression such as moclobemide, amitriptyline, desipramine, maprotiline, venlafaxine and paroxetine
- rimiterole and isoprenaline, used to treat respiratory diseases
- adrenaline, used for severe allergic reactions
- noradrenaline, dopamine and dobutamine, used to treat heart diseases and low blood pressure
- alpha-methyldopa, used to treat high blood pressure
- apomorphine, which is used to treat Parkinson's disease.

The effects of Corbilta may be weakened by certain medicines. These include:
- dopamine antagonists used to treat mental disorders, nausea and vomiting
- phenytoin, used to prevent convulsions
- papaverine used to relax the muscles.

Corbilta may make it harder for you to digest iron. Therefore, do not take Corbilta and iron supplements at the same time. After taking one of them, wait at least 2 to 3 hours before taking the other.

Corbilta with food and drink

Corbilta may be taken with or without food. For some patients, Corbilta may not be well absorbed if it is taken with, or shortly after eating protein-rich food (such as meats, fish, dairy products, seeds and nuts). Consult your doctor if you think this applies to you.

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

You should not breast-feed during treatment with Corbilta.

Driving and using machines

Corbilta may lower your blood pressure, which may make you feel light-headed or dizzy. Therefore, be particularly careful when you drive or when you use any tools or machines.

If you feel very drowsy, or if you sometimes find yourself suddenly falling asleep, wait until you feel fully awake again before driving or doing anything else that requires you to be alert. Otherwise, you may put yourself and others at risk of serious injury or death.

Corbilta contains sucrose

Corbilta contains sucrose (2.3 mg/tablet). If you have been told by your doctor that you have intolerance to some sugars, contact your doctor before taking this medicine.

This medicine contains less than 1 mmol (23 mg) sodium per maximum recommended daily dose, that is to say essentially 'sodium-free'.

3. How to take Corbilta

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

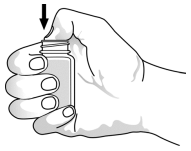
<u>For adults and elderly</u>:

- Your doctor will tell you exactly how many tablets of Corbilta to take each day.
- The tablets are not intended to be split or broken into smaller pieces.
- You should take only one tablet each time.
- Depending on how you respond to treatment, your doctor may suggest a higher or lower dose.
- If you are taking Corbilta 200 mg/50 mg/200 mg, do not take more than 7 tablets of this strength per day.

Talk to your doctor or pharmacist if you think the effect of Corbilta is too strong or too weak, or if you experience possible side effects.

To open the bottle for the first time: open the closure, and then press with your thumb on the seal until it breaks. See picture 1.

Picture 1



If you take more Corbilta than you should

If you have accidentally taken more Corbilta tablets than you should, talk to your doctor or pharmacist immediately. In case of an overdose you may feel confused or agitated, your heart rate may be slower or faster than normal or the colour of your skin, tongue, eyes or urine may change.

If you forget to take Corbilta

Do not take a double dose to make up for a forgotten tablet.

<u>If it is more than 1 hour until your next dose</u>:
Take one tablet as soon as you remember, and the next tablet at the normal time.

<u>If it is less than 1 hour until your next dose</u>:
Take a tablet as soon as you remember, wait 1 hour, then take another tablet. After that carry on as normal.

Always leave at least an hour between Corbilta tablets, to avoid possible side effects.

If you stop taking Corbilta

Do not stop taking Corbilta unless your doctor tells you to. In such a case your doctor may need to adjust your other antiparkinson medicines, especially levodopa, to give sufficient control of your symptoms. If you suddenly stop taking of Corbilta and other antiparkinsonian medicines it may result in unwanted side effects.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Many of the side effects can be relieved by adjusting the dose.

If you during the treatment with Corbilta experience the following symptoms, **contact your doctor immediately**:
- Your muscles get very rigid or jerk violently, you get tremors, agitation, confusion, fever, rapid pulse, or wide fluctuations in your blood pressure. These can be symptoms of neuroleptic malignant syndrome (NMS, a rare severe reaction to medicines used to treat disorders of the central nervous system) or rhabdomyolysis (a rare severe muscle disorder).

- Allergic reaction, the signs may include hives (nettle rash), itching, rash, swelling of your face, lips, tongue or throat. This may cause difficulties in breathing or swallowing.

Very common (*may affect more than 1 in 10 people)*:
- uncontrolled movements (dyskinesias)
- feeling sick (nausea)
- harmless reddish-brown discolouration of urine
- muscle pain
- diarrhoea.

Common (*may affect up to 1 in 10 people*):
- light-headedness or fainting due to low blood pressure, high blood pressure
- worsening of Parkinson's symptoms, dizziness, drowsiness
- vomiting, abdominal pain and discomfort, heartburn, dry mouth, constipation
- inability to sleep, hallucinations, confusion, abnormal dreams (including nightmares), tiredness
- mental changes – including problems with memory, anxiety and depression (possibly with thoughts of suicide)
- heart or artery disease events (e.g. chest pain), irregular heart rate or rhythm
- more frequent falling
- shortness of breath
- increased sweating, rashes
- muscle cramps, swelling of legs
- blurred vision
- anaemia
- decreased appetite, decreased weight
- headache, joint pain
- urinary tract infection.

Uncommon (*may affect up to 1 in 100 people*):
- heart attack
- bleeding in the gut
- changes in the blood cell count which may result in bleeding, abnormal liver function tests
- convulsions
- feeling agitated
- psychotic symptoms
- colitis (inflammation of the colon)
- discolourations other than urine (e.g. skin, nail, hair, sweat)
- swallowing difficulties
- inability to urinate.

Not known (*frequency cannot be estimated from the available data*):
Craving for large doses of Corbilta in excess of that required to control motor symptoms, known as dopamine dysregulation syndrome. Some patients experience severe abnormal involuntary movements (dyskinesias), mood swings or other side effects after taking large doses of Corbilta.

The following side effects have also been reported:
- hepatitis (inflammation of the liver)
- itching.

You may experience the following side effects:
- Inability to resist the impulse to perform an action that could be harmful, which may include:
  - strong impulse to gamble excessively despite serious personal or family consequences
  - altered or increased sexual interest and behaviour of significant concern to you or to others, for example, an increased sexual drive
  - uncontrollable excessive shopping or spending
  - binge eating (eating large amounts of food in a short time period) or compulsive eating

(eating more food than normal and more than is needed to satisfy your hunger).

Tell your doctor if you experience any of these behaviours; they will discuss ways of managing or reducing the symptoms.

Reporting of side effects
If you get any side effects talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Corbilta

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the bottle and the carton. The expiry date refers to the last day of that month.

This medicinal product does not require any special storage conditions.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What Corbilta contains

- The active substances of Corbilta are levodopa, carbidopa and entacapone.
- Each Corbilta 200 mg/50 mg/200 mg tablet contains 200 mg of levodopa, 50 mg of carbidopa and 200 mg of entacapone.
- The other ingredients in the tablet core are croscarmellose sodium, magnesium stearate, maize starch, mannitol (E421) and povidone (E1201).
- The ingredients in the film-coating are glycerol (85 per cent) (E422), hypromellose, magnesium stearate, polysorbate 80, red iron oxide (E172), sucrose and titanium dioxide (E171).

What Corbilta looks like and contents of the pack

Corbilta 200 mg/50 mg/200 mg: dark brownish red, oval, unscored film-coated tablets marked with “LCE 200” on one side.

Corbilta 200 mg/50 mg/200 mg tablet comes in five different pack sizes (10, 30, 100, 130 or 175). Not all pack sizes may be marketed.

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Orion Corporation
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For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder.

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Other sources of information

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