ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Ongentys 25 mg hard capsules
Ongentys 50 mg hard capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Ongentys 25 mg hard capsules

Each hard capsule contains 25 mg of opicapone.

Excipient(s) with known effect

Each hard capsule contains 171.9 mg of lactose (as monohydrate).

Ongentys 50 mg hard capsules

Each hard capsule contains 50 mg of opicapone.

Excipient(s) with known effect

Each hard capsule contains 148.2 mg of lactose (as monohydrate).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Hard capsule (capsule)

Ongentys 25 mg hard capsules

Light blue capsules, size 1, approximately 19 mm, imprinted “OPC 25” on the cap and “Bial” on the body.

Ongentys 50 mg hard capsules

Dark blue capsules, size 1, approximately 19 mm, imprinted “OPC 50” on the cap and “Bial” on the body.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Ongentys is indicated as adjunctive therapy to preparations of levodopa/ DOPA decarboxylase inhibitors (DDCI) in adult patients with Parkinson’s disease and end-of-dose motor fluctuations who cannot be stabilised on those combinations.

4.2 Posology and method of administration

Posology

The recommended dose is 50 mg of opicapone.
Ongentys should be taken once-daily at bedtime at least one hour before or after levodopa combinations.

Dose adjustments of antiparkinsonian therapy
Ongentys is to be administered as an adjunct to levodopa treatment and enhances the effects of levodopa. Hence, it is often necessary to adjust levodopa dose by extending the dosing intervals and/or reducing the amount of levodopa per dose within the first days to first weeks after initiating the treatment with opicapone according to the clinical condition of the patient (see section 4.4).

Missed dose
If one dose is missed, the next dose should be taken as scheduled. The patient should not take an extra dose to make up for the missed dose.

Special populations

Elderly
No dose adjustment is needed for elderly patients (see section 5.2).
Caution must be exercised in patients ≥ 85 years of age as there is limited experience in this age group.

Renal impairment
No dose adjustment is necessary in patients with renal impairment, as opicapone is not excreted by the kidney (see section 5.2).

Hepatic impairment
No dose adjustment is necessary in patients with mild hepatic impairment (Child-Pugh Class A).
There is limited clinical experience in patients with moderate hepatic impairment (Child-Pugh Class B). Caution must be exercised in these patients and dose adjustment may be necessary (see section 5.2).
There is no clinical experience in patients with severe hepatic impairment (Child-Pugh Class C), therefore, opicapone is not recommended in these patients (see section 5.2).

Paediatric population
There is no relevant use of Ongentys in the paediatric population with Parkinson's disease and motor fluctuations.

Method of administration

Oral use.

The capsules should be swallowed whole with water.

4.3 Contraindications

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

Phaeochromocytoma, paraganglioma, or other catecholamine secreting neoplasms.

History of neuroleptic malignant syndrome and/or non-traumatic rhabdomyolysis.

Concomitant use with monoamine oxidase (MAO-A and MAO-B) inhibitors (e.g. phenelzine, tranylcypromine and moclobemide) other than those for the treatment of Parkinson's disease (see section 4.5).

4.4 Special warnings and precautions for use

Dose adjustments of antiparkinsonian therapy

Ongentys is to be administered as an adjunct to levodopa treatment. Hence, the precautions valid for levodopa treatment should also be taken into account for Ongentys. Opicapone enhances the effects of levodopa. To reduce levodopa-related dopaminergic adverse reactions (e.g. dyskinesia, hallucinations, nausea, vomiting and orthostatic hypotension), it is often necessary to adjust the daily dose of levodopa by extending the dosing intervals and/or reducing the amount of levodopa per dose within the first days to first weeks after initiating treatment with Ongentys, according to the clinical condition of the patient (see section 4.2).

If Ongentys is discontinued it is necessary to adjust the dosing of the other antiparkinsonian treatments, especially levodopa, to achieve a sufficient level of control of the symptoms.

Psychiatric disorders

Patients and care-givers should be made aware that 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. Patients should be monitored regularly for the development of impulse control disorders and review of treatment is recommended if such symptoms develop.

Others

Increases in liver enzymes were reported in studies with nitrocatechol inhibitors of catechol-*O*-methyltransferase (COMT). 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.

Excipients

Ongentys contains lactose. Patients with rare hereditary problems of galactose intolerance, the total lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.

Ongentys contains less than 1 mmol sodium (23 mg) per capsule, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Monoamino oxidase (MAO) inhibitors

Combination of opicapone and MAO inhibitors could result in inhibition of the majority of the pathways responsible for the metabolism of catecholamines. Because of this, concomitant use of opicapone with MAO inhibitors (e.g. phenelzine, tranylcypromine and moclobemide) other than those for the treatment of Parkinson's disease is contraindicated (see section 4.3).
Concomitant use of opicapone and MAO inhibitors for the treatment of Parkinson's disease, e.g. rasagiline (up to 1 mg/day) and selegiline (up to 10 mg/day in oral formulation or 1.25 mg/day in buccal absorption formulation), is permissible.

There is no experience with opicapone when used concomitantly with the MAO-B inhibitor safinamide. Therefore, their concomitant use should be considered with appropriate caution.

Medicinal products metabolised by COMT

Opicapone may interfere with the metabolism of medicinal products containing a catechol group that are metabolised by COMT, e.g. rimiterole, isoprenaline, adrenaline, noradrenaline, dopamine, dopexamine or dobutamine, leading to potentiated effects of these medicinal products. Careful monitoring of patients being treated with these medicinal products is advised when opicapone is used.

Tricyclic antidepressants and noradrenaline re-uptake inhibitors

There is limited experience with opicapone when used concomitantly with tricyclic antidepressants and noradrenaline re-uptake inhibitors (e.g. venlafaxine, maprotiline and desipramine). Thus, their concomitant use should be considered with appropriate caution.

Quinidine

A study conducted in healthy volunteers showed that when a single dose of 50 mg opicapone was co-administered (within 1 hour) with a single dose of quinidine (600 mg), systemic exposure of opicapone decreased by 37% ($AUC_{0\text{-tlast}}$). Thus, particular consideration should be given to cases where quinidine needs to be administered together with opicapone as their co-administration should be avoided.

CYP2C8 and OATP1B1 substrates

Opicapone is a weak *in vitro* inhibitor of CYP2C8 and OATP1B1, whereas repaglinide is a sensitive CYP2C8 and OATP1B1 substrate. A study conducted in healthy subjects showed that there were no changes in repaglinide's exposure when repaglinide was administered following multiple once-daily administration of opicapone 50 mg.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no or limited amount of data from the use of opicapone in pregnant women. Opicapone crossed the placenta in rats. Animal studies are insufficient with respect to reproductive toxicity (see section 5.3). Ongentys is not recommended during pregnancy and in women of childbearing potential not using contraception.

Breast-feeding

Opicapone levels in the milk of lactating rats were equivalent to those in plasma. It is unknown whether opicapone or its metabolites are excreted into human milk. A risk to the newborns/infants cannot be excluded. Breast-feeding should be discontinued during treatment with Ongentys.

Fertility

The effects of opicapone on fertility in humans have not been studied. Animal studies with opicapone do not indicate harmful effects with respect to fertility (see section 5.3).

4.7 Effects on ability to drive and use machines

Opicapone in association with levodopa may have major influence on the ability to drive and use machines. Opicapone may, together with levodopa, cause dizziness, symptomatic orthostatism and somnolence. Therefore, caution should be exercised when driving or using machines.

4.8 Undesirable effects

Summary of the safety profile

The most common adverse reactions reported were nervous system disorders. Dyskinesia was the most frequently reported treatment-emergent adverse reaction (17.7%).

Tabulated list of adverse reactions

In the table below (Table 1) all adverse reactions are presented by System Organ Class and frequency. Frequency categories are defined as follows: 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).

Table 1 – Frequency of adverse reactions (MedDRA) in placebo-controlled Phase 3 studies

System Organ Class	Very common	Common	Uncommon
Metabolism and nutrition disorders			Decreased appetite, Hypertriglyceridaemia
Psychiatric disorders		Abnormal dreams, Hallucination, Hallucination visual, Insomnia	Anxiety, Depression, Hallucination auditory, Confusional state, Nightmare, Sleep disorder
Nervous system disorders	Dyskinesia	Dizziness, Headache, Somnolence	Dysgeusia, Hyperkinesia, Syncope
Eye disorders			Dry eye
Ear and labyrinth disorders			Ear congestion
Cardiac disorders			Palpitations
Vascular disorders		Orthostatic Hypotension	Hypertension, Hypotension
Respiratory, thoracic and mediastinal disorders			Dyspnoea
Gastrointestinal disorders		Constipation, Dry mouth, Nausea, Vomiting	Abdominal distention, Abdominal pain, Abdominal pain upper, Dyspepsia
Musculoskeletal and connective tissue disorders		Muscle spasms	Muscle twitching, Musculoskeletal stiffness, Myalgia, Pain in extremity
Renal and urinary disorders			Chromaturia, Nocturia
General disorders and administration site conditions			Fatigue
Investigations		Blood creatine phosphokinase increased	Weight decreased

Injury, poisoning and procedural complications			Fall

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

There is no known specific antidote. Symptomatic and supportive treatment should be administered as appropriate. Removal of opicapone by gastric lavage and/or inactivation by administering activated charcoal should be considered.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anti-parkinson drugs, other dopaminergic agents, ATC code: N04BX04

Mechanism of action

Opicapone is a peripheral, selective and reversible catechol-*O*-methyltransferase (COMT) inhibitor endowed with a high binding affinity (sub-picomolar) that translates into a slow complex dissociation rate constant and a long duration of action (>24 hours) *in vivo*.

In the presence of a DOPA decarboxylase inhibitor (DDCI), COMT becomes the major metabolising enzyme for levodopa, catalysing its conversion to 3-*O*-methyldopa (3-OMD) in the brain and periphery. In patients taking levodopa and a peripheral DDCI, such as carbidopa or benserazide, opicapone increases levodopa plasma levels thereby improving the clinical response to levodopa.

Pharmacodynamic effects

Opicapone showed a marked (>90%) and long-lasting (>24 hours) COMT inhibition in healthy subjects after administration of 50 mg opicapone.

At steady state, 50 mg opicapone significantly increased the extent of levodopa systemic exposure approximately 2 fold compared to placebo following a single oral administration of either 100/25 mg levodopa/carbidopa or 100/25 mg levodopa/benserazide administered 12 h after the opicapone dose.

Clinical efficacy and safety

The efficacy and safety of opicapone has been demonstrated in two Phase 3 double-blind, placebo and active (Study 1 only) controlled studies in 1,027 randomized adult patients with Parkinson's disease treated with levodopa/DDCI (alone or in combination with other antiparkinsonian medicinal products) and end-of-dose motor fluctuations for up to 15 weeks. At screening, the mean age was similar in all treatment groups in both studies, ranging between 61.5 and 65.3 years. Patients had disease severity stages 1 to 3 (modified Hoehn and Yahr) at ON, were treated with 3 to 8 daily doses of levodopa/DDCI and had a daily average OFF-time of at least 1.5 hours. In both studies, 783 patients were treated with 25 mg or 50 mg of opicapone or placebo. In Study 1, 122 patients were treated with 5 mg of opicapone and 122 patients were treated with 200 mg of entacapone (active comparator). The majority of patients treated in both pivotal studies were treated with immediate-release

levodopa/DDCI. There were 60 patients in the combined Phase 3 studies who were predominantly using controlled-release levodopa (i.e. >50% of their levodopa/DDCI formulations), 48 of whom were treated solely with controlled-release formulations of levodopa. Although there is no evidence that either the efficacy or safety of opicapone would be affected by use of controlled-release levodopa preparations, the experience with such preparations is limited.

Opicapone demonstrated clinical efficacy superior to placebo during the double-blind treatment, both for the primary efficacy variable used in both pivotal studies, i.e. reduction in OFF-time (Table 2), the proportion of OFF-time responders (i.e. a subject who had a reduction in OFF-time of at least 1 hour from baseline to endpoint) (Table 3) and for most diary-derived secondary endpoints.

The LS mean reduction in absolute OFF-time from baseline to endpoint in the entacapone group was -78.7 minutes. The difference in LS mean change in OFF-time of entacapone to placebo in Study 1 was -30.5 minutes. The difference in LS mean change in OFF-time of opicapone 50 mg to entacapone was -24.8 minutes and non-inferiority of opicapone 50 mg to entacapone was demonstrated (95% confidence interval: -61.4, 11.8).

Table 2 – Change in absolute OFF-time and ON-time (minutes) from baseline to endpoint

Treatment	N	LS mean	95% CI	p-value
Study 1				
Change in OFF-time				
Placebo	121	-48.3	--	--
OPC 5 mg	122	-77.6	--	--
OPC 25 mg	119	-73.2	--	--
OPC 50 mg	115	-103.6	--	--
OPC 5 mg – Placebo	--	-29.3	-65.5, 6.8	0.0558
OPC 25 mg – Placebo	--	-25.0	-61.5, 11.6	0.0902
OPC 50 mg – Placebo	--	-55.3	-92.0, -18.6	0.0016
Change in total ON-time without troublesome dyskinesias[a]				
Placebo	121	40.0	--	--
OPC 5 mg	122	75.6	--	--
OPC 25 mg	119	78.6	--	--
OPC 50 mg	115	100.8	--	--
OPC 5 mg – Placebo	--	35.6	-2.5, 73.7	0.0670
OPC 25 mg – Placebo	--	38.6	0.2, 77.0	0.0489
OPC 50 mg – Placebo	--	60.8	22.1, 99.6	0.0021
Study 2				
Change in OFF-time				
Placebo	136	-54.6	--	--
OPC 25 mg	125	-93.2	--	--
OPC 50 mg	150	-107.0	--	--
OPC 25 mg – placebo	--	-38.5	-77.0, -0.1	0.0900
OPC 50 mg – placebo	--	-52.4	-89.1, -15.7	0.0101
Change in total ON-time without troublesome dyskinesias[a]				
Placebo	136	37.9	--	--
OPC 25 mg	125	79.7	--	--
OPC 50 mg	150	77.6	--	--
OPC 25 mg – placebo	--	41.8	0.7, 82.9	0.0839
OPC 50 mg – placebo	--	39.7	0.5, 78.8	0.0852

CI = confidence interval; LS mean = least square mean; N = number of non-missing values; OPC = opicapone.

a. ON-time without troublesome dyskinesias=ON-time with non-troublesome dyskinesias + ON-time without dyskinesias

Table 3 – OFF-time responder rates at endpoint

Response type	Placebo (N=121)	Entacapone (N=122)	OPC 5 mg (N=122)	OPC 25 mg (N=119)	OPC 50 mg (N=115)
Study 1					
OFF-time reduction					
Responders, n (%)	55 (45.5)	66 (54.1)	64 (52.5)	66 (55.5)	75 (65.2)
Difference to placebo					
p-value	--	0.1845	0.2851	0.1176	0.0036
(95% CI)		(-0.039; 0.209)	(-0.056; 0.193)	(-0.025; 0.229)	(0.065; 0.316)
Study 2					
OFF-time reduction					
Responders, n (%)	65 (47.8)	NA	NA	74 (59.2)	89 (59.3)
Difference to placebo					
p-value	--	--	--	0.0506	0.0470
(95% CI)				(0.001; 0.242)	(0.003; 0.232)

CI = confidence interval; N = total number of patients; n = number of patients with available information; NA = not applicable; OPC = opicapone

Note: A responder was a patient who had a reduction of at least 1 hour in absolute OFF-time (OFF-time responder)

The results of the open-label (OL) extension studies of 1 year duration in 862 patients who continued treatment from the double-blind studies (Study 1-OL and Study 2-OL) indicated maintenance of the effect achieved during DB study periods. In the OL studies, all patients began at a dose of 25 mg opicapone for the first week (7 days), regardless of their prior treatment in the double-blind period. If end-of-dose motor fluctuations were not sufficiently controlled and tolerability allowed, the opicapone dose could be increased to 50 mg. If unacceptable dopaminergic adverse events were seen, the levodopa dose was to be adjusted. If not sufficient to manage the adverse events, the opicapone dose could then be down titrated. For other adverse events, the levodopa and/or opicapone dose could be adjusted.

Paediatric population

The European Medicines Agency has waived the obligation to submit the results of studies with opicapone in all subsets of the paediatric population with Parkinson's disease and motor fluctuations (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Absorption

Opicapone presents a low absorption (~20%). Pharmacokinetic results showed that opicapone is rapidly absorbed, with a t_{max} of 1.0 h to 2.5 h following once-daily multiple-dose administration up to 50 mg opicapone.

Distribution

In vitro studies over the opicapone concentration range 0.3 to 30 mcg/mL showed that binding of ^{14}C-opicapone to human plasma proteins is high (99.9%) and concentration-independent. The binding of ^{14}C-opicapone to plasma proteins was unaffected by the presence of warfarin, diazepam, digoxin and tolbutamide, and the binding of ^{14}C-warfarin, 2-^{14}C-diazepam, ^{3}H-digoxin and ^{14}C-tolbutamide was unaffected by the presence of opicapone and opicapone sulphate, the major human metabolite.

After oral administration, the apparent volume of distribution of opicapone at a dose of 50 mg was 29 L with an inter-subject variability of 36%.

Biotransformation

Sulphation of opicapone appears to be the major metabolic pathway in humans, yielding the inactive opicapone sulphate metabolite. Other metabolic pathways include glucuronidation, methylation and reduction.

The most abundant peaks in plasma after a single-dose of 100 mg ^{14}C-opicapone are metabolites BIA 9-1103 (sulphate) and BIA 9-1104 (methylated), 67.1 and 20.5% of radioactive AUC respectively. Other metabolites were not found in quantifiable concentrations in the majority of plasma samples collected during a clinical mass balance study.

The reduced metabolite of opicapone (found to be active in non-clinical studies) is a minor metabolite in human plasma and represented less than 10% of total systemic exposure to opicapone.

In *in vitro* studies in human hepatic microsomes, minor inhibition of CYP1A2 and CYP2B6 was observed. All reductions in activity essentially occurred at the highest concentration of opicapone (10 mcg/mL).

An *in vitro* study showed opicapone inhibited CYP2C8 activity. A single dose study with opicapone 25 mg showed an average increase of 30 % in the rate, but not the extent, of exposure to repaglinide (a CYP2C8 substrate), when the two drugs were co-administered. A second study conducted showed that, at steady state, opicapone 50 mg had no effect on repaglinide systemic exposure.

Opicapone reduced CYP2C9 activity through competitive / mixed type mode of inhibition. However, clinical interaction studies conducted with warfarin showed no effect of opicapone on the pharmacodynamics of warfarin, a substrate of CYP2C9.

Elimination

In healthy subjects, the opicapone elimination half-life ($t_{1/2}$) was 0.7 h to 3.2 h following once-daily multiple-dose administration up to 50 mg opicapone.
Following once-daily multiple oral doses of opicapone in the dose range of 5 to 50 mg, opicapone sulphate presented a long terminal phase with elimination half-life values ranging from 94 h to 122 h and, as a consequence of this long terminal elimination half-life, opicapone sulphate presented a high accumulation ratio in plasma, with values close of up to 6.6.

After oral administration, the apparent total body clearance of opicapone at a dose of 50 mg was 22 L/h, with an inter-subject variability of 45%.

Following administration of a single oral dose of ^{14}C-opicapone, the main excretion route of opicapone and its metabolites was faeces, accounting for 58.5% to 76.8% of the administered radioactivity (mean 67.2%). The remainder of the radioactivity was excreted in urine (mean 12.8%) and via expired air (mean 15.9%). In urine, the primary metabolite was the glucuronide metabolite of opicapone, while parent drug and other metabolites were generally below the limit of quantification. Overall, it can be concluded that the kidney is not the primary route of excretion. Therefore, it can be presumed that opicapone and its metabolites are mainly excreted in the faeces.

Linearity/non-linearity

Opicapone exposure increased in a dose proportional manner following once-daily multiple dose administration up to 50 mg opicapone.

Transporters

Effect of transporters on opicapone

In vitro studies have shown that opicapone is not transported by OATP1B1, but is transported by OATP1B3, and efflux transported by P-gp and BCRP. BIA 9-1103, its major metabolite, was transported by OATP1B1 and OATP1B3, and efflux transported by BCRP, but is not a substrate for the P-gp/MDR1 efflux transporter.

Effect of opicapone on transporters
At clinically relevant concentrations, opicapone is not expected to inhibit OAT1, OAT3, OATP1B1, OATP1B3, OCT1, OCT2, BCRP, P-gp/MDR1, BSEP, MATE1 and MATE2-K transporters as suggested by *in vitro* and *in vivo* studies.

Elderly (≥ 65 years old)

The pharmacokinetics of opicapone was evaluated in elderly subjects (aged 65-78 years old) after 7-day multiple-dose administration of 30 mg. An increase in both the rate and extent of systemic exposure was observed for the elderly population when compared to the young population. The S-COMT activity inhibition was significantly increased in elderly subjects. The magnitude of this effect is not considered to be of clinical relevance.

Weight

There is no relationship between exposure of opicapone and body weight over the range of 40-100 kg.

Hepatic impairment

There is limited clinical experience in patients with moderate hepatic impairment (Child-Pugh Class B). The pharmacokinetics of opicapone was evaluated in healthy subjects and moderate chronic hepatic impaired patients after administration of a single-dose of 50 mg. The bioavailability of opicapone was significantly higher in patients with moderate chronic hepatic impairment and no safety concerns were observed. However, as opicapone is to be used as adjunctive levodopa-therapy, dose adjustments may be considered based on a potentially enhanced levodopa dopaminergic response and associated tolerability. There is no clinical experience in patients with severe hepatic impairment (Child-Pugh Class C) (see section 4.2).

Renal impairment

The pharmacokinetics of opicapone was not directly evaluated in subjects with chronic renal impairment. However, an evaluation with 50 mg opicapone was performed in subjects included in both phase 3 studies with GFR/1.73 m^2 <60 mL/min (i.e. moderately decreased renal elimination capacity), and using pooled BIA 9-1103 data (major metabolite of opicapone). BIA 9-1103 plasma levels were not affected in patients with chronic renal impairment, and as such, no dose adjustment needs to be considered.

5.3 Preclinical safety data

Non-clinical data revealed no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and carcinogenic potential.

In rats, opicapone did not affect male and female fertility or prenatal development at exposure levels 22 times the therapeutic exposure in humans. In pregnant rabbits, opicapone was less well tolerated resulting in maximum systemic exposure levels around or below the therapeutic range. Although embryo-foetal development was not negatively influenced in rabbits, the study is not considered predictive for human risk assessment.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule content

Lactose monohydrate
Sodium starch glycolate, Type A
Maize starch, pregelatinized
Magnesium stearate

Capsule shell

Gelatin
Indigo carmine aluminium lake (E 132)
Erythrosine (E 127)
Titanium dioxide (E 171)

Printing ink

Ongentys 25 mg hard capsules
Shellac
Propylene glycol
Ammonia solution, concentrated
Indigo carmine aluminium lake (E 132)

Ongentys 50 mg hard capsules
Shellac
Titanium dioxide (E 171)
Propylene glycol
Ammonia solution, concentrated
Simeticone

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

HDPE bottles: 3 years
Blisters: 5 years

6.4 Special precautions for storage

This medicinal product does not require any special temperature storage conditions.

Blisters: Store in the original blister in order to protect from moisture.

HDPE bottles: Keep the bottle tightly closed in order to protect from moisture.

6.5 Nature and contents of container

Ongentys 25 mg hard capsules
White high density polyethylene (HDPE) bottles with polypropylene (PP) child resistant closures containing 10 or 30 capsules.

OPA/Al/PVC//Al blisters containing 10 or 30 capsules.

Ongentys 50 mg hard capsules

White high density polyethylene (HDPE) bottles with polypropylene (PP) child resistant closures containing 10, 30 or 90 capsules.

OPA/Al/PVC//Al blisters containing 10, 30 or 90 capsules

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

Bial - Portela & Cª, S.A.
À Av. da Siderurgia Nacional
4745-457 S. Mamede do Coronado
Portugal
Tel:+351 22 986 61 00
Fax: +351 22 986 61 90
e-mail: info@bial.com

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/15/1066/001-010

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 24 June 2016
Date of latest renewal: 18 February 2021

10. DATE OF REVISION OF THE TEXT

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

ANNEX II

A. MANUFACTURER 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 RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release
Bial - Portela & C[a], S.A.
À Av. da Siderurgia Nacional
4745-457 S. Mamede do Coronado
Portugal

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

HDPE BOTTLE

1. NAME OF THE MEDICINAL PRODUCT

Ongentys 25 mg hard capsules
opicapone

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each capsule contains 25 mg of opicapone.

3. LIST OF EXCIPIENTS

Contains lactose.

See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

10 hard capsules
30 hard capsules

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

Keep the bottle tightly closed in order to protect from moisture

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

Bial - Portela & Cª, S.A.
À Av. da Siderurgia Nacional
4745-457 S. Mamede do Coronado
Portugal
(only for outer packaging)

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/15/1066/009 10 hard capsules
EU/1/15/1066/010 30 hard capsules

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

ongentys 25 mg *(only on the outer packaging)*

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.
(only for outer packaging)

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN
(only for outer packaging)

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

BOX (BLISTER OPA/Al/PVC//Al)

1. NAME OF THE MEDICINAL PRODUCT

Ongentys 25 mg hard capsules
opicapone

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each capsule contains 25 mg of opicapone.

3. LIST OF EXCIPIENTS

Contains lactose.

See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

10 hard capsules
30 hard capsules

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

Store in the original blister in order to protect from moisture.

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

Bial - Portela & Cª, S.A.
À Av. da Siderurgia Nacional
4745-457 S. Mamede do Coronado
Portugal

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/15/1066/001 10 hard capsules
EU/1/15/1066/008 30 hard capsules

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

ongentys 25 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER OPA/Al/PVC//Al

1. NAME OF THE MEDICINAL PRODUCT

Ongentys 25 mg capsules
opicapone

2. NAME OF THE MARKETING AUTHORISATION HOLDER

BIAL

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

HDPE BOTTLE

1. NAME OF THE MEDICINAL PRODUCT

Ongentys 50 mg hard capsules
opicapone

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each capsule contains 50 mg of opicapone.

3. LIST OF EXCIPIENTS

Contains lactose.

See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

10 hard capsules
30 hard capsules
90 hard capsules

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

Keep the bottle tightly closed in order to protect from moisture

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

Bial - Portela & Cª, S.A.
À Av. da Siderurgia Nacional
4745-457 S. Mamede do Coronado
Portugal
(only for outer packaging)

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/15/1066/005 10 hard capsules
EU/1/15/1066/006 30 hard capsules
EU/1/15/1066/007 90 hard capsules

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

ongentys 50 mg *(only on the outer packaging)*

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.
(only for outer packaging)

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN
(only for outer packaging)

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

BOX (BLISTER OPA/Al/PVC//Al)

1. NAME OF THE MEDICINAL PRODUCT

Ongentys 50 mg hard capsules
opicapone

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each capsule contains 50 mg of opicapone.

3. LIST OF EXCIPIENTS

Contains lactose.

See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

10 hard capsules
30 hard capsules
90 hard capsules

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

Store in the original blister in order to protect from moisture.

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

Bial - Portela & Cª, S.A.
À Av. da Siderurgia Nacional
4745-457 S. Mamede do Coronado
Portugal

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/15/1066/002 10 hard capsules
EU/1/15/1066/003 30 hard capsules
EU/1/15/1066/004 90 hard capsules

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

ongentys 50 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER OPA/Al/PVC//Al

1. NAME OF THE MEDICINAL PRODUCT

Ongentys 50 mg capsules
opicapone

2. NAME OF THE MARKETING AUTHORISATION HOLDER

BIAL

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

Ongentys 25 mg hard capsules
opicapone

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 Ongentys is and what it is used for

Ongentys contains the active substance opicapone. It is used to treat Parkinson's disease and associated movement problems. Parkinson's disease is a progressive disease of the nervous system that causes shaking and affects your movement.

Ongentys is for use in adults who are already taking medicines containing levodopa and DOPA decarboxylase inhibitors. It increases the effects of levodopa and helps to relieve the symptoms of Parkinson's disease and movement problems.

2. What you need to know before you take Ongentys

Do not take Ongentys:
- if you are allergic to opicapone or any of the other ingredients of this medicine (listed in section 6);
- if you have a tumour of the adrenal gland (known as phaeochromocytoma), or of the nervous system (known as paraganglioma), or any other tumour which increase the risk of severe high blood pressure;
- if you have ever suffered from neuroleptic malignant syndrome which is a rare reaction to antipsychotic medicines;
- if you have ever suffered from a rare muscle disorder called rhabdomyolysis which was not caused by injury;
- if you are taking certain antidepressants called monoamine-oxidase (MAO) inhibitors (e.g. phenelzine, tranylcypromine or moclobemide). Ask your doctor or pharmacist if you can take your antidepressant together with Ongentys.

Warnings and precautions
Talk to your doctor or pharmacist before taking Ongentys:
- if you have severe liver problems and suffered from loss of appetite, weight loss, weakness, or exhaustion within a short period of time. Your doctor may need to reconsider your treatment.

Talk to your doctor or pharmacist 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 you or others. These behaviours are called 'impulse control disorders' and can include: addictive gambling, an abnormally high sex drive or an increased preoccupation with sexual thoughts or feelings. Behaviours such as these have been reported in patients using other medicines for Parkinsons´s disease.
Your doctor may need to review your treatments.

Children and adolescents
Children and adolescents under the age of 18 years must not take this medicine. It has not been studied in these age groups since treatment of Parkinson's disease is not relevant in children and adolescents.

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

Tell your doctor if you are taking:
- medicines for depression or anxiety such as venlafaxine, maprotiline and desipramine. Taking Ongentys with these medicines may increase the risk of side effects. Your doctor may need to adjust your treatment;
- safinamide used for Parkinson's disease. There is no experience taking Ongentys and safinamide together. Your doctor may need to adjust your treatment;
- medicines to treat asthma such as rimiterole or isoprenaline. Ongentys may increase their effect;
- medicines used to treat allergic reactions such as adrenaline. Ongentys may increase their effect;
- medicines used to treat heart failure such as dobutamine, dopamine or dopexamine. Ongentys may increase their effects;
- medicines for high cholesterol such as rosuvastatin, simvastatin, atorvastatin or pravastatin Ongentys may increase their effects;
- medicines that affect the immune system such as methotrexate. Ongentys may increase its effect;
- medicines containing quinidine, a medicine used to treat abnormal heart rhythms or malaria. Taking Ongentys and quinidine together, i.e. at the same time, may decrease the effect of Ongentys.

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

Ongentys is not recommended if you are pregnant. You should use effective contraception if you might become pregnant.

It is not known if Ongentys passes into breast milk in humans. Since the risk to the baby/infant cannot be excluded, you should stop breast-feeding during treatment with Ongentys.

Driving and using machines
Ongentys taken with levodopa may make you feel light-headed, dizzy, or sleepy.
Do not drive or operate machinery if you experience any of these side effects.

Ongentys contains lactose and sodium
- Lactose: If you have been told by your doctor that you have intolerance to some sugars, contact your doctor before taking this medicine.
- Sodium: This medicine contains less than 1 mmol sodium (23 mg) per capsule, that is to say essentially 'sodium-free'.

3. How to take Ongentys

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

The recommended dose is 50 mg once daily.
Ongentys should be taken preferably at bedtime.

Take Ongentys at least one hour before or after taking your levodopa medicine.

Doses of other medicines to treat Parkinson's disease
The dose of other medicines to treat Parkinson's disease may need to be adjusted when you start taking Ongentys. Follow the instructions that your doctor has given you.

Method of administration
Ongentys is for oral use.
Swallow the capsule whole with a glass of water.

If you take more Ongentys than you should
If you take more Ongentys than you should, tell your doctor or pharmacist, or go to a hospital immediately. Take the medicine package and this leaflet with you. This will help the doctor identify what you have taken.

If you forget to take Ongentys
If you forget to take one dose, you should continue the treatment and take the next dose as scheduled. Do not take a double dose to make up for a forgotten dose.

If you stop taking Ongentys
Do not stop taking Ongentys unless your doctor tells you to as your symptoms may get worse.
If you stop taking Ongentys your doctor may need to adjust the dose of other medicines that you are taking to treat Parkinson's disease.

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.

Side effects caused by Ongentys are usually mild to moderate and occur mostly within the first weeks of treatment. Some side effects may be caused by the increased effects of using Ongentys together with levodopa.

Contact your doctor straight away if you experience any side effects at the start of treatment. Many of the side effects can be managed by your doctor adjusting your levodopa medicine.

Tell your doctor as soon as possible if you notice any of the following side effects:

Very common: may affect more than 1 in 10 people
- involuntary and uncontrollable, or difficult or painful body movements

Common: may affect up to 1 in 10 people
- constipation
- dry mouth
- feeling sick (nausea)
- vomiting (being sick)
- increased levels of the enzyme (creatine kinase) in your blood
- muscle spasm
- dizziness

- headache
- sleepiness
- difficulty falling or staying asleep
- strange dreams
- experiencing or seeing things which do not exist (hallucinations)
- a fall in blood pressure on standing up which causes dizziness, light-headedness or fainting

Uncommon: may affect up to 1 in 100 people
- palpitations or irregular heartbeat
- blocked ear
- dry eye
- pain or swelling of the abdomen
- indigestion
- weight loss
- loss of appetite
- increased levels of triglycerides (fats) in your blood
- muscle twitching, stiffness or pain
- pain in arms or legs
- altered sense of taste
- excessive body movements
- fainting
- anxiety
- depression
- hearing things which do not exist
- feeling confused
- nightmares
- sleep disorder
- abnormal colour of urine
- need to wake and pass urine at night
- shortness of breath
- high or low blood pressure
- having falls
- feeling low in energy or tired

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 Ongentys

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/blister/carton after EXP. The expiry date refers to the last day of that month.

This medicine does not require any special temperature storage conditions.
Blisters: Store in the original blister in order to protect from moisture.
Bottles: Keep the bottle tightly closed in order to protect from moisture.

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 protect the environment.

6. Contents of the pack and other information

What Ongentys contains

- The active substance is opicapone. Each hard capsule contains 25 mg of opicapone.
- The other ingredients are:
  - capsule content: lactose monohydrate, sodium starch glycolate (Type A), pregelatinized maize starch and magnesium stearate
  - capsule shell: gelatine, indigo carmine aluminium lake (E 132), erythrosine (E 127) and titanium dioxide (E 171)
  - printing ink: shellac, propylene glycol, ammonia solution, concentrated, indigo carmine aluminium lake (E132)

What Ongentys looks like and contents of the pack

Ongentys 25 mg hard capsules are light blue, approximately 19 mm length, with “OPC 25” and “Bial” printed on the capsules.

The capsules are packaged in bottles or blisters.

Bottles: 10 or 30 capsules.
Blisters: 10 or 30 capsules.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Bial - Portela & Cª, S.A.
À Av. da Siderurgia Nacional
4745-457 S. Mamede do Coronado
Portugal
tel: +351 22 986 61 00
fax: +351 22 986 61 90
e-mail: info@bial.com

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

België/Belgique/Belgien/
Deutschland/ Ελλάδα/France/
Ireland/ Italia/Κύπρος/
Luxembourg/Luxemburg/
Malta/Nederland/ Österreich/Polska/Portugal/
România
BIAL - Portela & Cª, S.A.
Tél/Tel/Tlf/Τηλ: + 351 22 986 61 00

España
Laboratorios BIAL, S.A.
Tel: + 34 91 562 41 96

България
Medis Pharma Bulgaria EOOD
Тел.: +359(0)24274958

Česká republika
Medis Pharma s.r.o.
Tel: +386(0)15896900

Danmark
Nordicinfu Care AB
Tlf: +45 (0) 70 28 10 24

Eesti / Latvija/ Lietuva
Medis Pharma Lithuania UAB
Tel: +386(0)15896900

Hrvatska
Medis Adria d.o.o.

Tel.: +385(0)12303446

Suomi/Finland
Nordicinfu Care AB
Puh/Tel: +358 (0) 207 348 760

Magyarország
Medis Hungary Kft
Tel: +36(0)23801028

Ísland / Sverige
Nordicinfu Care AB
Tel / Sími: +46 (0) 8 601 24 40

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Slovenská republika
Medis Pharma Slovakia s.r.o.
Tel: +42(1)232393403

This leaflet was last revised in {MM/YYYY}.

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 patient

Ongentys 50 mg hard capsules
opicapone

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 Ongentys is and what it is used for

Ongentys contains the active substance opicapone. It is used to treat Parkinson's disease and associated movement problems. Parkinson's disease is a progressive disease of the nervous system that causes shaking and affects your movement.

Ongentys is for use in adults who are already taking medicines containing levodopa and DOPA decarboxylase inhibitors. It increases the effects of levodopa and helps to relieve the symptoms of Parkinson's disease and movement problems.

2. What you need to know before you take Ongentys

Do not take Ongentys:
- if you are allergic to opicapone or any of the other ingredients of this medicine (listed in section 6);
- if you have a tumour of the adrenal gland (known as phaeochromocytoma), or of the nervous system (known as paraganglioma), or any other tumour which increase the risk of severe high blood pressure;
- if you have ever suffered from neuroleptic malignant syndrome which is a rare reaction to antipsychotic medicines;
- if you have ever suffered from a rare muscle disorder called rhabdomyolysis which was not caused by injury;
- if you are taking certain antidepressants called monoamine-oxidase (MAO) inhibitors (e.g. phenelzine, tranylcypromine or moclobemide). Ask your doctor or pharmacist if you can take your antidepressant together with Ongentys.

Warnings and precautions
Talk to your doctor or pharmacist before taking Ongentys:
- if you have severe liver problems and suffered from loss of appetite, weight loss, weakness, or exhaustion within a short period of time. Your doctor may need to reconsider your treatment.

Talk to your doctor or pharmacist 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 you or others. These behaviours are called 'impulse control disorders' and can include: addictive gambling, an abnormally high sex drive or an increased preoccupation with sexual thoughts or feelings. Behaviours such as these have been reported in patients using other medicines for Parkinsons´s disease.
Your doctor may need to review your treatments.

Children and adolescents
Children and adolescents under the age of 18 years must not take this medicine. It has not been studied in these age groups since treatment of Parkinson's disease is not relevant in children and adolescents.

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

Tell your doctor if you are taking:
- medicines for depression or anxiety such as venlafaxine, maprotiline and desipramine. Taking Ongentys with these medicines may increase the risk of side effects. Your doctor may need to adjust your treatment;
- safinamide used for Parkinson's disease. There is no experience taking Ongentys and safinamide together. Your doctor may need to adjust your treatment;
- medicines to treat asthma such as rimiterole or isoprenaline. Ongentys may increase their effect;
- medicines used to treat allergic reactions such as adrenaline. Ongentys may increase their effect;
- medicines used to treat heart failure such as dobutamine, dopamine or dopexamine. Ongentys may increase their effects;
- medicines for high cholesterol such as rosuvastatin, simvastatin, atorvastatin or pravastatin Ongentys may increase their effects;
- medicines that affect the immune system such as methotrexate. Ongentys may increase its effect
- medicines containing quinidine, a medicine used to treat abnormal heart rhythms or malaria. Taking Ongentys and quinidine together, i.e. at the same time, may decrease the effect of Ongentys.

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

Ongentys is not recommended if you are pregnant. You should use effective contraception if you might become pregnant.

It is not known if Ongentys passes into breast milk in humans. Since the risk to the baby/infant cannot be excluded, you should stop breast-feeding during treatment with Ongentys.

Driving and using machines
Ongentys taken with levodopa may make you feel light-headed, dizzy, or sleepy.
Do not drive or operate machinery if you experience any of these side effects.

Ongentys contains lactose and sodium
- Lactose: If you have been told by your doctor that you have intolerance to some sugars, contact your doctor before taking this medicine.
- Sodium: This medicine contains less than 1 mmol sodium (23 mg) per capsule, that is to say essentially 'sodium-free'.

3. How to take Ongentys

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

The recommended dose is 50 mg once daily.

Ongentys should be taken preferably at bedtime.

Take Ongentys at least one hour before or after taking your levodopa medicine.

Doses of other medicines to treat Parkinson's disease
The dose of other medicines to treat Parkinson's disease may need to be adjusted when you start taking Ongentys. Follow the instructions that your doctor has given you.

Method of administration
Ongentys is for oral use.
Swallow the capsule whole with a glass of water.

If you take more Ongentys than you should
If you take more Ongentys than you should, tell your doctor or pharmacist, or go to a hospital immediately. Take the medicine package and this leaflet with you. This will help the doctor identify what you have taken.

If you forget to take Ongentys
If you forget to take one dose, you should continue the treatment and take the next dose as scheduled. Do not take a double dose to make up for a forgotten dose.

If you stop taking Ongentys
Do not stop taking Ongentys unless your doctor tells you to as your symptoms may get worse.
If you stop taking Ongentys your doctor may need to adjust the dose of other medicines that you are taking to treat Parkinson's disease.

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.

Side effects caused by Ongentys are usually mild to moderate and occur mostly within the first weeks of treatment. Some side effects may be caused by the increased effects of using Ongentys together with levodopa.

Contact your doctor straight away if you experience any side effects at the start of treatment. Many of the side effects can be managed by your doctor adjusting your levodopa medicine.

Tell your doctor as soon as possible if you notice any of the following side effects:

Very common: may affect more than 1 in 10 people
- involuntary and uncontrollable, or difficult or painful body movements

Common: may affect up to 1 in 10 people
- constipation
- dry mouth
- feeling sick (nausea)
- vomiting (being sick)

- increased levels of the enzyme (creatine kinase) in your blood
- muscle spasm
- dizziness
- headache
- sleepiness
- difficulty falling or staying asleep
- strange dreams
- experiencing or seeing things which do not exist (hallucinations)
- a fall in blood pressure on standing up which causes dizziness, light-headedness or fainting

Uncommon: may affect up to 1 in 100 people
- palpitations or irregular heartbeat
- blocked ear
- dry eye
- pain or swelling of the abdomen
- indigestion
- weight loss
- loss of appetite
- increased levels of triglycerides (fats) in your blood
- muscle twitching, stiffness or pain
- pain in arms or legs
- altered sense of taste
- excessive body movements
- fainting
- anxiety
- depression
- hearing things which do not exist
- feeling confused
- nightmares
- sleep disorder
- abnormal colour of urine
- need to wake and pass urine at night
- shortness of breath
- high or low blood pressure
- having falls
- feeling low in energy or tired

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 Ongentys

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/blister/carton after EXP. The expiry date refers to the last day of that month.

This medicine does not require any special temperature storage conditions.
Blisters: Store in the original blister in order to protect from moisture.
Bottles: Keep the bottle tightly closed in order to protect from moisture.

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 protect the environment.

6. Contents of the pack and other information

What Ongentys contains
- The active substance is opicapone. Each hard capsule contains 50 mg of opicapone.
- The other ingredients are:
  - capsule content: lactose monohydrate, sodium starch glycolate (Type A), pregelatinized maize starch and magnesium stearate
  - capsule shell: gelatine, indigo carmine aluminium lake (E 132), erythrosine (E 127) and titanium dioxide (E 171)
  - printing ink: shellac, titanium dioxide (E 171), propylene glycol, ammonia solution, concentrated, simeticone

What Ongentys looks like and contents of the pack
Ongentys 50 mg hard capsules are dark blue, approximately 19 mm length, with “OPC 50” and “Bial” printed on the capsules.

The capsules are packaged in bottles or blisters.

Bottles: 10, 30 or 90 capsules.
Blisters: 10, 30 or 90 capsules.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer
Bial - Portela & Cª., S.A.
À Av. da Siderurgia Nacional
4745-457 S. Mamede do Coronado
Portugal
tel: +351 22 986 61 00
fax: +351 22 986 61 90
e-mail: info@bial.com

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

België/Belgique/Belgien/
Deutschland/ Ελλάδα/France/
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Luxembourg/Luxemburg/
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Other sources of information

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

ANNEX IV

SCIENTIFIC CONCLUSIONS AND GROUNDS FOR THE VARIATION TO THE TERMS OF THE MARKETING AUTHORISATION(S)

Scientific conclusions

Taking into account the PRAC Assessment Report on the PSUR(s) for opicapone, the scientific conclusions of PRAC are as follows:

In view of available data on confusional state from clinical trials, spontaneous reports, including in some cases a close temporal relationship, a positive de-challenge and in view of a plausible mechanism of action, the PRAC considered that a causal relationship between opicapone and confusional state is at least a reasonable possibility. The PRAC concluded that the product information of products containing opicapone should be amended accordingly.

Having reviewed the PRAC recommendation, the CHMP agrees with the PRAC overall conclusions and grounds for recommendation.

Grounds for the variation to the terms of the marketing authorisation(s)

On the basis of the scientific conclusions for opicapone the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing opicapone is unchanged subject to the proposed changes to the product information

The CHMP recommends that the terms of the marketing authorisation(s) should be varied.