SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Cabergoline Aurobindo 0.5 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 0.5 mg of cabergoline.

Excipients with known effect: Each film-coated tablet contains 74.75 mg of lactose (as monohydrate).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet

White to off-white, capsule shaped, approximately 8mm x 4mm, flat faced, bevel edged, uncoated tablets debossed with 'C 0.5' on one side and break line on other side.
The tablet can be divided into equal doses.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Inhibition or suppression of postpartum lactation:
Cabergoline Aurobindo is indicated for the prevention of postpartum lactation immediately after delivery and for the suppression of ongoing lactation for medical reasons, such as:

- After delivery, when breastfeeding is contraindicated for mother- or child-related medical reasons.
- After stillbirth or abortion
- Hyperprolactinemia postpartum after a pregnancy following treatment with a dopamin-agonist

Treatment of hyperprolactinaemic disorders:
Cabergoline Aurobindo is indicated for the treatment of dysfunctions related to hyperprolactinaemia, such as amenorrhoea, oligomenorrhoea, anovulation and galactorrhoea. Cabergoline Aurobindo is indicated in patients with prolactin-secreting pituitary adenoma (micro- and macroprolactinoma), idiopathic hyperprolactinaemia or empty sella syndrome associated with hyperprolactinaemia.

4.2 Posology and method of administration

Posology

The maximum dose of 3 mg/day of Cabergoline Aurobindo must not be exceeded.

Inhibition of post-partum lactation:
Cabergoline Aurobindo should be administered during the first 24 hours post-partum. The recommended therapeutic dosage is 1 mg (2 tablets of 0.5 mg) Cabergoline Aurobindo given as a single dose.

Suppression of established postpartum lactation
The recommended therapeutic dosage regimen is 0.25 mg (one half of one 0.5 mg tablet) every 12 hours for two days (1 mg total dose). This dosage regimen has been demonstrated to be better tolerated than the single dose regimen in women electing to suppress lactation having a lower incidence of adverse events, in particular of hypotensive symptoms.

Treatment of hyperprolactinaemic disorders:

The recommended initial dosage is 0.5 mg Cabergoline Aurobindo per week given in one or two doses (e.g. on Monday and Thursday) per week. The weekly dose should be increased gradually, preferably by adding 0.5 mg Cabergoline Aurobindo per week at monthly intervals until an optimal therapeutic response is achieved.

The therapeutic dosage is usually 1 mg Cabergoline Aurobindo per week and ranges from 0.25 mg to 2 mg Cabergoline Aurobindo per week. Doses of up to 4.5 mg Cabergoline Aurobindo per week have been used in hyperprolactinaemic patients.

Depending to the patient's tolerability the weekly dose may be given as a single administration or divided into two or more doses per week. Division of the weekly dose into multiple administrations is advised when doses higher than 1 mg Cabergoline Aurobindo per week are to be given since the tolerability of doses greater than 1 mg Cabergoline Aurobindo taken as a single weekly dose has been evaluated only in a few patients.

Patients should be evaluated during dose escalation to determine the lowest dosage that produces the therapeutic response. Monitoring of serum prolactin levels at monthly intervals is advised since, once the effective therapeutic dosage regimen has been reached, serum prolactin normalisation is usually observed within two to four weeks.

After Cabergoline Aurobindo withdrawal, recurrence of hyperprolactinaemia is usually observed. However, persistent suppression of prolactin levels has been observed for several months in some patients. Of the group of women followed up, most had ovulatory cycles which continued for greater than 6 months after Cabergoline Aurobindo discontinuation.

Special populations
Elderly:
As a consequence of the indications for which Cabergoline Aurobindo is presently proposed, the experience in elderly is very limited. Available data do not indicate a special risk.

Patients with hepatic impairment
Cabergoline Aurobindo is not indicated in patients with severe hepatic impairment, see section 4.3, 4.4 and 5.2.

Patients with renal impairment
No change in dose is needed in patients with moderate to severe renal insufficiency.
Patients having end-stage renal failure or patients on haemodialysis should be treated with caution, as pharmacokinetics have not been studied, see section 4.4 and 5.2.

Paediatric population
The safety and efficacy of Cabergoline Aurobindo has not been established in subjects less than 16 years of age.

Method of administration
Cabergoline Aurobindo is to be administered by the oral route.

In order to reduce the risk of gastrointestinal undesirable effects it is recommended that Cabergoline Aurobindo is taken with meals for all therapeutic indications.

4.3 Contraindications

- Hypersensitivity to the active substance, any ergot alkaloid or to any excipient listed in section 6.1.
- Severe hepatic impairment, see section 4.2, 4.4 and 5.2
- Pre-eclampsia, eclampsia
- Post-partum hypertension or uncontrolled hypertension.
- History of pulmonary, pericardial and retroperitoneal fibrotic disorders.
- History of psychosis or risk of post-partum psychosis
- For long-term treatment: evidence of cardiac valvulopathy as determined by pre-treatment echocardiography (See section 4.4 Special warnings and precautions for use – Fibrosis and cardiac valvulopathy and possibly related clinical phenomena).

4.4 Special warnings and precautions for use

General:
Cabergoline should be given with caution to patients with severe cardiovascular disease, hepatic diseases (see section 4.2, 4.3 and 5.2), renal impairment (see section 4.2 and 5.2), hypotension, Raynaud's syndrome, peptic ulcer or gastrointestinal bleeding or with a history of serious, particularly psychotic, mental disorders.

Serious adverse events including hypertension, myocardial infarction, seizures, stroke or psychiatric disorders have been reported in postpartum women treated with cabergoline for inhibition of lactation. In some patients the development of seizures or stroke was preceded by severe headache and/or transient visual disturbances. Blood pressure should be carefully monitored during the treatment. If hypertension, suggestive chest pain, severe, progressive, or unremitting headache (with or without visual disturbances), or evidence of central nervous system toxicity develop, cabergoline should be discontinued and the patient evaluated promptly.

The effects of alcohol on overall tolerability of cabergoline are currently unknown.

Postural Hypotension:
Postural hypotension can occur following administration of cabergoline. Care should be exercised when administering cabergoline concomitantly with other drugs known to lower blood pressure.

Fibrosis and cardiac valvulopathy and possibly related clinical phenomena:
Fibrotic and serosal inflammatory disorders such as pleuritis, pleural effusion, pleural fibrosis, pulmonary fibrosis, pericarditis, pericardial effusion, cardiac valvulopathy involving one or more valves (aortic, mitral and tricuspid) or retroperitoneal fibrosis have occurred after prolonged usage of ergot derivatives with agonist activity at the serotonin 5HT2B receptor, such as cabergoline. In some cases, symptoms or manifestations of cardiac valvulopathy improved after discontinuation of cabergoline.

Erythrocyte sedimentation rate (ESR) has been found to be abnormally increased in association with pleural effusion/fibrosis. Chest x-ray examination is recommended in cases of unexplained ESR increases to abnormal values.

Valvulopathy has been associated with cumulative doses, therefore, patients should be treated with the lowest effective dose. At each visit, the risk benefit profile of cabergoline treatment for the patient should be reassessed to determine the suitability of continued treatment with cabergoline.

Before initiating long-treatment:
All patients should undergo a cardiovascular evaluation, including echocardiogram, to assess the potential presence of asymptomatic valvular disease. It is also appropriate to perform baseline investigations of erythrocyte sedimentation rate or other inflammatory markers, lung function/chest x-ray and renal function prior to initiation of therapy.

In patients with valvular regurgitation, it is not known whether cabergoline treatment might worsen the underlying disease. If fibrotic valvular disease is detected, the patient should not be treated with cabergoline. (See Section 4.3 Contraindications).

During long-term treatment:

Fibrotic disorders can have an insidious onset and patients should be regularly monitored for possible manifestations of progressive fibrosis. Therefore, during treatment, attention should be paid to the signs and symptoms of:

- Pleuro-pulmonary disease such as dyspnoea, shortness of breath, persistent cough or chest pain.
- Renal insufficiency or ureteral/abdominal vascular obstructions that may occur with pain in the loin/flank and lower limb oedema as well as any possible abdominal masses or tenderness that may indicate retroperitoneal fibrosis.
- Cardiac failure; cases of valvular and pericardial fibrosis have often manifested as cardiac failure. Therefore, valvular fibrosis (and constrictive pericarditis) should be excluded if such symptoms occur.

Clinical diagnostic monitoring for development of fibrotic disorders, as appropriate, is essential. Following treatment initiation, the first echocardiogram must occur within 3-6 months, thereafter, the frequency of echocardiographic monitoring should be determined by appropriate individual clinical assessment with particular emphasis on the above-mentioned signs and symptoms, but must occur at least every 6 to 12 months.

Cabergoline should be discontinued if an echocardiogram reveals new or worsened valvular regurgitation, valvular restriction or valve leaflet thickening (see section 4.3 Contraindications).

The need for other clinical monitoring (e.g. physical examination including, cardiac auscultation, X-ray, CT scan) should be determined on an individual basis.

Additional appropriate investigations such as erythrocyte sedimentation rate, and serum creatinine measurements should be performed if necessary to support a diagnosis of a fibrotic disorder.

Hypotension:
Symptomatic hypotension can occur within 6 hours following administration of cabergoline: particular attention should be paid when administering cabergoline concomitantly with other medicinal product known to lower blood pressure. Because of its elimination half-life hypotensive effects may persist for a few days after cessation of therapy. Monitoring of treatment with regular checks of blood pressure is recommended in the first 3-4 days after initiation of treatment.

Low blood pressure (≥ 20 mmHg systolic and ≥ 10 mmHg diastolic) has been reported in the 3-4 days following a single dose of 1 mg cabergoline in post-partum studies. The undesirable effects generally occur in the first two weeks, and then decline or disappear. 3% of the patients had their treatment discontinued on account of the undesirable effects.

Somnolence/Sudden Sleep Onset:
Cabergoline has been associated with somnolence. Dopamine agonists can be associated with sudden sleep onset episodes in patients with Parkinson's disease. A reduction of dosage or termination of reatment may be considered (See section 4.7 Effects on ability to drive and use machines).

Psychiatric:
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 including cabergoline. Dose reduction/tapered discontinuation should be considered if such symptoms develop.

Inhibition/suppression of physiologic lactation:
As with other ergot derivatives, cabergoline should not be used in women with pregnancy induced hypertension, for example, preeclampsia or post-partum hypertension.

A single dose of 0.25 mg of cabergoline should not be exceeded in nursing women treated for suppression of established lactation to avoid potential postural hypotension. (See section 4.2 Posology and method of administration – Inhibition/suppression of physiologic lactation and subsection above – Postural hypotension).

Treatment of hyperprolactinaemic disorders:
Because hyperprolactinaemia accompanied with amenorrhoea/galactorrhea and infertility may be associated with pituitary tumour, a complete evaluation of the pituitary is indicated before treatment with cabergoline is initiated.

Cabergoline restores ovulation and fertility in women with hyperprolactinemic hypogonadism.

Before administration of cabergoline, pregnancy should be excluded. Because clinical experience is still limited and the product has a long half-life, as a precautionary measure it is recommended that once regular ovulatory cycles have been achieved women seeking pregnancy discontinue cabergoline one month before intended conception.

Because pregnancy might occur prior to reinitiation of menses, a pregnancy test is recommended at least every 4 weeks during the amenorrheic period and, once menses are reinitiated, every time a menstrual period is delayed by more than 3 days. Women should be advised to use mechanical contraception during treatment with cabergoline and for at least one month after discontinuation of cabergoline. As a precautionary measure, women who become pregnant should be monitored to detect signs of pituitary enlargement since expansion of pre-existing pituitary tumors may occur during gestation.

Monitoring of serum prolactin levels at monthly intervals is advised since, once the effective therapeutic dosage regimen has been reached, serum prolactin normalisation is usually observed within two to four weeks.

After cabergoline withdrawal, recurrence of hyperprolactinaemia is usually observed. However, persistent suppression of prolactin levels has been observed for several months in some patients.

Renal insufficiency:
The pharmacokinetics of cabergoline has not been studied in patients having end-stage renal failure, or in patients on haemodialysis; these patients should be treated with caution.

Lactose:
Cabergoline Aurobindo contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant use not recommended:

No information is available about interaction between cabergoline and other ergot alkaloids; therefore the concomitant use of these medications during long-term treatment with cabergoline is not recommended.

Since cabergoline exerts its therapeutic effect by direct stimulation of dopamine receptors, it should not be concurrently administered with drugs that have dopamine antagonist activity (such as phenothiazines, butyrophenones, thioxanthenes, metoclopramide) since these might reduce the prolactin-lowering effect of cabergoline.

As with other ergot derivatives, cabergoline should not be used with macrolide antibiotics (e.g. erythromycin) due to increased systemic bioavailability of cabergoline.

Interactions with other medicinal products that reduce blood pressure should be taken into consideration.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no adequate and well-controlled studies from the use of cabergoline in pregnant women. Animal studies have not demonstrated teratogenic effects, but reduced fertility and embryo-toxicity were observed in association with pharmacodynamic activity (see section 5.3).

In a twelve year observational study on pregnancy outcomes following cabergoline therapy, information is available on 256 pregnancies. Seventeen of these 256 pregnancies (6.6%) eventuated in major congenital malformations or abortion. Information is available on 23/258 infants who had a total of 27 neonatal abnormalities, both major and minor. Musculoskeletal malformations were the most common neonatal abormality (10), followed by cardiopulmonary abnormalities (5). There is no information on perinatal disorders or long-term development of infants exposed to intra-uterine cabergoline. Based on recent published literature, the prevalence of major congenital malformations in the general population has been reported to be 6.9% or greater. Rates of congenital abnormality vary between different populations. It is not possible to accurately determine if there is an increased risk as no control group was included.

Cabergoline should only be used during pregnancy if clearly indicated and after an accurate benefit/risk evaluation. (See section “Special warning and precautions for use” – Treatment of Hyperprolactinemic Disorders).

Due to the long half-life of the drug and limited data on in utero exposure, women planning to become pregnant should discontinue cabergoline one month before intended conception. If conception occurs during therapy, treatment should be discontinued as soon as pregnancy is confirmed to limit foetal exposure to the drug.

Contraception should be continued for at least 4 weeks after stopping cabergoline.

Breast feeding
In rats, cabergoline and/or its metabolites are excreted in milk.No information is available on the excretion in breast milk in humans; however, mothers should be advised not to breast-feed in case of failed lactation inhibition/suppression by cabergoline.Since it prevents lactation, cabergoline should not be administered to mothers with hyperprolactinemic disorders who wish to breast-feed their infants.

Fertility
Cabergoline restores ovulation and fertility in women with hyperprolactinaemic hypogonadism: since pregnancy might occur prior to reinitiation of menses, pregnancy testing is recommended as appropriate during the amenorrhoeic period and, once menses are reinitiated, every time a menstrual

period is delayed by more than three days. Women not seeking pregnancy should be advised to use effective non-hormonal contraception during treatment and after cabergoline withdrawal. Because of limited experience on the safety of foetal exposure to cabergoline, it is advisable that women seeking pregnancy conceive at least one month after cabergoline discontinuation. As a precautionary measure, women who become pregnant should be monitored to detect signs of pituitary enlargement since expansion of pre-existing pituitary tumours may occur during gestation.

4.7 Effects on ability to drive and use machines

Patients should be careful when performing actions which require fast and accurate reaction during treatment initiation.

Patients treated with cabergoline and presenting with somnolence and/or sudden sleep episodes must be informed to refrain from driving or engaging in activities where impaired alertness may put themselves or others at risk of serious injury or death (e.g., operating machines) until such episodes and somnolence have resolved (see section 4.4 Special warnings and precautions for use Somnolence/sudden sleep onset).

4.8 Undesirable effects

The undesirable effects are usually dose-dependent, and can be reduced by decreasing the dose gradually.

Inhibition of lactation: Approximately 14% of the patients experience undesirable effects. The most common are low blood pressure (12%), dizziness (6%) and headaches (5%). Long-term treatment increases the frequency of undesirable effects to approximately 70%.

The following undesirable effects have been observed and reported during treatment with cabergoline with the following frequencies: 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).

MedDRA System Organ Class	**Frequency**	**Undesirable Effects**
Immune system disorders	Uncommon	Hypersensitivity reaction
Psychiatric disorders	Common	Depression, sleep disorders
	Uncommon	Increased libido
	Not Known	Aggression, delusions, hypersexuality, pathological gambling, psychotic disorder, hallucinations
Nervous system disorders	Very Common	Headache*, dizziness/vertigo*
	Common	somnolence
	Uncommon	Transient hemianopsia, syncope, paraesthesia
	Not Known	Sudden sleep onset, tremor
Eye disorders	Not Known	Visual impairment
Cardiac disorders	Very Common	Valvulopathy (including regurgitation) and related disorders (pericarditis and pericardial effusion)
	Uncommon	Palpitations
	Not Known	Angina pectoris
Vascular disorders	Common	Cabergoline generally exerts a hypotensive effect in patients on long-term treatment; Postural hypotension, hot flushes**
	Uncommon	Digital vasospasm, fainting
Respiratory, thoracic and mediastinal disorders	Uncommon	Dyspnoea, pleural effusion, fibrosis, (including pulmonary fibrosis), epistaxis
	Very rare	Pleural fibrosis

	Not Known	Respiratory disorder, respiratory failure, pleuritis chest pain
Gastrointestinal disorders	Very Common	Nausea*, dyspepsia, gastritis, abdominal pain*
	Common	Constipation, vomiting**
	Rare	Epigastric pain
Hepato-biliary disorders	Not Known	Hepatic function abnormal
Skin and subcutaneous tissue disorders	Uncommon	Rash, alopecia
Musculoskeletal and connective tissue disorders	Uncommon	Leg cramps
Reproductive system and breast disorders	Common	Breast pain
General disorders and administration site conditions	Very Common	Asthenia***, fatigue
	Uncommon	Oedema, peripheral oedema
Investigations	Common	Asymptomatic decreases in blood pressure (≥ 20 mmHg systolic and ≥ 10 mmHg diastolic)
	Uncommon	A decrease in haemoglobin values have been observed in amenhorrheic women during the first few months after menses.
	Not Known	Blood creatinine phosphokinase increased, liver function tests abnormal

*Very common in patients treated for hyperprolactinaemin disorders; Common in patients treated for inhibition/suppression of lactation
** Common in patients treated for hyperprolactinaemic disorders; Uncommon in patients treated for inhibition/suppression of lactation
*** Very common in patients treated for hyperprolactinaemic disorders; Uncommon in patients treated for inhibition/suppression of lactation

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 including Cabergoline Aurobindo (see section 4.4 Special warnings and precautions for use).

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

Symptoms of overdose would likely be those of over-stimulation of dopamine receptors, eg, nausea, vomiting, gastric complaints, postural hypotension, reduced blood pressure, confusion/psychosis or hallucinations.

Supportive measures should be taken to remove unabsorbed drug and maintain blood pressure, if necessary.In addition, the administration of dopamine antagonist drugs may be advisable.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Prolactin inhibitor ATC code: G02CB03

Cabergoline is a dopaminergic ergoline derivative endowed with a potent and long-lasting PRL-lowering activity. It acts by direct stimulation of the D2-dopamine receptors on pituitary lactotrophs, thus inhibiting PRL secretion. In rats the compound decreases PRL secretion at oral doses of 3-25 µg/kg, and in vitro at a concentration of 45 pg/ml. In addition, Cabergoline exerts a central dopaminergic effect via D2 receptor stimulation at oral doses higher than those effective in lowering serum PRL levels.

The long-lasting PRL-lowering effect of cabergoline is probably due to its long persistence in the target organ as suggested by the slow elimination of total radioactivity from the pituitary after a single oral dose in rats (t1/2 of approximately 60 hours).

The pharmacodynamic effects of cabergoline have been studied in healthy volunteers, puerperal women and hyperprolactinaemic patients. After a single oral administration of cabergoline (0.3 – 1.5 mg), a significant decrease in serum PRL levels was observed in each of the populations studied. The effect is prompt (within 3 hours from administration) and persistent (up to 7 – 28 days in healthy volunteers and hyperprolactinaemic patients, and up to 14 – 21 days in puerperal women). The PRL-lowering effect is dose-related both in terms of degree of effect and duration of action.

With regard to the endocrine effects of cabergoline not related to the antiprolactinaemic effect, available data from humans confirm the experimental findings in animals indicating that the test compound is endowed with a very selective action with no effect on basal secretion of other pituitary hormones or cortisol.

The pharmacodynamic actions of cabergoline not correlated with the therapeutic effect only relate to blood pressure decrease. The maximal hypotensive effect of cabergoline as single dose usually occurs during the first 6 hours after active substance intake and is dosedependent both in terms of maximal decrease and frequency.

5.2 Pharmacokinetic properties

Absorption
After oral administration cabergoline is rapidly absorbed from the gastrointestinal tract as the peak plasma concentration is received within 0.5 to 4 hours.

Food does not appear to affect absorption and disposition of cabergoline.

Distribution
"In-vitro" experiments showed that cabergoline at concentrations of 0.1 – 10 ng/ml is 41-42% bound to plasma proteins.

Biotransformation
In urine, the main metabolite identified is 6-allyl-8ß-carboxy-ergoline, which accounts for 4-6% of the dose. Three additional metabolites are identified in urine, which account overall for less than 3% of the dose. The metabolites have been found to be much less potent than cabergoline in inhibiting prolactin secretion "in-vitro".

Elimination
The elimination half-life of cabergoline, is long; (63-68 hours in healthy volunteers and 79-115 hours in hyperprolactinaemic patients.

On the basis of the elimination half-life, steady state conditions should be achieved after 4 weeks, as confirmed by the mean peak plasma levels of cabergoline obtained after a single dose (37 ± 8 pg/ml) and after a 4 week multiple-regimen (101 ± 43 pg/ml) for 0.5mg cabergoline dose.

Ten days after administration about 18% and 72% of the dose is recovered in urine and faeces, respectively. Unchanged cabergoline in urine accounts for 2-3% of the dose.

Linearity/Non-linearity
The pharmacokinetic profile is linear up to 7 mg per day.

Hepatic impairment
Compared to normal volunteers and those with lesser degrees of hepatic insufficiency, an increase in AUC has been seen in patients with severe hepatic insufficiency (Child-Pugh Class C) who received a single 1 mg dose. See section 4.2, 4.3 and 4.4.

Renal impairment
No overall differences in the pharmacokinetics of cabergoline were observed in moderate to severe renal disease. The pharmacokinetics of cabergoline has not been studied in patients having end-stage renal failure or in patients on haemodialysis; see section 4.2 and 4.4.

5.3 Preclinical safety data

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

There were maternotoxic effects but no teratogenic effects in mice given cabergoline at doses up to 8 mg/kg/day (approximately 55 times the maximum recommended human dose) during the period of organogenesis.

A dose of 0.012 mg/kg/day (approximately 1/7 the maximum recommended human dose) during the period of organogenesis in rats caused an increase in post-implantation embryo foetal losses. These losses could be due to the prolactin inhibitory properties of cabergoline in rats. At daily doses of 0.5 mg/kg/day (approximately 19 times the maximum recommended human dose) during the period of organogenesis in the rabbit, cabergoline caused maternotoxicity characterized by a loss of body weight and decreased food consumption. Doses of 4 mg/kg/day (approximately 150 times the maximum recommended human dose) during the period of organogenesis in the rabbit caused an increased occurrence of various malformations. However, in another study in rabbits, no treatment-related malformations or embryofoetotoxicity were observed at doses up to 8 mg/kg/day (approximately 300 times the maximum recommended human dose).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Leucine
Lactose monohydrate
Magnesium stearate

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store in the original package in order to protect from light.

6.5 Nature and contents of container

Cabergoline Aurobindo tablets are available in white opaque round HDPE container closed with white opaque polypropylene child resistant closure. Each HDPE container contains a desiccant sachet/canister with silica gel, which should not be swallowed.

HDPE container: 2 & 8 tablets

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Aurobindo Pharma (Malta) Limited,
Vault 14, Level 2, Valleta Waterfront,
Floriana, FRN 1913,
Malta

8. MARKETING AUTHORISATION NUMBER(S)

MA807/11101

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

25th September 2023

10. DATE OF REVISION OF THE TEXT