PRODUCT NAME:	CABERGOLINE TABLETS BP 0.5 MG

MODULE 1 - ADMINISTRATIVE AND PRODUCT INFORMATION

1.3.1 Summary of Product Characteristics (SmPC)

1. Name of drug product

CABERGOLINE TABLETS BP 0.5 MG

1.1 (Trade) name of product

CABERGOLINE TABLETS BP 0.5 MG

1.2 Strength

Composition:

Each Uncoated tablet contains:

Cabergoline BP ..... 0.5 mg

Excipients… ..... Q.S.

Colour: Titanium Dioxide

1.3 Pharmaceutical Dosage Form

Oral solid

PRODUCT NAME:	CABERGOLINE TABLETS BP 0.5 MG

MODULE 1 - ADMINISTRATIVE AND PRODUCT INFORMATION

2. Qualitative & Quantitative Composition

2.1 Qualitative Declaration

Composition:

Each Uncoated tablet contains:

Cabergoline BP ..... 0.5 mg

Excipients… ..... Q.S.

Colour: Titanium Dioxide

2.2 Quantitative Declaration

Batch Formula:

Batch Size: 1,00,000 tablets

Sr. No.	Ingredients	Specifications	Reason For Inclusion	Label Claim	Overages (%)	Quantity/ Unit (mg)	Quantity/ Batch (kg)
1.	Cabergoline	BP	Active	0.5 mg	---	0.500	0.050
2.	L -Leucine	BP	Lubricant	---	---	7.100	0.710
3.	Cross Carmellose Sodium	BP	Disintegrant	---	---	16.000	1.600
4.	Avicel 112	BP	Disintegrant	---	---	44.000	4.000
5.	Lactose Anhydrous	BP	Diluent	---	---	99.000	9.900
6.	Magnesium stearate	BP	Lubricant	---	---	1.200	0.120
7.	Aerosil	BP	Lubricant	---	---	1.200	0.120
8.	HPMC	BP	Matrix polymer	---	---	2.000	0.200

MODULE 1 - ADMINISTRATIVE AND PRODUCT INFORMATION

3. Pharmaceutical Dosage Form

Oral solid

4. Clinical Particulars

4.1 Therapeutic Indications

Cabergoline is indicated for the inhibition of physiological lactation soon after delivery and for suppression of already established lactation:

1. After parturition, when the mother elects not to breast feed the infant or when breast feeding is contraindicated due to medical reasons related to the mother or the new-born.
2. After stillbirth or absorption.

Cabergoline prevents/suppresses physiological lactation by inhibiting prolactin secretion.

In controlled clinical trials, cabergoline given as a single 1 mg administration during the first day post-partum, was effective inhibiting milk secretion, as well as breast engorgement and pain in 90% of the women. Less than 5% of women experienced rebound breast symptomatology during the third post-partum week (which was usually mild in severity).

Suppression of milk secretion and relief of breast engorgement and pain are obtained in approximately 85% of nursing women treated with a total dose of 1 mg cabergoline given in four divided deses over two days. Rebound breast symptomatology after day 10 is uncommon (approximately 2% of cases).

Treatment of hyperprolactinaemic disorders

Cabergoline is indicated for the treatment of dysfunctions associated with hyperprolactinaemia, including amenorrhoea, oligomenorrhoea, anovulation and galactorrhoea. Cabergoline is indicated in patients with prolactin-secreting pituitary adenomas (micro and macroprolactinomas), idiopathic hyperprolactinaemia, which represent the basic underlying pathologies contributing to the above clinical manifestations.

On chronic therapy, cabergoline at doses ranging between 1 and 2 mg per week, was effective in normalizing serum prolactin level in approximately 84% of hyperprolactinaemic patients. Regular cycles were resumed in 83 % of previously amennorhoeic women. Restoration of ovulation was

document in 89% of women with progesterone levels monitored during the luteal phase. Galactorrhoea disappeared in 90% of cases showing this symptom before therapy. Reduction in tumour size was obtained in 50-90% of female and male patients with micro or macroprolactinima.

4.2 Posology and Method of Administration

Cabergoline is to be administered by the oral route. In clinical studies, cabergoline has been mainly administered with food and since the tolerability of this class of compounds is improved with food, it is recommended that cabergoline is preferably taken with meals for all the therapeutic indications.

Treatment of Hyperprolactinaemic disorders:

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

The therapeutic dosage is usually 1 mg per week and ranges from 0.25 mg to 2 mg per week. Doses of up to 4.5 mg per week have been used in hyperprolactinaemic patients. The maximum dose on any one day should not exceed 3 mg.

The weekly dose may be given as a single administration or divided into two or more doses per week according to patient tolerability. Division of the weekly dose into multiple administrations is advised when doses higher than 1 mg per week are to be given since the tolerability of doses greater than 1 mg 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 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 discontinuation.

For inhibition of puerperal lactation:

Cabergoline should be administered during the first day post-partum. The recommended therapeutic dosage is 1 mg (two 0.5 mg tablets) given as a single dose.

For suppression of established 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. **Paediatric population:**

The safety and efficacy of cabergoline has not been established in subjects less than 16 years of age. **Use in the elderly:**

As a consequence of the indications for which cabergoline is presently proposed, the experience in elderly is very limited. Available data do not indicate a special risk

4.3 Contraindications

Hypersensitivity to cabergoline or to any of the excipients listed in section 6.1 or any ergot alkaloid.

Cabergoline is contraindicated in patients with hepatic insufficiency and with toxaemia of pregnancy.

History of pulmonary, pericardial and retroperitoneal fibrotic disorders.

For long-term treatment: Evidence of cardiac valvulopathy as determined by pre-treatment echocardiography. (See section 4.4)

Cabergoline should not be co-administered with anti-psychotic medications or administered to women with a history of puerperal psychosis.

4.4 Special Warnings and Precautions for Use

MODULE 1 - ADMINISTRATIVE AND PRODUCT INFORMATION

The safety and efficacy of cabergoline have not yet been established in patients with renal and hepatic disease. As with other ergot derivatives, cabergoline should be given with caution to patients with severe cardiovascular disease, Raynaud's syndrome, renal insufficiency, peptic ulcer or gastrointestinal bleeding, or with a history of serious, particularly psychotic, mental disorders. Ken when patients are taking concomitant psychoactive medication.

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Symptomatic hypotension can occur with cabegoline administration for any indication. Car should be exercised when administering cabergoline concomitantly with other drugs known to lower blood pressure.

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

Before cabergoline administration, pregnancy should be excluded and after treatment pregnancy should be prevented for at least one month.

4.5 Interaction with other medicinal products and other forms of interaction

The concomitant use of other drugs during early puerperium, particularly of ergot alkaloids, was not associated with detectable interactions modifying the efficacy and safety of cabergoline.

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 which 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.

4.6 Fertility, pregnancy and lactation

MODULE 1 - ADMINISTRATIVE AND PRODUCT INFORMATION

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 abnormality (10), followed by cardio-pulmonary 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 accuratebenefit/risk evaluation. (see section 4.4).

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.

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.

4.7 Effects on ability to drive and operate machine

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

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Patients being treated with cabergoline and presenting with somnolence 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).

4.8 Undesirable effects

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**
Cardiac disorders	Very Common	Valvulopathy (including regurgitation) and related disorders (pericarditis and pericardial effusion)
	Uncommon	Palpitations
	Not Known	Angina pectoris
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
Immune system disorders	Uncommon	Hypersensitivity reaction
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
Psychiatric disorders	Common	Depression
	Uncommon	Increased libido
	Not Known	Aggression, delusions, hypersexuality, pathological gambling, psychotic disorder, hallucinations
Vascular disorders	Common	Cabergoline generally exerts a hypotensive effect in patients on long-term treatment; Postural hypotension, hot flushes**
	Uncommon	Digital vasospasm, fainting
Gastrointestinal disorders	Very common	Nausea*, dyspepsia, gastritis, abdominal pain*

	Common	Constipation, vomiting**
	Rare	Epigastric pain
General disorders and administration site conditions	Very Common	Asthenia***, fatigue
	Uncommon	Oedema, peripheral oedema
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
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

4.9 Overdose

Symptoms of overdose would likely be those of over-stimulation of dopamine receptors, e.g. nausea, vomiting, gastric complaints, postural hypotension, 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 Pharmacodynamics property

Pharmacotherapeutic group: histamine H2 receptor antagonist

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 mcg/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 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 persisten (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 effect of cabergoline not related to 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 drug intake and is dose dependent both in term of maximal decrease and frequency.

5.2 Pharmacokinetic properties

The pharmacokinetic and metabolic profiles of cabergoline have been have been studied in healthy volunteers of both sexes and in female hyperprolactinaemic patients.

After oral administration of the labelled compound, radioactivity was rapidly absorbed from the gastrointestinal tract as the peak of radioactivity in plasma was between 0.5 and 4 hours.

Ten days after administration about 18% and 72% of the radioactivity dose was recovered in urine and faeces, respectively. Unchanged drug in urine accounted for 2-3 of the dose.

In urine, the main metabolite identified was 6-allyl-8β-carboxy-ergoline, which accounted for 4-6% of the dose. Three additional metabolites were identified in urine, which accounted 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. Cabergoline biotransformation was also studied in plasma

of healthy male volunteers treated with [14C]- cabergoline: a rapid and extensive biotransformation of cabergoline was shown.

The low urinary excretion of unchanged cabergoline has been confirmed also in studied with non-radioactive product. The elimination half-life of cabergoline, estimated from urinary excretion rates, is long (63-68 hours in healthy volunteers (using a radio-immuno assay), 79-115 hours in hyperprolactinaemic patients (using a HPLC method).

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

In vitro experiments showed that the drug at concentrations of 0.1-10 ng/ml is 41-42% bound to plasma proteins. Food does not appear to affect absorption and disposition of cabergoline.

5.3 Preclinical safety data

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).

PRODUCT NAME:	CABERGOLINE TABLETS BP 0.5 MG

MODULE 1 - ADMINISTRATIVE AND PRODUCT INFORMATION

6. Pharmaceutical particulars

6.1 List of excipients

L -Leucine

Cross Carmellose Sodium

Avicel 112

Lactose Anhydrous

Magnesium stearate

Aerosil

HPMC

6.2 Incompatibilities

Not Applicable.

6.3 Shelf-Life

36 Months

6.3 Special Precautions for Storage

Do not store above 30°C. Keep vials in the outer carton in order to protect from light.

6.4 Nature and Contents of Container

2 Tablets pack in ALU/ALU Blister. Such 4 Blister packed in a carton along with package insert.

PRODUCT NAME:	CABERGOLINE TABLETS BP 0.5 MG

MODULE 1 - ADMINISTRATIVE AND PRODUCT INFORMATION

7. Marketing authorisation holder

RESTORE HEALTHCARE LTD

99 PORT HARCOURT' ROAD FEGGE

ONITSHA ANAMBRA STATE NIGERIA.

8. Marketing authorisation number(s)

9. Date of first authorisation/renewal of the authorisation

10. Date of revision of the text

PRODUCT NAME:	CABERGOLINE TABLETS BP 0.5 MG

MODULE 1 - ADMINISTRATIVE AND PRODUCT INFORMATION

For the use of a medical practitioner, hospital or a laboratory

Carefully read the accompanying instructions before use. If necessary, ask your physician for further information

COMPOSITION:
Each uncoated tablet contains:

Cabergoline B.P. 0.5 mg

THERAPEAUTIC INDICATIONS :

Cabergoline is indicated for the inhibition of physiological lactation soon after delivery and for suppression of already established lactation:
1. After parturition, when the mother elects not to breast feed the infant or when breast feeding is contraindicated due to medical reasons related to the mother or the new-born.
2. After stillbirth or abortion.

Cabergoline prevents/suppresses physiological lactation by inhibiting prolactin secretion.

In controlled clinical trials, cabergoline given as a single 1 mg administration during the first day post-partum, was effective inhibiting milk secretion, as well as breast engorgement and pain in - 90% of the women. Less than 5% of women experienced rebound breast symptomatology during the third post-partum week (which was usually mild in severity).

Suppression of milk secretion and relief of breast engorgement and pain are obtained in approximately 85% of nursing women treated with a total dose of 1 mg cabergoline given in four divided doses over two days. Rebound breast symptomatology after day 10 is uncommon (approximately 2% of cases).

Treatment of hyperprolactinaemic disorders

Cabergoline is indicated for the treatment of dysfunctions associated with hyperprolactinaemia, including amenorrhoea, oligomenorrhoea, anovulation and galactorrhoea. Cabergoline is indicated in patients with prolactin-secreting pituitary adenomas (micro- and macroprolactinomas), idiopathic hyperprolactinaemia, or empty sella syndrome with associated hyperprolactinaemia, which represent the basic underlying pathologies contributing to the above clinical manifestations.

On chronic therapy, cabergoline at doses ranging between 1 and 2 mg per week, was effective in normalising serum prolactin levels in approximately 84% of hyperprolactinaemic patients. Regular cycles were resumed in 83% of previously amennorhoeic women. Restoration of ovulation was documented in 89% of women with progesterone levels monitored during the luteal phase. Galactorrhoea disappeared in 90% of cases showing this symptom before therapy. Reduction in tumour size was obtained in 50 - 90% of female and male patients with micro- or macroprolactinoma.

CONTRAINDICATIONS:

Hypersensitivity to cabergoline, any of the excipients listed in section 6.1 or any ergot alkaloid.

History of pulmonary, pericardial and retroperitoneal fibrotic disorders.

Cabergoline is contraindicated in patients with hepatic insufficiency and with toxaemia of pregnancy. Cabergoline should not be co-administered with anti-psychotic medications or administered to women with a history of puerperal psychosis.

For long-term treatment: Evidence of cardiac valvulopathy as determined by pre-treatment echocardiography.

SPECIAL WARNINGS AND PRECAUTION FOR USE :

The safety and efficacy of cabergoline have not yet been established in patients with renal and hepatic disease. As with other ergot derivatives, cabergoline should be given with caution to patients with severe cardiovascular disease, Raynaud's syndrome, renal insufficiency, peptic ulcer or gastrointestinal bleeding, or with a history of serious, particularly psychotic, mental disorders. Particular care should be ken when patients are taking concomitant psychoactive medication.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Symptomatic hypotension can occur with cabergoline administration for any indication. Care should be exercised when administering cabergoline concomitantly with other drugs known to lower blood pressure.

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

Before cabergoline administration, pregnancy should be excluded and after treatment pregnancy should be prevented for at least one month.

PHARMACOKINETIC PROPERTIES :

The pharmacokinetic and metabolic profiles of cabergoline have been studied in healthy volunteers of both sexes and in female hyperprolactinaemic patients.

After oral administration of the labelled compound, radioactivity was rapidly absorbed from the gastrointestinal tract as the peak of radioactivity in plasma was between 0.5 and 4 hours.

Ten days after administration about 18% and 72% of the radioactive dose was recovered in urine and faeces, respectively. Unchanged drug in urine accounted for 2-3% of the dose.

In urine, the main metabolite identified was 6-allyl-8β-carboxy-ergoline, which accounted for 4-6% of the dose. Three additional metabolites were identified in urine, which accounted 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*. Cabergoline biotransformation was also studied in plasma of healthy male volunteers treated with [^{14}C]-cabergoline: a rapid and extensive biotransformation of cabergoline was shown.

The low urinary excretion of unchanged cabergoline has been confirmed also in studies with non-radioactive product. The elimination half-life of cabergoline, estimated from urinary excretion rates, is long (63-68 hours in healthy volunteers (using a radio-immuno assay), 79-115 hours in hyperprolactinaemic patients (using a HPLC method).

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).

In vitro experiments showed that the drug at concentrations of 0.1-10 ng/ml is 41-42% bound to plasma proteins. Food does not appear to affect absorption and disposition of cabergoline.

PHARMACODYNAMIC PROPERTIES :

Cabergoline is a dopaminergic ergoline derivative endowed with a potent and long-lasting PRL-lowering activity. It acts by direct stimulation of the D_2-dopamine receptors on pituitary lactotrophs, thus inhibiting PRL secretion. In rats the compound decreases PRL secretion at oral doses of 3-25 mcg/kg, and *in-vitro* at a concentration of 45 pg/ml. In addition, cabergoline exerts a central dopaminergic effect via D_2 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 single oral dose in rats ($t_{½}$ 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 drug intake and is dose-dependent both in terms of maximal decrease and frequency.

OVERDOSE:

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

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

STORAGE CONDITIONS:

Store at room temperature protech from light & Moisture

PRESENTATION: 2 Tablets

SPECIFICATION: BP

KEEP OUT OF REACH OF CHILDREN.

Neutral Code : HP/06/200

Mfd. in India by: Alliaance Biotech
(WHO-GMP Certified, An ISO 9001:2015 Co.)
440/3, Vill. Katha, Baddi, Solan (H.P.) - 173 205