CABERGOLINE- cabergoline tablet
Teva Pharmaceuticals USA, Inc.

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use CABERGOLINE TABLETS safely and effectively. See full prescribing information for CABERGOLINE TABLETS.

CABERGOLINE tablets, for oral use
Initial U.S. Approval: 1996

RECENT MAJOR CHANGES

Indications and Usage (1)	4/2025
Warnings and Precautions, Cardiac Valvulopathy and Pericardial Fibrosis (5.1)	4/2025
Warnings and Precautions, Risks with Use of cabergoline tablets for Postpartum Lactation Inhibition or Suppression (5.4)	4/2025

INDICATIONS AND USAGE

Cabergoline tablets are an ergot derivative indicated for the treatment of hyperprolactinemic disorders, either idiopathic or due to pituitary adenomas in adults. (1)

Limitations of Use
Avoid use of cabergoline tablets for the inhibition or suppression of postpartum physiologic lactation because of the risk of serious adverse reactions. (5.4)

DOSAGE AND ADMINISTRATION

- Before initiating cabergoline tablets evaluate for valvular heart disease, including with an echocardiogram. If valvular disease is detected, do not administer cabergoline tablets. (2.1)
- Recommended starting dosage of cabergoline tablets is 0.25 mg orally twice weekly. (2.2)
- Titrate cabergoline tablets to achieve normal serum prolactin levels by increasing cabergoline tablets by 0.25 mg orally twice weekly at intervals of no less than 4 weeks. (2.2)
- Maximum recommended dosage is 1 mg orally, twice weekly. (2.2)

DOSAGE FORMS AND STRENGTHS

Tablets: 0.5 mg, white, with functional score. (3)

CONTRAINDICATIONS

- Uncontrolled hypertension (4)
- Known hypersensitivity to ergot derivatives (4)
- History of cardiac valvular disorders, or pericardial fibrosis. (5.1)
- History of pleural, pulmonary, or retroperitoneal fibrotic disorders. (5.2)

WARNINGS AND PRECAUTIONS

- Cardiac Valvulopathy and Pericardial Fibrosis: Before initiating cabergoline tablets, perform a cardiovascular evaluation, including echocardiogram, to evaluate for valvular disease. During cabergoline tablets treatment, monitor for the development of valvulopathy with a cardiac echocardiogram at intervals of 6 to 12 months or as clinically indicated and monitor for chest pain and signs and symptoms of heart failure (if heart failure occurs, exclude valvular fibrosis and pericarditis). Consider additional clinical and diagnostic monitoring at baseline and as necessary during cabergoline tablets treatment. Use cabergoline tablets in patients treated with other drugs associated with valvulopathy only if the potential benefit of cabergoline tablets outweighs the risk. Discontinue cabergoline tablets if the patient has a new diagnosis of valvular regurgitation, valvular restriction, valve leaflet thickening, or pericarditis. (5.1)
- Pleural, Pulmonary and Retroperitoneal Fibrosis: During cabergoline tablets treatment monitor for signs and symptoms of progressive fibrosis, (e.g., pleuro-pulmonary disease, renal impairment, ureteral/abdominal vascular obstruction). Consider clinical and diagnostic monitoring for pleural, pulmonary, and retroperitoneal fibrosis at baseline and as necessary during cabergoline tablets treatment. If pleural, pericardial, retroperitoneal, or pulmonary fibrosis occur, discontinue cabergoline tablets. (5.2)
- Orthostatic Hypotension: Check blood pressure at baseline and during treatment with cabergoline tablets and monitor for orthostatic hypotension. (5.3)
- Risks with Use of cabergoline tablets for Postpartum Lactation Inhibition or Suppression: Avoid use of cabergoline tablets for the inhibition or suppression of physiologic lactation. Use of bromocriptine, another dopamine agonist for this unapproved use has been associated with cases of hypertension, stroke, myocardial infarction, seizures, and death. (5.4)
- Impulse Control Disorders and Compulsive Behaviors: Specifically ask patients about the development of new or increased gambling urges, sexual urges, uncontrolled spending, or other urges while being

treated with cabergoline tablets. Consider dosage reduction or stopping cabergoline tablets if a patient develops such urges while taking cabergoline tablets. (5.5)

ADVERSE REACTIONS

The most common adverse reactions (incidence >10%) are nausea, headache, and dizziness. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Teva at 1-888-838-2872 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

Cabergoline tablets, a dopamine receptor agonist, is not recommended for concomitant use with D2-antagonists, such as phenothiazines, butyrophenones, thioxanthenes, or metoclopramide. (7)

USE IN SPECIFIC POPULATIONS

Pregnancy: If conception occurs during cabergoline tablets therapy, discontinue cabergoline tablets if the risks to the mother or fetus outweigh the benefits to the mother (8.1)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 6/2025

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Cabergoline tablets are an ergot derivative indicated for the treatment of hyperprolactinemic disorders, either idiopathic or due to pituitary adenomas in adults.

Limitations of Use

Avoid use of cabergoline tablets for the inhibition or suppression of postpartum physiologic lactation because of the risk of serious adverse reactions *[see Warnings and Precautions (5.4)].*

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Evaluation Before Initiating cabergoline tablets

Before initiating cabergoline tablets evaluate for valvular heart disease, including with an echocardiogram. If valvular disease is detected, do not administer cabergoline tablets *[see Contraindications (4) and Warnings and Precautions (5.1)]*.

2.2 Recommended Dosage

The recommended starting dosage of cabergoline tablets is 0.25 mg orally twice weekly. Titrate cabergoline tablets to achieve normal serum prolactin levels by increasing cabergoline tablets by 0.25 mg orally twice weekly at intervals of no less than 4 weeks. The maximum recommended dosage is 1 mg orally, twice weekly *[see Warnings and Precautions (5.2)]*. Administer cabergoline tablets with or without food *[see Clinical Pharmacology (12.3)].*

If cabergoline tablets are discontinued, monitor the serum prolactin level periodically to determine whether cabergoline tablets should be reinstituted.

3 DOSAGE FORMS AND STRENGTHS

Tablets: 0.5 mg, white, oval-shaped, scored tablets, debossed “hourglass logo”, “0.5” with a score on one side and “5420” on the other side.

4 CONTRAINDICATIONS

Cabergoline tablets are contraindicated in patients with:

- Uncontrolled hypertension.
- Known hypersensitivity to ergot derivatives.
- History of cardiac valvular disorders, as suggested by anatomical evidence of valvulopathy of any valve, determined by pre-treatment evaluation including echocardiographic demonstration of valve leaflet thickening, valve restriction, or mixed valve restriction-stenosis, or history of pericardial fibrosis *[see Warnings and*

Precautions (5.1)].
- History of pleural, pulmonary, or retroperitoneal fibrotic disorders *[see Warnings and Precautions (5.2)].*

5 WARNINGS AND PRECAUTIONS

5.1 Cardiac Valvulopathy and Pericardial Fibrosis

Before initiating cabergoline tablets, perform a cardiovascular evaluation, including with an echocardiogram, to evaluate for valvular disease. cabergoline tablets are contraindicated in the presence of valvular disease or pericardial fibrosis *[see Contraindications (4)].*

Cases of valvular and pericardial fibrosis have often manifested as heart failure. Following cabergoline tablets treatment initiation, monitor for the development of valvulopathy with a cardiac echocardiogram at intervals of 6 to 12 months or as clinically indicated with new onset edema, cardiac murmur, dyspnea, or heart failure. During cabergoline tablets treatment, monitor for chest pain and signs and symptoms of heart failure and if heart failure occurs, valvular fibrosis and pericarditis should be excluded. Consider clinical and diagnostic monitoring such as erythrocyte sedimentation rate, serum creatinine measurements, chest-x- ray, and other investigations and cardiac imaging at baseline and as necessary while patients are treated with during cabergoline tablets treatment. Use cabergoline tablets in patients treated with other drugs associated with valvulopathy only if the potential benefit of cabergoline tablets outweighs the risk.

Discontinue cabergoline tablets if the patient has a new diagnosis of valvular regurgitation, valvular restriction, valve leaflet thickening, or pericarditis.

Postmarketing cases of cardiac valvulopathy have been reported in patients who received cabergoline tablets. These cases have generally occurred during administration of high doses of cabergoline tablets (>2 mg/day) for the treatment of Parkinson’s disease (PD) (cabergoline tablets is not approved for the treatment of PD). Cases of cardiac valvulopathy have also been reported in patients who received lower dosages of cabergoline tablets for the treatment of hyperprolactinemic disorders. In a 12-year, multi-country retrospective cohort study, the use of cabergoline tablets for PD was associated with an increased risk of cardiac valvular regurgitation (CVR). Compared to non-ergot- derived dopamine agonists and levodopa, CVR with cabergoline tablets use had an incidence rate per 10,000 person years of 68 (95% CI: 37, 115) versus 10 (95% CI: 5, 19) for non-ergot dopamine agonists and 11 (95% CI: 7, 17) for levodopa.

5.2 Pleural, Pulmonary and Retroperitoneal Fibrosis

Cabergoline tablets are contraindicated in patients with a history of pleural, pulmonary, or retroperitoneal fibrosis. During cabergoline tablets treatment monitor for signs and symptoms of progressive fibrosis, including:
- Pleuro-pulmonary disease (e.g., dyspnea, shortness of breath, persistent cough, chest pain).
- Renal impairment or ureteral/abdominal vascular obstruction (e.g., pain in the loin/flank, lower limb edema, abdominal masses or tenderness that may indicate retroperitoneal fibrosis).

Consider clinical and diagnostic monitoring for pleural, pulmonary, and retroperitoneal fibrosis such as with erythrocyte sedimentation rate, serum creatinine measurements, chest-x-ray, and other investigations at baseline and as necessary during cabergoline tablets treatment. If pleural, pericardial, retroperitoneal, or pulmonary fibrosis occur,

discontinue cabergoline tablets.

Postmarketing cases of pleural, pulmonary, and retroperitoneal fibrosis have been reported following cabergoline tablets administration. Some reports were in patients previously treated with other ergotinic dopamine agonists. Cabergoline tablets-treated patients who developed a pleural effusion or pulmonary fibrosis and subsequently discontinued cabergoline tablets had improvement of their pulmonary symptoms.

5.3 Orthostatic Hypotension

Check blood pressure at baseline and during treatment with cabergoline tablets and monitor for orthostatic hypotension. Warn patients about the risk of orthostatic hypotension and precautions to take when rising from a supine or sitting position. Instruct patients to report dizziness or lightheadedness with changes in position to their healthcare provider.

Cabergoline tablets can cause orthostatic hypotension *[see Adverse Reactions (6.1)].* In a 4-week, placebo-controlled trial in patients with hyperprolactinemic disorders, the percentage of cabergoline tablets-treated patients and placebo-treated patients who developed orthostatic hypotension was 4% and 0%, respectively *[see Adverse Reactions (6.1)]*. The risk of orthostatic hypotension is greater in cabergoline tablets-treated patients when taking concomitant drugs that lower blood pressure.

5.4 Risks with Use of cabergoline tablets for Postpartum Lactation Inhibition or Suppression

Avoid use of cabergoline tablets for the inhibition or suppression of postpartum physiologic lactation because of the risk of serious adverse reactions. Use of bromocriptine, another dopamine agonist for this unapproved use has been associated with cases of hypertension, stroke, myocardial infarction seizures, and death.

5.5 Impulse Control Disorders and Compulsive Behaviors

Because patients may not recognize impulse control and compulsive behaviors as abnormal, it is important for health care providers to specifically ask patients about the development of new or increased gambling urges, sexual urges, uncontrolled spending, or other urges while being treated with cabergoline tablets. Consider dosage reduction or stopping cabergoline tablets if a patient develops such urges while taking cabergoline tablets.

Patients can experience intense urges to gamble or to spend money, increased sexual urges, binge eating, and/or other intense urges, and the inability to control these urges while taking one or more drugs that increase central dopaminergic tone, including cabergoline tablets. In some cases, these urges were reported to have stopped when the dosage was reduced, or the drug was stopped.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in the labeling:

- Cardiac Valvulopathy and Pericardial Fibrosis *[see Warnings and Precautions (5.1)]*.
- Pleural, Retroperitoneal, and Pulmonary Fibrosis *[see Warnings and Precautions (5.2)]*.
- Orthostatic Hypotension *[see Warnings and Precautions (5.3)]*.
- Impulse Control Disorders and Compulsive Behaviors *[see Warnings and Precautions (5.5)]*.

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of cabergoline tablets has been evaluated in more than 900 patients with hyperprolactinemic disorders. In a 4-week, double-blind, placebo-controlled trial (cabergoline tablets vs. placebo) *[see Clinical Studies (14)],* the incidence of the most common adverse reactions during the placebo-controlled trial in patients with hyperprolactinemic disorders is presented in Table 1.

Table 1. Adverse Reactions (n (%)* During the 4-Week, Double-Blind, Placebo-Controlled Trial in Hyperprolactinemic Females

	Cabergoline Tablets (n=168)	Placebo (n=20)
Nausea	45 (27%)	4 (20%)
Headache	43 (26%)	5 (25%)
Dizziness	25 (15%)	1 (5%)
Constipation	16 (10%)	0%
Fatigue	12 (7%)	0%
Postural hypotension	6 (4%)	0%
Dyspepsia	4 (2%)	0%
Vomiting	4 (2%)	0%
Nervousness	4 (2%)	0%
Vertigo	2 (1%)	0%
Paresthesia	2 (1%)	0%
Breast pain	2 (1%)	0%
Dysmenorrhea	2 (1%)	0%
Abnormal vision	2 (1%)	0%

* Adverse reactions that occurred ≥1% in the cabergoline tablets group and frequency more than that reported in the placebo group.

In the 8-week, double-blind period of the comparative trial with bromocriptine, 2% (4/221) of cabergoline tablets-treated patients (0.5 mg twice weekly) discontinued treatment because of an adverse event and 6% (14/231) of bromocriptine-treated patients (at a dose of 2.5 mg twice daily) discontinued treatment because of an adverse event. The most common reasons for cabergoline tablets discontinuation were headache, nausea, and vomiting (3, 2, and 2 patients, respectively). The incidence of the most common adverse events during the double-blind period of the comparative trial with bromocriptine is presented in Table 2.

Table 2. Adverse Events* During the 8-Week, Double-Blind Period of the Comparative Trial in Hyperprolactinemic Females

	Cabergoline Tablets (n=221)	Bromocriptine (n=231)
Nausea	63 (29%)	100 (43%)
Headache	58 (26%)	62 (27%)
Dizziness	38 (17%)	42 (18%)
Constipation	15 (7%)	21 (9%)
Asthenia	13 (6%)	15 (6%)
Abdominal pain	12 (5%)	19 (8%)
Dyspepsia	11 (5%)	16 (7%)
Fatigue	10 (5%)	18 (8%)

Vertigo	9 (4%)	10 (4%)
Vomiting	9 (4%)	16 (7%)
Depression	7 (3%)	5 (2%)
Hot flashes	6 (3%)	3 (1%)
Breast pain	5 (2%)	8 (3%)
Dry mouth	5 (2%)	2 (1%)
Paresthesia	5 (2%)	6 (3%)
Somnolence	5 (2%)	5 (2%)
Diarrhea	4 (2%)	7 (3%)
Flatulence	4 (2%)	3 (1%)
Pain	4 (2%)	6 (3%)
Acne	3 (1%)	0%
Anorexia	3 (1%)	3 (1%)
Anxiety	3 (1%)	3 (1%)
Hypotension	3 (1%)	4 (2%)
Insomnia	3 (1%)	2 (1%)
Syncope	3 (1%)	3 (1%)
Abnormal vision	2 (1%)	2 (1%)
Arthralgia	2 (1%)	0%
Dependent edema	2 (1%)	1 (<1%)
Dysmenorrhea	2 (1%)	1 (<1%)
Impaired concentration	2 (1%)	1 (<1%)
Influenza-like symptoms	2 (1%)	0%
Malaise	2 (1%)	0%
Nervousness	2 (1%)	5 (2%)
Palpitation	2 (1%)	5 (2%)
Periorbital edema	2 (1%)	2 (1%)
Peripheral edema	2 (1%)	1 (<1%)
Pruritus	2 (1%)	1 (<1%)
Rhinitis	2 (1%)	9 (4%)
Throat irritation	2 (1%)	0%
Toothache	2 (1%)	0%

* Adverse events reported ≥1% in the cabergoline tablets group. Abbreviation: n=number of patients.

Events that were reported at an incidence of <1% in the clinical studies follow:

- Body As a Whole: facial edema, influenza-like symptoms, malaise
- Cardiovascular System: hypotension, syncope, palpitations
- Digestive System: dry mouth, flatulence, diarrhea, anorexia
- Metabolic and Nutritional System: weight loss, weight gain
- Nervous System: somnolence, nervousness, paresthesia, insomnia, anxiety
- Respiratory System: nasal stuffiness, epistaxis
- Skin and Appendages: acne, pruritus
- Special Senses: abnormal vision
- Urogenital System: dysmenorrhea, increased libido

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of cabergoline tablets. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

- Psychiatric: impulse control disorders and compulsive behaviors including,

hypersexuality, increased libido, pathological gambling; psychotic disorder, aggression
- Skin and subcutaneous: alopecia

7 DRUG INTERACTIONS

Cabergoline tablets, a dopamine receptor agonist, is not recommended for concomitant use with D2-antagonists, such as phenothiazines, butyrophenones, thioxanthenes, or metoclopramide.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

If conception occurs during cabergoline tablets therapy, discontinue cabergoline tablets if the risks to the mother or fetus outweigh the benefits to the mother. There are risks to the mother associated with the use of cabergoline tablets (*see Clinical Considerations*).

The estimated background risk of major birth defects and miscarriage in patients with hyperprolactinemic disorders, either idiopathic or due to pituitary adenomas is unknown. All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Clinical Considerations

Maternal Adverse Reactions: In general, avoid use of dopamine agonists, including cabergoline tablets, during pregnancy and the postpartum period. The risks of cabergoline tablets use increase in pregnant females with pregnancy-induced hypertension, preeclampsia, and eclampsia.

Data

Human Data: Published case reports have not reported a clear association with cabergoline tablets and major birth defects, miscarriage, or adverse fetal outcomes when cabergoline tablets was used during early pregnancy. However, these case reports cannot definitely establish the absence of cabergoline tablets-associated risk.

Animal Data: Embryo-fetal development studies have been performed with cabergoline administered by oral gavage in mice, rats, and rabbits:
- There were no teratogenic effects in the presence of maternal toxicity in mice given cabergoline at doses up to 8 mg/kg/day (approximately 55 times the maximum recommended human dose based on body surface area) during the period of organogenesis.
- A dose of 0.012 mg/kg/day (approximately 0.14 times the maximum recommended human dose) administered during the period of organogenesis in rats caused an increase in post-implantation loss. This finding is likely due to the role of prolactin in implantation in rats and is not thought to be relevant to humans.
- At doses of 0.5 mg/kg/day (approximately 19 times the maximum recommended human dose) administered during the period of organogenesis in rabbits, cabergoline caused maternal toxicity 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) administered 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 embryofetal toxicity were observed at doses up to 8 mg/kg/day (approximately 300 times the maximum recommended human dose).

8.2 Lactation

Risk Summary

Cabergoline tablets are not recommended in postpartum women who are breastfeeding or who are planning to breastfeed. Avoid use of cabergoline tablets for the inhibition or suppression of physiologic lactation *[see Indications and Usage (1) and Warnings and Precautions (5.4)]*.

8.4 Pediatric Use

Safety and effectiveness of cabergoline tablets in pediatric patients have not been established.

8.5 Geriatric Use

Clinical studies of cabergoline tablets did not include sufficient numbers of patients 65 years of age and older to determine whether they respond differently from younger adult patients.

8.6 Hepatic Impairment

The use of cabergoline tablets in patients with severe hepatic impairment (HI) (Child-Pugh C) is not recommended. When using cabergoline tablets in patients with moderate HI (Child-Pugh B) increase monitoring of cabergoline tablets-associated adverse reactions. The recommendations for use of cabergoline tablets in patients with mild HI (Child Pugh A) is the same as those with normal hepatic function.

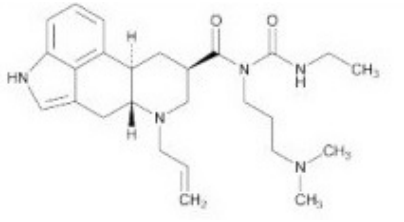
Patients with moderate or severe HI had increased cabergoline exposure *[see Clinical Pharmacology (12.3)],* which may increase the risk of cabergoline tablets-associated adverse reactions.

10 OVERDOSAGE

Take measures to support blood pressure, if necessary. Consider contacting the Poison Help line (1-800-222-1222) or a medical toxicologist for additional overdose management recommendations.

11 DESCRIPTION

Cabergoline, USP is an ergot derivative and dopamine receptor agonist. The chemical name for cabergoline, USP is 1-[(6-allylergolin-8β-yl)-carbonyl]-1-[3-(dimethylamino)propyl]-3-ethylurea and has the following structural formula:



$C_{26}H_{37}N_5O_2$ M.W. 451.6

Cabergoline, USP is a white powder soluble in ethyl alcohol, chloroform, and N, N-dimethylformamide (DMF); slightly soluble in 0.1N hydrochloric acid; very slightly soluble in n-hexane; and insoluble in water.

Each cabergoline tablet USP, for oral administration, contains 0.5 mg of cabergoline, USP and has the following inactive ingredients: anhydrous lactose and leucine.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Cabergoline is an ergot derivative and dopamine receptor agonist with a high affinity for D2 receptors. Results of *in vitro* studies demonstrate that cabergoline exerts a direct inhibitory effect on the secretion of prolactin by rat pituitary lactotrophs. Cabergoline decreased serum prolactin levels in reserpinized rats. Receptor-binding studies indicate that cabergoline has low affinity for dopamine D1, α1- and α2-adrenergic, and 5-HT1- and 5- HT2-serotonin receptors.

12.2 Pharmacodynamics

The exposure-response relationship and time course of pharmacodynamic response for the safety and effectiveness of cabergoline tablets have not been fully characterized.

12.3 Pharmacokinetics

Absorption

The time to reach maximum cabergoline plasma concentration was 2 to 3 hours after single oral doses of 0.5 mg to 1.5 mg (1.5 times the maximum recommended dose) of cabergoline tablets in healthy subjects. Following dosing of cabergoline tablets between 0.5 mg to 7 mg (7 times the maximum recommended dose), cabergoline plasma levels appeared to be dose-proportional. The absolute bioavailability of cabergoline is unknown. A significant fraction of the administered dose undergoes a first-pass effect.

Effect of Food: High-fat food did not alter the pharmacokinetics of cabergoline *[see Dosage and Administration (2.2)].*

Distribution

Protein binding of cabergoline was 40% to 42%.

Elimination

The elimination half-life of cabergoline estimated from urinary data of 12 healthy subjects ranged between 63 to 69 hours.

Metabolism: Cabergoline is extensively metabolized, predominately via hydrolysis of the acylurea bond or the urea moiety. Hydrolysis of the acylurea or urea moiety abolishes the prolactin-lowering effect of cabergoline, and major metabolites identified thus far do not contribute to the therapeutic effect.

Excretion: After oral dosing of radioactive cabergoline to 5 healthy volunteers, approximately 22% and 60% of the dose was excreted within 20 days in the urine and

feces, respectively. Less than 4% of the dose was excreted unchanged in the urine. Nonrenal and renal clearances for cabergoline are about 3.2 L/min and 0.08 L/min, respectively. Urinary excretion in hyperprolactinemic patients was similar.

Specific Populations

Patients with Hepatic Impairment:

In a pharmacokinetic hepatic impairment (HI) study *[see Use in Specific Populations (8.6)]*:

- In 4 cabergoline tablets-treated patients with mild HI (Child-Pugh A), no effect on mean area under the cabergoline plasma concentration-time curve (AUC) was observed.
- In 4 cabergoline tablets-treated patients with moderate HI (Child-Pugh B) there was a 1.5-fold increase in mean cabergoline AUC.
- In 4 cabergoline tablets-treated patients with severe HI (Child-Pugh C) there was a 5.6-fold increase in the mean cabergoline AUC.

Male and Female Patients: Males aged 20 to 34 years were shown to have had higher C_{max} than females aged 20 to 27 years) while males aged 66 to 75 years had lower C_{max} compared to females aged 66 to 74 years. The clinical significance of the findings is unknown.

Patients with Renal Impairment: The pharmacokinetics of cabergoline were not altered in 12 patients with moderate-to-severe renal impairment as assessed by creatinine clearance.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Carcinogenicity studies were conducted in mice and rats with cabergoline given by gavage at doses up to 0.98 mg/kg/day and 0.32 mg/kg/day, respectively. These doses are 7 times and 4 times the maximum recommended human dose calculated on a body surface area basis using total mg/m^2/week in rodents and mg/m^2/week for a 50 kg human.

There was a slight increase in the incidence of cervical and uterine leiomyomas and uterine leiomyosarcomas in mice. In rats, there was a slight increase in malignant tumors of the cervix and uterus and interstitial cell adenomas. The occurrence of tumors in female rodents may be related to the prolonged suppression of prolactin secretion because prolactin is needed in rodents for the maintenance of the corpus luteum. In the absence of prolactin, the estrogen/progesterone ratio is increased, thereby increasing the risk for uterine tumors. In male rodents, the decrease in serum prolactin levels was associated with an increase in serum luteinizing hormone, which is thought to be a compensatory effect to maintain testicular steroid synthesis. Since these hormonal mechanisms are thought to be species-specific, the relevance of these tumors to humans is not known.

Mutagenesis

The mutagenic potential of cabergoline was evaluated and found to be negative in a battery of *in vitro* tests. These tests included the bacterial mutation (Ames) test with *Salmonella typhimurium,* the gene mutation assay with *Schizosaccharomyces pombe* P_1

and V79 Chinese hamster cells, DNA damage and repair in *Saccharomyces cerevisiae* D_4, and chromosomal aberrations in human lymphocytes. Cabergoline was also negative in the bone marrow micronucleus test in the mouse.

Impairment of Fertility

In female rats, a daily cabergoline dose of 0.003 mg/kg for 2 weeks prior to mating and throughout the mating period inhibited conception. This dose represents approximately 0.04 times the maximum recommended human dose calculated on a body surface area basis using total mg/m^2/week in rats and mg/m^2/week for a 50 kg human.

This finding is likely due to the role of prolactin in implantation in rats and is not thought to be relevant to humans.

14 CLINICAL STUDIES

The prolactin-lowering efficacy of cabergoline tablets was demonstrated in 647 females with hyperprolactinemic disorders (including 55% microprolactinomas, 7% macroprolactinomas, 3% empty sella syndromes, and 3% idiopathic) in two randomized, double-blind, studies: one 4-week placebo-controlled dose-response study with an 12-month open-label extension (Study 1) and one 8-week active comparator study comparing cabergoline tablets and bromocriptine with 16-week open extension (Study 2).

Study 1: 4-Week Placebo-Controlled Dose-Response Study

Study 1 enrolled 188 non-pregnant, hyperprolactinemic females (these patients had a prolactin level >20 ng/ml (the upper normal reference limit)) with the following hyperprolactinemic etiologies: macroprolactinoma (60%, n=113), idiopathic (36%, n=67) and another etiology (4%, n= 8). Patients had a mean age of 32 years (range, 16-46 years of age), 99% were White (n=186), 0.5% were Asian (n=1) and 0.5% were another race (n=1). Patients were randomized one of the following five oral treatments given twice weekly for four weeks (for the cabergoline tablets groups, the first week the cabergoline tablets dosage was lower to reduce the risk of hypotensive reactions):

- Group 1: placebo twice weekly (n=20)
- Group 2: 0.0625 mg of cabergoline tablets twice weekly for the first week followed by 0.125 mg twice weekly for the next three weeks (n=42)-this dosage is not recommended because this dosage was not effective and results from this group are not presented below *[see Dosage and Administration (2.2)],*
- Group 3: 0.25 mg of cabergoline tablets twice weekly for the first week followed 0.5 mg twice weekly for the next three weeks (n=42),
- Group 4: 0.375 mg of cabergoline tablets twice weekly for the first week followed 0.75 mg twice weekly for the next three weeks (n=42), and
- Group 5: 0.5 mg of cabergoline tablets twice weekly for the first week followed 1 mg twice weekly for the next three weeks 0.75 mg, (n=42).

In Study 1, the endpoint was the percentage of patients who achieved a normal serum prolactin level (<20 ng/dL) at the end of the 4-week treatment period. At 4-weeks, 0%, 76%, 74% and 95% of patients in the placebo group (group 1), group 3, group 4, and group 5, achieved normal serum prolactin levels, respectively ($p < 0.0001$ across all the cabergoline tablets groups vs. placebo).

Study 2: 8-Week Active Comparator Study

Study 2 was an 8-week, randomized, double-blind active-control study that compared cabergoline tablets (n=223) with bromocriptine (n=236) for the treatment of hyperprolactinemic amenorrhea. In this study, patients had a mean age of 31 years

(range 16 – 46 years of age). Patients were randomized to oral cabergoline tablets 0.5 mg twice weekly or oral bromocriptine 2.5 mg twice daily for eight weeks (there was an attrition rate respectively of 46% and 43%, in the cabergoline tablets and bromocriptine groups, respectively). Endpoints included percentage of patients who achieved the following at 8 weeks:

- A normal serum prolactin level (<20 ng/dL)
- Restoration of menses
- Disappearance of galactorrhea

In Study 2, at 8 weeks, cabergoline tablets-treated and bromocriptine-treated patients had a normal serum prolactin level (77% and 59%, respectively), restoration of menses (77% and 70% respectively), and disappearance of galactorrhea, 73% and 56%, respectively).

The durability of the efficacy of cabergoline tablets beyond 24 months of therapy has not been established.

16 HOW SUPPLIED/STORAGE AND HANDLING

Cabergoline tablets USP, 0.5 mg are available as white, oval-shaped, scored tablets, debossed “hourglass logo”, “0.5” with a score on one side and “5420” on the other side containing 0.5 mg cabergoline, USP packaged in unit-of-use bottles of 8 tablets (NDC 0093-5420-88).

Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature].

Dispense in original container.

Keep this and all medications out of the reach of children.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Fibrotic Conditions

There is a risk of cardiac valvulopathy, and pericardial, pleural, pulmonary, and retroperitoneal fibrosis with cabergoline tablets treatment Advise patients to notify their healthcare provider if they develop shortness of breath, chest pain, persistent cough, difficulty with breathing when lying down, or swelling in their extremities *[see Warnings and Precautions (5.1)]*.

Orthostatic Hypotension

Warn patients about the risk of orthostatic hypotension and instruct patients to rise slowly from a supine or sitting position. Advise patients to notify their healthcare provider if they develop dizziness or lightheadedness *[see Warnings and Precautions (5.3)]*.

Impulse Control Disorders and Compulsive Behaviors

Patients should be alerted to the possibility that patients may experience intense urges to spend money uncontrollably, intense urges to gamble, increased sexual urges, and other intense urges and the inability to control these urges while taking cabergoline tablets. Advise patients to inform their health care provider if they develop new or increased uncontrolled spending, gambling urges, sexual urges, or other urges while being treated with cabergoline tablets *[see Warnings and Precautions (5.5)]*.

Pregnancy

Advise patients to notify their health care provider if they suspect they are pregnant, become pregnant, or intend to become pregnant during therapy. A pregnancy test should be done if there is any suspicion of pregnancy and continuation of cabergoline tablets treatment should be discussed with their health care provider *[see Use in Specific Populations (8.1)]*.

Manufactured In Czech Republic By:

Teva Czech Industries s.r.o.

Opava-Komarov, Czech Republic

Manufactured For:

Teva Pharmaceuticals

Parsippany, NJ 07054

Rev. H 6/2025

PATIENT INFORMATION
Cabergoline (ka ber′ goe leen) Tablets
for oral use

What are cabergoline tablets?
Cabergoline tablets are a prescription medicine used to treat a condition called hyperprolactinemia (increased levels of prolactin) in adults.
Cabergoline tablets are not for use to prevent or suppress breastfeeding after having given birth (postpartum lactation).
It is not known if cabergoline tablets are safe and effective in children.

Who should not take cabergoline tablets?
Do not take cabergoline tablets if you:
- have uncontrolled high blood pressure.
- are allergic to medicines called ergot derivatives.
- have a history of heart valve disorders.
- have a history of fibrosis in your heart, chest, lungs or abdomen.

Before taking cabergoline tablets, tell your health care provider about all of your medical conditions, including if you:
- have heart problems.
- have low blood pressure.
- have liver problems.
- are pregnant or plan to become pregnant. It is not known if cabergoline tablets will harm your unborn baby. Tell your health care provider if you become pregnant or think you are pregnant during treatment with cabergoline tablets. A pregnancy test should be done if you think you may be pregnant. You and your health care provider should discuss whether to continue treatment with cabergoline tablets.
- are breastfeeding or plan to breastfeed. Talk to your health care provider about the best way to feed your baby if you take cabergoline tablets. **Do not breastfeed during treatment while taking cabergoline tablets**.
- **Tell your health care provider about all the medicines you take**, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Cabergoline tablets may

affect the way other medicines work, and other medicines may affect the way cabergoline tablets work.

How should I take cabergoline tablets?

- Take cabergoline tablets exactly how your health care provider tells you to take it.
- Your health care provider should check for heart valve problems before starting treatment with cabergoline tablets.
- Take cabergoline tablets by mouth 2 times weekly or as directed by your health care provider.
- Take cabergoline tablets with or without food.
- Your health care provider should check your prolactin levels about every 4 weeks initially, and periodically thereafter, and may change your dose if needed.

If you take too many cabergoline tablets, call your Poison Help line at 1-800-222-1222 or go to the nearest hospital emergency room right away.

What are the possible side effects of cabergoline tablets?

Cabergoline tablets can cause serious side effects, including:

- **Heart valve problems and fibrosis (scarring).** Cabergoline tablets can cause heart valve problems and fibrosis in the heart, chest, lungs or areas of the stomach (abdomen). Call your health care provider right away if you get any of the following signs or symptoms of heart valve problems and fibrosis:
  - shortness of breath
  - chest pain
  - persistent cough
  - difficulty with breathing when lying down
  - swelling in the arms or legs
  - pain in the side (flank)
  - lump or tenderness in abdomen
- **Decreased blood pressure (orthostatic hypotension).** You may feel dizzy or lightheaded when you rise too quickly from a sitting or lying position. Talk to your health care provider if you have dizziness or lightheadedness.
- **Unusual and uncontrollable (compulsive) urges.** Some people taking cabergoline tablets have had unusual strong urges to gamble and gambling that cannot be controlled (compulsive gambling), and other compulsive urges including sexual urges, shopping, and eating or binge eating. Talk to your health care provider if you notice that you are having new or unusual strong urges or behaviors.

The most common side effects of cabergoline tablets include:

◦ nausea	◦ headache	◦ dizziness

These are not all the possible side effects of cabergoline tablets. For more information, ask your health care provider including your pharmacist. Call your health care provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store cabergoline tablets?

- Store cabergoline tablets at room temperature between (20°C to 25°C) 68°F to 77°F in the original container.

Keep cabergoline tablets and all medicines out of the reach of children.

General Information about the safe and effective use of cabergoline tablets.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information Leaflet. Do not use cabergoline tablets for a condition for which it was not prescribed. Do not give cabergoline tablets to other people, even if they have the same symptoms you have. It may

harm them. You can ask your health care provider, including your pharmacist, for information that is written for health care providers.

What are the ingredients in cabergoline tablets?
Active ingredient: cabergoline.
Inactive ingredients: anhydrous lactose and leucine.
Manufactured In Czech Republic By: **Teva Czech Industries s.r.o**., Opava-Komarov, Czech Republic
Manufactured For: **Teva Pharmaceuticals,** Parsippany, NJ 07054
For more information, call Teva at 1-888-838-2872.

This Patient Information has been approved by the U.S. Food and Drug Administration.
Rev. A 6/2025

PRINCIPAL DISPLAY PANEL

NDC 0093-5420-88

Cabergoline Tablets, USP

0.5 mg

Each tablet contains: cabergoline, USP 0.5 mg

Dispense in original container.

Rx only

8 Tablets Unit-Of-Use

CABERGOLINE

cabergoline tablet

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0093-5420
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
CABERGOLINE (UNII: LL60K9J05T) (CABERGOLINE - UNII:LL60K9J05T)	CABERGOLINE	0.5 mg

Inactive Ingredients	
Ingredient Name	**Strength**
ANHYDROUS LACTOSE (UNII: 3SY5LH9PMK)	

LEUCINE (UNII: GMW67QNF9C)	

Product Characteristics			
Color	white	**Score**	2 pieces
Shape	OVAL	**Size**	8mm
Flavor		**Imprint Code**	0;5;5420
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0093-5420-88	1 in 1 CARTON	03/07/2007	
1		8 in 1 BOTTLE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA077750	03/07/2007	

Labeler - Teva Pharmaceuticals USA, Inc. (001627975)

Revised: 6/2025 Teva Pharmaceuticals USA, Inc.