

Cabergoline

Cabergoline, an ergot derivative, is a potent dopamine receptor agonist on D2 receptors. It also acts on dopamine receptors in lactophilic hypothalamus cells to suppress prolactin production in the pituitary gland. It is frequently used as a second-line agent in the management of prolactinomas when bromocriptine is ineffective.

Following a single oral dose, resorption of cabergoline from the gastrointestinal (GI) tract is highly variable, typically occurring within 0.5 to 4 hours. Ingestion with food does not alter its absorption rate. Human bioavailability has not been determined since the drug is intended for oral use only. In mice and rats the absolute bioavailability has been determined to be 30 and 63 percent, respectively. Cabergoline is rapidly and extensively metabolized in the liver and excreted in bile and to a lesser extent in urine. All metabolites are less active than the parental drug or inactive altogether. The human elimination half-life is estimated to be 63 to 68 hours in patients with Parkinson's disease and 79 to 115 hours in patients with pituitary tumors. Average elimination half-life is 80h.

Uses

Cabergoline is used to treat different types of medical problems that occur when too much of the hormone prolactin is produced. It can be used to treat certain menstrual problems, fertility problems in men and women, and pituitary prolactinomas (tumors of the pituitary gland).

It works by stopping the brain from making and releasing the prolactin hormone from the pituitary. Cabergoline use is usually stopped when prolactin levels are normal for 6 months. It may be given again if symptoms of too much prolactin occur again.

- Monotherapy of Parkinson's disease in the early phase.

- Combination therapy, together with levodopa and a decarboxylase inhibitor such as carbidopa, in progressive-phase Parkinson's disease.
- Adjunctive therapy of prolactin-producing pituitary gland tumors (prolactinomas).
- Also for ablactation and dysfunctions associated with hyperprolactinemia (amenorrhea, oligomenorrhea, anovulation, and galactorrhea).

It has at times been used as an adjunct to SSRI antidepressants as there is some evidence that it counteracts certain side effects of those drugs, such as reduced libido and anorgasmia. It also has been suggested that it has a possible recreational use in reducing or eliminating the male refractory period. It is also used by bodybuilders to control gynecomastia caused by elevated prolactin levels through the use of anabolic steroids such as Nandrolone and Trenbolone. Additionally, a study that recently concluded Phase III trials is showing it to decrease the risk of ovarian hyperstimulation syndrome (OHSS) in females undergoing stimulated cycles of in vitro fertilization (IVF). A study on rats found that cabergoline reduces voluntary alcohol consumption.

Contraindications and precautions

- Hypersensitivity to ergot derivatives
- Pediatric patients (no clinical experience)
- Severely impaired liver function or cholestasis
- Co-medication with drugs metabolized mainly by CYP P450 such as erythromycin and ketoconazole, because increased plasma levels of cabergoline may result (although cabergoline undergoes minimal CYP450 metabolism).
- Cautions: severe cardiovascular disease, Raynaud's disease, gastroduodenal ulcers, active gastrointestinal bleeding, hypotension.

- **Pregnancy:** The incidence of spontaneous abortions and congenital abnormalities was comparable to non-treated patients. Nevertheless, women wishing to become pregnant should wait a period of four weeks after discontinuation of cabergoline. Patients becoming pregnant under therapy should terminate cabergoline immediately, if possible.
- **Lactation:** In rats cabergoline was found in the maternal milk. Since it is not known if this effect also occurs in humans, breastfeeding women should not be treated.

It is important that your doctor check your progress at regular visits while you are taking this medicine to make sure that this medicine is working properly and to check for unwanted effects.

This medicine may cause some people to become drowsy, dizzy, or less alert than they are normally. Make sure you know how you react to this medicine before you drive, use machines, or do other jobs that require you to be alert.

Dizziness, lightheadedness, or fainting may occur, especially when you get up from a lying or sitting position. Getting up slowly may help.

Tell your doctor immediately if you think you have become pregnant. You and your doctor should discuss whether you should continue to take this medicine during pregnancy.

Check with your doctor immediately if you have symptoms of fainting, hallucinations, lightheadedness, stuffy nose, or racing heart.

This medicine may increase your risk of having problems with your heart valves. Check with your doctor right away if you notice any signs or symptoms of heart disease, such as chest pain or tightness; troubled breathing; shortness of breath; extreme tiredness; or swelling in your hands, ankles, or feet.

Also tell your doctor if you have persistent cough along with shortness of breath or troubled breathing while you are using this medicine. This could be symptoms of a serious lung disorder called pulmonary fibrosis.

Side effects

These side effects were chiefly mild or moderate:

In a combination study with 2,000 patients also treated with levodopa, the incidence and severity of side effects was comparable to monotherapy. Encountered side effects required a termination of cabergoline treatment in 15% of patients. Additional side effects were infrequent cases of hematological side effects, and an occasional increase in liver enzymes or serum creatinine without signs or symptoms.

As with other ergot derivatives, pleuritis, exudative pleura disease, pleura fibrosis, lung fibrosis, and pericarditis are seen. These side effects are noted in less than 2% of patients. They require immediate termination of treatment. Clinical improvement and normalization of X-ray findings are normally seen soon after cabergoline withdrawal.

The reported incidence and severity of side effects in hyperprolactinemic patients was comparable.

The use of antihypertensive drugs should be intensively monitored because excessive hypotension may result from the combination.

Along with its needed effects, a medicine may cause some unwanted effects. Although not all of these side effects may occur, if they do occur they may need medical attention.

Check with your doctor as soon as possible if any of the following side effects occur:

More common

- Abdominal pain
- Sensation that you are moving in space or that objects are moving around you (vertigo)
- Constipation
- Dizziness
- Headache
- Nausea or stomach discomfort
- Weakness

Other side effects not listed may also occur in some patients. If you notice any other effects, check with your healthcare professional.

Some side effects may occur that usually do not need medical attention. These side effects may go away during treatment as your body adjusts to the medicine. Also, your health care professional may be able to tell you about ways to prevent or reduce some of these side effects. Check with your health care professional if any of the following side effects continue or are bothersome or if you have any questions about them:

Before Using

In deciding to use a medicine, the risks of taking the medicine must be weighed against the good it will do. This is a decision you and your doctor will make. For this medicine, the following should be considered:

Allergies

Inform your doctor about allergies of any kind so that adequate precautions can be taken. It is important to inform the doctor about any other medicines that you may be taking. Avoid using alcohol while taking this drug.

Pediatric

Appropriate studies have not been performed on the relationship of age to the effects of cabergoline in the pediatric population. Safety and efficacy have not been established.

Geriatric

Appropriate studies performed to date have not demonstrated geriatrics-specific problems that would limit the usefulness of cabergoline in the elderly. However, elderly patients are more likely to have age-related liver, kidney, or heart problems, which may require caution and adjustment of dosage in patients receiving cabergoline.

Pregnancy

	Pregnancy Category	Explanation
All Trimesters	B	Animal studies have revealed no evidence of harm to the fetus, however, there are no adequate studies in pregnant women OR animal studies have shown an adverse effect, but adequate studies in pregnant women have failed to demonstrate a risk to the fetus.

Breastfeeding

Studies suggest that this medication may alter milk production or composition. If an alternative to this medication is not prescribed, you should monitor the infant for side effects and adequate milk intake.

Other Medical Problems

The presence of other medical problems may affect the use of this medicine. Make sure you tell your doctor if you have any other medical problems, especially:

- Fibrotic disorders (scar-like tissues in the heart or lungs),

- High blood pressure, uncontrolled—Should not be used in patients with these conditions.
- Heart disease (or history of)
- Lung disorder (or history of)—Use with caution. Cabergoline may worsen these conditions.
- High blood pressure
- High blood pressure of pregnancy (or history of)—Cabergoline usually decreases blood pressure but at times it may increase blood pressure and worsen these conditions.
- Liver disease, mild to severe—Cabergoline may worsen this condition; a lower dose of cabergoline may be required.

Dosage

- Parkinson’s disease: Monotherapy: Initial dose should be 0.5 mg daily. The usual maintenance dose is 2 to 4 mg daily. Combination therapy: Usually 2 to 6 mg daily.
- Tumors of the pituitary gland and other hyperprolactinemic conditions: Initially 0.5 mg per week slowly titrated to 4.5 mg per week, if necessary.
- Ablactation: According to specific treatment scheme.
- For disorders of high prolactin levels:
 - Adults—0.25 milligram (mg) two times a week. Dose may be increased every four weeks as needed, according to body prolactin levels, up to 1 mg two times a week.
 - Children—Use and dose must be determined by the doctor.

It is important that your doctor check your progress at regular visits while you are taking cabergoline to make sure that cabergoline is working properly and to check for unwanted effects.