



CIGNA MEDICAL COVERAGE POLICY

The following Coverage Policy applies to all plans administered by CIGNA Companies including plans administered by Great-West Healthcare, which is now a part of CIGNA.

Effective Date 5/15/2010
Next Review Date..... 5/15/2011
Coverage Policy Number 5021

Subject **Cabergoline**

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Hyperlink to Related Coverage Policies

INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans as well as benefit plans formerly administered by Great-West Healthcare. Please note, the terms of a participant's particular benefit plan document [Group Service Agreement (GSA), Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a participant's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a participant's benefit plan document **always supercedes** the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable group benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. Proprietary information of CIGNA. Copyright ©2010 CIGNA

Coverage Policy

CIGNA covers cabergoline as medically necessary for the treatment of hyperprolactinemic disorders.

Note: There is a quantity limit of 16 tablets per 28 days.

FDA Approved Indications

Cabergoline tablets are indicated for the treatment of hyperprolactinemic disorders, either idiopathic or due to pituitary adenomas.

FDA Recommended Dosing

The recommended dosage of cabergoline tablets for initiation of therapy is 0.25 mg twice a week. Dosage may be increased by 0.25 mg twice weekly up to a dosage of 1 mg twice a week according to the patient's serum prolactin level. Before initiating treatment, cardiovascular evaluation should be performed and echocardiography should be considered to assess for valvular disease. Dosage increases should not occur more rapidly than every 4 weeks, so that the physician can assess the patient's response to each dosage level. If the patient does not respond adequately, and no additional benefit is observed with higher doses, the lowest dose that achieved maximal response should be used and other therapeutic approaches considered. Patients receiving long term treatment with cabergoline should undergo periodic assessment of their cardiac status and echocardiography should be considered. After a normal serum prolactin level has been maintained for 6 months, cabergoline may be discontinued, with periodic monitoring of the serum prolactin level to determine whether or when treatment

with cabergoline should be reinstated. The durability of efficacy beyond 24 months of therapy with cabergoline has not been established.

Drug Availability

Cabergoline tablets are available as white, oval-shaped, scored tablets, debossed "0.5" with a score on one side and "5420" on the other side containing 0.5 mg Cabergoline, packaged in bottles of 8 tablets.

General Background

Pharmacology

Cabergoline is a long-acting, selective dopamine receptor agonist, exhibiting high affinity for D₂ receptors and low affinity for D₁, alpha₁- and alpha₂-adrenergic, and serotonin receptors. Cabergoline inhibits the synthesis and release of prolactin from the anterior pituitary by directly stimulating the D₂ receptors of the pituitary lactotrophs in a dose-related fashion. While cabergoline doses of up to 2 mg inhibited prolactin in healthy volunteers, similar inhibition did not occur for the other anterior pituitary hormones, including growth hormone, follicle-stimulating hormone, luteinizing hormone, corticotropin, and thyroid-stimulating hormone.

Peak cabergoline levels following oral administration are reached within two to three hours. Absorption is not affected by food. Plasma protein binding is 40–42%. Distribution is extensive throughout the body. The elimination half-life is estimated to be 63–69 hours. Cabergoline undergoes extensive metabolism and biliary excretion. The metabolites appear to be inactive. Cytochrome P450 mediated metabolism appears minimal. Less than 4% of the dose is excreted in the urine unchanged.

Guidelines

The National Comprehensive Cancer Network (NCCN) recommends cabergoline for primary treatment for prolactinoma (grade 2A).

Clinical Efficacy

The prolactin-lowering efficacy of cabergoline was demonstrated in hyperprolactinemic women in two randomized, double-blind, comparative studies—one with placebo and the other with bromocriptine. In the placebo-controlled study (placebo n=20; cabergoline n=168), cabergoline produced a dose-related decrease in serum prolactin levels, with prolactin normalized after four weeks treatment in 29%, 76%, 74%, and 95% of the patients receiving 0.125, 0.5, 0.75, and 1.0 mg twice weekly, respectively.

In the eighth week, double-blind period of the comparative trial with bromocriptine (cabergoline n=223; bromocriptine n=236, in the intent-to-treat analysis), prolactin was normalized in 77% of the patients treated with cabergoline at 0.5 mg twice weekly compared with 59% of those treated with bromocriptine at 2.5 mg twice daily. Restoration of menses occurred in 77% of the women treated with cabergoline, compared with 70% of those treated with bromocriptine. Among patients with galactorrhea, this symptom disappeared in 73% of those treated with cabergoline compared with 56% of those treated with bromocriptine.

Adverse Reactions/Contraindications

Cabergoline is contraindicated in patients with uncontrolled hypertension or known hypersensitivity to ergot alkaloids. Also, cabergoline use should be avoided in patients with pregnancy-induced hypertension unless the benefit is judged to outweigh the possible risk. It is recommended that cabergoline be used with caution in patients with hepatic dysfunction. The therapeutic effects of cabergoline may be reduced with concomitant use of dopamine (D₂) antagonists (e.g., phenothiazines, butyrophenones, thioxanthines or metoclopramide); therefore, these agents should not be administered with cabergoline.

The safety of cabergoline tablets has been evaluated in more than 900 patients with hyperprolactinemic disorders. Most adverse events were mild or moderate in severity. The most common adverse effects in patients with hyperprolactinemia included nausea, vomiting, headache, dizziness/vertigo, fatigue, weakness, abdominal pain, dyspepsia and constipation.

Coding/Billing Information

Note: This section is not in use.

References

1. McEvoy GK, ed. AHFS 2010 Drug Information. Bethesda, MD: American Society of Health-Systems Pharmacists, Inc; 2010.
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3. Rains CP, Bryson HM, Fitton A. Cabergoline: A review of its pharmacologic properties and therapeutic potential in the treatment of hyperprolactinaemia and inhibition of lactation. *Drugs*.1995;49:255-79.
4. Teva Pharmaceuticals USA. Cabergoline tablets prescribing information. Sellersville, PA: Teva Pharmaceuticals USA. Dec 2007.

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