Amber with Guidance (Amber-G) = To be recommended or initiated by a specialist with follow up prescribing and monitoring by primary care clinicians.*
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Cabergoline for hyperprolactinaemic disorders

The details of side-effects, cautions, contraindications and interactions are not a complete list and the current BNF (https://www.medicinescomplete.com/#/) and the SPC (https://www.medicines.org.uk/emc/) remain authoritative.

Background Information	Cabergoline is indicated for the treatment of hyperprolactinaemic disorders including amenorrhoea, oligomenorrhoea, anovulation and galactorrhoea associated with hyperprolactinaemia. Cabergoline is a dopaminergic ergoline derivative endowed with potent and long-lasting prolactin-lowering activity. It acts by direct stimulation of the D_2-dopamine receptors on pituitary lactotrophs, thus inhibiting prolactin secretion.
BNF therapeutic class[1]	6.7 Other Endocrine Drugs
Indication[1,2]	Hyperprolactinaemic disorders
Dosage and administration[1,2]	Initial dose: • 500 micrograms (orally) per week (either as a single dose or as 250 micrograms on two separate days e.g., Monday and Thursday). Maintenance dose: • Increase gradually in steps of 500 micrograms every month until optimal therapeutic response is achieved – the therapeutic dosage is usually 1 milligram per week and ranges from 0.25 milligrams to 2 milligrams per week. • If doses above 1 milligram per week are to be used, these should be given in divided doses. • If intolerance is suspected, reduce dose, and increase more gradually. • Doses of up to 4.5 milligrams per week have been used in hyperprolactinaemic disorders with no more than 3 milligrams to be taken per day. • Doses should be preferably taken with food.
Cautions and Contraindications[1,2]	Cabergoline should be used with caution in: • History of peptic ulcers (withdraw cabergoline if GI bleed occurs) • Raynaud's syndrome • Cardiovascular disease • History of serious, particularly psychotic, mental health disorders • Concomitant use with antihypertensives due to risk of symptomatic hypotension and postural hypotension post dose • postpartum hypertension • In hyperprolactinaemic patients, the source of the hyperprolactinaemia should be established (i.e. exclude pituitary tumour before treatment) Contraindications: • Hypersensitivity to cabergoline or any ergot alkaloid • Patients with cardiac valvulopathy • History of pulmonary, pericardial and retroperitoneal fibrotic disorders • Toxaemia of pregnancy (pre-eclampsia) • History of puerperal psychosis in women • Co-administration with anti-psychotic medications • Hepatic insufficiency

Pregnancy and breast feeding[1,2]	**Pregnancy (refer to monitoring section below)** • Exclude pregnancy before starting and perform monthly pregnancy tests during the amenorrhoeic period. • Discontinue if pregnancy occurs during treatment to limit foetal exposure to the drug (specialist advice needed). • Discontinue 1 month before intended conception due to the long half-life of the drug and limited data on in utero exposure (ovulatory cycles persist for 6 months). **Breast feeding** • Cabergoline suppresses lactation (cabergoline should not be administered to mothers with hyperprolactinemic disorders who wish to breast-feed their infants). • Avoid breast-feeding if lactation prevention fails (no information is available on the excretion in breast milk in humans).
Adverse Drug Reactions[1]	Very Common: • Valvulopathy* (including regurgitation) and related disorders (pericarditis and pericardial effusion), headache, dizziness/vertigo, nausea, dyspepsia, gastritis, abdominal pain, gastritis, dyspepsia, nausea, abdominal pain, asthenia, fatigue. Common: • Somnolence, depression, postural hypotension, hot flushes, constipation, vomiting, breast pain, asymptomatic decreases in blood pressure (≥ 20 mmHg systolic and ≥ 10 mmHg diastolic). Uncommon: • Palpitations, dyspnea, pleural effusion, fibrosis, (including pulmonary fibrosis), epistaxis, hypersensitivity reaction, transient hemianopsia, syncope, paresthesia, increased libido, digital vasospasm, fainting, oedema, peripheral oedema, rash, alopecia, leg cramps, a decrease in haemoglobin values have been observed in amenhorrheic women during the first few months after menses. Rare: • Epigastric pain Very Rare: • Pleural fibrosis *Cardiac valvulopathy This is documented as a common side-effect of cabergoline at higher doses. Published studies have shown that this is unlikely at the doses used to treat hyperprolactinaemic disorders [3]. However there is the possibility that this may very rarely occur [4]. Valvulopathy has been associated with cumulative doses. Patients should have an annual cardiovascular examination to screen for cabergoline associated valvulopathy (CAV) if they are on a high dose of cabergoline for hyperprolactinaemia (greater than 3 milligrams per week), or in the presence of valvular heart disease before therapy commences. However routine cardiovascular examinations are not necessary with lower doses. See SPC[1] for full list of adverse reactions.

Monitoring[1,2]	Initiation and baseline monitoring to be done by the specialist. GP to continue prescribing therapy and be aware of the following:
	• Monitoring of prolactin levels will be carried out by the specialist, and the dose adjusted to achieve normal prolactin levels; following this the specialist will advise on monitoring and dose adjustment only according to clinical need.
	• A baseline echocardiogram will be performed at initiation of therapy with any clinical issues highlighted being used to determine further monitoring and use.
	• Fibrotic disorders may occur: patients presenting with signs or symptoms of pleuro-pulmonary disorders, renal insufficiency, ureteral/ abdominal vascular obstruction or cardiac failure during treatment should be fully investigated.
	• Blood pressure should be monitored for a few days after starting treatment and following dose increases.
	• Monitoring for signs of pituitary enlargement is only necessary when a prolactinoma has been diagnosed.
	• Pregnancy:
	  ◦ Exclude pregnancy before starting treatment. Also, in hyperprolactinaemic hypogonadism, perform a pregnancy test at least every four weeks during the amenorrhoeic phase and then once menstruation is re-initiated, every time a menstrual period is delayed by more than three days.
	  ◦ If pregnancy occurs during treatment, cabergoline should be discontinued. As a precautionary measure, due to the prolonged half-life of cabergoline, once regular ovulatory cycles have been achieved, women should discontinue treatment one month prior to intended conception.
	  ◦ Mechanical contraception should only be used if fertility is not the therapy endpoint, during treatment with cabergoline, and after discontinuation of cabergoline until recurrence of anovulation.
	• **A routine smear test will be done as recommended by the public health cervical cancer screening programme. No further gynaecological monitoring is required for cabergoline use in hyperprolactinaemia.**

Interactions[1,2]	• Not recommended for use with other ergot alkaloids. • Avoid concomitant use with droperidol, prochlorperazine (and other phenothiazines), benperidol, haloperidol, flupentixol, zuclopenthixol and metoclopramide. These drugs have dopamine-antagonist activity and might reduce the prolactin-lowering effect of cabergoline. • Avoid with macrolide antibiotics (e.g., erythromycin) due to increased systemic bioavailability of cabergoline. • Caution required when using with any drug which can lower blood pressure due to the risk of symptomatic and postural hypotension. Please see the SPC[1] and BNF[2] for further information on interactions.
Ordering information	• Cabergoline is licensed in the UK and is available via standard wholesalers.

Contact names and details

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Development Process

This guidance has been produced following an AMBER-G classification status of cabergoline for hyperprolactinaemic disorders by the Barnsley Area Prescribing Committee. This guideline was ratified by the Area Prescribing Committee on 11th October 2023.