

Summary of medical product characteristics

1. Name of the medicinal product

Cerebonin[®] Forte 240 mg

2. Qualitative and quantitative composition

1 film-coated tablet contains:

240 mg dry extract from Ginkgo biloba leaves (35-67:1), extraction agent: acetone 60% (w/w). The extract is quantified of 52.8-64.8 mg flavonoids calculated as flavone glycosides; and 12.96-15.84 mg terpene lactones of which 6.72-8.16 mg ginkgolides A, B, C as well as 6.24 -7.68 mg bilobalide, and contains no more than 1.2µg ginkgolic acids for each film coated tablet.

For the full list of excipients, see 6.1.

3. Pharmaceutical form

Film-coated tablets

The film coated tablets are brown and oval

4. Clinical particulars

4.1 Therapeutic indications

Herbal medicine for the improvement of (age-associated) cognitive impairment and of quality of life in mild dementia in adults

4.2 Posology and method of administration

Adults are to take one film-coated tablet once a day (corresponds to 240 mg ginkgo extract per day.)

Do not take the film-coated tablets whilst in a lying position. The film-coated tablets should be swallowed whole with a sufficient quantity of liquid (preferably with a glass of water). They can be taken independent of meals.

Treatment is to last for at least eight weeks. If symptoms have not improved after three months or the symptoms worsen, a physician should review whether continuing treatment is justified.

Children and adolescents

There is no relevant indication for children and adolescents.

Use in patients with impaired renal / hepatic function

There are no adequate data about specific dosage recommendations for patients with impaired liver or kidney function (see section 5.2).

4.3 Contraindications

Hypersensitivity to the active substance (ginkgo biloba) or to any of the excipients listed in section 6.1; pregnancy.

4.4 Special warnings and precautions for use

Patients with a greater risk of bleeding (bleeding diathesis) who are also taking anticoagulants and platelet aggregation inhibitors should only use this medicine after having consulted a doctor.

As a precaution, use of this drug is to be discontinued three to four days before surgery because there are individual reports which indicate that ginkgo products may increase the tendency to bleed.

The possibility cannot be ruled out that taking ginkgo products may promote the occurrence of seizures in epileptic patients.

Using ginkgo biloba products and efavirenz at the same time is not recommended (see section 4.5).

This drug contains less than 1mmol sodium (23 mg) per film-coated tablet, which means it is practically sodium-free.

4.5 Interactions with other medicinal products and other forms of interaction

When Cerebonin[®] forte[®] 240 mg is taken at the same time as anticoagulants (such as phenprocoumon or warfarin) or platelet aggregation inhibitors (such as clopidogrel, acetylsalicylic acid and other non-steroidal anti-inflammatory drugs), it cannot be ruled out that it will enhance the effect of these drugs.

Available research about warfarin shows no evidence of interactions between warfarin and ginkgo biloba. However, the appropriate lab tests should be performed at the beginning of treatment, when dosage is changed, when treatment ends or if there is a change in medication.

As with all medicinal products, the possibility cannot be ruled out that Cerebonin® forte® 240 mg may act on the metabolism of various other medicinal preparations via cytochrome P450-3A4,-1A2,-2C19, which may influence the potency and/or duration of the effect of the preparation concerned. There is no adequate research into these effects.

Using ginkgo biloba products and efavirenz at the same time is not recommended; together they lower the concentration of active substance in the blood. (see section 4.4)

4.6 Fertility, pregnancy and lactation

Pregnancy

This drug is not to be taken during pregnancy since individual reports have shown that there is a possibility of ginkgo products increasing the risk of bleeding (see section 4.3).

Animal studies in three species showed no evidence of embryotoxic or teratogenic effects caused by the quantified extract EGb 761® in Cerebonin® forte® 240 mg (see section 5.3).

Lactation

This drug should not be used during breastfeeding since not enough research is available. It is not known whether the extract components pass into breast milk.

Fertility

There are no data about the potential effects of ginkgo extracts on human fertility. The quantified extract EGb 761® in Cerebonin® forte® 240 mg did not have any adverse effects on male or female fertility in rats (see section 5.3).

4.7. Effects on ability to drive and use machines

There has been no research on the effects on the ability to drive and use machines.

4.8. Adverse effects

Like all pharmaceuticals, Cerebonin® forte® 240 mg may also have side effects, although they do not affect everyone.

Adverse reactions are listed based on the following information about their frequency:

Very common:	$\geq 1/10$
Common:	$\geq 1/100, < 1/10$
Uncommon:	$\geq 1/1000, < 1/100$
Rare:	$\geq 1/10,000, < 1/1,000$
Very rare:	$< 1/10,000$
Not known:	Cannot be estimated from the available data

Possible side effects (listed by organ system and frequency):

Diseases of the blood and the lymphatic system:

- Bleeding of individual organs (eye, nose, brain, gastrointestinal tract); frequency not known

Diseases of the nervous system:

- Headache; very common
- Light-headedness / dizziness; common

Diseases of the gastrointestinal tract:

- Diarrhoea, stomach pain, nausea, vomiting; common

Diseases of the nervous system:

- Hypersensitivity reactions (allergic shock); frequency not known

Diseases of the skin and subcutaneous tissue:

- Allergic skin reactions (erythema, oedema, pruritus); frequency not known

The patient-information leaflet informs the patient to discontinue the drug and consult a physician in the event of adverse effects.

Reporting suspected adverse effects

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form: <https://sideeffects.health.gov.il>

In addition, suspected adverse events can be reported directly to Dr. Samuelov's drug safety department at: drugsafety@drsamuelov.co.il

4.9 Overdose

There have been no reports of overdosage to date.

Specific antidotes to treat overdose are not known. Treatment should be based upon on the clinical picture.

5. Pharmacological properties

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Herbal anti-dementia drug
ATC Code N06DP01

The exact mechanism of action is not known.

Human pharmacological data in the EEG of older patients (57 to 77) show greater alertness, greater viscosity of the blood, increased perfusion in certain areas of the brain in healthy men ages 60 to 70, and reduced platelet aggregation. Furthermore, vasodilatory effects were

observed in the blood vessels of the forearms with a subsequent increase of regional perfusion.

Clinical trials demonstrated the efficacy of ginkgo biloba extract in patients with mild dementia, especially those over the age of 50. A meta-analysis of 7 placebo-controlled studies of 2625 patients, 1396 of whom were treated with EGb 761[®], supports these findings.

5.2. Pharmacokinetic properties

After oral application of 120 mg EGb 761[®] in humans, the terpene lactones ginkgolide A, ginkgolide B and bilobalide showed absolute bioavailability of 80% for ginkgolide A, 88% for ginkgolide B and 79% for bilobalide. Maximum plasma concentrations were in a range from 16 ng/ml to 22 ng/ml for ginkgolide A, 8 ng/ml to 10 ng/ml for ginkgolide B and 27 ng/ml to 54 ng/ml for bilobalide after administering ginkgo dry extract as a tablet. The corresponding half-lives were 3-4 hours (ginkgolide A), 4-6 hours (ginkgolide B) and 2-3 hours (bilobalide).

In patients with moderate liver failure (Child-Turcotte-Pugh class B), the C_{max} and AUC of ginkgolide A, ginkgolide B and bilobalide (a total of approx. 7% of ginkgo dry extract) after oral administration of a single dose of 120 mg and a single dose of 240 mg was unchanged versus healthy volunteers.

5.3 Preclinical safety data

The findings of conventional preclinical studies on safety pharmacology and toxicity after individual and repeated dosage showed no specific threat to human health.

Reproduction toxicity:

Animal experiments with the quantified extract EGb 761[®] in Cerebonin[®] forte[®] 240 mg yielded no evidence of an influence either on fertility or on pre- and postnatal development.

In a report in the literature, a not clearly specified ginkgo extract caused dose-dependent subcutaneous bleeding, hypopigmentation, growth inhibition and anophthalmia in chicken embryos.

Mutagenicity:

A weak positive result was seen in the Ames test and the mouse lymphoma test. The cause of this is the well-established effect of the herbal substance quercetin; however, it is safe for human use. The lack of genotoxic potential of the ginkgo extract was confirmed in a host-mediated assay, a chromosome aberration test with human lymphocytes, a V79 cell mutation test and a micronucleus test in mice.

Carcinogenicity:

Carcinogenicity studies of EGb 761[®] conducted on mice and rats show no evidence of carcinogenic effects.

In a carcinogenicity study of a ginkgo extract manufactured in a different manner, rodent-specific effects were observed. These, however, are not relevant to humans.

6. Clinical particulars

6.1 The other constituents are:

Microcrystalline cellulose; croscarmellose sodium; magnesium stearate (Ph. Eur.); hypromellose (viscosity 6 mPas); silica, precipitated; hypromellose (viscosity 15 mPas); iron (III)-hydroxide oxide x H₂O (yellow) (E 172), talcum, stearic acid, iron (III) oxide (red) (E 172).

6.2 Incompatibilities

None known.

6.3 Shelf-life

The expiry date is printed on both the cardboard box and the blister strip that holds the tablets. Cerebonin[®] forte[®] 240 mg should not be used after the expiry date.

6.4 Special precautions for storage

Keep out of reach of children. No special storage instructions, it is recommended to store in room temperature

6.5 Nature and contents of container

The container (blister pack) is made of PVC/PVDC foil and aluminium foil.

The following original package sizes are available:
Original package with 30 film-coated tablets

6.6 Special precautions for disposal / handling of the product

Not applicable.

7. Israeli marketing authorization holder and importer:

Dr. Samuelov Importing & Marketing Ltd.
13 Hasadna st, POB 2486
Ra'anana 4365007 Israel
Phone: 09 7483769

8. Manufacturer:

Dr. Willmar Schwabe GmbH & Co. KG
Willmar-Schwabe-Strasse 4
76227 Karlsruhe, Germany

9. Marketing authorisation number

177-41-36979-00

10. Date of first authorisation / renewal of authorisation

October 2024

11. Last updated

October 2024

12. Sales restrictions

Prescription only