



Primolut® Depot 250 mg

ampoules
hydroxyprogesterone caproate

PROFESSIONAL DATASHEET Summary of Product Characteristics

This is a medicament

- ▶ A medicament is a product which affects your health and its consumption contrary to instructions is dangerous for you.
- ▶ Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.
- ▶ The doctor and the pharmacist are experts in medicine, its benefits and risks.
- ▶ Do not by yourself interrupt the period of treatment prescribed.
- ▶ Do not repeat the same prescription without consulting your doctor.

Keep medicament out of reach of children

Council of Arab Health Ministers
Union of Arab Pharmacists

1. NAME OF THE MEDICINAL PRODUCT

Primolut Depot 250 mg ampoules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One 1-ml ampoule contains 250 mg hydroxyprogesterone caproate.

Other constituents: 517.7 mg benzyl benzoate, 297.3 mg castor oil for injection

See section entitled "List of other constituents" for a full list of the other constituents.

3. DOSAGE FORM

Oily, pale yellow solution for injection, free of particles

4. CLINICAL PARTICULARS

4.1 Indications

Habitual and threatened abortion due to corpus luteum deficiency

4.2 Dosage, mode and duration of employment

Like all oily solutions Primolut Depot 250 mg must be injected via the intramuscular route. Experience has shown that the transient patient reactions that occur in rare cases during or immediately after the injection of oily solutions (urge to cough, coughing bouts, shortness of breath) can be prevented by injecting particularly slowly.

Dosage:

In line with the latest scientific knowledge any medicinal therapy in early pregnancy requires an unequivocal indication. This applies similarly to the use of hormonal preparations like Primolut Depot to maintain pregnancy. Consequently, Primolut Depot must only be used if the patient urgently wants to have a baby, especially if there is corpus luteum insufficiency or a history of miscarriage. To achieve this goal and to maintain pregnancy Primolut Depot must be injected in sufficiently high doses for a protracted period.

▶ Habitual abortion

As soon as pregnancy has been diagnostically confirmed, one to two ampoules of Primolut Depot 250 mg are to be injected at weekly intervals during the first months of pregnancy, in isolated cases even longer.

▶ Threatened abortion

Therapy is initiated by injecting 2 ampoules of Primolut Depot 250 mg i.m. twice to three times per week until bleeding ceases. Bed rest is strongly recommended during this time. After this one ampoule of Primolut Depot 250 mg is to be injected i.m. twice a week for several weeks, until such time as the patient demonstrates neither bleeding nor other complaints despite being mobile again.

Whether Primolut Depot should be given prophylactically for an even longer period depends on the individual case.

4.3 Contraindications

Hypersensitivity to the active ingredient or any other constituents;
a history of *herpes gestationis*;
past or present liver tumors.

4.4 Special warnings and precautions for use

A thorough general medical examination (including measurement of blood pressure, testing the urine for sugar, possibly also conducting special liver diagnostic tests) must be conducted before treatment begins in order to be able to detect any diseases needing treatment as well as any risk factors.

Special caution and monitoring are required in the case of diabetes mellitus.

Although there is no conclusive evidence that progestogens are effective in maintaining pregnancy after previous abortions, tentative treatment may be indicated, depending on the individual circumstances.

During the course of protracted therapy it is necessary to ensure that pregnancy is continuing by conducting appropriate checkups (e.g. sonography) and immunological tests, because a dead embryo may be retained owing to the relaxing effect that Primolut-Depot has on the uterus.

8 to 14 days after unsuccessful treatment of threatened abortion and the subsequent necessary curettage, withdrawal bleeding may sometimes occur owing to the continuing effect

of Primolut-Depot which subsides only gradually. No further measures are necessary, however.

Intravascular injection must be avoided at all costs.

4.5 Interactions with other medications and other interactions

The need for oral antidiabetics or insulin may change.

4.6 Pregnancy and lactation

Hydroxyprogesterone caproate must only be used if the patient urgently wants to have a baby, if there is corpus luteum insufficiency or a history of miscarriage.

There is no tangible evidence from clinical studies or postmarketing experience that the administration of Primolut during pregnancy is deleterious.

Because minute amounts of the hormone dose pass into the mother's milk the risk-benefit ratio should be weighed up very carefully before using during lactation.

4.7 Effects on ability to drive and use machines

not applicable

4.8 Side effects

Most of the serious adverse effects - in connection with the use of medicinal products containing progestogens only - are listed in section 4.4 "Warnings and special precautions for use". Moreover, the following undesired effects have been reported in users of Primolut Depot, although a causal link could not always be ascertained.

The table below lists the side effects arranged according to the MedDRA body system categories. Incidence figures are based on reports from postmarketing studies and literature reports.

Body system (MedDRA v.8.0)	Very common (≥ 1/10)	Common (≥ 1/100 and < 1/10)	Uncommon (≥ 1/1000 and < 1/100)	Rare (≥ 1/10000 and < 1/1000)	Very rare (< 1/10000)
Immune system diseases	Allergic skin reactions e.g. allergic rash, allergic urticaria, allergic edema				Anaphylactoid reactions
General disorders and complaints at the administration site	Complaints at the administration site, reddening, swelling, pain				

Respiratory, thoracic and mediastinal disorders

Experience has shown that the transient patient reactions that occur in rare cases during or immediately after the injection of oily solutions (urge to cough, coughing bouts, shortness of breath) can be prevented by injecting particularly slowly.

Gastrointestinal tract disorders

In rare cases after the use of hormonal active ingredients such as those that are contained in Primolut Depot, benign liver tumors, and even more rarely malignant liver tumors have been observed, which in isolated cases led to life-threatening hemorrhages in the abdominal cavity. If severe upper abdominal complaints, liver enlargement or signs of intraabdominal hemorrhage occur, differential diagnostic considerations should also include the possibility of hepatic tumor, and the drug must be discontinued as the case may be.

4.9 Overdose

On the strength of animal experimental studies into acute toxicity the risk of side effects from an overdose appears to be small.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic category:

Pregnene-4 derivatives

ATC code: G03DA03

Hydroxyprogesterone caproate is a long-acting progestogen which causes secretory transformation of the endometrium at a dose of 250 mg. The effect of hydroxyprogesterone caproate on the endometrium persists for about 10 days if an estrogen is administered at the same time.

Hydroxyprogesterone caproate is an ester of the naturally occurring hydroxyprogesterone and possesses progesterone-like progestogenic effects such as antigonadotropic effects, the secretory transformation of the endometrium and thickening of the cervical mucus. The transformation of the endometrium facilitates the implantation of a fertilized ovum and creates favorable conditions for the maintenance of any pregnancy.

In the case of parenteral administration the transformation dose of

hydroxyprogesterone caproate is 250 mg. The progestogen possesses only a minor inhibitory effect on LH secretion and no effect on the placental production of hormones like progesterone. Hydroxyprogesterone caproate has no estrogenic, androgenic, antiandrogenic or corticoid effects. Unlike the short-lived effect of progesterone, hydroxyprogesterone caproate possesses a distinct depot effect. For this reason, if a single intramuscular injection is performed when an estrogen is being administered at the same time, an effect on the endometrium lasting 10 days can be observed. The thermogenic effect of hydroxyprogesterone caproate is small. The retardant effect that all sexual hormones have on the anterior pituitary-hypothalamus system is relatively weak in the case of hydroxyprogesterone caproate: It inhibits neither the progesterone production in the corpus luteum phase nor hormone production in the placenta.

The thermogenic effect is small. Only doses of 500 mg and more increase basal temperature.

5.2 Pharmacokinetic properties

Hydroxyprogesterone caproate is not cleaved into the free steroid alcohol and the fatty acid residue. The active ingredient hydroxyprogesterone caproate is thus bioavailable to 100%. In vitro, 95% of the active ingredient is bound to plasma proteins (human plasma).

On the second day after intramuscular injection the level of active ingredient plus metabolites in the entire blood pool amounted to approx. 1 % of the dose.

Elimination is exclusively in the form of conjugates, with approx. 80 % being excreted via the bile and approx. 20 % via the kidneys.

The speed of release can be deduced from the elimination half-life of 6 days. The depot is exhausted after 3 - 4 weeks.

5.3 Preclinical safety data

Conventional animal studies into repeated dose toxicity, carcinogenicity or mutagenicity have not been conducted with Primolut Depot or its active substance hydroxyprogesterone caproate because this was not considered necessary for determining risk in humans.

Hydroxyprogesterone caproate is an ester of the hydroxyprogesterone occurring naturally in intermediary metabolism. For this reason - provided it is used in humans as prescribed - no symptoms of systemic intolerance or tumorigenic effects are to be expected. No mutagenic potential can be expected on account of its structure. On the other hand it must be remembered that sex steroids can trigger the growth of hormone-dependent tissue and tumors. Reproduction toxicology studies gave no indication that Primolut Depot has any teratogenic potential or any deleterious effects on reproductive capacity in the subsequent F1 generation.

6. PHARMACEUTICAL PARTICULARS

6.1 List of other constituents

Benzyl benzoate
Castor oil for injection

6.2 Incompatibilities

Not applicable

6.3 Special precautions for storage

Light protection needed
Store below 30°C.

6.4 Nature and contents of container

One 1-ml amber glass ampoule

6.5 Special precautions for disposal and other notes on handling

No special requirements

7. MANUFACTURER

Bayer Pharma AG
Berlin, Germany.

8. INFORMATION STATUS

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Prescription status / pharmacy-only?

Rp, pharmacy-only



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Primolut
Depot 250 mg

Bayer