Bayer logo

Proluton Depot

NAME OF THE MEDICINAL PRODUCT

Proluton Depot, 250mg, solution for intramuscular injection

QUALITATIVE AND QUANTITATIVE COMPOSITION

1ml Proluton Depot contains 250 mg hydroxyprogesterone caproate in oily solution.

PHARMACEUTICAL FORM

Oily solution for intramuscular injection.

CLINICAL PARTICULARS

Therapeutic indications

Habitual and imminent abortion

Dosage and method of administration

- **How to use Proluton Depot**

Proluton Depot must be administered always as a deep intramuscular injection, preferably intragluteal, alternatively into the upper arm. The injection must be administered extremely slowly (see section "Undesirable effects").

- Abortion

  According to the present state of scientific knowledge, medicinal therapy should be given in early pregnancy only if it is absolutely essential. This is also valid for the use of hormone preparations such as Proluton Depot for the maintenance of pregnancy. Consequently, Proluton Depot should only be prescribed if there is an urgent desire for children - primarily in the presence of corpus luteum insufficiency or a case history of abortion.

  Proluton Depot is indicated for both prophylaxis and treatment of abortion because it compensates for the hormone deficit, induces quiescence of the uterus and stimulates growth of an underdeveloped uterus.

  Prolonged treatment with an adequate dosage of Proluton Depot is necessary to achieve this objective and to maintain pregnancy.

Because Proluton Depot places the uterus at rest, it is possible for an already dead embryo to be retained. In the case of protracted therapy, it is therefore necessary to check the continued existence of pregnancy by means of appropriate examinations and immunological tests.

- Habitual abortion

  As soon as pregnancy has been confirmed by diagnosis, 250 - 500 mg Proluton Depot are injected i.m. at weekly intervals during the initial months or, in individual cases, for even longer.

- Imminent abortion

  The therapy is initiated with an i.m. injection of 500 mg Proluton Depot 2 - 3 times weekly until the bleeding ceases, bed rest being urgently recommended. The treatment must then be continued for several weeks with 250 mg Proluton Depot i.m. twice weekly until the patient remains free from complaints and bleeding despite mobilization. Whether Proluton Depot should be given prophylactically even beyond this point will depend on the individual case.

  8 to 14 days after unsuccessful treatment of imminent abortion and subsequent curettage withdrawal bleeding may occur in isolated cases owing to the continuing effect of Proluton Depot which subsides only gradually. However, no further measures are necessary.

Contraindications

Proluton Depot should not be used in the presence of any of the conditions listed below. Should any of the conditions appear during the use of Proluton Depot, the use of the preparation must be discontinued immediately.

- Active venous thromboembolic disorders

- Arterial and cardiovascular disease present or in history (e.g. myocardial infarction, cerebrovascular accident, ischemic heart disease)

- Diabetes mellitus with vascular involvement.

- Presence or history of severe hepatic disease as long as liver function values have not returned to normal.

- Presence or history of liver tumors (benign or malignant)

- Known or suspected sex hormone-dependent malignancies.

- Hypersensitivity to hydroxyprogesterone caproate or to any of the excipients.

Special warnings and special precautions for use

If any of the conditions/risk factors mentioned below is present or deteriorates, an individual risk-benefit analysis should be done before Proluton Depot is started or continued.

- Circulatory disorders

It has been concluded from epidemiological surveys that the use of oral estrogen/progestogen containing ovulation inhibitors is attended by an increased incidence of thromboembolic diseases. Therefore, one should keep the possibility of an increased thromboembolic risk in mind, particularly where there is a history of thromboembolic diseases.

Generally recognized risk factors for venous thromboembolism (VTE) include a positive personal or family history (VTE in a sibling or a parent at a relatively early age), age, obesity, prolonged immobilization, major surgery or major trauma.

The increased risk of thromboembolism in the puerperium must be considered.

Treatment should be stopped at once if there are symptoms of an arterial or venous thrombotic event or suspicion thereof.

- Tumors

In rare cases, benign liver tumors, and even more rarely, malignant liver tumors have been reported in users of hormonal substances such as the one contained in Proluton Depot. In isolated cases, these tumors have led to life-threatening intra-abdominal hemorrhages.

- Other conditions

Strict medical supervision is necessary if the patient suffers from diabetes.

Chloasma may occasionally occur, especially in women with a history of chloasma gravidarum. Women with a tendency to chloasma should avoid exposure to the sun or ultraviolet radiation when taking Proluton Depot**.**

Patients who have a history of psychic depression should be carefully observed and the drug discontinued if the depression recurs to a serious degree**.**

- Medical examination

A complete medical history should be taken and a physical and gynecological examination should be performed prior to the initiation or reinstitution of the use of Proluton Depot, guided by the "Contraindications" and "Special precautions and warnings for use" and these should be repeated during the use of Proluton Depot. The frequency and nature of these assessments should be adapted to the individual woman but should generally include special reference to blood pressure, breasts, abdomen and pelvic organs, and should also include cervical cytology. Pregnancy must be excluded in the appropriate indications.

Interaction with other medicaments and other forms of interaction

Drug interactions which result in an increased clearance of sex hormones can lead to decreased therapeutic efficacy. This has been established with many hepatic enzyme-inducing drugs (including phenytoin, barbiturates, primidone, carbamazepine, rifampicin, oxcarbazepine, St. John's Wort, and rifabutin); griseofulvin, is also suspected.

Sex steroids may interfere with the metabolism of other drugs. Accordingly, plasma and tissue concentrations may be affected (e.g. cyclosporin).

- laboratory tests

The use of progestogens may influence the results of certain laboratory tests

Pregnancy and lactation

Pregnancy

Pregnancy should be ruled out unless Proluton Depot is being used for the treatment of habitual and threatened abortion.

Epidemiological studies have revealed neither an increased risk of birth defects in children born to women who used sex steroids prior to pregnancy, nor a teratogenic effect when sex steroids were used inadvertently during early pregnancy.

A possible association between the administration of female sex hormones in early pregnancy and the occurrence of malformations has been the subject of discussions in recent years. According to the present state of scientific knowledge, the assumption that there may be a causal association can be regarded as unfounded. However, it must be clearly understood, that no drug including sex hormones can be claimed with absolute certainty to be free from teratogenic effects. This remaining uncertainty is the reason why, in certain indications, the exclusion of pregnancy is called for before the start of sex hormone therapy.

Lactation

Cyclical function is usually absent during lactation - particularly during short-lasting lactation. Since this is a physiological situation, there is no need to use Proluton Depot.

It is not known whether hydroxyprogesterone and its metabolites are excreted in human milk.

Effects on ability to drive or use machines

Not known.

Undesirable effects

The most serious undesirable effects associated with the use of progestogen only preparations are listed in “Special warnings and special precautions for use”. In addition the following undesirable effects have been reported in users of Proluton Depot although a causal relationship could not always be confirmed.

The table below reports adverse reactions by MedDRA system organ classes (MedDRA SOCs). The frequencies are based on reporting rates from postmarketing experience and literature.

System organ class	Common (≥1/100)	Uncommon (≥1/1,000 to <1/100)	Rare (≥1/10,000 to <1/1,000)	Very Rare (<1/10,000)
Immune system disorders	Allergic skin reaction, e.g. allergic rash, allergic urticarial, allergic edema			Anaphylactoid reaction
General disorders and administration site conditions	Injection site reaction, e.g. injection site redness, injection site swelling, injection site pain			

The most appropriate MedDRA term is used to describe a certain reaction and its synonyms and related conditions.

Respiratory, thoracic and mediastinal disorders.

Experience has shown that the short-lasting reactions (Urge to cough, Paroxysmal cough, Respiratory distress) which occur in isolated cases during or immediately after the injection of oily solutions can be avoided by injecting the solution extremely slowly.

Overdose

On the basis of studies into the acute toxicity in experimental animals, the risk of adverse effects due to overdose appears low.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties

Pharmacotherapeutic group: Progestogens

(ATC): G03D

Proluton Depot contains the progestogen hydroxyprogesterone caproate in oily solution. Hydroxyprogesterone caproate is an ester of the natural hydroxyprogesterone and exerts typical progestogenic effects in women, comparable to progesterone such as antigonadotrophic effects, secretory transformation of the endometrium and thickening of the cervical mucus. In opposite to the short-lasting progesterone, hydroxyprogesterone caproate has a progestogenic depot effect. Following intramuscular administration, maximum concentrations in the plasma are reached within 2-5 days. The thermogenic effect of the preparation is weak.

The administration of 250 mg hydroxyprogesterone caproate leads to secretory transformation of the endometrium; the effect lasts about 10 days if an estrogen is administered at the same time.

Proluton Depot does not inhibit the production of progesterone during the luteal phase and has no estrogenic, corticoid or androgenic effect. Moreover, it has no inhibitory effect on the placental production of hormones.

Pharmacokinetic properties

- Absorption

Within 30 days after intramuscular administration, hydroxyprogesterone caproate was gradually and completely realeased from the depot. Hydroxyprogesterone caproate is completely bioavailable. The parent compound reached maximum concentrations in serum of 17 ± 6 ng/ml within 2-5 days after administration. Thereafter, the serum levels of hydroxyprogesterone caproate decreased slowly, and the compound was eliminated from the serum within 23 – 28 days post dose.

- Distribution

There is no formation of secondary depots or deep compartments (e.g. fat) in the body. 33 34

- Metabolism

Hydroxyprogesterone caproate is predominately metabolized as the complete steroid ester. Only small amounts of estradiol and its metabolites could be detected. The parent compound was practically not detectable in urine and feces41 indicating an almost complete metabolism of hydroxyprogesterone caproate in humans.

- Elimination

Hydroxyprogesterone caproate and its metabolites were excreted with the bile and with the urine at a ratio of 8:2, respectively. An excretion half-life of about 6 days was calculated which characterizes the release of the drug from the depot.

- Steady state conditions

During a once-weekly administration regimen, an accumulation of hydroxyprogesterone caproate and its metabolites of 100 % or more can be expected in the serum.

Preclinical safety data

Conventional animal studies aimed at clarifying repeated dose toxicity, carcinogenicity or mutagenicity have not been carried out with Proluton Depot or with its active ingredient hydroxyprogesterone caproate. Nor are they considered necessary for risk estimation in humans. Hydroxyprogesterone caproate is an ester of hydroxyprogesterone which occurs physiologically in the intermediary metabolism. Therefore, if it is used in humans according to prescription, no symptoms of systemic intolerance or tumorigenic effects are to be expected. Due to the structure no mutagenic potential is to be expected.

However, it should be kept in mind that sex steroids might stimulate the growth of hormone dependent tissues and tumors.

Reproductive toxicity studies gave no indication of a teratogenic potential of Proluton Depot nor of a damaging influence on the reproductive capacity of the following F1-generation.

PHARMACEUTICAL PARTICULARS

List of excipients
Benzyl benzoate
castor oil for injection

Incompatibilities

In the absence of compatibility studies, this medicinal product should not be mixed with other medicinal products

Storage conditions

Protect from light

Store below 30°C

Store all drugs properly and keep them out of reach of children

Presentation

1ml containing 250mg per ampoule, 1 ampoule per box

Shelf-life

Please refer to labels

Manufacturer

Bayer AG

Mullerstrasse 178

13353 Berlin

Germany

Last date of text revision

Aug 2022

If you would like to report a side effect for any Bayer Pharmaceutical or Consumer Health product, you can do it easily using our online reporting portal: https://safetrack-public.bayer.com/ or scan the QR code available below. Please also remember to seek medical advice directly from your doctor or pharmacist.

SafeTrack