PRESCRIBING INFORMATION

[Pr] Progesterone Injection, USP

50 mg/mL
(500 mg/10 mL)

Progestogen

Indications: This drug is indicated in amenorrhea and abnormal uterine bleeding due to hormonal imbalance in the absence of organic pathology, such as submucous fibroids or uterine cancer.

Pediatrics: Safety and effectiveness in pediatric patients have not been established; therefore, Health Canada has not authorized an indication for pediatric use.

Contraindications: Thrombophlebitis, thromboembolic disorders, cerebral apoplexy or patients with a history of these conditions; known or suspected carcinoma of the breast; undiagnosed vaginal bleeding; missed abortion; as a diagnostic test for pregnancy; known sensitivity to the active substance (progesterone) or any ingredient in the drug formulation; known sensitivity to sesame oil/seeds; known or suspected carcinoma of the breast or genital organs; liver dysfunction or disease.

Warnings: THE USE OF PROGESTATIONAL AGENTS DURING THE FIRST FOUR MONTHS OF PREGNANCY IS NOT RECOMMENDED.

The physician should be alert to the earliest manifestations of thrombotic disorders (thrombophlebitis, cerebrovascular disorders, pulmonary embolism, and retinal thrombosis). Should any of these occur or be suspected, the drug should be discontinued immediately.

Discontinue medication pending examination of there is a sudden partial or complete loss of vision, or if there is a sudden onset of proptosis, diplopia, or migraine. If examination reveals papilledema or retinal vascular lesions, medication should be withdrawn.

Progestational agents have been used beginning with the first trimester of pregnancy in an attempt to prevent habitual abortion or threatened abortion. There is no adequate evidence that such use is effective and there is evidence of potential harm to the fetus when such drugs are given in the first four months of pregnancy. Furthermore, in the vast majority of women, the cause of abortion is a defective ovum which progestational agents could not be expected to influence. In addition, the use of progestational agents, with their uterine relaxant properties, in patients with fertilized defective ova may cause a delay in spontaneous abortion. Therefore, the use of such drugs during the first four months of pregnancy is not recommended.

Several reports suggest an association between intrauterine exposure to female sex hormones and congenital anomalies, including congenital heart defects and limb reduction defects. One study estimated a 4.7 fold increased risk of limb reduction defects in infants exposed in utero to sex hormones (oral contraceptives, hormone withdrawal tests for pregnancy, or attempted treatment for threatened abortion). Some of these exposures were very short and involved only a few days of treatment. The data suggests that the risk of limb reduction defects in exposed fetuses is somewhat less than 1 in 1000.

If the patient is exposed to progesterone during the first four months of pregnancy or if she becomes pregnant while taking this drug, she should be apprised of the potential risks to the fetus.

Detectable amounts of progestogens have been identified in the milk of the mothers receiving them. The effect of this on the nursing infant has not been determined.

Masculinization of female fetus has occurred when progestogens have been used in pregnant women.

Because progestational drugs may cause some degree of fluid retention, conditions which might be influenced by this condition, such as epilepsy, migraine, asthma, cardiac, or renal dysfunction, require careful observation.

In cases of breakthrough bleeding, as in all cases of irregular bleeding per vaginum, nonfunctional

causes should be borne in mind, and adequate diagnostic measures undertaken.

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

The pathologist should be advised of progestin therapy when relevant specimens are submitted.

There are possible risks which may be associated with the use of progestin treatment, including adverse effects on carbohydrate and lipid metabolism.

A decrease in glucose tolerance has been observed in a small percentage of patients on estrogen-progestin combination treatment. The mechanism of this decrease is obscure. For this reason, diabetic patients should be carefully observed while receiving such therapy.

Acute eosinophilic pneumonia has been reported in patients receiving progesterone in sesame oil. In reported cases associated with progesterone in sesame oil, patients developed fever, dyspnea with hypoxic respiratory insufficiency, and diffuse pulmonary infiltrates. In general, patients developed eosinophilic pneumonia 2 to 4 weeks after starting progesterone in sesame oil and improved when progesterone in sesame oil was discontinued and a different formulation of progesterone and/or steroid therapy was initiated. Patients who develop these signs and symptoms while receiving progesterone in sesame oil should undergo prompt medical evaluation, and progesterone in sesame oil should be discontinued immediately.

Special Populations:

Renal Insufficiency: The safety and effectiveness in patients with renal insufficiency have not been established. Since progesterone metabolites are excreted mainly by the kidneys, progesterone should be administered with caution and careful monitoring in this patient population.

Hepatic Insufficiency: The safety and effectiveness in patients with hepatic insufficiency have not been established. Since progesterone is metabolized by the liver, use in patients with liver dysfunction or disease is contraindicated.

Drug Interactions:

Ketoconazole is a known inhibitor of cytochrome P450 3A4 and these data suggest that ketoconazole or other known inhibitors of this enzyme may increase the bioavailability of progesterone. The clinical relevance of the in vitro findings is unknown.

Adverse Reactions: The following adverse reactions have been observed in women taking progestogens: breakthrough bleeding; spotting; change in menstrual flow; amenorrhea; edema; changes in weight (increase or decrease); changes in cervical erosion and cervical secretions; cholestatic jaundice; rash (allergic) with and without pruritus; anaphylactoid (life-threatening allergic) reaction; melasma or chloasma, and mental depression; pain, irritation, swelling, and/or redness at the injection area.

The following laboratory result may be altered by the use of progestogens: pregnanediol determination.

In addition, the following laboratory results may be altered by the concomitant use of estrogens with progestogens: (1) hepatic function, (2) coagulation tests: increase in prothrombin, Factors VII, VIII, IX and X, (3) increase in PBI, BEI, and a decrease in T_3 uptake and (4) metyrapone test.

A statistically significant association has been demonstrated between use of estrogen-progestin combination drugs and the following serious adverse reactions: thrombophlebitis; pulmonary embolism and cerebral thrombosis and embolism. For this reason patients on progestin therapy should be carefully observed.

Although available evidence is suggestive of an association, such a relationship has been neither confirmed nor refuted for the following serious adverse reactions: neuro-ocular lesions, e.g. retinal thrombosis and optic neuritis.

The following adverse reactions have been observed in patients receiving estrogen-progestin combination drugs: rise in blood pressure in

susceptible individuals; premenstrual-like syndrome; changes in libido; changes in appetite; cystitis-like syndrome; headache; nervousness; dizziness; fatigue; backache; hirsutism; loss of scalp hair; erythema multiforme; erythema nodosum; hemorrhagic eruption, and itching.

In view of these observations, patients on progestin therapy should be carefully observed for their occurrence.

Dosage and Administration:

Not for intravenous injection.

Amenorrhea – 5 to 10 mg for 6 to 8 consecutive days. If there has been sufficient ovarian activity to produce a proliferative endometrium, one can expect withdrawal bleeding 48 to 72 hours after the last injection. This may be followed by spontaneous normal cycles.
Functional Uterine Bleeding – 5 to 10 mg daily for 6 days. Bleeding may be expected to cease within 6 days. When estrogen is given as well, the administration of progesterone is begun after 2 weeks of estrogen therapy. If menstrual flow begins during the course of injections of progesterone, they are discontinued.

Progesterone is administered by intramuscular injection. It differs from other commonly used steroids in that it is irritating at the place of injection. This is true whether the preparation is in an oil or an aqueous vehicle. The latter is particularly painful.

Supplied: Each mL contains: Progesterone 50 mg, Benzyl Alcohol 10% as a preservative in Sesame Oil q.s. In multiple dose vials of 10 mL.

Store at 15°-30°C in original packaging.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html)
- For information on how to report online, by mail or by fax, or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Find the complete Prescribing Information that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (https://health-products.canada.ca/dpd-bdpp/index-eng.jsp) or by calling 1-833-847-0082.

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