MERCK

Crinone®

NAME OF THE MEDICINAL PRODUCT
Crinone® progesterone vaginal gel 8%.

QUALITATIVE AND QUANTITATIVE COMPOSITION
90 mg Progesterone

PHARMACEUTICAL FORM
Vaginal gel

CLINICAL PARTICULARS
Therapeutic Indications
Treatment of disorders associated with progesterone deficiency, such as:
• infertility due to inadequate luteal phase.
• for use during in-vitro fertilisation, where infertility ismainly due to tubal, idiopathic or endometriosis linked sterility associated with normal ovulatory cycles.

Posology and method of administration
Intravaginal application
• Treatment of infertility due to inadequate luteal phase: one application (1.125 g 8 %gel) every day, starting after documented ovulation or arbitrarily on the 18th-21st day of the cycle.
• When used during in-vitro fertilisation, daily application of Crinone® 8 % gel should be continued for 30 days if there is laboratory evidence of pregnancy. Children: not applicable.

Contra-indications
• known sensitivity to Crinone® (progesterone or any of the other ingredient)
• undiagnosed vaginal bleeding
• known or suspected malignancy of the breast or genital organ
• acute porphyria
• thrombophlebitis, thromboembolic disorders, cerebral apoplexy or patients with a history of these conditions
• missed abortion

Special warnings and special precautions for use
• Crinone® should be used with caution in patients with severe hepatic impairment.
• Discontinue drug immediately if thrombophlebitis, cerebrovascular disorders, pulmonary embolism and retinal thrombosis occur.
• The pretreatment physical examination should include special reference to breast and pelvic organs, as well as Papanicolaou smear.
• In cases of breakthrough bleeding, as in all cases of irregular vaginal bleeding, non-function causes should be considered. In cases of undiagnosed vaginal bleeding adequate diagnostic measures should be undertaken.
• The pathologist should be advised of progesterone therapy when relevant specimens are submitted.
• Because progestogens may cause some degree of fluid retention, conditions which might be influenced by this factor (e.g. epilepsy, migraine, asthma, cardiac or renal dysfunction) require careful observation.
• Patients who have a history of psychic depression should be carefully observed and the drug discontinued if the depression recurs to a serious degree.
• A decrease in glucose tolerance has been observed in a small percentage of patients on oestrogen-progestin combination drugs. The mechanism of this decrease is not known. For this reason, diabetic patients should be carefully observed while receiving progestin therapy.

Interaction
Although no interaction with other drugs have been reported. Crinone® is not recommended for use concurrently with other vaginal preparations.

Pregnancy and lactation
Use during pregnancy

In case of corpus luteum deficiency, Crinone® can be used during the first trimester of pregnancy. Controlled studies in women have not revealed foetal risks in the course of the first trimester.
Use during lactation
Do not use during lactation.

Effects on ability to drive and use machines
Crinone® has no influence on the ability to drive and use machines.

Undesirable effects
The adverse reactions reported below are classified according to frequency of occurrence as follows:

Very common (≤ 1/10)
Common (≤ 1/100 to < 1/10)
Uncommon (≤ 1/1,000 to < 1/100)
Rare (≤ 1/10,000 to < 1/1,000)
Very rare (< 1/10,000)

Crinone is generally well tolerated. In clinical studies, the following adverse events have been reported during Crinone® therapy. Most adverse events observed in clinical studies cannot be distinguished from the symptoms common in early pregnancy.

Common:
Breast tenderness, itching or burning.

Post Marketing Reports
For adverse reactions identified during post-marketing surveillance, the frequency is not known (cannot be estimated from the available data).

In addition, intermenstrual bleeding (spotting), hypersensitivity reactions usually manifesting as skin rash, vaginal irritation and other mild application site reactions have been reported post marketing.

Overdose
In the case of overdose, discontinue Crinone®, treat the patient symptomatically, and institute supportive measures.

PHARMACOLOGICAL PROPERTIES
Pharmacodynamic properties
Those of the naturally occuring progesterone with induction of a full secretory endometrium.

Pharmacokinetic properties
The progesterone vaginal gel is based on a Polycarbophil delivery system which attaches to the vaginal mucosa and provides a prolonged release of Progesterone for at least three days.

Preclinical safety data
In rabbits, Crinone® was an eye irritant categorized class IV (minimal effects clearing in less than 24 hours), but not a dermal irritant.
A moderate vaginal irritation was found in rabbits after application of 2.0 ml/day of 8 % gel for 5 days.

PHARMACEUTICAL PARTICULARS
List of excipients
Glycerin, Light Liquid Paraffin, Hydrogenated Palm Oil Glyceride, Carbomer 974P, Sorbic acid, Polycarbophil, Sodium hydroxide, Purified water.

Incompatibilities
No incompatibilities were found with the usual contraceptive devices.

Shelf life
36 months

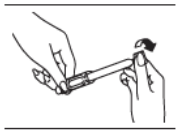
Special precautions for storage
Do not store above 30°C

Nature and contents of container
A single use, one piece, white polyethylene applicator with a twist-off top, designed for intravaginal application.

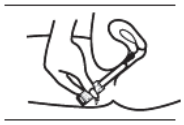
Each applicator delivers 1.125 g of gel. Each one is wrapped up and sealed in a paper/aluminium/polyethylene foil overwrap.
The applicators are packed in cardboard boxes containing 6 or 15 units.
Not all pack sizes may be marketed.

Instructions of use/handling
Crinone® is applied directly from the specially designed sealed applicator into the vaginal. Remove the applicator from the sealed wrapper. DO NOT remove the twist-off cap at this time.

1. Grip the applicator firmly by the thick end. Shake down like a thermometer to ensure that the contents are at the thin end.
2. Twist off the tab and discard.



3. The applicator may be inserted while you are in a sitting position or when lying on your back with the knees bent. Gently insert the thin end of applicator well into the vaginal.
4. Press the thick end of the applicator firmly to deposit gel. Remove the applicator and discard in a waste container.
5. Crinone® coats the vaginal mucosa to provide long-lasting release of progesterone.



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