1.3 Product Information

1.3.1 Summary of Product Characteristic

1. Name of the medicinal product

PROGESTERONE INJECTION BP (FERTLITE 100)

2. Qualitative and quantitative composition

Each ml contains

Progesterone BP	100 mg
Benzyl Alcohol BP (As preservatives)	200 mg
Ethyl Oleate BP	Q.S.

3. Pharmaceutical form

Solution for Injection.

Pale yellow colored liquid filled in clear glass ampoule USP Type-I.

4. Clinical particulars

4.1 Therapeutic indications

Fertlite 100 is indicated for the treatment of dysfunctional uterine bleeding. It is also indicated for the maintenance of early pregnancy in cases of documented history of repeated miscarriages due to luteal phase defect and in selected cases as an adjunct to successful treatment of infertility with techniques such as In-Vitro Ferilisation (IVF) or Gamete Intra- Fallopian Transfer (GIFT) in order to facilitate uterine implantation of the fertilised ovum.

4.2 Posology and method of administration

Dosage and Administration

Fertlite 100 is given by intra-muscular injection. It should be injected deep into the buttock, rather than the thigh or deltoid, using a 1.5 inch (3.8 cm) needle. This site has ample fat cells where a depot of progesterone can be formed for slow release.

Dysfunctional uterine bleeding: 5-10mg daily for 5-10 days until 2 days before anticipated onset of menstruation.
Maintenance of pregnancy: Twice weekly of more frequent (maximum: daily) injections of 25-100mg from approximately day 15, or day of transfer of embryo or gametes usually until 8- 16 weeks of pregnancy when secretion of progesterone from the placenta should be established. Daily dosage can be increased to 200mg at the discretion of the physician.

As the indications for Fertlite 100 are restricted to women of childbearing age, dosage recommendations for children and the elderly are not appropriate.

4.3 Contraindications

1.Current or past history of thrombophlebitis, thromboembolic disorders, or cerebral apoplexy.
2. Liver dysfunction or disease.
3. Known or suspected malignancy of breast or genital organs.
4. Undiagnosed vaginal bleeding.
5. Missed abortion.
6. Known sensitivity to progesterone injection.

4.4 Special warnings and precautions for use

Fertlite 100 should be used cautiously in patients with conditions that might be aggravated by fluid retention (eg. hypertension, cardiac disease, renal disease, epilepsy), with a history of mental depression, diabetes, mild to moderate hepatic dysfunction, acute intermittent porphyria, migraine or photosensitivity.

If unexplained, sudden or gradual, partial or complete loss of vision, proptosis or diplopia, papilloedema, retinal vascular lesions or migraine occur during therapy, the drug should be discontinued and appropriate diagnostic and therapeutic measures instituted.

PRECAUTIONS

General

The pretreatment physical examination should include special reference to breast and pelvic organs, as well as a Papanicolaou smear.

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*, non-functional 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 age of the patient constitutes no absolute limiting factor although treatment with Fertlite 100 may mask the onset of the climacteric.

The pathologist should be advised of Fertlite 100 therapy when relevant specimens are submitted.

There are possible risks which may be associated with the use of Fertlite 100 treatment, including adverse effects on carbohydrate and lipid metabolism. The dosage used may be important in minimizing these adverse effects.

A decrease in glucose tolerance has been observed in a small percentage of patients on estrogen-Fertlite 100 combination treatment. The mechanism of this decrease is obscure.

For this reason, diabetic patients should be carefully observed while receiving such therapy.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Progesterone at high doses is an antifertility drug and high doses would be expected to impair fertility until the cessation of treatment.

Geriatric Use: The safety and effectiveness in geriatric patients (over age 65) have not been established.

Pediatric Use: Safety and effectiveness in pediatric patients have not been established.
Nursing Mothers: Detectable amounts of drug have been identified in the milk of mothers receiving progestational drugs. The effect of this on the nursing infant has not been determined.

4.5 Interaction with other medicinal products and other forms of interaction

Fertlite 100 may interfere with the effects of bromocriptine.
Fertlite 100 may affect the results of laboratory tests of hepatic and/or endocrine functions.
Fertlite 100 may raise the plasma concentration of cyclosporine.
The metabolism of progesterone by human liver microsomes was inhibited by ketoconazole (IC50 < 01 μM). 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.

4.6 Fertility, pregnancy and lactation

Fertlite 100 may be used to maintain pregnancy where there is deficient production of endogenous progesterone from the corpus luteum. It should not be necessary to administer Fertlite 100 once there is adequate secretion of placental progesterone.
Fertlite 100 contains progesterone itself, the same as the naturally secreted hormone, and is not associated with masculinization of a female foetus as are synthetic progestins.
Detectable amounts of progesterone enter the breast milk. As the effect on the suckling infant has not been determined, theuse of Fertlite 100 during lactation is not recommended.

4.7 Effects on ability to drive and use machines

No Known Effect.

4.8 Undesirable effects

Breakthrough bleeding; spotting; change in menstrual flow; amenorrhea; edema; change in weight (increase or decrease); changes in cervical erosion and cervical secretions; cholestatic jaundice; breast tenderness and galactorrhea; pain, irritation, and/or redness at the injection area; skin sensitivity reactions consisting of urticaria, pruritus, edema and generalized rash; acne, alopecia and hirsutism; rash (allergic) with and without pruritus; anaphylactoid reactions; mental depression; pyrexia; insomnia; nausea; and somnolence.
A statistically significant association has been demonstrated between use of estrogen progestin combination drugs and pulmonary embolism and cerebral thrombosis and embolism. For this reason, patients on progestin therapy should be carefully observed.
There is also evidence suggestive of an association with 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 individual, premenstrual syndrome, changes in libido, changes in appetite, cystitis-like syndrome, headache, nervousness, fatigue, backache, hirsutism, loss of scalp hair, erythema multiforme, erythema nodosum, hemorrhagic eruption, itching, and dizziness.

The following laboratory results may be altered by the use of estrogen-progestin combination drugs: increased sulfobromophthalein retention and other hepatic function tests; coagulation tests: increase in prothrombin factors VII, VIII, IX, and X; metyrapone test; pregnanediol determinations; thyroid function: increase in PBI, and butanol extractable protein bound iodine and decrease in T_3 uptake values.

4.9 Overdose

This is unlikely and is not expected to produce any adverse effects. Treatment is observation and, if necessary, symptomatic and supportive measures should be provided.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Transforms proliferative endometrium into secretory endometrium.
Inhibits (at the usual dose range) the secretion of pituitary gonadotropins, which in turn prevents follicular maturation and ovulation.

5.2 Pharmacokinetic properties

Absorption: After intramuscular administration of 10 mg of progesterone in oil maximum plasma concentrations (geometric mean of 7 ng/mL) were reached within approximately 8 hours after injection and plasma concentrations remained above baseline for about 24 hours after injection. Injection of 10, 25, and 50 mg resulted in geometric mean values for maximum plasma concentration (C_{MAX}) of 7, 28, and 50 ng/mL, respectively.

Distribution: Progesterone is extensively bound to plasma proteins, primarily albumin (50-54%) and cortisol-binding protein (43-48%).

Metabolism: Progesterone is metabolized primarily in the liver by reduction to pregnanediol, pregnanetriol and pregnanolone. Subsequent conjugation results in the formation of glucuronide and sulfate metabolites. The mean plasma metabolic clearance rate in cycling women is 2510 ± 135 (SEM) L/day.

Excretion: The glucuronide and sulfate conjugates of pregnanediol and pregnanolone are excreted in the urine and bile. Progesterone metabolites which are excreted in the bile may undergo enterohepatic recycling or may be excreted in the feces.
The pharmacokinetic data was determined in a small number of patients, limiting the precision in which population values may be estimated.

5.3 Preclinical safety data

Progesterone is a well-known natural reproductive steroidal hormone in humans and animals, with no known toxicological effects. Therefore, no toxicity studies have been performed with this progesterone vaginal dosage form, with the exception of local tolerance and skin sensitization studies.

6. Pharmaceutical particulars

6.1 List of excipients
Ethyl oleate
Benzyl alcohol
Butylated Hydroxy Toluene

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
2 years

6.4 Special precautions for storage
Store Below 30°C. Do not freeze. Protect from light.
Keep out of reach of children.

6.5 Nature and contents of container
1 ml clear glass ampoules USP Type-I with green snap off band

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product
None

7. Manufactured By,
Ignite Pharma Nigeria Limited.
30, Ajegunle Village, Magboro Ogun State,
Nigeria

8. Drug Product Manufacturer
Montage Laboratories Private Limited.
Unit-I, Dhandha, Idar Road,
Himatnagar-383001, Gujarat, India

Exported by
Alvita Pharma Pvt. Ltd.
Ahmedabad-380015,
Gujarat, India

9. NAFDAC REGISTRATION NUMBER(S)