SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Progesterone 200mg Pessaries

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each pessary contains 200mg Progesterone
For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM
Off-white pessaries

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
Progesterone is indicated for the
1) Treatment of premenstrual syndrome, including premenstrual tension and depression.
2) Treatment of puerperal depression.

4.2 Posology and method of administration
200mg daily to 400mg twice a day, by vaginal or rectal insertion. For premenstrual syndrome commence treatment on day 14 of menstrual cycle and continue treatment until onset of menstruation. If symptoms are present at ovulation commence treatment on day 12.

*Use in special populations:* There is no experience with use of Progesterone in patients with impaired liver or renal function.

*Paediatric population:* There is no relevant use of Progesterone in the paediatric population.

*Elderly:* No clinical data have been collected in patients over age 65.
4.3 **Contraindications**

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Undiagnosed vaginal bleeding.
- Known or suspected progesterone sensitive malignant tumours.
- Porphyria.
- Severe hepatic dysfunction or disease
- Known missed abortion or ectopic pregnancy.
- Active arterial or venous thromboembolism or severe thrombophlebitis, or a history of these events.

4.4 **Special warnings and precautions for use**

Progesterone is not indicated in threatened miscarriage. Treatment should be discontinued in the event of a missed miscarriage.

Progesterone should be discontinued if any of the following conditions are suspected:
- myocardial infarction, cerebrovascular disorders, arterial or venous thromboembolism (venous thromboembolism or pulmonary embolism), thrombophlebitis or retinal thrombosis.

Although risk of thromboembolism has been associated with estrogens, a link with progestins remains questionable. Therefore, in women with generally recognised risk factors for thromboembolic events, such as personal or family history, treatment with Progesterone may further increase the risk. In these women, the benefits of Progesterone administration need to be weighed against the risks. It should be noted however, that pregnancy itself carries an increased risk of thrombo-embolic events.

Patients with a history of depression need to be closely observed. Consider discontinuation if symptoms worsen.

Because progesterone may cause some degree of fluid retention, conditions that might be influenced by this factor (e.g. epilepsy, migraine, asthma, cardiac or renal dysfunction) require careful observation.

A decrease in glucose tolerance has been observed in a small number of patients on estrogen-progestin combination drugs. The mechanism of this decrease is not known. For this reason, diabetic patients should be carefully observed while receiving progestin therapy.

Progesterone is metabolised in the liver and should be used with caution in patients with hepatic dysfunction.

Progesterone contains the hormone progesterone which is present in significant concentrations in women during the second half of the menstrual
cycle and during pregnancy. This should be borne in mind when treating patients with conditions that may be hormone-sensitive.

Abrupt discontinuation of progesterone dosing may cause increased anxiety, moodiness, and increased sensibility to seizures.

Use rectally if barrier methods of contraception are used.

Use rectally if patients suffer from vaginal infection (especially moniliasis) or recurrent cystitis or have recently given birth.

Use vaginally if patients suffer from colitis or faecal incontinence.

4.5 Interactions with other medicinal products and other forms of interaction

Drugs known to induce the hepatic cytochrome-P450-3A4 system (e.g. rifampicin, carbamazepine or phenytoin) may increase the elimination rate and thereby decrease the bioavailability of progesterone.

The effect of concomitant vaginal products on the exposure of progesterone from Progesterone has not been assessed and is therefore not recommended.

4.6 Pregnancy and lactation

Pregnancy
Progesterone should not be used during pregnancy. There is limited and inconclusive data on the risk of congenital anomalies, including genital abnormalities in male or female infants, following intrauterine exposure during pregnancy. The rates of congenital anomalies, spontaneous abortion and ectopic pregnancies observed during the clinical trial were comparable with the event rate described in the general population although the total exposure is too low to allow conclusions to be drawn.

Lactation
Progesterone is excreted in human milk and progesterone should not be used during breast-feeding.

4.7 Effects on ability to drive and use machines

None known

4.8 Undesirable effects
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), Not known (cannot be estimated from the available data)

<table>
<thead>
<tr>
<th>SYSTEM ORGAN CLASS</th>
<th>Common</th>
<th>Uncommon</th>
<th>Not known</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nervous system disorder</td>
<td>Somnolence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>Abdominal pain, Abdominal discomfort</td>
<td>Diarrhoea and flatulence may occur with rectal administration.</td>
<td></td>
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<tr>
<td>Reproductive system and breast disorders</td>
<td>Breast pain</td>
<td>Menstruation may occur earlier than expected, or, more rarely, menstruation may be delayed.</td>
<td></td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>Hypersensitivity reactions (e.g. rash, pruritus)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td></td>
<td>Soreness, some leakage of the pessary base</td>
<td></td>
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</tbody>
</table>

**Reporting of suspected adverse reactions**

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme; website: www.mhra.gov.uk/yellowcard

4.9 **Overdose**

There is a wide margin of safety with Progesterone pessaries, but overdosage may produce euphoria or dysmenorrhoea.

5. **PHARMACOLOGICAL PROPERTIES**

5.1 **Pharmacodynamic properties**

Pharmacotherapeutic group: Sex hormones and modulators of the genital system; Progestogens; Pregnen-(4) derivatives. ATC code: G03DA04.
Progesterone is a naturally occurring steroid that is secreted by the ovary, placenta, and adrenal gland.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

There are no preclinical data of relevance to the prescriber which are additional to those already included in other sections of the SmPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Also contains: vegetable fat.

6.2 Incompatibilities

None known

6.3 Shelf life

Shelf-life

Three years from the date of manufacture.

Shelf-life after dilution/reconstitution

Not applicable.
6.4 Special precautions for storage

Store below 25°C in a dry place

6.5 Nature and contents of container

The product may be supplied in strip packs contained in cartons:

Carton: White backed folding box board printed on white.

Strip pack: Aluminium foil lacquer-laminated to 20µm polypropylene foil and coated on the reverse with polythene (20mg/m²). The alternative is thermoplastic film and laminated PVC to 95µm and polyethylene to 27-30µm.

Pack sizes: 5s, 12s, 15s

6.6 Special precautions for disposal and handling

Not applicable.

7 MARKETING AUTHORISATION HOLDER

Actavis Group PTC ehf
Reykjavikurvegur 76-78,
220 Hafnarfjordur
Iceland
8 MARKETING AUTHORISATION NUMBER(S)
PL 30306/0322

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
10/03/2011

10 DATE OF REVISION OF THE TEXT
12/09/2016