9. OVERDOSE

With vaginal administration, no case of overdose has so far been reported. With oral administration, the undesirable effects described above are mostly symptomatic of overdosage. A reduction in dosage will cause such signs to regress spontaneously.

In some users, the usual dosage may prove to be too high, as evidenced by the persistence or recurrence of uncontrolled endogenous progesterone secretion, marked sensitivity to the product itself or concomitantly low levels of blood oestradiol. The following measures should be taken:

- Progesterone should be administered in the evening AT BEDTIME, over a 10-day period per cycle.
- In the event of breakthrough bleeding (spotting)/ shortening of the menstrual cycle, initiation of treatm ent should be deferred until later into the cycle (e.g. day 19 instead of day 17).
- Perimenopausal women/ women receiving HRT should be tested to ensure that blood oestradiol levels are sufficient.

10. PHARMACOLOGICAL PROPERTIES

➢ Pharmacodynamic properties

Pharmacotherapeutic group: Genitourinary system and sex hormones
ATC code: G03DA04

Utrogestan, which contains progesterone in micronised form, significantly increases plasma progesterone levels following oral and vaginal administration, thus making it possible to correct any deficits in progesterone.

➢ Pharmacokinetic properties

Elevation of blood progesterone levels starts from the first hour onwards, with peak plasma levels reached within 1 – 3 hours following administration.

Metabolisation: plasma and urinary metabolites are identical to those found during physiological corpus luteum secretion. Its main plasma metabolites include 20-alpha-hydroxy-delta-4-pregnenolone and 5-alpha-dihydroprogesterone. Urinary elimination occurs at a rate of 95% in the form of glucuronide-conjugated metabolites. Its main urinary metabolite is 3-alpha-5-beta pregnanediol (pregnandiol).

- **Oral route**

Owing to the tissue retention time of the hormone, it might be prudent to divide the dosage into two doses, to be taken at 12-hourly intervals approx., in order to ensure that impregnation is obtained throughout the entire 24-hour period.

- **Vaginal route**

At the standard recommended dose, **stable** physiological levels of plasma progesterone, similar to those obtained during the luteal phase of a normal, ovulatory menstrual cycle, can be reached and maintained.

Utrogestan Vaginal soft capsules, induce adequate endometrial maturity, thus promoting embryo implantation.
At higher doses, reached via gradual upward titration, this route of administration makes it possible to achieve blood progesterone levels similar to those observed during the first trimester of pregnancy.

11. PHARMACEUTICAL PARTICULARS

➢ Incompatibilities

Not applicable

➢ Shelf life

3 years in its sealed blister strip.

➢ Special precautions for storage

Store below 25° C

Store in the original package

➢ Nature and contents of container

Each box contains 30 units of 100 mg soft capsules packed in blister strips, for oral and vaginal administration.

➢ Special precautions for disposal

No special requirements.

Any unused product or waste material should be disposed of in accordance with local requirements.