SCHEDULING STATUS:

S4

PROPRIETARY NAME (and dosage form):

PROVERA™ 100 mg (Tablets)

PROVERA™ 500 mg (Tablets)

COMPOSITION:

Each tablet contains 100 mg or 500 mg medroxyprogesterone acetate.

Preservative: Sodium benzoate 0,07 % m/m

PHARMACOLOGICAL CLASSIFICATION:

A 21.8.2 Progesterone without oestrogens

PHARMACOLOGICAL ACTION:

The anticancer activity of PROVERA at pharmacological doses may be dependent upon its effect on the hypothalamic/pituitary/gonadal axis, oestrogen receptors and the metabolism of steroids at tissue level.

Like progesterone, medroxyprogesterone acetate is thermogenic. At the very high dosage levels used in the treatment of certain cancers (500 mg daily or more), corticoid-like activity may manifest.

PROVERA is an orally-active progestational steroid having an apparent half-life of about 30 hours.

The principal metabolite of medroxyprogesterone acetate that has been identified is 6 □-methyl-6ß17 □, 21-trihydroxy-4-pregnene-3,20-diono-17-acetate, which is excreted in the urine.

INDICATIONS:

PROVERA tablets are indicated in the palliative treatment of:

1. Recurrent and/or metastatic endometrial cancer.
2. Recurrent and/or metastatic renal cancer.
3. Recurrent and/or metastatic breast cancer in post-menopausal women.

CONTRA-INDICATIONS:

PROVERA is contra-indicated in patients who are known to be sensitive to medroxyprogesterone acetate, or any of the tablet excipients.

WARNING:

Though PROVERA has not causally been associated with the induction of thromboembolic disorders, any patient who develops signs and/or symptoms consistent with thromboembolic disorders should be re-evaluated before continuing treatment with PROVERA.

DOSAGE AND DIRECTIONS FOR USE:

PROVERA is not recommended as primary therapy, but as adjunctive and palliative treatment in advanced, inoperable cases including those with recurrent or metastatic disease.

For the treatment of endometrial and renal cancer a dosage of 200 mg to 600 mg PROVERA per day is recommended.

For the treatment of breast cancer in post-menopausal women, a dosage of 400 mg to 1200 mg PROVERA per day is recommended.

SIDE-EFFECTS AND SPECIAL PRECAUTIONS:

The following medical events, listed in order of seriousness rather than frequency of occurrence, have been associated with the use of progestogens:

- Anaphylaxis and anaphylactoid reactions.
- Thromboembolic disorders.
- Central nervous system - nervousness, insomnia, somnolence, fatigue, depression, dizziness and headache.
- Skin and mucous membranes - urticaria, pruritis, rash, acne, hirsutism and alopecia.
- Gastro-intestinal - nausea.
- Breast tenderness and galactorrhoea.
- Miscellaneous - pyrexia, change in weight and moon facies.

Precautions:

1. Before using PROVERA, the status of the patient should be carefully evaluated.
2. PROVERA, especially in high doses used for cancer therapy, may cause weight gain and fluid retention. With this in mind, caution should be exercised in treating any patient with a pre-existing medical condition that may be adversely affected by weight gain or fluid retention.
3. The high doses of PROVERA used in the treatment of cancer patients may, in some cases, produce cushingoid symptoms, e.g. moon facies, fluid retention, glucose intolerance and blood pressure elevations.

4. Some patients receiving low dose PROVERA may exhibit a decreased glucose tolerance. The mechanism for this is not known. The fact should be borne in mind when treating all patients and especially known diabetics.
5. Patients with a history of treatment for mental depression should be carefully monitored while receiving PROVERA therapy. Some patients may complain of premenstrual-like depression while on PROVERA therapy.
6. Pathologists should be informed of the patient's ingestion of PROVERA if endometrial or endocervical tissue is submitted for examination.
7. The following laboratory tests may be affected by the use of PROVERA.
    a. Gonadotrophin levels.
    b. Plasma progesterone levels.
    c. Urinary pregnanediol levels.
    d. Plasma testosterone levels (in males).
    e. Plasma oestrogen levels (in females).
    f. Plasma cortisol levels.
    g. Glucose tolerance test.
    h. Metyrapone test.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

Patients receiving pharmacological doses of PROVERA for the treatment of neoplasms (400 mg/day or greater) may exhibit effects resembling those of corticoid excess. Only observation is recommended for management, although it may be necessary to consider dose reduction. No symptoms of acute overdosage have been observed.

IDENTIFICATION:

PROVERA™ 100 mg tablets: A white, circular, flat, bevelled tablet marked U467 on one side and scored on the reverse.

PROVERA™ 500 mg tablets: A white, capsule-shaped tablet embossed Upjohn 717 on one side only.

PRESENTATION:

PROVERA™ 100 mg tablets are available in blister packs of 100 tablets.

PROVERA™ 500 mg tablets are available in blisters and glass bottles of 30 and 100 tablets.

STORAGE INSTRUCTIONS:

Store at room temperature (15 - 30 ^{0}C)

Keep out of reach of children.

Protect from light.

REGISTRATION NUMBERS:

PROVERA™ 100 mg tablets: S/21.8.2/1

PROVERA™ 500 mg tablets: W/21.8.2/462

NAME AND BUSINESS ADDRESS OF THE APPLICANT:

Pfizer Laboratories (Pty) Ltd

85 Bute Lane

Sandton 2196

South Africa

DATE OF PUBLICATION OF THIS PACKAGE INSERT:

15 August 1989

NAMIBIA: S2

Provera 100 mg: Reg. No. 90/21.8.2/001350

Provera 500 mg: Reg. No. 90/21.8.2/001351

BOTSWANA: S2

Provera 100 mg: Reg. No. B9312125