APPROVED PACKAGE INSERT FOR NORLEVO® TABLET

SCHEDULING STATUS:
S2

PROPRIETARY NAME (AND DOSAGE FORM):

NORLEVO® Tablet.

COMPOSITION:

Each tablet contains 0,75mg Levonorgestrel.

PHARMACOLOGICAL CLASSIFICATION:

A 21.8.2 Progesterones with or without oestrogens.

PHARMACOLOGICAL ACTION:

Levonorgestrel acts as a contraceptive by inhibiting ovulation and preventing the nidation of a fertilised ovum in the uterine mucosa.

Pharmacokinetics:

Oral bioavailability of levonorgestrel is approximately 100%. In the plasma it is strongly bound to SHBG. Levonorgestrel is eliminated metabolically via the kidney (60 – 80%) and liver (40 – 50%).

After oral administration of 1,5 mg levonorgestrel the plasma terminal half-life is estimated to be 43 hours. The maximal plasma concentration (approximately

40 nmol/l) are reached within 3 hours. Levonorgestrel is hydroxylated in the liver and the metabolites are excreted as glucoronide conjugates.

INDICATIONS:

NORLEVO® is indicated for the prevention of pregnancy within 72 hours of unprotected sexual intercourse or the recognisable failure of mechanical methods.

NORLEVO® is intended for emergencies only and is completely unsuitable for regular contraception. Its reliability is not as high as that of the familiar “pill”, which is taken for at least 21 days of the menstrual cycle.

CONTRA-INDICATIONS:

Pregnancy.

NORLEVO® should not be used if there is a possibility that pregnancy already exists, e.g. if unprotected sexual intercourse has already taken place in the same cycle or if the last menstrual period failed to occur.

Hypersensitivity to any of the ingredients.

NORLEVO® should not be given to patients with undiagnosed vaginal bleeding, nor to those with a history of, or current high risk of arterial disease.

Severe hepatic impairment.

The repeated use of NORLEVO® within a monthly cycle is to be avoided, since it constitutes undesirable hormonal stress and may result in severe cycle disturbances

WARNINGS:

Patients who become pregnant despite emergency contraception should be carefully evaluated for ectopic pregnancy.

Therefore, Norlevo® is not recommended for patients who are at risk of ectopic pregnancy (previous history of salpingitis or of ectopic pregnancy).

The effect of NORLEVO® on the conceptus in the event of a failure to prevent conception is not definitely known. Therefore, a pregnancy test must be performed if there is any doubt.

NORLEVO® is intended for emergencies only and is completely unsuitable for regular contraception. Its reliability is not as high as that of the familiar “pill”, which is taken for at least 21 days of the menstrual cycle.

INTERACTION:

Interactions with other medicines:

The metabolism of NORLEVO® is enhanced by the concomitant use of liver enzyme inducers: anticonvulsants (phenobarbitones, phenytoin, primidene, carbamazepine); rifabutin, rifampicin, griseofulvin, ritonavir, Hypericum perforatum (St John’s wart). The efficacy of NORLEVO® may be decreased in cases of concomitant intake of the above mentioned medicines.

PREGNANCY AND LACTATION:

NORLEVO® is not indicated in pregnancy.

NORLEVO® is secreted into breast milk and breastfeeding should not occur

within 6 hours of administration of NORLEVO® (See contra – indications).

DOSAGE AND DIRECTIONS FOR USE:

Take two tablets in a single administration as soon as possible, preferably within 12 hours, but not later than 72 hours after unprotected sexual intercourse.

The earlier NORLEVO® is used, the more effective it is. Even extremely high doses of hormone can no longer prevent pregnancy once a fertilised ovum has become implanted in the uterine mucosa.

All further unprotected sexual intercourse must be avoided until the next menstrual period; till then, only mechanical and/or chemical methods (condom, foam, pessary) of contraception may be used.

SIDE-EFFECTS AND SPECIAL PRECAUTIONS:

The following table gives the frequency of undesirable effects reported in clinical trials.

Body System	**Frequency of Adverse Reaction**	**Frequency of Adverse Reaction**
	Very common (>1/10)	Common (>1/100)
Endocrine System.	Bleeding not related to Menses.	Delay of menses more than 7 days. Irregular bleeding and Spotting.
Nervous System.		Dizziness. Headache.
Gastro-Intestinal	Nausea. Low abdominal pain.	Diarrhoea. Vomiting.

System.

Reproductive System and Breast.	Breast tenderness.
General.	Fatigue.

Side-effects:

The following side-effects have been reported and the frequencies are unknown.

Gastro-intestinal disorders:
Gastro-intestinal disturbances.

Endocrine disorders:
Premenstrual syndrome-like symptoms and altered menstrual cycles or irregular menstrual bleeding.

Certain progestogens may have an adverse effect on serum lipids.

Metabolism and nutrition disorders:
Changes in appetite or weight and fluid retention as well as oedema.

Skin and subcutaneous tissue disorders:
Acne, melasma or chloasma, allergic skin reactions, urticaria, hair loss or hirsutism and fever.

Psyciatric disorders:
Mental depression.

Reproductive system and breast disorders:
Breast changes, including discomfort or less frequently gynaecomastia and changes in libido.

Nervous system disorders:
Fatigue, drowsiness or insomnia.

Vascular disorders:
Headache.

Immune system disorders:
Anaphylaxis or anaphylactoid reactions may occur less frequently.

Hepato-biliary disorders:
Alterations in liver function tests have been reported.

Jaundice has been reported less frequently during prolonged Levonorgestrel administration.

Special Precautions.

Pregnancy, puerperium and perinatal conditions:

NORLEVO® is not recommended for patients who are at risk of an ectopic pregnancy.

NORLEVO® should not be used diagnostically for pregnancy testing and should not be given in missed or incomplete abortion.

The use of emergency contraception does not replace the necessary precautions against sexual transmitted diseases.

Endocrine disorders:
The next menstrual period may occur earlier or later than usual. A health professional should be consulted 3 weeks after taking NORLEVO® regardless of whether bleeding has occurred or not.

Psychiatric disorders:
NORLEVO® should be used with caution in patients with a history of mental depression.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

See side-effects and special precautions.

Treatment is symptomatic and supportive.

IDENTIFICATION:

White, round, biconvex tablet engraved with “NL” on both faces.

PRESENTATION:

2 Tablets in orange PVC/PE/PVDC plastic foil sealed on aluminium foil blisters strips.

1 blister strip packed in a printed cardboard box.

STORAGE INSTRUCTIONS:

Store in a cool place below 25° C.

Protect from moisture and light.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER:

33/21.8.2/0471

NAME AND BUSINESS ADDRESS OF THE APPLICANT:

Actor Pharma (Pty) Ltd

Unit 7, Royal Palm Business Estate

646 Washington Street

Halfway House

Midrand, 1685

DATE OF PUBLICATION OF THIS PACKAGE INSERT:

[17 April 2006]
Date of approval of the new dosage.