

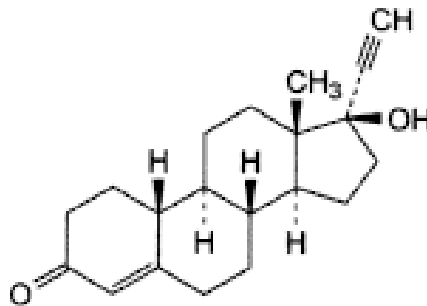
PRODUCT INFORMATION

NORIDAY[®] 28-DAY

norethisterone

NAME OF THE MEDICINE

The chemical name of norethisterone is 17-hydroxy-19-nor-17 α -pregn-4-en-20-yn-3-one. The chemical structure of norethisterone is shown below. The empirical formula is C₂₀H₂₆O₂ and the molecular weight is 298.4.



The CAS number is 68-22-4.

DESCRIPTION

Norethisterone (B.P.) is a white to creamy-white odourless crystalline powder with a slightly bitter taste, insoluble in water and sensitive to light.

Each NORIDAY tablet contains 0.35 mg norethisterone. The tablets are round, white, marked "SEARLE" on one side and "NY" on the reverse side.

PHARMACOLOGY

Norethisterone is a synthetic steroidal progestogen oral contraceptive. The mechanism of conception control is not known. Suggested mechanisms of action are increased viscosity of the cervical mucus, changes in the endometrium making it unsuitable for nidation to take place, some inhibition of the secretion of pituitary gonadotrophins.

INDICATIONS

NORIDAY is an oral contraceptive for women who will not, or cannot tolerate other oral contraceptives or intrauterine devices.

Advice to the Patient

This product (like all oral contraceptives) is intended to prevent pregnancy. It does not protect against HIV infection (AIDS) and other sexually transmitted diseases.

CONTRAINDICATIONS

- Thrombophlebitis, thromboembolic disorders, cerebral vascular disease, myocardial infarction, or a history of these conditions.
- Patients with liver disease or history of cholestatic jaundice of pregnancy and in Dubin-Johnson Syndrome or Rotor Syndrome.
- Known or suspected carcinoma of the breast and/or genital organs, or known or suspected hormone-dependent neoplasia.
- Undiagnosed abnormal genital bleeding.
- Known or suspected pregnancy.
- Sickle cell anaemia.
- Disturbed lipid metabolism.
- History of herpes of pregnancy.
- Otosclerosis with deterioration in previous pregnancy.
- Hypersensitivity to any component of the product.

PRECAUTIONS

The effects of long-term use with low dose single progestogen therapy remain to be determined. Until then, the same precautions (outlined below) associated with oestrogen-progestogen combination therapy should apply to progestogen-only contraceptives.

General

Before prescribing oral contraceptives, a complete medical family history and physical examination is desirable. The pre-treatment and periodic physical examinations should include special reference to blood pressure, breasts, abdomen and pelvic organs, including Papanicolaou smear and laboratory tests.

The effectiveness of progestogen only oral contraceptives, such as NORIDAY, is lower than that of the sequential or combination oral contraceptives containing both oestrogen and progestogen. If 100 women utilised an oestrogen containing oral contraceptive for a period of 1 year, generally less than 1 pregnancy would be expected to occur; however, if NORIDAY had been utilised approximately 4 pregnancies might occur.

An alteration in menstrual patterns in many patients is likely to be induced by using continuous progestogens. The amount and duration of flow, and cycle length, will probably be quite variable; therefore, the physician should be alert to the possibility of other causes of irregular genital bleeding and consider adequate diagnostic measures. The patient should be advised that if prolonged bleeding occurs she should consult her physician.

The efficacy of NORIDAY may be affected when absorption is impaired by vomiting or diarrhoea. If in doubt about the absorption of a tablet, the patient should be advised to treat the incident as a missed tablet (see **DOSAGE AND ADMINISTRATION**).

Thromboembolic Disorders

An increased risk of thromboembolic and thrombotic disease associated with the use of oral contraceptives is well established. The physician should be alert to the earliest manifestations of thrombotic and thromboembolic disorders, e.g., thrombophlebitis, cerebrovascular disorders (including haemorrhage), myocardial infarction, pulmonary embolism, mesenteric thrombosis and retinal thrombosis. Should any of these occur or be suspected, the drug should be discontinued immediately.

A two to six fold increase in relative risk of post-operative thromboembolic complications has been reported with the use of oral contraceptives, therefore, the physician should consider discontinuing therapy at least six weeks prior to and two weeks after elective surgery. It is also recommended that oral contraceptive therapy should be discontinued during prolonged periods of bed rest.

Myocardial Infarction

An increased risk of myocardial infarction associated with the use of oral contraceptives has been reported confirming a previously suspected association. Studies found that the greater the number of underlying risk factors for coronary artery disease (cigarette smoking, hypertension, hypercholesterolaemia, obesity, diabetes, history of pre-eclamptic toxemia) the higher the risk of developing myocardial infarction, regardless of whether the patient was an oral contraceptive user or not. Oral contraceptives, however, were found to be an additional factor. As the risk of myocardial infarction is substantially increased in women aged 40 or over, the use of oral contraceptives in women of this age group is not recommended.

In terms of relative risk, it has been estimated that oral contraceptive users who do not smoke (smoking is considered a major predisposing condition to myocardial infarction) are about twice as likely to have a fatal myocardial infarction as non-users who smoke.

Cigarette Smoking

Cigarette smoking increased the risk of serious adverse effects on the heart and blood vessels from oral contraceptive use. The risk increases with age particularly after 30 years and with heavy smoking (15 or more cigarettes per day) and is quite marked in women over 35 years of age. Women who use oral contraceptives should not smoke.

Elevated Blood Pressure

Susceptible women may experience a rise in blood pressure following the administration of contraceptive steroids. Blood pressure should be measured at intervals and care should be exercised in prescribing these preparations for patients with hypertension.

Ocular Lesions

There have been reports of neuro-ocular lesions such as optic neuritis or retinal thrombosis with the use of oral contraceptives. Oral contraceptives should be discontinued if there is gradual or sudden, partial or complete loss of vision; onset of proptosis or diplopia; onset or aggravation of migraine or development of headache of a new pattern which is recurrent, persistent or severe; papilloedema; or

any evidence of retinal vascular lesions. Appropriate diagnostic and therapeutic measures should be taken immediately.

Hepatic Tumours

Benign hepatic adenomas appear to be associated with the use of oral contraceptives. Although benign and rare, hepatic adenomas may rupture and cause death through intra-abdominal bleeding. This has been reported in short-term as well as long-term users of oral contraceptives, although one study relates risk with duration of use of the contraceptive. While hepatic adenoma is a rare lesion, it should be considered in women presenting with abdominal pain and tenderness, abdominal mass or shock.

A few cases of hepatocellular carcinoma have been reported in women taking oral contraceptives. The relationship of these drugs to this type of malignancy is not known at this time.

Carcinoma

Although there is no confirmed evidence to indicate that an increased risk of cancer is associated with the use of oral contraceptives, close clinical surveillance is nevertheless essential in all women taking these drugs. In cases of undiagnosed, persistent, or recurrent abnormal vaginal bleeding, appropriate diagnostic measures should be taken to eliminate the possibility of malignancy. Women with a strong family history of breast cancer or who have breast nodules, fibrocystic disease, or abnormal mammograms should be monitored with particular care.

Several epidemiological studies suggest that oral contraceptive use has been associated with an increase in the risk of cervical intra-epithelial neoplasia or invasive cervical cancer. It is not known whether the use of oral contraceptives is causative but an independent association has been consistently shown. The studies suggest that there is an “ever-used” effect in addition to the duration of use. These findings must be balanced against evidence of significant effects attributable to sexual behaviour, smoking, the presence of human papilloma virus and other factors. In view of the above, periodical cervical smears should form part of the routine follow up of women who have previously used oral contraceptives. As part of the routine counselling, advice that hormonal contraception does not protect against the transmission of sexually transmittable diseases, including human papilloma virus, should be made clear. Patients may not be aware that barrier contraceptive measures are necessary to reduce the risk of transmission of human papilloma virus.

Ectopic Pregnancy

Ectopic as well as intrauterine pregnancy may occur in contraceptive failures. However, in oral contraceptive failures, the ratio of ectopic to intrauterine pregnancies is higher than in women who are not receiving oral contraceptives, since the drugs are more effective in preventing intrauterine than ectopic pregnancies. The higher ectopic-intrauterine ratio has been reported with both combination products and progestogen-only oral contraceptives.

In addition, the symptoms of ectopic pregnancy and the adverse reactions to low dose progestogen administration (i.e. breakthrough bleeding, spotting, menstrual irregularity and amenorrhoea) are similar. The possibility of an ectopic pregnancy should be considered whenever a patient receiving a low-dose progestogen contraceptive experiences pelvic discomfort.

Carbohydrate and Lipid Effects

A decrease in glucose tolerance has been observed in a significant percentage of patients on oral contraceptives. For this reason, prediabetics and diabetics should be carefully observed while receiving oral contraceptives.

An increase in triglycerides and total phospholipids has been observed in patients receiving oral contraceptives.

Fluid Retention

Progestogens may cause some degree of fluid retention. Conditions which might be influenced by this factor, such as epilepsy, migraine, asthma, cardiac or renal dysfunction, require careful observation.

Depressive disorder

Oral contraceptives may cause depressive disorder. Patients with a history of depressive disorder should be carefully observed during treatment.

Prolonged Therapy

Any possible influence of prolonged NORIDAY therapy on pituitary, ovarian, adrenal, hepatic or uterine function awaits further study. The age of the patient constitutes no absolute limiting factor, although treatment with NORIDAY may mask the onset of the climacteric.

Use in Pregnancy

PREGNANCY CATEGORY: B3

Animal studies have shown that high doses of progestogens can cause masculinization of the female foetus.

Use in Lactation

Progestogen-only contraceptives seem to have no effect on lactation and the nursing child.

Effects on Laboratory Tests

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

INTERACTIONS WITH OTHER MEDICINES

There have been reports of contraceptive failure when women have taken oral contraceptives concomitantly with anti-convulsants (barbiturates, primidone, phenytoin and carbamazepine), rifampicin and other antibiotics such as ampicillin and griseofulvin.

NORIDAY should be administered at least 2 hours apart from antacids, as antacids may impair the absorption of NORIDAY.

ADVERSE EFFECTS

The following adverse reactions have been observed in women taking progestogens: break-through bleeding, spotting, change in menstrual flow, amenorrhoea, oedema, change in weight (increase or

decrease); change in cervical erosions and cervical secretions; cholestatic jaundice; rash (allergic) with or without pruritus; melasma or chloasma; mental depression; gastrointestinal disturbance; breast changes (tenderness, enlargement and secretion); masculinisation of the female foetus, hirsutism.

DOSAGE AND ADMINISTRATION

One NORIDAY 0.35 mg tablet should be taken daily, at about the same time each day starting on the first day of menstruation. Tablets should be taken continuously, without interruption, whether bleeding occurs or not. This is especially important for patients new to progestogen-only oral contraception. If a tablet is missed and there is a delay of more than 3 hours after the normal time of taking the tablet, protection is reduced and additional means of contraception should be used along with NORIDAY until menstrual bleeding occurs. The patient should be advised that if prolonged bleeding occurs, she should consult her physician.

If the patient has missed 1 or 2 tablets and does not have a period within 6 weeks of the last period, she should stop taking NORIDAY and use another method of nonhormonal contraception until pregnancy has been ruled out. If more than 2 tablets have been missed, NORIDAY should be discontinued immediately and a method of nonhormonal contraception should be used until menses has occurred or pregnancy has been excluded. Alternatively, if the patient has taken the tablets correctly, and if menses does not appear within 60 days from the last period, a method of nonhormonal contraception should be substituted until pregnancy is ruled out.

NORIDAY may be prescribed in the postpartum period either immediately or at the first postpartum examination whether or not menstruation has resumed.

OVERDOSAGE

Exact toxic doses have not been determined. When oral contraceptives are the sole medication taken as an acute overdose, the patient may remain clinically well. Overdosage may cause nausea, vomiting, breast distension, and withdrawal bleeding may occur in females.

In the case of overdosage or accidental ingestion, the patient should be observed and given supportive treatment, as there is no specific antidote. Contact the Poisons Information Centre for advice on the management of an overdose.

PRESENTATION AND STORAGE CONDITIONS

NORIDAY Tablets are available as round white tablets marked "SEARLE" on one side and "NY" on the reverse in "calendar" packs of 28 tablets.

Store below 25°C.

NAME AND ADDRESS OF THE SPONSOR

Pfizer Australia Pty Ltd
A.B.N. 5000 8422 348
38-42 Wharf Road
WEST RYDE NSW 2114

POISON SCHEDULE

S4, Prescription Only Medicine

DATE OF TGA APPROVAL

9 March 1993

DATE OF MOST RECENT AMENDMENT

24 April 2013

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