

NEXT CHOICE

Levonorgestrel Tablets 750mcg

Presentation

NEXT CHOICE 750mcg Tablets: Round, peach, uncoated tablets debossed '475' on one side and 'WATSON' on the other side. Each tablet contains 750mcg levonorgestrel.

Uses

Actions

The precise mode of action of NEXT CHOICE is not known. At the recommended regimen, levonorgestrel is thought to work mainly by preventing ovulation and fertilisation if the intercourse has taken place in the preovulatory phase, when the likelihood of fertilisation is the highest. NEXT CHOICE may also cause endometrial changes that discourage implantation. NEXT CHOICE is not effective once the process of implantation has begun.

At the recommended regimen, levonorgestrel is not expected to induce significant modification of blood clotting factors, and lipid and carbohydrate metabolism.

It has been estimated that levonorgestrel 750mcg (2 tablets 12 hours apart) prevents 85% of expected pregnancies. Efficacy appears to decline with time after intercourse (95% within 24 hours, 85% if used between 24 and 48 hours and/or 58% if used between 48 and 72 hours). Efficacy after 72 hours is unknown.

Pharmacokinetics

Orally administered levonorgestrel is rapidly and almost completely absorbed. Following ingestion of one tablet of levonorgestrel 750mcg tablet, maximum drug serum levels of 14.1 ng/ml were found at 1.6 hours. Thereafter, levonorgestrel serum levels decrease in two disposition phases with mean elimination half-lives which range from about 9 hours to 14.5 hours. Levonorgestrel is not excreted in unchanged form but as metabolites. Levonorgestrel metabolites are excreted in about equal proportions with urine and faeces. The biotransformation follows the known pathways of steroid metabolism; levonorgestrel is hydroxylated in the liver and the metabolites are excreted as glucuronide conjugates. No pharmacologically active metabolites are known.

Levonorgestrel is bound to serum albumin and sex hormone binding globulin (SHBG). Only about 1.5% of the total serum levels are present as free steroid, but 65% are specifically bound to SHBG. The absolute bioavailability of levonorgestrel was determined to be almost 100% of the dose administered.

About 0.1% of the maternal dose can be transferred via milk to the nursed infant.

Indications

NEXT CHOICE is an oral emergency contraceptive indicated for use within 72 hours of unprotected intercourse. It should be used only as an emergency measure.

Women who present for repeated courses of emergency contraception should be advised to consider long-term methods of contraception.

Dosage and Administration

The treatment requires two tablets to be taken. One tablet is taken as soon as possible (and not later than 72 hours) after unprotected intercourse. The second tablet should be taken 12 hours (and no later than 16 hours) after the first tablet.

If the patient vomits within three hours of taking either tablet another tablet should be taken immediately.

NEXT CHOICE can be used at any time during the menstrual cycle unless menstrual bleeding is overdue.

After using emergency contraception it is recommended to use a local barrier method (condom, cervical cap) until the next menstrual period starts. The use of NEXT CHOICE does not contraindicate the continuation of regular hormonal contraception.

Children

NEXT CHOICE is not recommended in children. Very limited data are available in women under 16 years of age.

Contraindications

NEXT CHOICE should not be given to pregnant women. If menstrual bleeding is overdue, if the last menstrual period was abnormal in timing or character, or if pregnancy is suspected for any other reason, pregnancy should be excluded (by pregnancy testing or pelvic examination) before treatment is given.

Hypersensitivity to the active substance levonorgestrel or any of the excipients.

Warnings and Precautions

Emergency contraception is an occasional method. NEXT CHOICE is not as effective as a conventional regular method of contraception and is suitable only as an emergency measure. It should not replace a regular contraceptive method.

Emergency contraception does not prevent a pregnancy in every instance. If there is uncertainty about the timing of the unprotected intercourse or if the woman has had unprotected intercourse more than 72 hours earlier in the same menstrual cycle,

conception may have occurred. Treatment with NEXT CHOICE following a second act of intercourse may therefore be ineffective in preventing pregnancy. If menstrual periods are delayed by more than 5 days or abnormal bleeding occurs at the expected date of menstrual periods or pregnancy is suspected for any other reason, pregnancy should be excluded.

If pregnancy occurs after treatment with NEXT CHOICE, the possibility of an ectopic pregnancy should be considered.

After taking NEXT CHOICE, menstrual periods are usually normal and occur at the expected date. They can sometimes occur earlier or later than expected by a few days. It is recommended to make a medical appointment to initiate or adapt a method of regular contraception. In case no menstrual period occurs in the next pill-free period following the use of NEXT CHOICE after regular hormonal contraception, pregnancy should be ruled out.

Repeated administration within a menstrual cycle is not advisable because of the possibility of disturbance of the cycle. Women who present for repeated courses of emergency contraception should be advised to consider long-term methods of contraception.

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

NEXT CHOICE is not recommended in patients with severe hepatic dysfunction. Severe malabsorption syndromes, such as Crohn's disease, might impair the efficacy of NEXT CHOICE.

Conditions which are considered relative contraindications include severe hypertension (BP>180+/110+), diabetes mellitus with nephropathy, retinopathy, neuropathy or vascular disease, ischaemic heart disease, stroke, or a past history of breast cancer. However, since exposure to levonorgestrel with NEXT CHOICE is brief, the risks of pregnancy in all women, including those with pre-existing medical conditions, are almost certainly greater than those associated with NEXT CHOICE.

Effect on ability to drive and use machines

No effect is known.

Preclinical safety data

Levonorgestrel is a well-established progestogen with anti-estrogenic activity. The safety profile following systemic administration is well documented and reveals no special concerns for use beyond that already listed in this text.

In acute toxicity studies performed in mice and rats levonorgestrel induced a decrease of body weight and dermatitis-like (non-irritative or non-allergic) changes on the skin. In repeat dose toxicity studies performed in mice, rats and rabbits, there were no overt signs of toxicity and no target organs or functions were identified other than the reproductive system.

Pregnancy and lactation

Use in Pregnancy

NEXT CHOICE should not be given to pregnant women and it will not interrupt the pregnancy. In the case of failure of emergency contraception, epidemiological studies indicate no adverse effects of progestogens on the fetus. It is generally considered that known teratogens will not produce malformations before organogenesis starts, which is later than 72 hours after fertilisation.

Use in Lactation

Levonorgestrel is secreted into breast milk. The potential exposure of an infant to levonorgestrel can be reduced if the breastfeeding woman takes the tablets immediately after feeding and avoids nursing following each NEXT CHOICE administration.

Adverse Effects

The following table gives the frequency of undesirable effects:

Effect	Percent of women with effect (n=977 women)*
Nausea	23.1
Low abdominal pain	17.6
Fatigue	16.9
Headache	16.8
Dizziness	11.2
Breast tenderness	10.8
Vomiting	5.6
All undesirable effects**	13.5

* Lancet, 1998, 352, 428-433;

** Mostly diarrhoea, irregular bleeding and spotting

Bleeding patterns may be temporarily disturbed, but most women will have their next menstrual period at the expected time.

If the next menstrual period is more than 5 days overdue, pregnancy should be excluded.

Interactions

The metabolism of levonorgestrel is enhanced by concomitant use of liver enzyme inducers. Drugs suspected of having the capacity to reduce the efficacy of levonorgestrel-containing medication includes: barbiturates, primidone, phenytoin, carbamazepine, herbal medicines containing *Hypericum perforatum* (St Johns' Wort), rifampicin, ritonavir, rifabutin and griseofulvin.

Medicines containing levonorgestrel may increase the risk of cyclosporin toxicity due to possible inhibition of cyclosporin metabolism.

Overdosage

Serious undesirable effects have not been reported following acute ingestion of large doses of oral contraceptives. Overdose may cause nausea, and withdrawal bleeding may occur. There are no specific antidotes and treatment should be symptomatic.

Medicine Classification

2 tablet pack - Restricted/Pharmacist Only Medicine

10 tablet pack - Prescription Only Medicine

Package quantities

NEXT CHOICE contains either one blister sleeve containing two tablets (Restricted/Pharmacist Only Medicine) or a carton containing five sleeves, each containing two tablets (Prescription Only Medicine).

Pharmaceutical precautions

Store below 25 °C.

Further information

Levonorgestrel is a white crystalline powder that is very slightly soluble in water, slightly soluble in alcohol and acetone, and soluble in chloroform. The chemical formula is $C_{21}H_{28}O_2$, molecular weight 312.45, CAS No. 797-63-7.

List of excipients

Lactose monohydrate, corn starch, povidone, colloidal silicon dioxide, magnesium stearate, FD&C Yellow #6.

Name and Address

Sponsor

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