Elisa

Drospirenone 3 mg
Ethinylestradiol 0.02 mg

Each *Elisa* Pack contains 28 Tablets, among these 24 tablets are light pink in a color which contains Drospirenone USP 3.0 mg & Ethinylestradiol USP 0.02 mg and remaining 4 white colored round tablets are without API.

DESCRIPTIONS

Elisa contains two active ingredients, Ethinylestradiol and Drospirenone. Ethinylestradiol is a synthetic version of oestrogen and Drospirenone is a synthetic form of progesterone. The hormonal components of *Elisa* inhibit ovulation by suppressing gonadotropin release. Secondary mechanisms, which may contribute to the effectiveness of *Elisa* as a contraceptive, include changes in the cervical mucus (which increase the difficulty of sperm penetration) and changes in the endometrium (which reduce the likelihood of implantation).

Drospirenone has antimineralocorticoid activity, counteracting oestrogen related sodium retention. In combination with ethinylestradiol, drospirenone displays a favourable lipid profile with an increase in high-density lipoprotein HDL. Drospirenone exerts antiandrogenic activity and does not counteract the ethinylestradiol-related sex hormone binding globulin (SHBG) increase which is useful for binding and inactivating the endogenous androgens.

PHARMACOKINETICS

Absorption

The absolute bioavailability of DRSP is about 76%. The absolute bioavailability of EE is approximately 40%. The absolute bioavailability of *Elisa* tablet, has not been evaluated. Serum concentrations of DRSP and EE reached peak levels within 1-2 hours after administration of Drospirenone & ethinyl estradiol tablets.

Food Effect

The rate of absorption of DRSP and EE following single administration of a formulation slower under fed (high fat meal).

Distribution

DRSP and EE serum concentrations decline in two phases. The apparent volume of distribution of DRSP does not bind to sex hormone binding globulin (SHBG) orcorticosteroid binding globulin (CBG) but binds about 97% to other serum proteins. EE is reported to be highly but non-specifically bound to serum albumin (approximately 98.5%) and induces an increase in the serum concentrations of both SHBG and CBG.

Metabolism

The two main metabolites of DRSP found in human plasma were identified to be the acid form of DRSP generated by opening of the lactone ring and the 4,5-dihydrodrospirenone-3-sulfate, formed by reduction and subsequent sulfation. These metabolites were shown not to be pharmacologically active. Drospirenone is also subject to oxidative metabolism catalyzed by CYP3A4.
EE has been reported to be subject to significant gut and hepatic first-pass metabolism. Metabolism of EE and its oxidative metabolites occur primarily by conjugation with glucuronide or sulfate.

Excretion

DRSP serum concentrations are characterized by a terminal disposition phase half-life of approximately 30 hours after both single and multiple dose regimens. Excretion of DRSP was nearly complete after ten days and amounts excreted were slightly higher in feces compared to urine.
For EE the terminal disposition phase half-life has been reported to be approximately 24 hours. EE is not excreted unchanged. EE is excreted in the urine and feces as glucuronide and sulfate conjugates and undergoes enterohepatic circulation.

INDICATIONS

- Oral Contraception
- Premenstrual syndrome (PMS)
- Moderate acne in women who are able to and wish to use the Pill for birth control

INSTRUCTIONS TO PATIENTS HOW TO TAKE THE PILL

IMPORTANT POINTS TO REMEMBER BEFORE YOU START TAKING YOUR PILLS:

1. BE SURE TO READ THESE DIRECTIONS:
   Before you start taking your pills.
   Anytime you are not sure what to do.
2. THE RIGHT WAY TO TAKE THE PILL IS TO TAKE ONE PILL EVERY DAY AT THE SAME TIME. *Elisa* CAN BE TAKEN WITHOUT REGARD TO MEALS.
   If you miss pills you could get pregnant. This includes starting the pack late. The more pills you miss, the more likely you are to get pregnant.
   See "WHAT TO DO IF YOU MISS PILLS" below.
3. MANY WOMEN HAVE SPOTTING OR LIGHT BLEEDING, OR MAY FEEL SICK TO THEIR STOMACH DURING THE FIRST 1-3 PACKS OF PILLS.
   If you do have spotting or light bleeding or feel sick to your stomach, do not stop taking the Pill. The problem will usually go away. If it does not go away, check with your healthcare provider.
4. MISSING PILLS CAN ALSO CAUSE SPOTTING OR LIGHT BLEEDING, even when you make up these missed pills. On the days you take two pills, to make up for missed pills, you could also feel a little sick to your stomach.
5. IF YOU HAVE VOMITING (within 3 to 4 hours after you take your pill), you should follow the instructions for "WHAT TO DO IF YOU MISS PILLS".

IF YOU HAVE DIARRHEA, or IF YOU TAKE CERTAIN MEDICINES, including some antibiotics and some herbal products such as St. John's Wort, your pills may not work as well. Use a back-up method (such as condoms or spermicides) until you check with your healthcare provider.

6. IF YOU HAVE TROUBLE REMEMBERING TO TAKE THE PILL, talk to your healthcare provider about how to make pill-taking easier or about using another method of birth control.
7. IF YOU HAVE ANY QUESTIONS OR ARE UNSURE ABOUT THE INFORMATION IN THIS LEAFLET, call your healthcare provider.

1) DECIDE WHAT TIME OF DAY YOU WANT TO TAKE YOUR PILL. It is important to take *Elisa* at about the same time every day. *Elisa* can be taken without regard to meals.
2) LOOK AT YOUR PILL PACK: – IT HAS 28 PILLS: The *Elisa*-pill pack has 24 light pink "active" pills (with hormones) to be taken for 24 days, followed by 4 white "reminder" pills (without hormones) to be taken for four days.
3) ALSO FIND
   - Where on the pack to start taking pills,
   - In what order to take the pills (follow the arrows)
   - The week numbers as shown in the diagram below
4) BE SURE YOU HAVE READY AT ALL TIMES:

- ANOTHER KIND OF BIRTH CONTROL (such as condoms or spermicides) to use as a back-up in case you miss pills.
- AN EXTRA, FULL PILL PACK.

WHEN TO START THE FIRST PACK OF PILLS
You have a choice for which day to start taking your first pack of pills. Decide with your healthcare provider which is the best day for you. Pick a time of day which will be easy to remember.

DAY 1 START

1. Take the first light pink "active" pill of the first pack during the first 24 hours of your period
2. Follow the day marking
3. Continue taking one light pink pill every day for 24 consecutive days. It's recommended to take pills everyday at the same time.
4. Then start taking your inactive (white color) 4 pills, one pill every day.

When Switching From A Different Birth Control Pill
When switching from another birth control pill, Elisa should be started on the same day that a new pack of the previous birth control pills would have been started.

WHAT TO DO DURING THE MONTH

1. TAKE ONE PILL AT THE SAME TIME EVERY DAY UNTIL THE PACK IS EMPTY
   Do not skip pills even if you are spotting or bleeding between monthly periods or feel sick to your stomach (nausea). Do not skip pills even if you do not have sex very often.
2. WHEN YOU FINISH A PACK OF PILLS
   Start the next pack on the day after your last white "reminder" pill. Do not wait any day between packs.

WHAT TO DO IF YOU MISS PILLS If you MISS 1 light pink "active" pill

1. Take it as soon as you remember. Take the next pill at your regular time. This means you may take two pills in one day.
2. You do not need to use a back-up birth control method if you have sex. If you

MISS 2 light pink "active" pills in a row in WEEK 1 OR WEEK 2 of your pack

1. Take two pills on the day you remember and two pills the next day.
2. Then take one pill a day until you finish the pack.
3. You COULD BECOME PREGNANT if you have sex in the 7 days after you restart your pills. You MUST use another birth control method (such as condoms or spermicides) as a back-up for those 7 days.

If you MISS 2 light pink "active" pills in a row in WEEK 3 or Week 4 of your pack

1. Keep taking pills according to mentioned days. Throw out the rest of the pink pills on 25th day.
2. You COULD BECOME PREGNANT if you have sex in the 7 days after you restart your pills. You MUST use another birth control method (such as condoms or spermicides) as a back-up for those 7 days.
3. You may not have your period this month but this is expected. However, if you miss your period two months in a row, call your doctor or clinic because you might be pregnant.

If you MISS 3 OR MORE light pink "active" pills in a row during ANY Week

1. Keep taking pills according to mentioned days. Throw out the rest of the pink pills on 25th day.
2. You COULD BECOME PREGNANT if you have sex in the 7 days after you restart your pills. You MUST use another birth control method (such as condoms or spermicides) as a back-up for those 7 days.
3. You may not have your period this month but this is expected. However, if you miss your period two months in a row, call your doctor or clinic because you might be pregnant.

If you MISS ANY of the 4 white "reminder" pills in Week 4 THROW AWAY the pills you missed. Keep taking one pill each day until the pack is empty. You do not need a back-up method.

When Switching From A Method Other Than A Birth Control Pill
When switching from a transdermal patch or vaginal ring, *Elisa* tablets should be started when the next application would have been due. When switching from an injection, *Elisa* tablets should be started when the next dose would have been due. When switching from an intrauterine contraceptive or an implant, *Elisa* tablets should be started on the day of removal.

Withdrawal bleeding usually occurs within 3 days following the last yellow tablet. If spotting or breakthrough bleeding occurs while taking *Elisa* tablets, instruct the patient to continue taking *Elisa* tablets by the regimen described above. Counsel her that this type of bleeding is usually transient and without significance; however, advise her that if the bleeding is persistent or prolonged, she should consult her healthcare provider.

Although the occurrence of pregnancy is low if *Elisa* tablets is taken according to directions, if withdrawal bleeding does not occur, consider the possibility of pregnancy. If the patient has not adhered to the prescribed dosing schedule (missed one or more active tablets or started taking them on a day later than she should have), consider the possibility of pregnancy at the time of the first missed period and take appropriate diagnostic measures. If the patient has adhered to the prescribed regimen and misses two consecutive periods, rule out pregnancy.

Discontinue *Elisa* tablets if pregnancy is confirmed.

The risk of pregnancy increases with each tablet missed. For additional patient instructions regarding missed pills, see the "WHAT TO DO IF YOU MISS PILLS" section in the FDA-Approved Patient Labeling. If breakthrough bleeding occurs following missed tablets, it will usually be transient and of no consequence. She should still be protected against pregnancy provided she begins taking a new cycle of tablets on the proper day.

For postpartum women who do not breastfeed or after a second time abortion, start *Elisa* tablets not before 4 weeks postpartum due to the increased risk of thrombo-embolism. If the patient starts *Elisa* tablets postpartum and has not yet had a period, evaluate for possible pregnancy, and instruct her to use an additional method of contraception until she has taken *Elisa* tablets for 7 consecutive days.

CONTRAINDICATIONS

Do not prescribe *Elisa* tablets to women who are known to have the following:

- Renal impairment
- Adrenal insufficiency
- A high risk of arterial or venous thrombotic diseases. Examples include women who are known to: Smoke, if over age 35
- Have deep vein thrombosis or pulmonary embolism, now or in the past
- Have cerebrovascular disease
- Have coronary artery disease
- Have thrombogenic valvular or thrombogenic rhythm diseases of the heart (for example, subacute bacterial endocarditis with valvular disease, or atrial fibrillation)
- Have inherited or acquired hypercoagulopathies
- Have uncontrolled hypertension
- Have diabetes mellitus with vascular disease
- Have headaches with focal neurological symptoms or have migraine headaches with or without aura if over age 35
- Undiagnosed abnormal uterine bleeding
- Breast cancer or other estrogen-or progestin-sensitive cancer, now or in the past
- Liver tumor (benign or malignant) or liver disease
- Pregnancy, because there is no reason to use COCs during pregnancy

SIDE EFFECTS

The following serious adverse reactions with the use of COCs are discussed elsewhere in the labeling:

- Serious cardiovascular events and stroke.
- Vascular events
- Liver disease

Adverse reactions commonly reported by COC users are:

- Irregular uterine bleeding
- Nausea
- Breast tenderness
- Headache

Serious Adverse Reactions

Depression, pulmonary embolism, toxic skin eruption, and uterine leiomyoma.

Precautions

Thromboembolic Disorders and Other Vascular Problems Stop *Elisa* tablets if an arterial or venous thrombotic (VTE) event occurs. Based on presently available information on *Elisa* tablets, DRSP-containing COCs may be associated with a higher risk of venous thromboembolism (VTE) than COCs containing the progestin levonorgestrel or some other progestins.

Hyperkalemia

Elisa tablets contains 3 mg of the progestin DRSP, which has anti-mineralocorti-coid activity, including the potential for hyperkalemia in high-risk patients, compara-ble to a 25 mg dose of spironolactone. Elisa tablet is contraindicated in patients with conditions that predispose to hyperkalemia (that is, renal impairment, hepatic impairment, and adrenal insufficiency).

Carcinoma of the Breasts and Reproductive Organs

Women who currently have or have had breast cancer should not use *Elisa* tablets because breast cancer is a hormonallysensitive tumor.
There is substantial evidence that COCs do not increase the incidence of breast cancer.

Liver Disease

Discontinue *Elisa* tablets if jaundice develops. Steroid hormones may be poorly metabolized in patients with impaired liver function. Acute or chronic disturbances of liver function may necessitate the discontinuation of COC use until markers of liver function return to normal and COC causation has been excluded.

High Blood Pressure

For women with well-controlled hypertension, monitor blood pressure and stop *Elisa* tablets if blood pressure rises significantly. Women with uncontrolled hypertension or hypertension with vascular disease should not use COCs. An increase in blood pressure has been reported in women taking COCs, and this increase is more likely in older women.

Gallbladder Disease

Studies suggest a small increased relative risk of developing gallbladder disease among COC users.

Carbohydrate and Lipid Metabolic Effects

Carefully monitor prediabetic and diabetic women who are taking *Elisa* tablets. COCs may decrease glucose tolerance in a dose-related fashion.
Consider alternative contraception for women with uncontrolled dyslipidemia. A small proportion of women will have adverse lipid changes while on COCs. Women with hypertriglyceridemia, or a family history thereof, may be at an increased risk of pancreatitis when using COCs.

Headache

If a woman taking *Elisa* tablets develops new headaches that are recurrent, persistent, or severe, evaluate the cause and discontinue *Elisa* tablets if indicated. An increase in frequency or severity of migraine during COC use.

Bleeding Irregularities

Unscheduled bleeding and spotting sometimes occur in patients on COCs, especially during the first three months of use. If bleeding persists or occurs after previously regular cycles, check for causes such as pregnancy or malignancy. If pathology and pregnancy are excluded, bleeding irregularities may resolve over time or with a change to a different COC.

PREGNANCY AND LACTATION

Pregnancy

There is little or no increased risk of birth defects in women who inadvertently use COCs during early pregnancy. Epidemiologic studies and meta-analyses have not found an increased risk of genital or non-genital birth defects (including cardiac anomalies and limb-reduction defects) following exposure to low dose COCs prior to conception or during early pregnancy.
The administration of COCs to induce withdrawal bleeding should not be used as a test for pregnancy. COCs should not be used during pregnancy to treat threatened or habitual abortion.
Women who do not breastfeed may start COCs no earlier than four weeks postpartum.

Nursing Mothers

When possible, advise the nursing mother to use other forms of contraception until she has weaned her child. Estrogen-containing COCs can reduce milk production in breastfeeding mothers. This is less likely to occur once breastfeeding is well-established; however, it can occur at any time in some women. Small amounts of oral contraceptive steroids and/or metabolites are present in breast milk. After oral administration of *Elisa* tablets, about 0.02% of the DRSP dose was excreted into the breast milk of postpartum women within 24 hours.

DRUG INTERACTION

Consult the labeling of all concurrently-used drugs to obtain further information about interactions with hormonal contraceptives or the potential for enzyme alterations.

EFFECTS OF OTHER DRUGS ON COCs

Substances Diminishing the Efficacy of COCs

Drugs or herbal products that induce certain enzymes, including cytochrome P450 3A4 (CYP3A4), may decrease the effectiveness of COCs or increase breakthrough bleeding. Some drugs or herbal products that may decrease the effectiveness of hormonal contraceptives include phenytoin, barbiturates, carbamazepine, bosentan, felbamate, griseofulvin, oxcarbazepine, rifampicin, topiramate and products containing St. John's wort. Interactions between oral contraceptives and other drugs may lead to breakthrough bleeding and/or contraceptive failure. Counsel women to use an alternative method of contraception or a back-up method when enzyme inducers are used with COCs, and to continue back-up contraception for 28 days after discontinuing the enzyme inducer to ensure contraceptive reliability.

Antibiotics

There have been reports of pregnancy while taking hormonal contraceptives and antibiotics, but clinical pharmacokinetic studies have not shown consistent effects of antibiotics on plasma concentrations of synthetic steroids.

Effects of Combined Oral Contraceptives on Other Drugs

COCs containing EE may inhibit the metabolism of other compounds. COCs have been shown to significantly decrease plasma concentrations of lamotrigine, likely due to induction of lamotrigine glucuronidation. This may reduce seizure control; therefore, dosage adjustments of lamotrigine may be necessary. Consult the labeling of the concurrently-used drug to obtain further information about interactions with COCs or the potential for enzyme alterations.

Potential to Increase Serum Potassium Concentration

There is a potential for an increase in serum potassium concentration in women taking *Elisa* with other drugs that may increase serum potassium concentration.

Interference with Laboratory Tests

The use of contraceptive steroids may influence the results of certain laboratory tests, such as coagulation factors, Liver Function Tests, Thyroid Function Tests, Lipoproteins, Gonadotropins,Glucose Tolerance.
DRSP causes an increase in plasma renin activity and plasma aldosterone induced by its mild anti-mineralocorticoid activity.

OVER DOSAGE

Symptoms of overdose may include nausea, vomiting, or vaginal bleeding. Available information from cases of accidental ingestion of oral contraceptives by children indicates no serious effects.

STORAGE

Store in a cool & dry place, protect from light & moisture. Keep out of the reach of children.

COMMERCIAL PACK

Each box contains single Alu-PVC blister pack which contains 1 x 24's light pink colored tablets and 4 white color placebo (inactive) Tablets.

**DRSP - Drospirenone*
**EE - Ethinylestradiol*

nuvista
Manufactured by:
Nuvista Pharma Limited
48 Tongi industrial area, Gazipur, Bangladesh
A subsidiary of Beximco Pharmaceuticals Ltd.
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