ARTWORK DETAIL LABEL

Product	Zinnia				
Buyer/Country	Malaysia				
Item Code	XXXXXXXX				
Dimension	Open Size: 134 x 223 mm, Folding size : 134 x 28 mm	**Component**	Leaflet	**Pack**	NA
Colour Shades	Black			**No. of Colours**	1
Non Printing Colour	Die Line				
Date	09-12-2024				
Special Instructions	NA				

Front **Back**

28 mm

223 mm

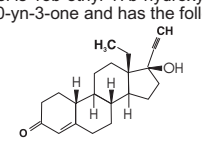
Space for Pharma Code

Zinnia

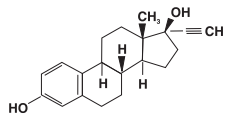
(Levonorgestrel and Ethinylestradiol Tablets)
21 Tablets

Composition
Each sugar coated tablet contains:
Levonorgestrel Ph. Eur 150 mcg
Ethinylestradiol Ph. Eur 30 mcg
Colour : Titanium Dioxide

Description
Levonorgestrel is 13b-ethyl-17b-hydroxy-18, 19-dinor-17a-pregn-4-en-20-yn-3-one and has the following structure.



Ethinylestradiol is 19-Nor-17 a -pregna-1,3,5(10)-trien-20-yne-3,17-diol and has the following structure.



Pharmaceutical Form
Sugar coated tablet.
Tablet is white, circular, biconvex.

Pharmacodynamics
Inhibits ovulation via a negative feedback mechanism on the hypothalamus, which alters the normal pattern of gonadotropin secretion of a follicle-stimulating hormone (FSH) and luteinizing hormone by the anterior pituitary gland.
Changes the cervical mucus to make it more viscid which increases the difficulty of sperm entry into the uterus. Changes the endometrium to reduce the likelihood of implantation.

Therapeutic Class
Hormonal Contraceptives.

Indications
Zinnia is indicated for the prevention of pregnancy.

Pharmacokinetics
Levonorgestrel and Ethinylestradiol are absorbed well from the gastro intestinal tract. Ethinylestradiol considerably undergoes first-pass metabolism having average bioavailability of 40-45%. Levonorgestrel does not exhibit first pass metabolism and hence completely bioavailable.
Levonorgestrel is largely plasma protein bound to both sex hormone binding globulin (SHBG) and albumin. However, Ethinylestradiol is bound in plasma to albumin only and increases the binding power of SHBG. After oral administration, peak plasma levels of each, Levonorgestrel and Ethinylestradiol, is noticed within 1 to 4 hours.
The elimination half-life of Ethinylestradiol is about 25 hours. It is mainly metabolised by aromatic hydroxylation but different variety of hydroxylated and methylated metabolites are formed which are present both as free and as conjugated with glucuronide and sulphate. Conjugated Ethinylestradiol is excreted in bile and may undergo enterohepatic recirculation system. Approximately 40 % of Ethinylestradiol is excreted in the urine and remaining 60 % in the faeces.
The elimination half-life for Levonorgestrel is about 24 hours. Levonorgestrel is mainly metabolised by reduction of the A ring followed by glucuronidation. Approximately 60 % of Levonorgestrel is excreted in the urine and remaining 40 % in the faeces.

Dosage and Administration
Tablets must be taken in the order directed on the package every day at about the same time with some liquid as needed. Tablet taking is continuous. One tablet is to be taken daily for 21 consecutive days. Each subsequent pack is started after a 7-day tablet free interval, during which time a withdrawal bleeding usually occurs. This usually starts on day 2-3 after the last tablet and may not have finished before the next pack is started.
How to start ZINNIA TABLET : - No preceding hormonal contraceptive use (in the past month) : Tablet-taking has to start on day 1 of the woman's natural cycle (i.e. the first day of her menstrual bleeding). Starting on days 2-5 is allowed, but during the first cycle a barrier method is recommended in addition for the first 7 days of tablet-taking. - Changing from a combined hormonal contraceptive (combined oral contraceptive/COC) : The woman should start with ZINNIA TABLET preferably on the day after the last active tablet (the last tablet containing the active substances) of her previous COC, but at the latest on the day following the usual tablet-free or placebo tablet interval of her previous COC. - Changing from a progestogen-only-method (minipill, injection, implant) The woman may switch any day from the minipill (from an implant on the day of its removal, from an injectable when the next injection would be due), but should in all of these cases be advised to additionally use a barrier method for the first 7 days of tablet-taking. - Following first-trimester abortion : The woman may start immediately. When doing so, she need not take additional contraceptive measures. - Following delivery or second-trimester abortion : Women should be advised to start at day 21 to 28 after delivery or second-trimester abortion. When starting later, the woman should be advised to additionally use a barrier method for the first 7 days of tablet-taking. However, if intercourse has already occurred, pregnancy should be excluded before the actual start of COC use or the woman has to wait for her first menstrual period. Management of missed tablets : If the user is less than 12 hours late in taking any tablet, contraceptive protection is not reduced. The woman should take the tablet as soon as she remembers and should take further tablets at the usual time. If she is more than 12 hours late in taking any tablet, contraceptive protection may be reduced. The management of missed tablets can be guided by the following two basic rules : 1. Tablet-taking must never be discontinued for longer than 7 days 2. 7 days of uninterrupted tablet-taking are required to attain adequate suppression of the hypothalamic-pituitary-ovarian-axis. Advice in case of gastro-intestinal disturbances : In case of severe gastro-intestinal disturbances, absorption may not be complete and additional contraceptive measures should be taken. If vomiting occurs within 3-4 hours after active tablet-taking, the advice concerning missed tablets, is applicable. If the woman does not want to change her normal tablet-taking schedule, she has to take the extra tablet(s) needed from another pack.

Route of Administration: Oral

Pregnancy and Lactation
The administration of Zinnia is contraindicated during pregnancy. Combination oral contraceptives do not appear to increase the risk of birth effects when they are used before Pregnancy. It have also been concluded from clinical studies that oral contraceptives when inadvertently during early pregnancy, do not seem to have a teratogenic effect.
Oral contraceptives are distributed into breast milk and may diminish its quality or shorten time of lactation.

Contraindications
1. Pregnancy
2. Severe disturbances of liver function, jaundice or persistent itching during a previous pregnancy, Dubin-Johnson syndrome, Rotor syndrome, previous or existing liver tumours.
3. Existing or a history of confirmed venous thromboembolism (VTE), family history of idiopathic VTE and other known risk factors for VTE.
4. Existing or previous arterial thrombotic or embolic processes, conditions which predispose to them e.g. disorders of the clotting processes, valvular heart disease and atrial fibrillation.
5. Sickle-cell anaemia
6. Mammary or endometrial carcinoma, or a history of these conditions
7. Severe diabetes mellitus with vascular changes
8. Disorders of lipid metabolism
9. History of herpes gestationis
10. Deterioration of otosclerosis during pregnancy
11. Undiagnosed abnormal vaginal bleeding
12. Hypersensitivity to any of the components

Side effects
In rare cases, headaches, gastric upsets, nausea, vomiting, breast tenderness, changes in body weight, changes in libido, depressive moods can occur. In predisposed women, use of ZINNIA TABLET can sometimes cause chloasma which is exacerbated by exposure to sunlight. Such women should avoid prolonged exposure to sunlight. Menstrual changes: 1. Reduction of menstrual flow: This is not abnormal and it is to be expected in some patients. Indeed, it may be beneficial where heavy periods were previously experienced. 2. Missed menstruation: Occasionally, withdrawal bleeding may not occur at all. If the tablets have been taken correctly, pregnancy is very unlikely. If withdrawal bleeding fails to occur at the end of a second pack, the possibility of pregnancy must be ruled out before resuming with the next pack. Intermenstrual bleeding: 'Spotting' or heavier 'breakthrough bleeding' sometimes occur during tablet taking, especially in the first few cycles, and normally cease spontaneously. Effect on blood chemistry: The use of oral contraceptives may influence the results of certain laboratory tests including biochemical parameters of liver, thyroid, adrenal and renal function, plasma levels of carrier proteins and lipid/lipoprotein fractions, parameters of carbohydrate metabolism and parameters of coagulation and fibrinolysis.

Drug interactions
Hepatic enzyme inducers such as barbiturates, primidone, phenobarbitone, phenytoin, phenylbutazone, rifampicin, carbamazepine and griseofulvin can impair the efficacy of ZINNIA TABLET. For women receiving long-term therapy with hepatic enzyme inducers, another method of contraception should be used. The use of ampicillin and other antibiotics may also reduce the efficacy of ZINNIA TABLET, possibly by altering the intestinal flora. Women receiving short courses of enzyme inducers or broad spectrum antibiotics should take additional, non-hormonal (except rhythm or temperature method) contraceptive precautions during the time of concurrent medication and for 7 days afterwards. With rifampicin, additional contraceptive precautions should be continued for 4 weeks after treatment stops, even if only a short course was administered. The requirement for oral antidiabetics or insulin can change as a result of the effect on glucose tolerance.

Interaction of Other Medicaments:
The metabolism of levonorgestrel is enhanced by concomitant use of liver enzyme inducers, mainly CYP3A4 enzyme inducers. Concomitant administration of efavirenz has been found to reduce plasma levels of levonorgestrel (AUC) by around 50%.
Drugs suspected of having similar capacity to reduce plasma levels of levonorgestrel include barbiturates, phenytoin, carbamazepine, herbal medicines containing Hypericum perforatum (St. John's wort), rifampicin, ritonavir, and griseofulvin.
For women who have used enzyme-inducing drugs in the past 4 weeks and need emergency contraception, the use of non-hormonal emergency contraception (i.e. a Cu-IUD) should be considered. Taking a double dose of levonorgestrel (i.e. 3 mg within 72 hours after the unprotected intercourse) is an option for women who are unable or unwilling to use a Cu-IUD, although this specific combination (a double dose of levonorgestrel during concomitant use of an enzyme inducer) has not been studied.

Precautions and warnings
The use of any combined oral contraceptive carries an increased risk of venous thromboembolism (VTE) compared with no use. The excess risk of VTE is highest during the first year a woman ever uses a combined oral contraceptive. This increased risk is less than the risk of VTE associated with pregnancy which is estimated as 60 cases per 100 000 pregnancies. Some epidemiological studies have reported a greater risk of VTE for women using combined oral contraceptives containing desogestrel or gestodene (the so-called 'third generation' pills) than for women using pills containing levonorgestrel (the so-called 'second generation' pills). Numerous epidemiological studies have been reported on the risks of ovarian, endometrial, cervical and breast cancer in women using combined oral contraceptives. The evidence is clear that combined oral contraceptives offer substantial protection against both ovarian and endometrial cancer. In rare cases benign and, in even rarer cases, malignant liver tumours leading in isolated cases to life-threatening intra-abdominal haemorrhage have been observed after the use of hormonal substances such as those contained in ZINNIA TABLET. If severe upper abdominal complaints, liver enlargement or signs of intra-abdominal haemorrhage occur, the possibility of a liver tumour should be included in the differential diagnosis. Assessment of women prior to starting oral contraceptives (and at regular intervals thereafter) should include a personal and family medical history of each woman. Physical examination should be guided by this and by the contraindications and warnings for this product. The frequency and nature of these assessments should be based upon relevant guidelines and should be adapted to the individual woman, but should include measurement of blood pressure and, if judged appropriate by the clinician, breast , abdominal and pelvic examination including cervical cytology. The following conditions require strict medical supervision during medication with oral contraceptives. Deterioration or first appearance of any of these conditions may indicate that use of the oral contraceptive should be discontinued: Diabetes mellitus, or a tendency towards diabetes mellitus (e.g. unexplained glycosuria), hypertension, varicose veins, a history of phlebitis, otosclerosis, multiple sclerosis, epilepsy, porphyria, tetany, disturbed liver function, Sydenham's chorea, renal dysfunction, family history of clotting disorders, obesity, family history of breast cancer and patient history of benign breast disease, history of clinical depression, systemic lupus erythematosus, uterine fibroids and migraine, gall-stones, cardiovascular diseases, chloasma, asthma, an intolerance of contact lenses, or any disease that is prone to worsen during pregnancy. Some women may experience amenorrhoea or oligomenorrhoea after discontinuation of oral contraceptives, especially when these conditions existed prior to use. Women should be informed of this possibility.

Symptoms and treatment of overdose
Overdosage may cause nausea, vomiting and, in females, withdrawal bleeding. There are no specific antidotes and treatment should be symptomatic..

Presentation(packing and pack size)
Blister pack of 21 Tablets (Aluminium foil & PVC / PVdC) packed in a carton along with pack insert.
1) Carton containing 1 Blister along with pack insert .
2) Carton containing 5 Blisters along with pack insert .
3) Carton containing 100 Blisters along with 25 pack inserts.

Storage instructions
Store below 30°C. Keep out of reach of Children.

Shelf Life : 3 years

Senador

Manufactured by:
Senador Laboratories Private Limited
Plot No.1606 - 1609, G.I.D.C., Sarigam, Tal: Umergam,
Dist - Valsad - 396 155, Gujarat, India

Product Registration Holder & Imported by:
UNIMED SDN BHD
53, Jalan Tembaga SD 5/2B
Bandar Sri Damansara 52200, Kuala Lumpur.

Revised date : 07/01/2025

XXXXXXXX

134 mm

134 mm