Levonorgestrel and Ethinyloestradiol Tablets I.P. with Ferrous Fumarate Tablets I.P.

OVRAL® 28 Tablets

PATIENTS SHOULD BE COUNSELED THAT THIS PRODUCT DOES NOT PROTECT AGAINST HIV INFECTION (AIDS) AND OTHER SEXUALLY TRANSMITTED DISEASES.

1. TRADENAME OF THE MEDICINAL PRODUCT

OVRAL 28

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each combipack contains 28 Tablets:
21 white tablets and 7 brown tablets

Each uncoated white tablet contains:
Levonorgestrel I.P.....0.15 mg
Ethinyloestradiol I.P. .....0.03 mg

Each film coated brown tablet contains:
Ferrous Fumarate I.P. .....75 mg
Approximately equivalent to ferrous Iron…..24 mg
Approved colours used: Red Oxide of Iron and Titanium Dioxide I.P.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Ovral 28 is available in the form of tablets.

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Licensed User – Pfizer Limited, India

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Ovral 28 is indicated for the prevention of pregnancy in women who elect to use an oral contraceptive.

4.2 Posology and Method of Administration

How to take Ovral 28
Tablets must be taken orally in the order directed on the package every day at about the same time. One white tablet is to be taken daily for 21 consecutive days. One brown tablet is to be taken for the next 7 consecutive days. Each subsequent pack is started on the day after the completion of previous pack. A withdrawal bleed usually starts on days 2-3 after the last white tablet and may not have finished before the next pack is started.

How to start Ovral 28

No preceding hormonal contraceptive use (in the past month)

Directions for use: Start taking white tablets according to the day of the week from 5th day of your menstrual cycle counting first day of bleeding as day one.

Changing from another COC (Combined Oral Contraceptive)

The woman should start Ovral 28 preferably on the day after the last tablet of her previous COC, but at the latest, on the day following the usual tablet-free or inactive tablet interval of her previous COC.

Changing from a progestin only method (progestin-only pill, injection, implant)

The woman may switch any day from the progestin-only pill and should begin Ovral 28 the next day. She should start Ovral 28 on the day of an implant removal or, if using an injection, the day the next injection would be due. In all of these situations, the woman should be advised to use a nonhormonal back-up method for the first 7 days of tablet taking.

Following first-trimester abortion: The woman may start Ovral 28 immediately. Additional contraceptive measures are not needed.

Following delivery or second-trimester abortion

Since the immediate post-partum period is associated with an increased risk of

thromboembolism, COCs should be started no earlier than Day 28 after delivery in the non lactating mother or after second-trimester abortion. The woman should be advised to use a non-hormonal back-up 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 must wait for her first menstrual period. (see Sections **4.3 Contraindications** and **4.4 Special Warnings and Special Precautions for Use**).

Management of Missed Tablets

Contraceptive protection may be reduced if active tablets are missed and particularly if the missed tablets extend the tablet free interval.

If one tablet is missed, but is less than 12 hours late, it should be taken as soon as it is remembered. Subsequent tablets should be taken at the usual time.

If one tablet is missed and is more than 12 hours late or if more than one active tablet is missed, contraceptive protection may be reduced. The last missed tablet should be taken as soon as it is remembered, even if this means taking two tablets in one day. Subsequent tablets should be taken at the usual time. In addition, a nonhormonal back-up method of birth control should be used for the next seven days.

If the seven days where back up is required run beyond the last active tablet in the current pack, the next pack must be started as soon as the current pack is finished, no gap should be left between packs. This prevents an extended break in tablet-taking which may increase the risk of escape ovulation. The user is unlikely to have a withdrawal bleed until the end of the second pack, but she may experience spotting or breakthrough bleeding on tablet-taking days. If the user does not have a withdrawal bleed at the end of the second pack, the possibility of pregnancy must be ruled out before resuming tablet-taking.

If two active tablets in a row are missed in Week 1 or Week 2 of a pack, two tablets should be taken on the day remembered and two tablets the next day. Subsequent tablets should be taken at the usual time. In addition, a nonhormonal back-up method of birth control should be used for the seven days after tablets are missed.

If two active tablets in a row are missed in Week 3 of a pack or if three or more active tablets in a row are missed in weeks 1-3 of a pack: Day 1 starters should throw out the rest of the pack and start a new pack that same day. Sunday starters should keep taking one tablet every day until Sunday; on Sunday, the rest of the pack is thrown out and a new pack started that same day. In addition, a nonhormonal back-up method should be used for the seven days after tablets are missed. The user may not have a withdrawal bleed until the end of the second pack. If the user does not have a withdrawal bleed at the

end of the second pack, the possibility of pregnancy must be ruled out before resuming tablet-taking.

Advice in case of vomiting

If vomiting occurs within 4 hours after tablet taking, absorption may not be complete. In such an event, the advice concerning MANAGEMENT OF MISSED TABLETS is applicable. The woman must take the extra active tablet(s) needed from a backup pack.

How to delay a period

To delay a period the woman should continue with another pack of Ovral 28. The extension can be carried on for as long as wished until the end of the second pack. During the extension the woman may experience breakthrough bleeding or spotting. Regular intake of Ovral 28 is then resumed after the completion of previous pack.

4.3 Contraindications

Ovral 28 must not be used in women with any of the following conditions:

- Deep vein thrombosis (current or history)
- Thromboembolism (current or history)
- Cerebrovascular or coronary artery disease
- Thrombogenic valvulopathies
- Thrombogenic rhythm disorders
- Hereditary or acquired thrombophilias
- Headache with focal neurological symptoms, such as aura
- Diabetes with vascular involvement
- Uncontrolled hypertension
- Known or suspected carcinoma of the breast or other known or suspected estrogens dependant neoplasia
- Hepatic adenomas or carcinomas or active liver disease, as long as liver function has not returned to normal.
- Undiagnosed vaginal bleeding
- Known or suspected pregnancy
- Hypersensitivity to any of the components of Ovral 28 tablets.

COCs are contraindicated for concomitant use with certain anti-viral hepatitis C virus (HCV) medicinal products such as ombitasvir, paritaprevir, ritonavir and dasabuvir (see Sections **4.4 Special Warnings and Special Precautions for Use** and **4.5 Interaction with Other Medicaments and Other Forms of Interaction**).

4.4 Special Warnings and Special Precautions for Use

Cigarette smoking increases the risk of serious cardiovascular adverse reactions from COC use. This risk increases with age and with the extent of smoking (in epidemiological studies, smoking 15 or more cigarettes per day was associated with a significantly increased risk), and is quite marked in women over 35 years of age. Women who use COCs should be strongly advised not to smoke.

1. VENOUS AND ARTERIAL THROMBOSIS AND THROMBOEMBOLISM

Use of Ovral 28 is associated with an increased risk of venous and arterial thrombotic and thromboembolic events.

For any particular estrogen/progestin combination, the dosage regimen prescribed should be one which contains the least amount of estrogen and progestin that is compatible with a low failure rate and the needs of the individual patient.

New acceptors of Ovral 28 should be started on preparations containing less than 50 µg of estrogens.

a. Venous thrombosis and thromboembolism

Use of COCs increases the risk of venous thrombotic and thromboembolic events. Reported events include deep venous thrombosis and pulmonary embolism. For information on retinal vascular thrombosis (see Section **4.4 Special Warnings and Special Precautions for Use - Ocular lesions**).

The use of any COC carries an increased risk of venous thrombotic and thromboembolic events compared with no use. The excess risk is highest during the first year a woman ever uses a combined oral contraceptive. This increased risk is less than the risk of venous thrombotic and thromboembolic events associated with pregnancy which is estimated as 60 cases per 100,000 women-years. Venous thromboembolism is fatal in 1-2% of cases.

The risk of venous thrombotic and thromboembolic events is further increased in women with conditions predisposing for venous thrombosis and thromboembolism. Caution must be exercised when prescribing COCs for such women.

Examples of predisposing conditions for venous thrombosis and thromboembolism are:
- obesity
- surgery or trauma with increased risk of thrombosis
- recent delivery or second-trimester abortion
- prolonged immobilization

- increasing age

Further risk factors, which represent contraindications for the use of COCs, are listed in (Section **4.3 Contraindications**).

The relative risk of postoperative thromboembolic complications has been reported to be increased two- to four-fold with the use of COCs. The relative risk of venous thrombosis in women with predisposing conditions is twice that of women without such conditions. If feasible, COCs should be discontinued:

- for four weeks prior to and for two weeks after elective surgery with increased risk of thrombosis, and
- during prolonged immobilization.

Since the immediate post-partum period is associated with an increased risk of thromboembolism, COCs should be started no earlier than Day 28 after delivery or second-trimester abortion.

b. Arterial thrombosis and thromboembolism

The use of COCs increases the risk of arterial thrombotic and thromboembolic events. Reported events include myocardial infarction and cerebrovascular events (ischemic and hemorrhagic stroke, transient ischaemic attack). For information on retinal vascular thrombosis (see Section **4.4 Special Warnings and Special Precautions for Use - Ocular lesions**).

The risk of arterial thrombotic and thromboembolic events is further increased in women with underlying risk factors.

Caution must be exercised when prescribing COCs for women with risk factors for arterial thrombotic and thromboembolic events.

Examples of risk factors for arterial thrombotic and thromboembolic events are:
- smoking
- hypertension
- hyperlipidemias
- obesity
- increasing age

COC users with migraine (particularly migraine with aura) may be at increased risk of stroke.
Further risk factors, which represent contraindications for the use of COCs, are listed in (Section **4.3 Contraindications**).

2. OCULAR LESIONS

With use of COCs, there have been reports of retinal vascular thrombosis, which may lead to partial or complete loss of vision. If there are signs or symptoms such as visual changes, onset of proptosis or diplopia, papilledema, or retinal vascular lesions, the COC should be discontinued and the cause immediately evaluated.

3. BLOOD PRESSURE

Increases in blood pressure have been reported in women taking COCs.

In women with hypertension, a history of hypertension or hypertension related diseases (including certain renal diseases), another method of contraception may be preferable. If COCs are used in such cases, close monitoring is recommended and, if a significant increase in blood pressure occurs, COCs should be discontinued.

Elevated blood pressure associated with COC use will generally return to baseline after stopping COCs, and there appears to be no difference in the occurrence of hypertension among ever- and never- users.

COC use is contraindicated in women with uncontrolled hypertension (see Section **4.3 Contraindications**).

4. CARCINOMA OF THE REPRODUCTIVE ORGANS

The most important risk factor for cervical cancer is persistent human papillomavirus infection.

Some studies suggest that COC use may be associated with an increase in the risk of cervical intraepithelial neoplasia or invasive cervical cancer in some populations of women.

However, there continues to be controversy about the extent to which such findings may be due to differences in sexual behavior and other factors. In cases of undiagnosed abnormal genital bleeding, adequate diagnostic measures are indicated.

A meta-analysis from 54 epidemiological studies reported that there is a slightly increased relative risk (RR = 1.24) of having breast cancer diagnosed in women who are using COCs compared to never-users. The increased risk gradually disappears during the course of the 10 years after cessation of COC use. These studies do not provide evidence for causation. The observed pattern of increased risk of breast cancer diagnosis may be due to earlier detection of breast cancer in COC users (due to more regular clinical

monitoring), the biological effects of COCs, or a combination of both. Because breast cancer is rare in women under 40 years of age, the excess number of breast cancer diagnoses in current and recent COC users is small in relation to the lifetime risk of breast cancer. Breast cancers diagnosed in ever-users tend to be less advanced clinically than the cancers diagnosed in never-users.

5. HEPATIC NEOPLASIA/LIVER DISEASE/HEAPTITIS C

In very rare cases, hepatic adenomas, and in extremely rare cases, hepatocellular carcinoma may be associated with COC use. The risk appears to increase with duration of COC use. Rupture of hepatic adenomas may cause death through intra-abdominal hemorrhage.

Women with a history of COC-related cholestasis or women with cholestasis during pregnancy are more likely to have this condition with COC use. If these patients receive a COC they should be carefully monitored and, if the condition recurs, the COC should be discontinued.

Hepatocellular injury has been reported with COC use. Early identification of drug-related hepatocellular injury can decrease the severity of hepatotoxicity when the drug is discontinued. If hepatocellular injury is diagnosed, patients should stop their COC, use a nonhormonal form of birth control, and consult their doctor.

Acute or chronic disturbances of liver function may necessitate the discontinuation of COC use until liver function has returned to normal.

Hepatitis C

During clinical trials with patients treated for HCV infections with the medicinal products containing ombitasvir/paritaprevir/ritonavir and dasabuvir with or without ribavirin, transaminase (ALT) elevations higher than 5 times the upper limit of normal (ULN) occurred significantly more frequently in women using ethinylestradiol-containing medications such as COCs (see Sections **4.3 Contraindications** and **4.5 Interaction with Other Medicaments and Other Forms of Interaction**).

6. MIGRAINE/HEADACHE

The onset or exacerbation of migraine or development of headache with a new pattern that is recurrent, persistent or severe requires discontinuation of COCs and evaluation of the cause.

Women with migraine (particularly migraine with aura) who take COCs may be at increased risk of stroke (see Section **4.3 Contraindications**).

PRECAUTIONS

1. GENERAL

Patients should be counseled that this product does not protect against HIV infection (AIDS) and other sexually transmitted diseases.

Diarrhea and/or vomiting may reduce hormone absorption resulting in decreased serum concentrations.

2. PHYSICAL EXAMINATION AND FOLLOW UP

A complete personal and family medical history and physical examination, including blood pressure, should be taken prior to the initiation of COC use.

Such medical examinations should be repeated periodically during the use of COCs.

3. CARBOHYDRATE AND LIPID EFFECTS

Glucose intolerance has been reported in COC users. Women with impaired glucose tolerance or diabetes mellitus who use COCs should be carefully monitored.

A small proportion of women will have adverse lipid changes while taking OCs. Nonhormonal contraception should be considered in women with uncontrolled dyslipidemias. Persistent hypertriglyceridemia may occur in a small proportion of COC users. Elevations of plasma triglycerides may lead to pancreatitis and other complications.

Estrogens increase serum high-density lipoproteins (HDL cholesterol), whereas a decline in serum HDL cholesterol has been reported with many progestational agents. Some progestins may elevate low-density lipoprotein (LDL) levels and may render the control of hyperlipidemias more difficult. The net effect of a COC depends on the balance achieved between doses of estrogen and progestin and the nature and absolute amount of progestins used in the contraceptive. The amount of both hormones should be considered in the choice of a COC.

Women who are being treated for hyperlipidemias should be followed closely if they elect to use COCs.

4. GENITAL BLEEDING

In some women withdrawal bleeding may not occur during the "tablet-free" interval. If the COC has not been taken according to directions prior to the first missed withdrawal bleed, or if two consecutive withdrawal bleeds are missed, tablet-taking should be discontinued and a nonhormonal back-up method of contraception should be used until the possibility of pregnancy is excluded.

Breakthrough bleeding/spotting may occur in women taking COCs, especially during the first three months of use. The type and dose of progestin may be important. If this bleeding persists or recurs, nonhormonal causes should be considered and adequate diagnostic measures may be indicated to rule out pregnancy, infection, malignancy, or other conditions. If pathology has been excluded, continued use of the COC or a change to another formulation may solve the problem.

Some women may encounter post-pill amenorrhea (possibly with an ovulation) or oligomenorrhea, especially when such a condition was preexistent.

5. DEPRESSION

Women with a history of depression who use COCs should be carefully observed and the drug discontinued if depression recurs to a serious degree. Patients becoming significantly depressed while taking COCs should stop the medication and use an alternate method of contraception in an attempt to determine whether the symptom is drug-related.

4.5 Interaction with Other Medicaments and Other Forms of Interaction

Interactions between ethinyl estradiol (EE) and other substances may lead to decreased or increased serum EE concentrations, respectively.

Concomitant use with the medicinal products containing ombitasvir/paritaprevir/ritonavir and dasabuvir, with or without ribavirin may increase the risk of ALT elevations (see Sections **4.3 Contraindications** and **4.4 Special Warnings and Special Precautions for Use**).

Therefore, COC users must switch to an alternative method of contraception (e.g., progestogen-only contraception or non-hormonal methods) prior to starting therapy with anti-viral HCV medicinal products such as ombitasvir, paritaprevir, ritonavir, dasabuvir. COCs can be restarted 2 weeks following completion of treatment with an anti-viral HCV medicinal product.

Decreased EE serum concentrations may cause an increased incidence of breakthrough bleeding and menstrual irregularities and may possibly reduce efficacy of the COC.

During concomitant use of EE-containing products and substances that may lead to decreased EE serum concentrations, it is recommended that a nonhormonal back-up method of birth control (such as condoms and spermicide) be used in addition to the regular intake of Ovral 28. In the case of prolonged use of such substances COCs should not be considered the primary contraceptive.

After discontinuation of substances that may lead to decreased EE serum concentrations, use of a nonhormonal back-up method is recommended for at least 7 days. Longer use of a back-up method is advisable after discontinuation of substances that have lead to induction of hepatic microsomal enzymes, resulting in decreased EE serum concentrations. It may sometimes take several weeks until enzyme induction has completely subsided, depending on dosage, duration of use and rate of elimination of the inducing substance.
Examples of substances that may decrease serum EE concentrations:

- Any substance that reduces gastrointestinal transit time and, therefore, EE absorption
- Substances that induce hepatic microsomal enzymes, such as rifampicin, rifabutin, barbiturates, primidone, phenylbutazone, phenytoin, dexamethasone, griseofulvin, topiramate, some protease inhibitors, modafinil
- *Hypericum perforatum*, also known as St. John's wort, and ritonavir* (possibly by induction of hepatic microsomal enzymes)

Examples of substances that may increase serum EE concentrations:

- Atorvastatin
- Competitive inhibitors for sulfation in the gastrointestinal wall, such as ascorbic acid (vitamin C) and paracetamol (acetaminophen)
- Substances that inhibit cytochrome P 450 3A4 isoenzymes such as indinavir, fluconazole, and troleandomycin

Troleandomycin may increase the risk of intrahepatic cholestasis during coadministration with COCs.

EE may interfere with the metabolism of other drugs by inhibiting hepatic microsomal enzymes, or by inducing hepatic drug conjugation, particularly glucuronidation. Accordingly, plasma and tissue concentrations may either be increased (e.g., cyclosporine, theophylline, corticosteroids) or decreased (e.g., lamotrigine).

In patients treated with flunarizine, use of oral contraceptives has been reported to increase the risk of Galactorrhea.

There have been reports of pregnancy when COCs were co-administered with certain antibiotics (e.g., ampicillin and other penicillins, tetracyclines).

The prescribing information of concomitant medications should be consulted to identify potential interactions.

*Although ritonavir is an inhibitor of cytochrome P 450 3A4, treatment with ritonavir has been shown to decrease EE serum concentrations (see above).

INTERFERENCE WITH LABORATORY AND OTHER DIAGNOSTIC TESTS

Effects on laboratory parameters

The use of COCs may cause certain physiologic changes which may be reflected in the results of certain laboratory tests, including

a. Biochemical parameters of liver function (including a decrease in bilirubin and alkaline phosphatase), thyroid function (increased total T_3 and T_4 due to increased TBG, decreased free T_3 resin uptake), adrenal function (increased plasma cortisol, increased cortisol binding globulin, decreased dehydroepiandrosterone sulfate (DHEAS), and renal function (increased plasma creatinine and creatinine clearance).
b. Plasma levels of (carrier) proteins, such as corticosteroid-binding globulin and lipid/lipoprotein fractions
c. Parameters of carbohydrate metabolism
d. Parameters of coagulation and fibrinolysis
e. Decreased serum folate levels

4.6 Pregnancy and Lactation

Extensive epidemiological studies have revealed no increased risk of birth defects in children born to women who used COCs prior to pregnancy.

Studies do not suggest a teratogenic effect; particularly insofar as cardiac anomalies and limb-reduction defects are concerned, when taken inadvertently during early pregnancy (see Section **4.3 Contraindications**).

Small amounts of contraceptive steroids and/or metabolites have been identified in the milk of nursing mothers and a few adverse effects on the child have been reported, including jaundice and breast enlargement. Lactation may be influenced by COCs as they may reduce the quantity and change the composition of breast milk.

The use of COCs is generally not recommended until the nursing mother has completely weaned her child.

4.7 Effects on Ability to Drive and Use Machines

There is no clinical data available on effect of levonorgestrel and ethinylestradiol on ability to drive or use machines.

4.8 Adverse Reactions

Adverse reactions are listed in the Table per CIOMS frequency categories:

Very Common:	≥10%
Common:	≥1% and <10%
Uncommon:	≥0.1% and <1%
Rare:	≥0.01% and <0.1%
Very rare:	<0.01%

Use of COCs has been associated with:

- an increased risk of arterial and venous thrombotic and thromboembolic events, including myocardial infarction, stroke, transient ischemic attack, venous thrombosis and pulmonary embolism
- an increased risk of cervical intraepithelial neoplasia and cervical cancer
- an increased risk of being diagnosed with breast cancer
- an increased risk of benign hepatic tumors (e.g., Focal nodular hyperplasia, hepatic adenoma).

(see Section **4.4 Special Warnings and Special Precautions for Use**).

System Organ Class	**Adverse Reaction**
Infections and Infestations	
Common	Vaginitis, including candidiasis
Neoplasms benign, malignant, and unspecified	
Very Rare	Hepatocellular carcinomas
Immune system disorders	
Rare	Anaphylactic/anaphylactoid reactions, including very rare cases of urticaria, angioedema, and severe reactions with respiratory and circulatory symptoms
Very Rare	Exacerbation of systemic lupus erythematosus

Metabolism and nutrition disorders	
Uncommon	Changes in appetite (increase or decrease)
Rare	Glucose intolerance
Very Rare	Exacerbation of porphyria
Psychiatric disorders	
Common	Mood changes, including depression; changes in libido
Nervous system disorders	
Very common	Headache, including migraines
Common	Nervousness; dizziness
Very Rare	Exacerbation of chorea
Eye disorders	
Rare	Intolerance to contact lenses
Very Rare	Optic neuritis*, retinal vascular thrombosis
Vascular disorders	
Very Rare	Aggravation of varicose veins
Gastrointestinal disorders	
Common	Nausea; vomiting; abdominal pain
Uncommon	Abdominal Cramps; bloating
Very Rare	Pancreatitis, ischemic colitis
Hepato-biliary disorder	
Rare	Cholestatic jaundice
Very Rare	Gallbladder disease, including gallstones**
Skin and subcutaneous tissue disorders	
Common	Acne
Uncommon	Rash; chloasma (melasma), which may persist;
	hirsutism; alopecia
Rare	Erythema nodosum
Very Rare	Erythema multiforme
Renal and urinary disorders	
Very Rare	Hemolytic uremic syndrome
Reproductive system and breast disorders	
Very common	Breakthrough bleeding/spotting
Common	Breast pain, tenderness, enlargement, secretion; dysmenorrhea; change in menstrual flow; change in cervical ectropion and secretion; amenorrhea
General disorders and administration site conditions	
Common	Fluid retention/edema
Investigations	

Common	Changes in weight (increase or decrease)
Uncommon	Increase in blood pressure; changes in serum lipid levels, including hypertriglyceridemia
Rare	Decrease in serum folate levels***

* Optic neuritis may lead to partial or complete loss of vision.
** COCs may worsen existing gallbladder disease and may accelerate the development of this disease in previously asymptomatic women.
*** Serum folate levels may be depressed by COC therapy. This may be of clinical significance if the woman becomes pregnant shortly after discontinuing COCs.

4.9 Overdosage

Symptoms of oral contraceptive overdosage in adults and children may include nausea, vomiting, breast tenderness, dizziness, abdominal pain, drowsiness/fatigue; withdrawal bleeding may occur in females. There is no specific antidote and further treatment of overdose, if necessary, is directed to the symptoms.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

When taken consistently and correctly, the probable failure rate of COCs is 0.1% per year; however, the failure rate during typical use is 5% per year for all types of oral contraceptives. The efficacy of most methods of contraception depends upon the reliability with which they are used. Method failure is more likely if COC tablets are missed.

NON-CONTRACEPTIVE HEALTH BENEFITS
The following noncontraceptive health benefits related to the use of COCs are supported by epidemiological studies which largely utilized COC formulations containing doses exceeding 35 µg of EE or 50 µg of mestranol.

Effects on menses
Improved menstrual cycle regularity
Decreased blood loss and decreased incidence of iron-deficiency anemia
Decreased incidence of dysmenorrhea

Effects related to inhibition of ovulation
Decreased incidence of functional ovarian cysts
Decreased incidence of ectopic pregnancies

Other noncontraceptive health benefits
Decreased incidence of fibroadenomas and fibrocystic disease of the breast
Decreased incidence of acute pelvic inflammatory disease

Decreased incidence of endometrial cancer
Decreased incidence of ovarian cancer
Decreased severity of acne

MODE OF ACTION

COCs suppress gonadotropins in a manner that inhibits ovulation, which leads to contraception.

The hormonal components of Ovral 28 inhibit ovulation by suppressing gonadotropin release. Secondary mechanisms which may contribute to the effectiveness of Ovral 28 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).

5.2 Pharmacokinetic Properties

Absorption:
Ethinyl estradiol and levonorgestrel are rapidly and almost completely absorbed from the gastrointestinal tract. Ethinyl estradiol is subject to considerable first-pass metabolism with a mean bioavailability of 40%-45%. Levonorgestrel does not undergo first-pass metabolism and is thereby completely bioavailable.

Metabolism:
Levonorgestrel is extensively plasma protein bound both to sex hormone binding globulin (SHBG) and albumin. Ethinyl estradiol, however, is bound in plasma only to albumin and enhances the binding capacity of SHBG. Following oral administration, peak plasma levels of each drug occur within 1 to 4 hours.

Excretion:
The elimination half-life for ethinyl estradiol is approximately 25 hours. It is primarily metabolized by aromatic hydroxylation but a wide variety of hydroxylated and methylated metabolites are formed, and these are present both free and as conjugates with glucuronide and sulfate. Conjugated ethinyl estradiol is excreted in bile and subject to enterohepatic recirculation. About 40% of the drug is excreted in the urine and 60% is eliminated in the feces.

The elimination half-life for levonorgestrel is approximately 24 hours. The drug is primarily metabolized by reduction or hydroxylation followed by conjugation with sulfate and glucuronide. About 60% of levonorgestrel is excreted in the urine and 40% is eliminated in the feces.

5.3 Preclinical Safety Data

No information available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients:

White Oral Contraceptive tablets:
Lactose (70 mesh) IP
Microcrystaline Cellulose (PH101) IP
Indion 234
Magnesium Stearate IP
Red Ferrous Fumarate Tablets:
Lactose (70 mesh) IP
Microcrystalline Cellulose (PH101) IP
Starch (2%) IP
Magnesium Stearate IP
Opadry II (85G86806) brown

6.2 Incompatibilities

None

6.3 Shelf-life

36 Months

6.4 Special Precautions for Storage

Store below 30°C. Protect from moisture.

6.5 Nature and Contents of Container

28 Tablets are blister packed using rear printed Aluminium foil and front clear PVC film

6.6 Instruction for Use/Handling

Keep out of the reach of children