Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

Novella 0.15mg tablet

2. Qualitative and quantitative composition

Each film coated tablet contains;
Levonorgestrel 150mcg
Ethinylestradiol 30mcg

Excipent of known effect
The tablet also contains 62 mg of lactose monohydrate
For full list of excipients see section 6.1

3. Pharmaceutical form

Round, biconvex, yellow film coated tablet of about 6 mm in diameter, debossed with 'C1' on one side and plain on the other side.
The tablet should not be divided.

4. Clinical particulars

4.1 Therapeutic indications

Ethinylestradiol/Levonorgestrel 30µg/150µg tablet is oral combined hormonal contraceptive (CHC) agent for women

4.2 Posology and method of administration

Posology

The tablets should be taken every day at about the same time, if necessary with some liquid, in the sequence indicated on the blister pack. One tablet is to be taken daily over a period of 28 consecutive days. The next pack is started the day after the last tablet from the previous pack was taken. Two or three days after starting on the placebo tablets, withdrawal bleed usually begins, and this may still be continuing when the new pack has been started.

Starting to take Novella

•When no hormonal contraceptives were taken in the previous month:

The course may be started on day 1 of the cycle (day 1 of menstruation). If alternatively the course isstarted on any other day of the cycle, an additional non-hormonal (barrier) method of contraception should be used during the first 7 days of taking the tablets.

• When changing from another combination product to hormonal contraception (combined oral contraceptive(COC), vaginal ring, transdermal patch):

Depending upon the type of combined oral contraceptive used before Novella is taken, the course should be started either on the day after the usual tablet-free interval, which follows the last active tablet, or ontheday after the last placebo tablet of the combined oral contraceptive. If a vaginal ring or a transdermal patchwas previously used, then Novella should be started on the day after the usual interval, during which neitherring nor patch was used.

When changing from a progestogen-only product (mini pill, injection preparation, implant) or from an intrauterine system (IUS)

When changing from a progestogen-only product, the switch can take place on any day. When changing from an implant or an intrauterine system, it should take place on the day of its removal, or, when switching from an injectable, on the day the next injection would have been due. In any event, an additional non hormonal contraceptive method (barrier method) is necessary during the first 7 days of taking Novella

Following a first or second trimester abortion

Novella can be started immediately . In this case, no additional contraceptive precautions are necessary.

Following delivery

Breast-feeding women

Novella should not be used in the first 6 months of breast-feeding, as milk production may be reduced and small quantities of the active substances may pass into the milk. Novella may be used by breast-feeding women after 6 months.

Non-breast-feeding women

Since the risk of a thromboembolic event is increased during the period directly following delivery, women who are not breast-feeding should not start taking oral contraceptives earlier than day 21 following delivery. A longer period of up to 42 days should be allowed when there are risk factors for venous thromboembolism (VTE), such as previous VTE, thrombophilia, immobility, transfusion at delivery, BMI > 30 kg/m2 , postpartum haemorrhage, history of pre-eclampsia, caesarean delivery,smoking. During the first 7 days of taking Novella, she should use an additional non-hormonal (barrier) contraceptive method. If she has already had sexual intercourse, pregnancy must be ruled out or she should wait for her first menstrual bleed before starting to take the product.

Duration of administration

Novella can be used as long as a hormonal contraceptive method is desired and there are no healthrisks contraindicating it (see section 4.4 for regular checkups).

If a tablet has been missed

The contraceptive efficacy may be decreased if Novella is not taken regularly. The following two basic rules apply when a tablet has been missed:

1. Taking the active tablets must never be discontinued for more than 7 days.
2. The tablets should be taken regularly, without interruption, for seven days in order to attain an adequate suppression of the hypothalamic-pituitary-ovarian axis function.

Single delayed tablet

A single delayed tablet should be taken as soon as possible, even if two tablets have to be taken on the same day. If this can be done within 12 hours, contraceptive protection is maintained. All subsequent tablets should then be taken at the usual time.

If the user is more than 12 hours late taking the tablet, contraceptive protection is no longer assured. During the next 7 days, the woman should use an additional non-hormonal (barrier) contraceptive method.

If the user forgot to take only one active tablet once in week 2, then it is not necessary to take additional contraceptive precautions. If the usual withdrawal bleed does not occur following the active tablets in the sequence with the forgotten tablet, pregnancy must be ruled out before a new blister pack is started.

More than one forgotten tablet

If the user forgot to take more than one active tablet, she should use an additional non-hormonal(barrier) contraceptive method, until the next usual withdrawal bleed appears.

1. If there are fewer than seven days between the forgotten tablets and the last active tablet in thepresent pack, then the user should start immediately, without taking the placebo tablets, with the first active tabletof the next blister pack. Therefore, the usual withdrawal bleed will probably not occur until all the active tablets from this second pack have been taken. An increase in breakthrough bleeding and spotting can occur, however.
2. Alternatively, the user can stop taking the active tablets and start taking the placebo tablets fromthe present pack. Following a placebo interval of up to seven days, including the days on which she forgotto take the tablets, the user then continues by taking the active tablets from the next pack.

Forgetting placebo tablets has no effect on contraceptive protection.

What to do in case of vomiting or diarrhoea

In the event of vomiting or severe diarrhoea within the first four hours after taking Novella, the active substances may possibly not be completely absorbed. Therefore additional contraceptive measures should be used. The same instructions apply as in the case of forgotten tablets (see also sections 4.4 and 4.5). If the user wishes to keep to her accustomed tablet-taking schedule, the additional tablet has to be taken from another blister pack. She should use additional non-hormonal contraceptive methods and consult a doctor in the event of persistent or repeated gastro-intestinal disturbances.

4.2.6 Delaying the withdrawal bleed In order to postpone the withdrawal bleed the user should continue taking tablets from the next pack of Novella immediately, without taking any placebo tablets. The withdrawal bleed can be delayed for as long as desired by taking only the first 21 active tablets from each pack, though evidence for this is limited beyond 2 years. Increased breakthrough bleeding and spotting can occur during this time. Following the subsequent regular seven-day period of taking the placebo tablets, the user may continue to take Novella as usual.

4.3 Contraindications

Combined hormonal contraceptives (CHCs) must not be used if any of the following points apply to you. Should any of the conditions appear for the first time during CHC use, product should be stopped immediately.

- if you have a blood clot in a blood vessel of the legs (deep vein thrombosis, DVT), lungs (pulmonary embolism, LE) or any other organ (or have had one in the past)
- if you are known to suffer from a blood-clotting disorder – for example, protein C deficiency, protein S deficiency, antithrombin III deficiency, Factor V Leiden or antiphospholipid antibodies
- if you need surgery or have been bedridden for a prolonged period of time (see section "Blood clots")
- if you have ever had a heart attack or stroke
- if you have (or have ever had) angina pectoris (a condition that causes severe chest pain and may be the first sign of a heart attack) or a transient ischaemic attack (TIA – temporary symptoms of stroke)
- if you suffer from any of the following diseases which may increase the risk of a blood clot in an artery:
- severe diabetes with damage to the blood vessels or very high blood pressure
- very high blood fat levels (cholesterol or triglycerides) or a disease known as hyperhomocysteinaemia
- if you suffer from a certain form of migraine (called "migraine with aura") (or have done so in the past)
- if you have a past or present history of severe liver disorders, unless your liver counts have returned to normal
- if you have a past or present history of liver tumours if you have a past or present history of breast cancer or genital cancer, or suspicion thereof
- if you have any unexplained vaginal bleeding
- if you are missing your monthly period, possibly due to diet or physical activity
- if you are allergic to ethinylestradiol, levonorgestrel or any of the other ingredients of this tablet (listed in section 6).This may cause itching, rash or swelling.

Do not use Ethinylestradiol/ Levonorgestrel tablet if you have hepatitis C and are taking any tablets containing ombitasvir/paritaprevir/ritonavir and/or dasabuvir.

4.4 Special warnings and precautions for use

Warnings

If any of the conditions or risk factors mentioned below are present, the suitability of Ethinylestradiol/ Levonorgestrel tablet should be discussed with the woman.

In the event of aggravation, or first appearance of any of these conditions or risk factors, the woman should be advised to contact her doctor to determine whether the use of should be discontinued.

- If you notice possible signs of a blood clot which might mean that you have a blood clot in your leg (i.e. deep vein thrombosis), a blood clot in the lungs (i.e. pulmonary embolism), or you are having a heart attack or stroke.
- If a close relative has, or has ever had, breast cancer
- If you are known to have a liver or gallbladder disease
- If you suffer from diabetes mellitus
- If you suffer from depression
- If you have Crohn's disease or ulcerative colitis (chronic inflammatory bowel disease)
- If you have systemic lupus erythematosus (SLE - a disease that affects your natural defence system)
- If you have a haemolytic uraemic syndrome (HUS - a blood-clotting disorder which leads to kidney failure)
- If you have sickle cell anaemia (a hereditary disease of the red blood cells)
- If you have high blood fat levels (hypertriglyceridaemia) or a family history of this disease. Hypertriglyceridaemia has been associated with an increased risk of pancreatitis (inflammation of the pancreas)
- If you need surgery or have been bedridden for a prolonged period of time
- If you have recently given birth, your risk of blood clots is increased. . Ask your doctor how soon after childbirth you can start using this medicine
- If you have inflammation in the veins beneath the skin (superficial thrombophlebitis)
- If you have varicose veins (varices)
- If you suffer from epilepsy (see "Other tablets andEthinylestradiol/Levonorgestrel 30µg/150µg tablets")
- If you have ever experienced a disorder that occurred for the first time during pregnancy or previous use of sex hormones, e.g. hardness of hearing, a blood disease called porphyria, a blister-type rash during pregnancy (herpes gestationis), a nerve disorder where sudden, involuntary body movements occur (Sydenham's chorea)
- If you have a past or present history of yellowish-brown pigment patches (chloasma), also known as the "mask of pregnancy", mainly on the face. In this case, it is advisable to avoid exposure to direct sunlight or ultraviolet light.
- If you suffer from hereditary angioedema (sudden swelling of the skin, mucous membranes, internal organs or brain): tablets containing oestrogens can trigger or worsen the symptoms. You should consult your doctor immediately if you notice symptoms of angioedema, such as swelling of the face, tongue and/or throat and/or swallowing difficulties or skin rash together with breathing problems.

<u>Blood clots</u>
When using a combined hormonal contraceptive such as Ethinylestradiol/Levonorgestrel 30µg/150µg tablets, your risk for blood clot formation is higher than if you do not use one. In rare cases, a blood clot can block blood vessels and cause serious problems.

Blood clots can occur

- in veins (known as “venous thrombosis”, “venous thromboembolism” or VTE)
- in the arteries (known as “arterial thrombosis”, “arterial thromboembolism” or ATE).

Blood clot in a vein

Use of combined hormonal contraceptives has been associated with a higher risk of blood clots in a vein (venous thrombosis). However, these side effects rarely occur. They usually happen in the first year of using a combined hormonal contraceptive.

- If a blood clot occurs in a vein in the leg or foot, this can cause deep vein thrombosis (DVT).
- If a blood clot migrates from the leg to the lung and gets stuck there, it can cause a pulmonary embolism.
- Very rarely, a blood clot may form in a vein of another organ, e.g. the eye (retinal vein thrombosis).

Risk of developing a blood clot in a vein.

- The risk of developing a blood clot in a vein is greatest during the first year of first-time use of a combined hormonal contraceptive. The risk may also be increased if you start using a combined hormonal contraceptive again (same or different medicinal product) after a break of 4 or more weeks. The risk decreases after the first year, but always remains slightly higher than if no combined hormonal contraceptive has been used.

- The risk depends on your natural risk for VTE and the type of combined hormonal contraceptive you are using.

The overall risk of a blood clot in the leg or lungs (DVT or PE) with this tablet is low.

- Around 2 out of 10,000 women who are neither pregnant nor using a combined hormonal contraceptive will suffer a blood clot during the course of a year.
- Around 5-7 out of 10,000 women using a Levonorgestrel-containing combined hormonal contraceptive will suffer a blood clot during the course of a year.
- The risk of blood clot formation varies according to your personal medical history (see following section “Risk factor for blood clot in a vein”)

Symptoms of VTE (deep vein thrombosis (DVT) and pulmonary embolism (PE)):

In the event of symptoms, women should be advised to seek urgent medical attention and to inform the healthcare professional that she is taking a CHC.

Symptoms of deep vein thrombosis (DVT) can include:

- unilateral swelling of the leg and/or foot or along a vein in the leg;

- pain or tenderness in the leg which may be felt only when standing or walking,
- increased warmth in the affected leg; red or discoloured skin on the leg.

Symptoms of pulmonary embolism (PE) can include:
- sudden onset of unexplained shortness of breath or rapid breathing;
- sudden coughing which may be associated with haemoptysis;
- sharp chest pain;
- severe light headedness or dizziness;
- rapid or irregular heartbeat

Some of these symptoms (e.g. “shortness of breath”, “coughing”) are non-specific and might be misinterpreted as more common or less severe events (e.g. respiratory tract infections).
Other signs of vascular occlusion can include: sudden pain, swelling and slight blue discoloration of an extremity.
If the occlusion occurs in the eye symptoms can range from painless blurring of vision which can progress to loss of vision. Sometimes loss of vision can occur almost immediately

Risk Factor for blood clot in a vein
The risk of a blood clot with combined hormonal contraceptives is low, but is increased as a result of some diseases and risk factors. The risk is increased:
- if you are severely overweight (Body Mass Index or BMI over30 kg/m2);
- if one of your close relatives has experienced a blood clot in the leg, lung or any other organ at a young age (i.e. below 50 years). In this case, you might have a hereditary blood-clotting disorder;
- if you need surgery or have been bedridden for a prolonged period of time due to injury or illness or your leg is in plaster. You may have to stop using this tablet several weeks prior to surgery or if your mobility is impaired. If you have to stop using this tablet, ask your doctor when you can start using it again.
- if you are of a certain age (especially from about 35 years of age); if you have had a baby within the last few weeks.

The risk of blood clot formation increases with the number of diseases and risk factors present. Air travel (> 4 hours) can temporarily increase your risk of blood clots, especially if you have any other of the factors listed.

- Blood clots in an artery

Just like a blood clot in a vein, a clot in an artery can cause serious problems. It can cause a heart attack or stroke.

Risk Factor for blood clot in an artery

It is important to note that the risk of a heart attack or stroke due to combined hormonal contraceptives use is very low, but may rise:

- with increasing age (over 35 years of age);
- if you smoke. When using a combined hormonal contraceptive such as Ethinylestradiol/Levonorgestrel 30µg/150µg tablets, it is advised that you stop smoking. If you cannot stop smoking and are over 35 years of age, your doctor may advise you to use a different type of contraception;
- if you are overweight;
- if you have high blood pressure;
- if one of your close relatives has had a heart attack or stroke at a young age (below 50 years). In this case, you might also be at increased risk of heart attack or stroke;
- if you or one of your close relatives have high blood fat levels (cholesterol or triglycerides);
- if you have migraine and especially migraine with aura;
- if you suffer from heart problems (heart valve disease, a heart rhythm disorder called atrial fibrillation);
- if you have diabetes.

Symptoms of a cerebrovascular accident can include:
- sudden numbness or weakness of the face, arm or leg, especially on one side of the body;
- sudden trouble walking, dizziness, loss of balance or coordination;
- sudden confusion, trouble speaking or understanding;
- sudden trouble seeing in one or both eyes;
- sudden, severe or prolonged headache with no known cause;
- loss of consciousness or fainting with or without seizure.

Temporary symptoms suggest the event is a transient ischaemic attack (TIA).

Symptoms of myocardial infarction (MI) can include
- pain, discomfort, pressure, heaviness, sensation of squeezing or fullness in the chest, arm, or below the breastbone;
- discomfort radiating to the back, jaw, throat, arm, stomach;
- feeling of being full, having indigestion or choking;
- sweating, nausea, vomiting or dizziness;
- extreme weakness, anxiety, or shortness of breath;
- rapid or irregular heartbeats.

<u>Tumours</u>
An increased risk of cervical cancer in long-term users of COCs has been reported in some epidemiological studies, but there continues to be controversy about the extent to which this finding is attributable to the confounding effects of sexual behaviour and other factors such as human papilloma virus (HPV).

<u>Breast Cancer</u>
A meta-analysis of 54 epidemiological studies showed that there is a slightly increased relative risk (RR = 1.24) of having breast cancer diagnosed in women who are currently using COCs. The excess risk gradually disappears

during the course of the 10 years after cessation of COC use. 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 overall risk of breast cancer.
In rare cases, benign liver tumours, and even more rarely, malignant liver tumours have been reported in users of COCs. In isolated cases, these tumours have led to life-threatening intra-abdominal haemorrhages. A hepatic tumour should be considered in the differential diagnosis when severe upper abdominal pain, liver enlargement or signs of intra-abdominal haemorrhage occur in women taking COCs.

Other conditions
Women with hypertriglyceridaemia, or a family history thereof, may be at an increased risk of pancreatitis when using COCs.
Although small increases in blood pressure have been reported in many women taking COCs, clinically relevant increases are rare. Only in these rare cases an immediate discontinuation of COC use is justified. A systemiatic relationship between COC use and clinical hypertension has not been established.If, during the use of a COC in pre-existing hypertension, constantly elevated blood pressure values or a significant increase in blood pressure do not respond adequately to antihypertensive treatment, the COC must be withdrawn. Where considered appropriate, COC use may be resumed if normotensive values can be achieved with antihypertensive therapy.
The following conditions have been reported to occur or deteriorate during both pregnancy and COC use, but the evidence of an association with COC use is inconclusive: jaundice and/or pruritus related to cholestasis, gallstones, porphyria, systemic lupus erythematosus, haemolytic uremic syndrome, Sydenham's chorea, herpes gestationis, otosclerosis-related hearing loss, depressive mood.
In women with hereditary angioedema exogenous oestrogens may induce or exacerbate symptoms of angioedema.
Acute or chronic disturbances of liver function may necessitate the discontinuation of COC use until the liver function values return to normal.
Recurrence of cholestatic jaundice and/or cholestasis-related pruritus which previously occurred during pregnancy or previous use of sex steroids necessitates discontinuation of COCs.
Although COCs may have an effect on peripheral insulin resistance and glucose tolerance, there is no evidence for a need to alter the therapeutic regimen in diabetics using low-dose COCs. However, diabetic women should be carefully monitored, particularly in the early stage of COC use.
Worsening of endogenous depression, of epilepsy, of Crohn's disease and of ulcerative colitis has been reported during COC use.
Chloasma may occasionally occur, especially in women with a history of chloasma gravidarum. Women with a tendency to chloasma should avoid exposure to the sun or ultraviolet radiation whilst taking COCs.

Levonorgestrel / Ethinylestradiol tablet contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or

glucose-galactose malabsorption who are on a lactose-free diet should take this amount into consideration.

Medical examination/consultation
Prior to the initiation or reinstitution of Levonorgestrel / Ethinylestradiol tablet a complete medical history (including family history) should be taken and pregnancy must be ruled out. Blood pressure should be measured and a physical examination should be performed, guided by the contra-indications (see section 4.3 Contraindications) and warnings (see section 4.4 Special Warnings and special precautions for use). The woman should also be instructed to carefully read the user leaflet and to adhere to the advice given. The frequency and nature of examinations should be based on established practice guidelines and be adapted to the individual woman. Women should be advised that oral contraceptives do not protect against HIV infections (AIDS) and other sexually transmissible diseases.

Reduced efficacy
The efficacy of COCs may be reduced in the event of e.g. missed tablets, vomiting or diarrhea or concomitant medication.

Reduced cycle control
With all COCs, irregular bleeding (spotting or breakthrough bleeding) may occur, especially during the first months of use. Therefore, the evaluation of any irregular bleeding is only meaningful after an adaptation period of about three cycles. In users of COC's with the same active substances, any bleeding (spotting and/or break-through bleeding) was reported by more than 50% during the first 6 months of use.
If bleeding irregularities persist or occur after previously regular cycles, then non-hormonal causes should be considered and adequate diagnostic measures are indicated to exclude malignancy or pregnancy. These may include curettage.
In some women withdrawal bleed may not occur during the tablet-free interval. If the COC has been taken according to the directions described in section 4.2 Posology and method of administration, it is unlikely that the woman is pregnant. However, if the COC has not been taken according to these directions prior to the first missed withdrawal bleed or if two withdrawal bleeds are missed, pregnancy must be ruled out before COC use is continued.

ALT elevations
During clinical trials with patients treated for hepatitis C virus infections (HCV) with the medicinal products containing ombitasvir/paritaprevir/ritonavir and dasabuvir with or without transaminase (ALT) elevations higher than 5 times the upper limit of normal (ULN) occurred significantly more frequent in women using ethinylestradiol-containing medications such as combined hormonal contraceptives (CHCs) (see sections 4.3 and 4.5

4.5 Interaction with other medicinal products and other forms of interaction

Interactions

Hepatic enzyme inducers

Interactions can occur with drugs that induce microsomal enzymes (especially cytochrome P450 3A4) which can result in increased clearance of sex hormones and which may lead to breakthrough bleeding and/or contraceptive failure.

Enzyme induction can already be observed after a few days of treatment. Maximal enzyme induction is generally seen within a few weeks. After the cessation of drug therapy enzyme induction may be sustained for about 4 weeks.

Women on short-term treatment with any of these drugs should temporarily use a barrier method in addition to the COC or choose another method of contraception. The barrier method should be used during the time of concomitant drug administration and for 28 days after their discontinuation. If the period during which the barrier method is used runs beyond the end of a pack, the next pack should be started without a break. In this situation, a withdrawal bleed should not be expected until the end of the second pack. If the patient does not have a withdrawal bleed during the tablet-free interval following the end of the second pack, the possibility of pregnancy must be ruled out before resuming with the next pack.

For women receiving long-term therapy with hepatic enzyme inducers, another method of contraception should be used.

The following have been shown to have clinically important interactions with COCs:

Antiretroviral agents: ritonavir, nelfinavir, nevirapine.

Anticonvulsants: barbiturates (including phenobarbitone), primidone, phenytoin, carbamazepine, oxcarbazepine, topiramate. or felbamate

Antibiotics/antifungals: griseofulvin, rifampicin,

Calcium Channel blockers: Verapamil,diltiazem

Herbal remedies: St John's wort (*Hypericum perforatum*)

Substances decreasing the clearance of COCs (enzyme inhibitors)

Strong and moderate CYP3A4 inhibitors such as azole antifungals (e.g. itraconazole, voriconazole, fluconazole) and macrolides (e.g. erythromycin, clarithromycin) can increase plasma concentrations of the oestrogen or the progestin or both.

Etoricoxib increase plasma concentrations of ethinylestradiol.

Effects on other drugs

Oral contraceptives may affect the metabolism of certain other drugs. Accordingly, plasma and tissue concentrations may either increase (e.g. cyclosporin, tizanidine, theophylline) or decrease (e.g. lamotrigine).

Pharmacodynamics interactions

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 and 4.4).

Therefore, Levonorgestrel / Ethinylestradiol tablets-users must switch to an alternative method of contraception (e.g., progestagen-only contraception or

non-hormonal methods) prior to starting therapy with this combination drug regimen. Levonorgestrel / Ethinylestradiol tablets can be restarted 2 weeks following completion of treatment with this combination drug regimen.

Laboratory tests
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, e.g. corticosteroid binding globulin and lipid/lipoprotein fractions, parameters of carbohydrate metabolism and parameters of coagulation and fibrinolysis. Laboratory staff should therefore be informed about oral contraceptive use when laboratory tests are requested

4.6 Pregnancy and Lactation

Pregnancy
Ethinylestradiol/ Levonorgestrel tablet is not indicated during pregnancy. If pregnancy occurs during treatment with Levonorgestrel / Ethinylestradiol tablet, further intake must be stopped. However, extensive epidemiological studies have revealed neither an increased risk of birth defects in children born to women who used COCs prior to pregnancy, nor a teratogenic effect when COCs were taken inadvertently during early pregnancy.

Breast-feeding
The use of Ethinylestradiol/ Levonorgestrel tablet during lactation may lead to a reduction in the volume of milk produced and to a change in its composition. Minute amounts of the active substances are excreted with the milk. These amounts may affect the child particularly in the first 6 weeks' post-partum. Mothers who are breast-feeding may be advised instead to use another method of contraception.

4.7 Effects on ability to drive and use machines

Ethinylestradiol / Levonorgestrel have no effects or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

All adverse drug reactions are listed by system organ class and frequency: Very common > 1/10), Common (≥1/100, < 1/10), Uncommon (≥1/1000, < 1/100), Rare (≥ 1/10,000, < 1/1000), Very Rare (< 1/10,000), not known (cannot be estimated from the available data).
The following adverse events have been reported during use of Ethinylestradiol / Levonorgestrel

Table 1: tabulated adverse reactions

System Organ Class	**Common Side effects (≥ 1/100)**	**Uncommon Side effects (≥ 1/1000, <1/100)**	**Rare Side effects (< 1/1000)**
Eye disorders			contact lens intolerance, Blood clots in eyes
Gastrointestinal disorders	nausea, abdominal pain	vomiting, diarrhoea	
Immune system disorders			hypersensitivity
Investigations	weight increased		weight decreased
Metabolism and nutrition disorders		fluid retention	
Nervous system disorders	headache	migraine	
Gastrointestinal disorders			Blood clots occur in stomach or intestine
Hepatobiliary disorders			
Psychiatric disorders	depressed mood, mood altered	libido decreased	libido increased
Reproductive system and breast disorders	breast pain, breast tenderness	breast hypertrophy	vaginal discharge, breast discharge
Skin and subcutaneous tissue disorders		rash, urticaria	erythema nodosum, erythema multiforme

Moreover, the following adverse drug reactions have been reported in connection with the use ofcombined oral contraceptives. (The frequency of these reactions cannot be calculated from the reports.)
- optic neuritis (may cause partial or complete loss of vision),
– worsening of varicose veins,
- pancreatitis with a currently existing severe lipid metabolic disturbance,
– gall bladder disease, including gall stones (combined oral contraceptives can cause gall bladder diseaseor worsen existing gall bladder disease),
– haemolytic-uraemic syndrome,
– Herpes gestationis, – otosclerosis,
– worsening of systemic lupus erythematosus,
– worsening of porphyria,
– worsening of Chorea minor (Sydenham's chorea),
– worsening of depression, –

worsening of chronic-inflammatory intestinal diseases (Crohn's disease and ulcerative colitis)

4.9 Overdose

Symptoms of an overdose with oral contraceptives in the case of adults and children may include: nausea, vomiting, chest tightness, giddiness, abdominal pain, sleepiness / tiredness; vaginal bleeding can occurringwomen and girls. There is no specific antidote. The treatment is symptomatic.

5 Pharmacological properties

5.2 Pharmacodynamic properties

Pharmacotherapeutic group: progestrogens and estrogens, ATC code: G03AA07
Levonorgestrel / Ethinylestradiol tablet is an oestrogen-progestogen combination which acts by inhibiting ovulation by suppression of the mid-cycle surge of luteinising hormone, the inspissation of cervical mucus producing a barrier to sperm, and the rendering of the endometrium unreceptive to implantation

5.3 Pharmacokinetic properties

Levonorgestrel

Absorption

Levonorgestrel is absorbed rapidly and completely following oral administration. Following single dose administration of 2 tablets of Novella in healthy volunteers, the mean (± SD) levonorgestrel Cmax value was 9.7 (±3.6) ng/ml, the corresponding value for AUC was 145 (±91) ng.h/ml, and the mean levonorgestrel tmax value was 1.7 (±0.6) hours.

Distribution

Levonorgestrel is bound to serum albumin and sex-hormone binding globulin (SHBG). Only 1.1% of the total serum concentration of the active pharmaceutical substance is present as free steroid; 65 % is specifically bound to SHBG and about 35 % non-specifically to albumin. The rise of SHBG, induced by ethinylestradiol, affects the relative distribution of levonorgestrel in different protein fractions. The induction of the binding protein causes a rise of the SHBG-bound fraction and a decrease in the albumin-bound fraction. The apparent volume of distribution of levonorgestrel is 129 L following a singledose.

Metabolism

Levonorgestrel is primarily metabolised through reduction of the Δ4-3-oxo group and through hydroxylation at positions 2α, 1β and 16β and by subsequent conjugation. Most of the metabolites that circulate in blood are sulphates of 3α, 5β-tetrahydrolevonorgestrel, while excretion occurs predominantly in the form of glucuronides. Part of the unchanged levonorgestrel also circulates as 17β sulphate. Metabolic clearance can differ

inter-individually by several fold, which may partially explain the broad fluctuations in levonorgestrel concentrations among users.

Elimination
The serum levels of levonorgestrel decrease in two phases. The terminal phase is characterised by a half-life of approximately 25 hours. Levonorgestrel and its metabolites are primarily eliminated in urine (40 - 68%) and about 16 - 48 % in faeces. Dynamic equilibrium (steady state) Levonorgestrel levels in serum increase by about three-fold during continuous use, and attain dynamic equilibrium (steady state) during the second half of the treatment cycle. The pharmacokinetics of levonorgestrel are affected by the SHBG levels in serum, which rise by between 1.5 – 1.6 fold during theuse of estradiol. This is why the clearance rate from serum and the distribution volume are slightly decreased (0.7 ml/min/kg or respectively about 100 L) with dynamic equilibrium (steady state).

Ethinylestradiol
Absorption
Ethinylestradiol is absorbed rapidly and completely following oral administration. Ethinylestradiolis exhaustively metabolised during absorption and first-pass hepatic metabolism, leading to a mean oral bioavailability of 45 % (inter-individual fluctuation is about 20 - 65 %). Following single dose administration of 2 tablets of Novella in healthy volunteers, the mean (± SD) ethinylestradiol Cmax value was 152 (±49) pg/ml, the corresponding value for AUC was 1076 (±504) pg.h/ml, and the mean ethinylestradiol tmax value was 1.7 (±0.3)hours.

Distribution
Ethinylestradiol is highly (approximately 98%) but non-specifically bound to serum albumin, and induces an increase in the serum concentrations of SHBG. The apparent volume of distribution of ethinylestradiolis 2.8–8.6 L/kg.

Metabolism
Ethinylestradiol is metabolised by presystemic conjugation in the small intestine mucosa and in the liver. Ethinylestradiol is primarily metabolised by aromatic hydroxylation, during which a wide variety of hydroxylated and methylated metabolites are formed. These can be detected in serum as free metabolitesor as glucuronide or sulphate conjugates. Ethinylestradiol is subject to an enterohepatic cycle.

Elimination
The serum levels of ethinylestradiol decrease in two phases, which are characterised by half-lives of approximately 1 hour and 10 to 20 hours, respectively. Ethinylestradiol is not eliminated in its unchanged form. The metabolites are eliminated via urine and bile in a ratio of 4 to 6. Dynamic equilibrium (steady state) The ethinylestradiol serum concentration almost doubles following continuous use. Due to daily use and the variable half-life in the terminal phase of serum clearance, dynamic equilibrium (steady state) isreached after approximately one week

5.4 Preclinical safety data

The toxicity profiles of ethinylestradiol and levonorgestrel are well known. Because of the pronounced differences in species, results from animal experimental testing withoestrogens possess limited predictive value for administration to humans.
In experimental animals, ethinylestradiol exhibits an embryo-lethal effect in relatively smalldosage; malformations of the urogenital system and feminization of male foetuses have been observed. Levonorgestrel showed an embryo-lethal effect in animal experiments and, in high doses, a virilizingeffect on female foetuses. Reproduction-toxicological studies in rats, mice and rabbits did not furnish any indication of a teratogenic effect. Preclinical data for ethinylestradiol and levonorgestrel from conventional studies on chronic toxicity, genotoxicity and on carcinogenic potential do not show relevant risks for humans beyond those already described.

6 Pharmaceutical Particulars

6.2 List of Excipients

Tablet core:
Lactose monohydrate BP/EP
Maize starch EP
Povidone K30 USP
Poloxamer 407 EP
Magnesium stearate EP
Colloidal silicon dioxide EP

Film-coating:
Polyvinyl Alcohol- Part. Hydrolyzed (USP, FCC, Ph.Eur, JPE)- E1203
Titanium Dioxide (USP,FCC,PhEur,JP,ChP,GB) - E171
Macrogol/PEG (USP,FCC,PhEur,JECFA,JP - E1521
Iron Oxide Yellow (NF,JPE,ChP, JECFA) - E172
Iron Oxide Red (NF,JPE,JECFA, ChP) - E172

6.3 Incompatibilities

Not applicable

6.4 Shelf-Life

24 months

6.5 Special Precautions for storage

Store below 30C. Store in the original package. Protect from light

6.6 Nature and Content of container

Ethinylestradiol/Levonorgestrel 30µg/150µg Tablets are available in clear PVC/PVDC-Alu blister card containing 21 tablets. One blister card and one patient information leaflet per carton. 10 such cartons in one master carton.

Ethinylestradiol/Levonorgestrel 30µg/150µg Tablets are available in a pack of 1 blister card containing 21 tablets.

6.7 Special precautions for disposal and other handling

Tablets should not be disposed of via wastewater or household waste. Any unused product or waste material should be disposed of in accordance with local requirements.

7 Marketing Authorization Holder

HLL Lifecare Limited,
(A Govt. of India Enterprise)
Unipill Block, Kanagala,
Belagavi District,
Karnataka,
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Tel: 08333-279239/682/244
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Email : enquiry@lifecarehll.com

8 Marketing Authorization Number

CTD10652

9 Date of first authorization/renewal of the authorization

29/06/2023

10 Date of revision of the text

10/05/2025