NEW ZEALAND DATA SHEET

LO-ORALCON 20 ED

1. Product Name

Lo-Oralcon 20 ED, 0.1 mg levonorgestrel and 0.02 mg ethinylestradiol, tablet.

2. Qualitative and Quantitative Composition

Each active tablet contains 0.1 mg levonorgestrel and 0.02 mg ethinylestradiol. Each blister pack contains 21 active tablets and 7 placebo tablets.

Excipients with known effect: Maize starch, sucrose and lactose

Allergen Declaration: Sulfites and lactose

For the full list of excipients, see section 6.1.

3. Pharmaceutical Form

Active tablets: pink tablets.

Non-hormonal (placebo) tablets: yellow tablets.

4. Clinical Particulars

4.1 Therapeutic indications

Oral contraception.

4.2 Dose and method of administration

Combined oral contraceptives (COCs), such as Lo-Oralcon 20 ED, when taken correctly, have a failure rate of approximately 1% per year. The failure rate may increase when pills are missed or taken incorrectly.

How to take Lo-Oralcon 20 ED

Tablets must be taken in the order directed on the package every day at about the same time with some water as needed. Tablet-taking is continuous. One tablet is to be taken daily for 28 consecutive days. Each subsequent pack is started the day after the last tablet of the previous pack following the directional arrows. Withdrawal bleeding usually occurs while taking the 7 yellow placebo tablets (last row). This usually starts on day 2 - 3 after starting the yellow placebo tablets and may not have finished before the next pack is started.

How to start Lo-Oralcon 20 ED

START WITH THE FIRST TABLET FROM THE BLUE SECTION MARKED WITH THAT DAY OF THE WEEK, in accordance with one of the following:

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 - 3 is allowed, but during the first cycle an additional barrier contraceptive method is recommended for the first 7 days of tablet taking.

Changing from another combined oral contraceptive (COC), vaginal ring or transdermal patch

The woman should start with Lo-Oralcon 20 ED preferably on the day after her 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.

In case a vaginal ring or transdermal patch has been used, the woman should start taking Lo-Oralcon 20 ED preferably on the day of removal, but at the latest when the next application would have been due.

Changing from a progestogen-only method (minipill, injection, implant) or progestogen-releasing intrauterine system (IUS)

The woman may switch any day from the minipill, from an implant or IUS on the day of its removal, or from an injectable when the next injection would be due. In all of these cases, the woman should be advised to additionally use a barrier contraceptive 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

The woman should be advised to start at day 21 to 28 after delivery or second-trimester abortion. When starting later than this, the woman should be advised to additionally use a barrier contraceptive method for the first 7 days of tablet taking. However, if intercourse has already occurred, pregnancy should be excluded before starting Lo-Oralcon 20 ED or the woman has to wait for her first menstrual period.

For breastfeeding women, see Section 4.6

Management of missed tablets

Errors in taking the yellow placebo tablets contained in Lo-Oralcon 20 ED can be ignored. However, they should be discarded to avoid unintentionally prolonging the placebo tablet phase. The following advice only refers to missed pink active tablets (rows 1-3 of the blister):

If the user is **less than 12 hours** late in taking any pink active tablet, contraceptive protection is not reduced. The woman should take the tablet as soon as she remembers and should take subsequent tablets at the usual time.

If she is **more than 12 hours** late in taking any pink active tablet, contraceptive protection may be reduced.

There is a particularly high risk of pregnancy if tablets are missed just before or immediately after taking the yellow placebo tablets. If tablets are missed in the first week of taking the pink active tablets following the yellow placebo tablets and intercourse took place in the preceding 7 days, the possibility of pregnancy should be considered.

The management of missed tablets can be guided by the following two basic rules:

1. Active tablet taking must never be discontinued for longer than 7 days.
2. Seven days of uninterrupted active tablet taking are required to attain adequate suppression of the hypothalamic-pituitary-ovarian axis.

These rules form the basis of the instructions to patients provided in the package insert.

Extra Contraceptive Precautions

When you need extra contraceptive precautions, either:

- don't have sex; or
- use a cap plus spermicide; or
- use a condom

Do not use the rhythm or temperature methods as extra contraceptive precautions. This is because oral contraceptives alter the usual menstrual cycle changes, such as changes in temperature and cervical mucus.

The 7 Day Rule

- Continue taking your Pills.
- You will not be protected from pregnancy until you have taken your daily pink active Pill for the next 7 days in a row.
- Use another method of contraception (see above) such as condoms or do not have sexual intercourse for these next 7 days.
- If there are fewer than 7 pink active Pills left in the pack, or before the yellow placebo Pills in the pack, go straight on to the pink active Pills in the blue section of the next pack. This means that you miss out the yellow placebo Pills. You may not have a period until the end of the next pack. This is not harmful.

If the woman missed active tablets and subsequently has no withdrawal bleed in the placebo tablet phase, the possibility of a pregnancy should be considered.

Advice in case of vomiting or severe diarrhoea

If vomiting or severe diarrhoea occurs within 3-4 hours after taking an active tablet, absorption may not be complete and additional barrier contraceptive measures should be used. In such an event, 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.

How to shift periods or how to delay a period

To delay a period the woman should continue with the pink active tablets from another pack of Lo-Oralcon 20 ED without taking the yellow placebo tablets from her current pack. The extension can be carried on for as long as desired until the end of the pink active tablets in the second pack. During the extension the woman may experience breakthrough bleeding or spotting. Regular intake of Lo-Oralcon 20 ED is then resumed after the usual 7 day placebo tablet phase.

To shift her periods to another day of the week than the woman is used to with her current scheme, she can be advised to shorten her forthcoming placebo tablet phase by as many days as she likes. The shorter the hormone-free interval, the higher the risk that she does not have a withdrawal bleed and will experience breakthrough-bleeding and spotting during the second pack (just as when delaying a period).

Special populations

Use in the Elderly

Lo-Oralcon 20 ED is not indicated after menopause.

Patients with hepatic impairment

Lo-Oralcon 20 ED is contraindicated in women with severe hepatic disease as long as liver function values have not returned to normal (see section 4.3).

Patients with renal impairment

Lo-Oralcon 20 ED has not been specifically studied in renal impaired patients. There is no data suggesting the need for a dosage adjustment in patients with renal impairment.

Paediatric Use

Lo-Oralcon 20 ED is only indicated after menarche.

4.3 Contraindications

COCs should not be used in the presence of any of the conditions listed below. Should any of the conditions appear for the first time during their use, the product should be stopped immediately.

- Presence or risk of venous thromboembolism (VTE) (See section 4.4)
  - Current VTE (on anticoagulants) or history of deep venous thrombosis [DVT] or pulmonary embolism [PE]
  - Known hereditary or acquired predisposition for venous thromboembolism, such as APC-resistance (including Factor V Leiden), antithrombin-III-deficiency, protein C deficiency, protein S deficiency
  - Major surgery with prolonged immobilisation
  - A high risk of venous thromboembolism due to the presence of multiple risk factors

- Presence or risk of arterial thromboembolism (ATE) (see section 4.4)
  - Current ATE or history of ATE (e.g. myocardial infarction or stroke) or prodromal condition (e.g. angina pectoris or transient ischaemic attack [TIA])
  - Known hereditary or acquired predisposition for arterial thromboembolism, such as hyperhomocysteinaemia and antiphospholipid-antibodies (e.g. Anticardiolipin antibodies and lupus anticoagulant)
  - History of migraine with focal neurological symptoms
  - A high risk of arterial thromboembolism due to multiple risk factors or to the presence of one serious risk factor such as:
    - diabetes mellitus with vascular symptoms
    - severe hypertension
    - severe dyslipoproteinaemia
- Severe hepatic disease as long as liver function values have not returned to normal
- Concomitant use with the medicinal products glecaprevir, pibrentasvir, sofosbuvir, velpatasvir, voxilaprevir, ombitasvir, paritaprevir, or dasabuvir, and combinations of these (see sections 4.4 and 4.5)
- Presence or history of liver tumours (benign or malignant)
- Known or suspected sex-steroid influenced malignancies (e.g. of the genital organs or the breasts)
- Undiagnosed vaginal bleeding
- Known or suspected pregnancy
- Hypersensitivity to any of the active substances or excipients of Lo-Oralcon 20 ED.

4.4 Special warnings and precautions for use

The clinical and epidemiological evidence for COCs like Lo-Oralcon 20 ED is predominantly based on experience with COCs in general. Therefore, the following warnings related to the use of COCs apply also to the use of Lo-Oralcon 20 ED.

If any of the conditions/risk factors mentioned below are present, the benefits of Lo-Oralcon 20 ED use should be weighed against the possible risks for each individual woman and discussed with the woman before she decides to start using it. In the event of aggravation, exacerbation or first appearance of any of these conditions or risk factors, the woman should contact her physician. The physician should then decide whether the Lo-Oralcon 20 ED should be discontinued.

Circulatory disorders

Epidemiological studies have suggested an association between the use of COCs containing ethinylestradiol and an increased risk of arterial and venous thrombotic and thromboembolic diseases such as myocardial infarction, stroke, deep venous thrombosis and pulmonary embolism. These events occur rarely in average-risk women.

Risk of venous thromboembolism (VTE)

The use of any COC increases the risk of VTE compared with no use. The woman should be advised that her VTE risk is highest in the first ever year of use and that there is some evidence that the risk is increased when a COC is re-started after a break in use of 4 weeks or more.

Data from a large, prospective 3-arm cohort study suggest that this increased risk is mainly present during the first 3 months.

Post Authorisation Safety Studies (PASS) have shown that the frequency of VTE diagnosis ranges from 7-10 per 10,000 woman-years in low-oestrogen-dose (< 50 µg ethinylestradiol) COC users. The most recent data suggest that the frequency of VTE diagnosis is approximately 4 per 10,000 woman-years in non-pregnant non-COC users and ranges from 20 to 30 per 10,000 woman-years in pregnant women or in the post-partum period.

Overall the risk of VTE in users of low oestrogen dose (< 50 µg ethinylestradiol) COCs is two to threefold higher than for non-users of COCs who are not pregnant and remains lower than the risk associated with pregnancy and delivery.

It is important that women understand that VTE associated with COC use is rare in average-risk women. The risk in pregnancy (5-20 per 10,000 women over 9 months) and the risk in the post-partum period (45-65 per 10,000 women over 12 weeks) is higher than that associated with COC use.

An additional increase in VTE risk for COCs containing ≥ 50 µg ethinylestradiol cannot be excluded.

The decision to use any product other than one with the lowest VTE risk should be taken only after a discussion with the woman to ensure she understands the risk of VTE with COCs and how her current risk factors influence this risk.

The increased risk of VTE during the postpartum period must be considered if re-starting Lo-Oralcon 20 ED (see sections 4.2 and 4.6).

VTE may be life-threatening or may have a fatal outcome (in 1-2% of cases).

Extremely rarely, thrombosis has been reported to occur in COC users in other blood vessels, e.g. hepatic, mesenteric, renal or retinal veins and arteries.

The risk for venous thromboembolic complications in COC users may increase substantially in a woman with additional risk factors, particularly if there are multiple risk factors (see list below).

Lo-Oralcon 20 ED is contraindicated if a woman has multiple risk factors that put her at high risk of venous thrombosis. If a woman has more than one risk factor, it is possible that the increase in risk is greater than the sum of the individual factors – in this case her total risk of VTE should be considered. If the balance of benefits and risks is considered to be negative a COC should not be prescribed.

When considering risk/benefit, the doctor should take into account that the adequate treatment of a condition may reduce the associated risk of thrombosis.

RiskfactorsforVTE

- Obesity (body mass index over 30 kg/m²). Risk increases substantially as BMI rises

- Prolonged immobilisation, major surgery, any surgery to the legs or pelvis, neurosurgery, or major trauma
- Temporary immobilisation including air travel >4 hours can also be a risk factor for VTE, particularly in women with other risk factors
- Positive family history (venous thromboembolism ever in a sibling or parent especially at a relatively early age e.g. before 50)
- Biochemical factors that may be indicative of hereditary or acquired predisposition for VTE include Activated Protein C (APC) resistance (including Factor V Leiden), antithrombin-III deficiency, protein C deficiency, protein S deficiency
- Other medical conditions associated with VTE include
  - Cancer
  - Systemic lupus erythematosus
  - Haemolytic uraemic syndrome
  - Chronic inflammatory bowel disease (e.g. Crohn's disease or ulcerative colitis)
  - Sickle cell disease.
- Increasing age, particularly above 35 years
- Smoking

In women at risk of prolonged immobilisation (including major surgery, any surgery to the legs or pelvis, neurosurgery, or major trauma), it is advisable to discontinue use of Lo-Oralcon 20 ED (in the case of elective surgery at least four weeks in advance) and not resume until two weeks after complete remobilisation. Another method of contraception should be used to avoid unintentional pregnancy. Antithrombotic treatment should be considered if Lo-Oralcon 20 ED has not been discontinued in advance.

If a hereditary predisposition to VTE is suspected, the woman should be referred to a specialist for advice before deciding about any COC use.

There is no consensus about the possible role of varicose veins and superficial thrombophlebitis in venous thromboembolism.

SymptomsofVTE(DVTandPE)
Women should be informed of the symptoms of VTE and be advised to seek urgent medical attention if VTE symptoms develop and to inform the healthcare professional that she is taking a COC.

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 or sudden severe pain in the chest which may increase with deep breathing
- severe light headedness or dizziness
- rapid or irregular heartbeat

Some of these symptoms (e.g. "shortness of breath", "coughing") are nonspecific 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 of arterial thromboembolism (ATE)

Epidemiological studies have associated the use of COCs with an increased risk for arterial thromboembolism (e.g. myocardial infarction, angina pectoris, stroke or TIA). Arterial thromboembolic events may be fatal.

The risk of arterial thromboembolic complications in COC users increases in women with risk factors. Lo-Oralcon 20 ED is contraindicated if a woman has one serious or multiple risk factors for ATE that puts her at high risk of arterial thrombosis. If a woman has more than one risk factor, it is possible that the increase in risk is greater than the sum of the individual factors - in this case her total risk should be considered. If the balance of benefits and risks is considered to be negative a COC should not be prescribed.

RiskfactorsforATE

- Increasing age, particularly above 35 years
- Smoking
- Hypertension
- Obesity
- Positive family history (arterial thromboembolism ever in a sibling or parent especially at relatively early age e.g. below 50)
- Biochemical factors that may be indicative of hereditary or acquired predisposition for ATE include: hyperhomocysteinaemia and antiphospholipid antibodies (e.g. anticardiolipin antibodies, and lupus anticoagulant)
- Migraine
- Other medical conditions associated with adverse vascular events:
    - Diabetes mellitus
    - Hyperhomocysteinaemia
    - Valvular heart disease
    - Atrial fibrillation
    - Dyslipoproteinaemia
    - Systemic lupus erythematosus

Women should be advised not to smoke if they wish to use a COC. Women over 35 years who continue to smoke should be strongly advised to use a different method of contraception.

If a hereditary predisposition is suspected, the woman should be referred to a specialist for advice before deciding about any COC use.

An increase in frequency or severity of migraine during COC use (which may be prodromal of a cerebrovascular event) may be a reason for immediate discontinuation.

SymptomsofATE

Women should be informed of the symptoms of ATE and be advised to seek urgent medical attention if ATE symptoms develop and to inform the healthcare professional that she is taking a COC.

Symptoms of a stroke 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, slurred speech or aphasia
- sudden partial or complete loss of vision; diplopia
- 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

Tumours

The most important risk factor for cervical cancer is persistent human papilloma virus (HPV) infection. Some epidemiological studies have indicated that long-term use of COCs may further contribute to this increased risk but there continues to be controversy about the extent to which this finding is attributable to confounding effects, e.g. cervical screening and sexual behaviour including use of barrier contraceptives.

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 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. These studies do not provide evidence for causation. The observed pattern of increased risk may be due to an earlier diagnosis of breast cancer in COC users, the biological effects of COCs or a combination of both. The breast cancers diagnosed in ever-users tend to be less advanced clinically than the cancers diagnosed in never-users.

In rare cases, benign, 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 liver 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.

Malignancies may be life-threatening or may have a fatal outcome.

Other conditions

Women with hypertriglyceridemia, 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. However, if a sustained clinically significant hypertension develops during the use of a COC, then it is prudent for the physician to withdraw the COC and treat the hypertension. 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 with both pregnancy and COC use, but the evidence of an association with COC use is inconclusive: jaundice and/or pruritus related to cholestasis; gallstone formation; porphyria; systemic lupus erythematosus; haemolytic uremic syndrome; Sydenham's chorea; herpes gestationis; otosclerosis-related hearing loss.

In women with hereditary angioedema exogenous oestrogen may induce or exacerbate symptoms of angioedema.

Acute or chronic disturbances of liver or kidney function may necessitate the discontinuation of COC use until markers of liver or kidney function return to normal. Recurrence of cholestatic jaundice which occurred first during pregnancy or previous use of sex steroids necessitates the 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 taking low-dose COCs

(containing < 0.05 mg ethinylestradiol). However, diabetic women should be carefully observed while taking COCs.

Crohn's disease and ulcerative colitis have been associated with 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.

Each pink active tablet contains 48.2 mg of lactose; each yellow placebo tablet contains 52.5 mg of lactose. Patients with rare hereditary problems of galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption who are on a lactose free diet should take this amount into consideration.

Medical examination/consultation

A complete medical history and physical examination should be taken prior to the initiation or reinstitution of Lo-Oralcon 20 ED, guided by sections 4.3 and 4.4. This should be repeated at least annually during the use of Lo-Oralcon 20 ED. Periodic medical assessment is also of importance because contraindications (e.g. a transient ischemic attack, etc.) or risk factors (e.g. a family history of venous or arterial thrombosis) may appear for the first time during the use of Lo-Oralcon 20 ED. The frequency and nature of these assessments should be adapted to the individual woman but should generally include special reference to blood pressure, breasts, abdomen and pelvic organs, including cervical cytology, and relevant laboratory tests.

Sexually transmitted diseases including Human Immunodeficiency Virus (HIV) infections and Acquired Immune Deficiency Syndrome (AIDS)

Women should be advised that preparations like Lo-Oralcon 20 ED do not protect against HIV infections (AIDS) and other sexually transmissible diseases (STIs). The woman should be advised that additional barrier contraceptive measures are needed to prevent transmission of STDs.

Reduced efficacy

The efficacy of Lo-Oralcon 20 ED may be reduced in the event of missed active tablets (see section 4.2), vomiting or severe diarrhoea (see section 4.2) or concomitant medication (see section 4.5).

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 interval of about three cycles.

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 bleeding may not occur while taking the 7 yellow placebo tablets. If the COC has been taken according to the directions described in section 4.2, 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.

Alanine transaminase (ALT) elevations

In patients treated with hepatitis C antiviral medications including glecaprevir, pibrentasvir, ombitasvir, paritaprevir or dasabuvir, ALT elevations may occur in women using ethinylestradiol-containing medications such as CHCs (see sections 4.3 and 4.5). Prescribers should consult the relevant antiviral medicine product safety information. Patients taking a CHC should therefore be

switched to an alternative method of contraception (e.g., progestogen-only contraception or non-hormonal methods) prior to starting therapy.

4.5 Interaction with other medicines and other forms of interaction

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

Effects of other Medicines on Lo-Oralcon 20 ED

Interactions can occur with medicines that induce microsomal enzymes which can result in increased clearance of sex hormones and which may lead to breakthrough bleeding and/or oral 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 treatment with any of these medicines 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 medicine administration and for 28 days after its discontinuation. If the period during which the barrier method is used runs beyond the end of the pink active tablets in the Lo-Oralcon 20 ED pack, the yellow placebo tablets should be omitted and the next Lo-Oralcon 20 ED pack should be started.

Substances increasing the clearance of COCs (diminished efficacy of COCs by enzyme-induction), e.g.:

Phenytoin, barbiturates, primidone, carbamazepine, rifampicin, and possibly also oxcarbazepine, topiramate, felbamate, griseofulvin and products containing St John's Wort.

Substances with variable effects on the clearance of COCs:

When co-administered with COCs, many human immunodeficiency virus (HIV)/hepatitis C virus (HCV) protease inhibitors and non-nucleoside reverse transcriptase inhibitors can increase or decrease plasma concentrations of oestrogen or progestogen. These changes may be clinically relevant in some cases.

Substances decreasing the clearance of COCs (enzyme inhibitors)

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

Etoricoxib doses of 60 to 120 mg/day have been shown to increase plasma concentrations of ethinylestradiol 1.4 to 1.6-fold, respectively when taken concomitantly with a combined hormonal contraceptive containing 0.035 mg ethinylestradiol.

Influence of Lo-Oralcon 20 ED on other Medicines

Oral contraceptives such as Lo-Oralcon 20 ED may interfere with the metabolism of other medicines. Accordingly, plasma and tissue concentrations may either increase (e.g. cyclosporin) or decrease (e.g. lamotrigine).

In vitro, ethinylestradiol is a reversible inhibitor of CYP2C19, CYP1A1 and CYP1A2 as well as a mechanism based inhibitor of CYP3A4/5, CYP2C8, and CYP2J2. In clinical studies, administration of a hormonal contraceptive containing ethinylestradiol lead to no, or a weak increase in CYP3A4 substrates (e.g. midazolam) and a weak (e.g. theophylline) to moderate (e.g. melatonin, tizanidine) increase of CYP1A2 substrates.

Pharmacodynamic Interactions

Co-administration of ethinylestradiol-containing medicinal products with direct-acting antiviral (DAA) medicinal products containing ombitasvir, paritaprevir, or dasabuvir, and combinations of these has been shown to be associated with increases in alanine aminotransferase (ALT) levels to greater than 20 times the upper limit of normal in healthy female subjects and HCV infected women (see sections 4.3 and 4.4). ALT elevations have also been observed with HCV anti-viral medicinal products including glecaprevir/pibrentasvir. Patients taking a CHC should therefore be switched to an alternative method of contraception (e.g., progestogen-only contraception or non-hormonal methods) prior to starting therapy.

Laboratory Tests

The use of preparations like Lo-Oralcon 20 ED 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. Changes generally remain within the normal laboratory range.

4.6 Fertility, pregnancy and lactation

Pregnancy

Pregnancy Category B3.

Lo-Oralcon 20 ED is contraindicated during pregnancy (see section 4.3). If pregnancy occurs during treatment with Lo-Oralcon 20 ED, further intake must be stopped.

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.

Breastfeeding

Lactation may be influenced by COCs as they may reduce the quantity and change the composition of breast milk. Small amounts of the contraceptive steroids and/or their metabolites may be excreted with the milk. Therefore the use of COCs should generally not be recommended until the nursing mother has completely weaned her child.

Fertility

No data available.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. No effects on ability to drive and use machines have been observed in users of COCs.

4.8 Undesirable effects

Serious undesirable effects of Lo-Oralcon 20 ED have been referred to in sections 4.3 and 4.4.

The most commonly reported adverse reactions with Lo-Oralcon 20 ED are nausea, abdominal pain, increased weight, headache, depressed mood, altered mood, breast pain and breast tenderness. They occur in ≥ 1 % of users.

Serious adverse reactions are arterial and venous thromboembolism.

In addition, the following undesirable effects have been reported in users of COCs such as Lo-Oralcon 20 ED, although the causal relationships have not been confirmed:

System organ class	Common (≥ 1/100)	Uncommon (≥ 1/1000 and < 1/100)	Rare (< 1/1000)
Eye disorders			Contact lens intolerance
Gastrointestinal disorders	Nausea, abdominal pain	Vomiting, diarrhoea	
Immune system disorders			Hypersensitivity
Investigations	Increased weight		Decreased weight
Metabolism and nutrition disorders		Fluid retention	
Nervous system disorders	Headache	Migraine	
Psychiatric disorders	Depressed mood, altered mood	Decreased libido	Increased libido
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
Vascular disorder			Venous and arterial thromboembolic event**

** - Estimated frequency, from epidemiological studies encompassing a group of combined oral contraceptives.

- 'Venous and arterial thromboembolic events' summarizes the following Medical Entities: Peripheral deep venous occlusion, thrombosis and embolism/Pulmonary vascular occlusion, thrombosis, embolism and infarction/Myocardial infarction/Cerebral infarction and stroke not specified as haemorrhagic.

In women with hereditary angioedema exogenous oestrogen may induce or exacerbate symptoms of angioedema.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://pophealth.my.site.com/carmreportnz/s/.

4.9 Overdose

There have been no reports of serious deleterious effects from overdose.

Symptoms

Symptoms that may occur in case of taking an overdose of active tablets are nausea, vomiting and withdrawal bleeding. The last may even occur in girls before their menarche, if they have accidentally taken the medicinal product.

Treatment

There are no antidotes and further treatment should be symptomatic.

For risk assessment and advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5. Pharmacological Properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: hormonal contraceptives for systemic use, ATC code: G03AA07

Mechanism of action

The contraceptive effect of Lo-Oralcon 20 ED is based on the interaction of various factors, the most important of which are seen as the inhibition of ovulation and the changes in the cervical secretion. When Lo-Oralcon 20 ED is taken according to instructions, the egg cells are prevented from maturing to the point at which they can be fertilised, the cervical mucus remains thick so as to constitute a barrier to sperm, and the endometrium is rendered unreceptive to implantation.

As well as protection against pregnancy, oestrogen/progestogen combinations have several positive properties which, next to the negative properties (see sections 4.4 and 4.8) can be useful in deciding on the method of birth control.

With combined oral contraceptives (COCs) the cycle is more regular and menstruation is often less painful and bleeding is lighter. The latter may result in a decrease in the occurrence of iron deficiency. Apart from this there is evidence of a reduced risk of endometrial cancer and ovarian cancer. With the higher-dosed combined oral contraceptives containing 0.05 mg ethinylestradiol, there is evidence of a reduced risk of ovarian cysts, pelvic inflammatory disease, benign breast disease and ectopic pregnancy. Whether this also applies to lower-dosed COCs remains to be confirmed.

5.2 Pharmacokinetic properties

Levonorgestrel

Absorption

Orally administered levonorgestrel is rapidly and completely absorbed. Peak serum concentrations of 2.3 nanograms/mL are reached 1.3 hours after single ingestion.

Levonorgestrel is almost completely bioavailable after oral administration.

Distribution

Levonorgestrel is bound to serum albumin and sex hormone binding globulin (SHBG). Only around 1.1% of the total serum medicine concentrations are present as free steroid, approximately 65% are specifically bound to SHBG and about 34% non-specifically bound to albumin. The ethinylestradiol induced increase in SHBG influences the proportion of levonorgestrel bound to the serum proteins, causing an increase of the SHBG-bound fraction and a decrease of the albumin-bound fraction.

The apparent volume of distribution of levonorgestrel is 129 L after single administration.

Biotransformation

Levonorgestrel is extensively metabolized. The major metabolites in plasma are the unconjugated and conjugated forms of 3α, 5β-tetrahydrolevonorgestrel. Additionally, based on in vitro and in vivo studies, CYP3A4 is the main enzyme involved in the oxidative metabolism of levonorgestrel.

The metabolic clearance rate from serum is approximately 1.0 mL/min/kg.

Elimination

Levonorgestrel serum levels decrease in two phases. The terminal disposition phase is characterised by a half-life of approximately 25 hours.

Levonorgestrel is not excreted in unchanged form. Its metabolites are excreted at a urinary to biliary ratio of about 1:1. The half-life of metabolite excretion is about 1 day.

Steady-state conditions

Following daily ingestion, medicine serum levels increase about three-fold reaching steady-state conditions during the second half of the treatment cycle. Levonorgestrel pharmacokinetics are influenced by SHBG levels, which are increased 1.5 - 1.6 fold when co-administered with ethinylestradiol. At steady-state, clearance rate and volume of distribution are slightly reduced to 0.7 mL/min/kg and about 100 L, respectively.

Ethinylestradiol

Absorption

Orally administered ethinylestradiol is rapidly and completely absorbed. Peak serum concentrations of about 50 pg/mL are reached within 1 - 2 hours. During absorption and first-pass liver passage, ethinylestradiol is metabolized extensively, resulting in a mean oral bioavailability of about 45% with a large interindividual variation of about 20 - 65%.

Distribution

Ethinylestradiol is highly but non-specifically bound to serum albumin (approx. 98%), and induces an increase in the serum concentrations of SHBG. An apparent volume of distribution of about 2.8 - 8.6 L/kg was reported.

Biotransformation

Ethinylestradiol is subject to presystemic conjugation in both small bowel mucosa and the liver. Ethinylestradiol is primarily metabolized by aromatic hydroxylation but a wide variety of hydroxylated and methylated metabolites are formed, and these are present as free metabolites and as conjugates with glucuronides and sulfate. The metabolic clearance rate was reported to be 2.3 - 7 mL/min/kg.

Elimination

Ethinylestradiol serum levels decrease in two disposition phases characterized by half-lives of about 1 hour and 10 - 20 hours, respectively. Ethinylestradiol is not excreted as unchanged drug. Ethinylestradiol metabolites are excreted at a urinary to biliary ratio of 4:6. The half-life of metabolite excretion is about 1 day.

Steady-state conditions

Ethinylestradiol serum concentrations increase about two-fold after daily oral administration of Lo-Oralcon 20 ED. According to the variable half-life of the terminal disposition phase from serum and the daily ingestion, steady-state serum levels of ethinylestradiol will be reached after about one week.

5.3 Preclinical safety data

Preclinical data reveal no special risks for humans based on conventional studies of repeated dose toxicity, genotoxicity, carcinogenic potential and toxicity to reproduction. However, it should be borne in mind that sex steroids can promote the growth of certain hormone-dependent tissues and tumours.

6. Pharmaceutical Particulars

6.1 List of excipients

Lo-Oralcon 20 ED tablets also contain:

- lactose
- microcrystalline cellulose
- croscarmellose sodium
- polyvinyl pyrrolidone
- magnesium stearate
- povidone K-90
- purified talc
- glycerol
- sucrose
- calcium carbonate
- macrogol 6000
- titanium dioxide
- ferric oxide (red)
- ferric oxide (yellow)

- carnauba wax

Non-hormonal (placebo) tablets contain:

- lactose
- glycerol
- macrogol 6000
- calcium carbonate
- purified talc
- povidone K-90
- sucrose
- titanium dioxide
- magnesium stearate
- carnuaba wax
- maize starch
- ferric oxide (yellow)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Store at or below 25°C.

6.5 Nature and contents of container

PVC/PVdC/Al blister packs of 84 (3 x 28 tablets).

6.6 Special precautions for disposal

Not applicable.

7. Medicines Schedule

Prescription Medicine

8. Sponsor Details

MAPLE HEALTHCARE LIMITED
Level 11, 41 Shortland Street,
Auckland,1010, NZ
info@maplehealthcare.com.au

9. Date of First Approval

15 December 2011

10. Date of Revision of the Text

03 September 2025

Summary table of changes

Section	Summary of new information
-	Updation of Sponsor details - Maple Healthcare Limited
-	-
-	-