NEW ZEALAND DATA SHEET

1. PRODUCT NAME

MICROLUT 0.03 milligram tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One tablet contains 0.03 milligrams levonorgestrel.

Excipients with known effect

Lactose monohydrate 32.97 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Sugar-coated tablets

The tablets are white, biconvex, round and 5.7 mm in diameter. Each blister contains 28 small white tablets, each containing levonorgestrel 0.03 mg.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Oral contraception.

4.2. Dose and method of administration

The dosage of MICROLUT is one tablet daily without any break, taken at the same time each day with some liquid as needed.

How to take MICROLUT

Tablets must be taken in the order directed on the package for the full 28 days without regard to bleeding. This means that after the first pack has been finished, the next should be started without interruption. The number of 28 tablets per pack is not related to the menstrual cycle. The days of the week are printed on the pack for convenience.

It is important to maintain an interval of exactly 24 hours between tablets. This interval should by no means be exceeded by more than 3 hours. If, for example, the patient chooses 7 a.m. as the time for taking her tablets, she should try to always take them at this time. Whenever this is impossible, the tablet must be taken by 10 a.m. at the very latest, otherwise protection against conception may decline. The greatest possible reliability of MICROLUT can be assured only by adhering as closely as possible to the 24-hour-intervals.

How to start MICROLUT

No preceding hormonal contraceptive use (in the past month)

Tablet taking has to start on the first day of the menstrual bleeding.

Changing from a combined oral contraceptive (COC)

The woman should start with MICROLUT immediately on the day after the last active hormonal tablet of her previous COC and omit the pill-free interval of this COC.

Changing from another progestogen-only pill

When switching from another progestogen-only pill, the woman may start with MICROLUT on any day, without any break between the tablets.

Changing from another progestogen-only method (injection or implant)

The woman may switch from an implant on the day of its removal, from an injectable when the next injection would be due, but should in both cases be advised to additionally use a barrier contraceptive method for the first 7 days of tablet taking.

Following abortion

The woman may start immediately.

Following delivery

For breast-feeding women, refer to Section 4.6 Fertility, Pregnancy and Lactation – Use in Lactation.

Non-breast-feeding women should be advised to start in the fourth week after delivery. When starting later, 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 the actual start of MICROLUT use or the woman has to wait for her first menstrual period.

Management of missed tablets

If even 1 tablet is taken late (i.e. if it is more than 27 hours since the last tablet was taken, i.e. more than three hours later than it should have been taken) or if even 1 tablet is missed, protection against conception may be impaired. The user should take the last missed tablet as soon as she remembers, even if this means taking 2 tablets at the same time. She then continues to take tablets at her usual time. In addition, a barrier method should be used for the next 7 days. If intercourse took place in the preceding 7 days, the possibility of a pregnancy should be considered. The more tablets are missed, the higher the risk of a pregnancy.

Advice in case of vomiting or diarrhoea

If vomiting and/or diarrhoea occur within 3 - 4 hours after tablet taking, absorption may not be complete and additional contraceptive measures should be taken. In such an event, the advice concerning missed tablets, as given in the section “Management of missed tablets, is applicable. The last tablet(s) in the pack should be used for the replacement tablet.

4.3. Contraindications

MICROLUT should not be used in the presence of any of the conditions listed below. Should any of the conditions appear during the use of MICROLUT, the use of the preparation must be discontinued immediately.

- Known or suspected pregnancy
- Active venous thromboembolic disorder
- Arterial and cardiovascular disease present or in history (e.g. myocardial infarction, cerebrovascular accident, ischaemic heart disease)
- Diabetes mellitus with vascular involvement
- Presence or history of severe hepatic disease as long as liver function values have not returned to normal
- Presence or history of liver tumours (benign or malignant)
- Known or suspected sex hormone-dependent malignancies e.g. of the breast
- Undiagnosed vaginal bleeding
- Known hypersensitivity to any of the components of MICROLUT

4.4. Special warnings and precautions for use

Medical examination/consultation

A complete medical history should be taken and a physical and gynaecological examination should be performed prior to the initiation or reinstitution of the use of MICROLUT, guided by the Contraindications and Precautions, and these should be repeated at least annually during the use of MICROLUT. The frequency and nature of these assessments should be based on established practice guidelines and adapted to the individual woman but should generally include special reference to blood pressure, breasts, abdomen and pelvic organs, and should also include cervical cytology.

Women should be advised that oral contraceptives do not protect against HIV infections (AIDS) and other sexually transmitted diseases.

If any of the conditions/risk factors mentioned below is present, the benefits of using MICROLUT 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 on whether MICROLUT should be discontinued.

Circulatory Disorders

An increased risk of thromboembolic and thrombotic disease associated with the use or oral contraceptive is well established. Increased risk of thrombotic and thromboembolic events, including cerebrovascular event and myocardial infarction, have been associated with the use of combined oral contraceptives. The available literature, which is limited because of infrequent use of progestogen only contraceptives, does not suggest an increased risk of these conditions. However, there have been reports of these conditions coincident with the use of progestogen only contraceptives. Therefore, the possibility of thrombosis should be considered. The doctor should be alert to the earliest manifestations of these disorders (e.g. thrombophlebitis, pulmonary embolism, cerebrovascular insufficiency, cerebral

haemorrhage, cerebral thrombosis, coronary occlusion, retinal thrombosis, mesenteric thrombosis). Should any of these occur or be suspected, the drug should be discontinued immediately.

A fourfold to six fold increased risk of thromboembolic complications following surgery has been reported in users of combined oral contraceptives. If feasible, oral contraceptives should be discontinued at least four weeks before surgery associated with an increased risk of thromboembolism or prolonged immobilisation.

Myocardial infarction and coronary artery disease – An increased risk of myocardial infarction associated with the use of oral contraceptives has been reported. Studies found that the greater the number of underlying risk factors for coronary artery disease (cigarette smoking, hypertension, hypercholesterolaemia, obesity, diabetes, history of pre-eclamptic toxaemia) the higher the risk of developing myocardial infarction, regardless of whether or not the patient used an oral contraceptive. Oral contraceptives, however, were found to be a clear additional factor.

The increased risk of thromboembolism in the puerperium must be considered.

Treatment should be stopped at once if there are symptoms of an arterial or venous thrombotic event or suspicion thereof.

Tumours

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 mainly using estrogen-progestogen preparations. 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. The risk of having breast cancer diagnosed in progestogen-only pill users is possibly of similar magnitude to that associated with COC. However, for progestogen-only preparations, the evidence is based on much smaller populations of users and so is less conclusive than that for COCs. 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 OCs 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 oral contraceptives. 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 MICROLUT.

Some epidemiological studies also suggest that combination oral contraceptive use has been associated with an increase in the risk of cervical intraepithelial neoplasia in some populations of women, although 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).

Other conditions

Progestogen-only pills generally do not appear to affect blood pressure in normotensive women. However, if a sustained clinically significant hypertension develops during the use of MICROLUT, it is advisable to withdraw MICROLUT and treat the hypertension.

Recurrence of cholestatic jaundice and/or pruritus which occurred first during pregnancy or previous use of sex steroids necessitates the discontinuation of MICROLUT.

Although MICROLUT may have a slight effect on peripheral insulin resistance and glucose tolerance, there is generally no need to alter the therapeutic regimen in diabetics using progestogen-only pills. However, diabetic women and those with a history of gestational diabetes mellitus should be carefully observed while taking MICROLUT.

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 MICROLUT.

Pregnancies that occur among users of progestogen-only pills are more likely to be ectopic than are pregnancies among users of COCs. In women with a history of extrauterine pregnancy or an impairment of tube function, the use of MICROLUT should be decided on only after carefully weighing the benefits against the risks.

If lower abdominal pain occurs together with an irregular cycle pattern (amenorrhoea or amenorrhoea followed by persistent bleeding), an ectopic pregnancy must be considered.

Persistent ovarian follicles (often referred to as functional ovarian cysts) may occur during the use of MICROLUT. Most of these follicles are asymptomatic, although some may be accompanied by pelvic pain or dyspareunia. In most cases, the enlarged follicles disappear spontaneously during 2 - 3 months of observation.

Oral contraceptives may cause mental depression. Patients with a history of mental depression should be carefully observed and the drug discontinued if depression recurs to a serious degree.

These agents may cause some degree of fluid retention. Women with cardiac or renal dysfunction, convulsive disorders, migraine, or asthma require careful observation since these conditions may be exacerbated by the fluid retention which may occur in users of oral contraceptives.

Steroid hormones may be poorly metabolised in patients with impaired liver function and should be administered with caution to such patients.

Users or oral contraceptives may have disturbances in normal tryptophan metabolism which may result in a relative pyridoxine deficiency. The clinical significance of this is yet to be determined.

Serum folate levels may be depressed by oral contraceptive use. Women who became pregnant shortly after discontinuing these drugs may have a greater chance of developing folate deficiency and its complications.

<u>Ocular lesions</u>

Discontinue oral contraceptives and institute appropriate diagnostic and therapeutic measures if there is unexplained, gradual or sudden, partial or complete loss of vision; proptosis or diplopia; papilloedema; or any evidence of retinal vascular lesions or optic neuritis.

Elevated blood pressure

An increase in blood pressure has been reported in patients receiving oral contraceptives. In some women, hypertension may occur within a few months of beginning use. In the first year of use, the prevalence of women with hypertension is low but the incidence increases with increased exposure. Age is also strongly correlated with the development of hypertension in oral contraceptive users. Women who previously have had hypertension during pregnancy may be more likely to develop an elevation of blood pressure when given oral contraceptives. If blood pressure rises markedly, the drug should be discontinued. Hypertension that develops as a result of taking oral contraceptives usually returns to normal after discontinuing the drug.

Gall bladder disease

Studies report an increased risk of surgically confirmed gall bladder disease in users of oral contraceptives.

Headache

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

Carbohydrate and lipid metabolic effects

An increase in triglycerides and total phospholipids has been observed in patients receiving oral contraceptives.

Bleeding irregularities

Breakthrough bleeding, spotting and amenorrhoea are frequent reasons for patients discontinuing oral contraceptives. In breakthrough bleeding, as in all cases or irregular bleeding from the vagina, nonfunctional causes should be borne in mind. In undiagnosed persistent or recurrent abnormal bleeding from the vagina, appropriate diagnostic measures are indicated to rule out pregnancy or malignancy. If pathology has been excluded, time or a change to another formulation may solve the problem. Changing from a progestin only oral contraceptive to an estrogen-progestin oral contraceptive, whilst potentially useful in minimising menstrual irregularity, should be done only if necessary, since this may increase the risk of thromboembolic disease.

An alteration in menstrual patterns is likely to occur in women using progestin only oral contraceptives. The amount and duration of flow, cycle length, breakthrough bleeding, spotting and amenorrhoea will probably be quite variable. Bleeding irregularities occur more frequently with the use of progestin only oral contraceptives than with estrogen-progestin oral contraceptives.

Women with a history of oligomenorrhoea or secondary amenorrhoea or young women without regular cycles may have a tendency to remain anovulatory or to become amenorrhoeic after discontinuation of oral contraceptives. Women with these

pre-existing problems should be advised of this possibility and encouraged to use another method of contraception. Post-use anovulation, possibly prolonged, may also occur in women without previous irregularities.

Reduced efficacy

The efficacy of MICROLUT may be reduced in the event of missed tablets (see Section 4.2 Dose and Method of Administration), vomiting and/or diarrhoea (see Section 4.2 Dose and Method of Administration – Advice in case of vomiting and diarrhoea), or concomitant medication (see Section 4.5 Interaction with other medicines and other forms of interactions).

Reduced cycle control

Menstrual bleeding

Menstrual bleeding occurs at normal intervals and is of normal duration and intensity in the majority of cases. However, both shortened and lengthened intervals are observed.

For this reason the possibility of such changes in menstrual rhythm should, as a precaution, be pointed out to the patient before the start of tablet taking. The changes occur mainly during the first few months of use, but with continuing treatment the cycle pattern tends to stabilise, and in most cases an individual pattern is established. The patient should be encouraged to keep a record of bleeding on the calendar contained in each pack.

Procedure in the event of intermenstrual bleeding

Intermenstrual bleeding of varying intensity may occur, particularly during the first few months. It is not a medical reason to stop tablet taking, as long as organic causes for such bleeding can be ruled out by means of adequate diagnostic measures.

It is inadvisable to attempt to influence cycle disturbances by the additional administration of an oestrogen. This would only serve to reverse the changes brought about by MICROLUT in the cervical mucus, thereby considerably jeopardising the contraceptive effect.

Absence of withdrawal bleeding

Amenorrhoea may occur in some women, in most cases only for one or two menstrual periods. In rare cases bleeding may fail to occur at longer intervals.

If no menstrual bleeding has occurred within 6 weeks after the last menstrual bleeding, pregnancy must be excluded before tablet taking is continued.

Use in Children

MICROLUT is only indicated after menarche.

Use in the Elderly

MICROLUT is not indicated after menopause.

Patients with Hepatic Impairment

MICROLUT is contraindicated in women with severe hepatic disease as long as liver function values have not returned to normal (see section 4.3 Contraindications).

Patients with Renal Impairment

MICROLUT has not been specifically studied in renally impaired patients.

4.5. Interaction with other medicines and other forms of interaction

Note: The data sheet of concomitant medications should be consulted to identify potential interactions.

Effects of other medicinal products on MICROLUT

Interactions can occur with drugs that induce microsomal enzymes, which can result in increased clearance of sex hormones which may lead to changes in the uterine bleeding profile and/or contraceptive failure.

Women on treatment with any of these drugs should temporarily use a barrier method in addition to MICROLUT 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.

Substances increasing the clearance of levonorgestrel (diminished efficacy of MICROLUT by enzyme-induction)

Phenytoin, barbiturates, primidone, carbamazepine, rifampicin and possibly also, oxcarbazepine, topiramate, felbamate, rifabutin, griseofulvin and products containing St John's Wort (*Hypericum perforatum*).

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.

For women on rifampicin, a barrier method should be used in addition to the POP during the time of rifampicin administration and for 28 days after its discontinuation.

Substances with variable effects on the clearance of levonorgestrel

When co-administered with sex hormones, many HIV/HCV protease inhibitors and non-nucleoside reverse transcriptase inhibitors can increase or decrease plasma concentrations of the progestin.

These changes may be clinically relevant in some cases.

Substances decreasing the clearance of levonorgestrel (enzyme inhibitors)

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

Increased intermenstrual bleeding and occasional pregnancies have been reported during concomitant administration of oral contraceptives and ampicillin, sulfamethoxypyridazine, chloramphenicol, nitrofurantoin, phenoxymethylpenicillin and neomycin. The mechanism appears to be reduced enterohepatic circulation of sex steroid due to change in bowel flora. It may be prudent for women to use supplemental forms of contraception during therapy with these antibiotics.

Combination oral contraceptives have been reported to antagonise the effectiveness of oral anticoagulants, antihypertensive agents, anticonvulsants, and hypoglycaemic

agents. Patients should be carefully monitored for a decreased response to these drugs.

Combination oral contraceptives may interfere with the oxidative metabolism of diazepam and chlordiazepoxide, resulting in plasma accumulation of the parent compound. Patients receiving these benzodiazepines on a long-term basis should be monitored for increased sedative effects.

The effects of benzodiazepines on oral contraceptive metabolism have not been determined.

Effects of MICROLUT on other medicinal products

Oral contraceptives may affect the metabolism of certain other drugs. Accordingly, plasma and tissue concentrations may be affected (e.g. cyclosporin).

Other forms of Interaction

Laboratory tests

The use of contraceptive steroids 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.

Papanicolaou smears should be performed before prescribing these drugs and periodically during their administration.

4.6. Fertility, pregnancy and lactation

Effects on fertility

No data available.

Use in Pregnancy (Category B3)

MICROLUT is not indicated during pregnancy. If pregnancy occurs during treatment with MICROLUT, further intake must be stopped. However, extensive epidemiological studies have revealed no significant effects on foetal development associated with the use of combined oral contraceptives before pregnancy or taken inadvertently during early pregnancy. There have been an insufficient number of pregnancies in patients using levonorgestrel only contraceptives to rigorously evaluate the potential for developmental toxicity; however based on the experience with combined oral contraceptives, an increase in foetal abnormalities is not expected.

Use in Lactation

Progestogens do not appear to affect the quantity or quality of breast milk. However, levonorgestrel is secreted into breast milk following oral administration to lactating women. Very rarely, adverse effects on the child have been reported, including jaundice.

4.7. Effects on ability to drive and use machines

There are no observed effects.

4.8. Undesirable effects

Summary of the safety profile

The most commonly reported adverse reactions with progestogen-only pills including MICROLUT are menstrual disturbances (e.g. frequent and/or irregular bleeding, amenorrhea). They occur in ≥ 1% of users.

Tabulated list of adverse reactions

In addition to the adverse effects listed under "Precautions", the following undesirable effects have been reported in users of progestogen-only pills, although the causal relationship with progestogen-only pills could not always be confirmed:

A review (McCann MF and Poter LS Contraception 1994; 50 (Suppl 1) S9-S198) provided estimates of adverse effects from several studies that included levonorgestrel only oral contraceptive use in women who were not breast feeding. Approximate incidence levels associated with these studies were as follows:

	Very Common (≥ 1/10)	**Common (≥ 1/100 and < 1/10)**	**Uncommon (≥ 1/1000 and < 1/100)**	**Rare (< 1/1000)**
Gastrointestinal disorders		Nausea, vomiting		
Investigations			Change in body weight	
Nervous system disorders		Headache, dizziness		
Psychiatric disorders		Depressed mood		
Reproductive system and breast disorders	Menstrual disturbances (e.g. frequent and/or irregular bleeding, amenorrhea)	Breast tenderness	Change in vaginal secretion	
Skin and subcutaneous tissue disorders			Pigmentation changes	Acne Hirsutism

The following reactions, as a general rule, are seen much less frequently or only occasionally in users of progestogen-only pills, however, that does not necessarily mean that these reactions have been reported in association with MICROLUT:

gastrointestinal disturbances such as bloating and abdominal cramps, chloasma or melasma which may be persistent, breast enlargement, and secretion, change in cervical erosion or cervical secretion, rash (allergic), vaginal candidiasis.

The following adverse reactions have been reported in users of combined oral contraceptives, but the association has been neither confirmed nor refuted: premenstrual like syndrome, changes in appetite, cystitis like syndrome, nervousness, loss of scalp hair, erythema multiforme, erythema nodosum, haemorrhagic eruption, vaginitis, oedema.

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: chorea, porphyria, haemolytic uraemic syndrome.

The following conditions have been reported with user of POP pills however their frequency is unknown: Contact lens intolerance, hypersensitivity, change in libido, various skin disorder.

Post Marketing Information

The following post marketing event have been reported for MICROLUT with a low frequency and causality has not been determined: Skin disorder including acne, dermatitis acneform, chloasma, rash and skin desquamation, visual disturbance, abdominal pain, diarrhoea, migraine, alopecia.

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.

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

Symptoms

Symptoms that may occur in this case are nausea, vomiting and slight vaginal bleeding.

Treatment

There are no antidotes and further treatment should be symptomatic.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Progestogens, levonorgestrel

ATC Code: G03AC03

MICROLUT contains the oral progestogen levonorgestrel in a very low dose. The continuous daily ingestion of 0.03 mg levonorgestrel prevents conception in several independent ways. Mainly, there are changes in the cervical mucus which make the migration and ascent of sperm difficult or block this. Furthermore, changes in the endometrium throughout the cycle can be considered as having the effect of rendering nidation difficult. Ovulation is not inhibited in the majority of women, but MICROLUT can impair the midcycle gonadotrophin peaks and the corpus luteum function which may contribute to the contraceptive action.

The pregnancy rates of oral progestogen only contraceptives are slightly higher than that of combined progestogen-estrogen oral contraceptives. However, when taken correctly (without missing tablets), the chance of becoming pregnant is very low.

5.2. Pharmacokinetic properties

Absorption

Orally administered levonorgestrel is rapidly and completely absorbed. Peak serum concentrations of 0.8 ng/mL are reached about 1 hour after single ingestion of MICROLUT. In a study of 18 healthy women the absolute bioavailability of levonorgestrel from MICROLUT is about 82 ± 16%. The mean volume of distribution of levonorgestrel was 106 ± 37.5 L.

Distribution

Levonorgestrel is bound to serum albumin and to sex hormone-binding globulin (SHBG). Only about 1.5% of the total serum drug concentrations is present as free steroid and about 65% is specifically bound to SHBG. The relative distribution of levonorgestrel in serum (free, albumin-bound, SHBG-bound) depends on the actual SHBG concentrations. The apparent volume of distribution of levonorgestrel is about 106 L.

Levonorgestrel distributes into mother's milk and about 0.1% of the maternal dose can be transferred to the breast-fed infant.

Metabolism

Levonorgestrel is completely metabolised by the known pathways of steroid metabolism. The metabolic clearance rate from serum is between 1 and 1.5mL/min/kg.

Elimination

Levonorgestrel serum levels decrease in two phases which are characterised by half-lives of about 1 hour and about 20 hours, respectively. Levonorgestrel is not excreted in unchanged form. Its metabolites are excreted at about equal parts via urine and faeces. The half-life of metabolite excretion is about 1 day.

Steady-state conditions

Following daily repeated administration of levonorgestrel, drug serum levels reach steady-state after about 2-3 weeks, when SHBG levels achieve steady-state. The pharmacokinetics of levonorgestrel is influenced by serum levels of SHBG. In a study of 12 healthy women administered 0.150 mg levonorgestrel for 28 days, there

was a 50% decrease in SHBG serum levels and thus, a 40% reduction in levonorgestrel trough levels after 2 - 3 weeks. The extent of the effect of MICROLUT on these binding proteins is not known.

5.3. Preclinical safety data

Acute toxicity studies did not indicate a risk of acute adverse effects in case of inadvertent intake of a multiple of the daily contraceptive dose.

Genotoxicity

The genotoxic potential of levonorgestrel has not been fully investigated, although limited data available to date suggest that it did not appear to be genotoxic.

Carcinogenicity

A long-term study in dogs showed that levonorgestrel was associated with an increased incidence of mammary tumours, although similar findings were not apparent in studies in mice, rats or monkeys. The occurrence of these mammary tumours in dogs may be due in part to a hormonal feed-back mechanism. The clinical relevance of this finding to humans remains largely unknown. Numerous epidemiological studies have been conducted to determine the incidence of breast, endometrial, ovarian and cervical cancer in women using combination oral contraceptives. Some of these studies have shown an increased relative risk of breast cancer in certain subgroups of combination oral contraceptive users. Women with a strong family history of breast cancer or who have breast nodules, fibrocystic disease or abnormal mammograms should be monitored with particular care. Benign hepatic adenomas have been found to be associated with the use of oral contraceptives containing sex hormones such as levonorgestrel. Although benign, hepatic adenomas may rupture and cause death through intra-abdominal haemorrhage. Some epidemiological studies also suggest that combination oral contraceptive use has been associated with an increase in the risk of cervical intraepithelial neoplasia in some populations of women, although 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). It must also be borne in mind that sexual steroids can promote the growth of certain hormone-dependent tissues and tumours (also see Section 4.4 Special warnings and precautions for use).

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Calcium carbonate, glycol montanate, lactose monohydrate, macrogol 6000, magnesium stearate, maize starch, povidone, purified talc, sucrose.

Microlut is gluten free.

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

3 years

6.4. Special precautions for storage

Store below 30°C. Storage conditions and expiry date are printed on the pack.

6.5. Nature and contents of container

PVC/Aluminium blisters. Pack sizes of 1 x 28, 3 x 28 or 4 x 28 tablets.

Not all pack sizes may be marketed.

6.6. Special precautions for disposal

Any unused medicine or waste material should be disposed of in accordance with local requirements.

7. MEDICINE SCHEDULE

Prescription Medicine

8. SPONSOR

Bayer New Zealand Limited
PO Box 2825
Shortland Street
Auckland 1140
New Zealand

Free Phone: 0800 233 988

9. DATE OF FIRST APPROVAL

08 February 1973

10. DATE OF REVISION OF THE TEXT

16 June 2025

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
1	Adopted Data Sheet format
2, 3, 4.2, 4.3,	Editorial changes
4.4	Addition and revision of safety information and re-arrangement

	of text
4.5	Addition of text
4.6	Revision of text
4.8	Revision of the presentation of undesirable effects including addition of information and change to reporting web address
5.2	Revision and addition of text.
6.3	Change to the shelf life to 3 years
6.4	Addition of 4 x 28 tablet presentation
8	Update of sponsor address