Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:
Microlut 30 microgram coated tablets

2. Qualitative and quantitative composition
Levonorgestrel

One coated tablet contains:
Levonorgestrel.....30 µg

Other constituents with known effect: 33 mg lactose monohydrate and 19.6 mg sucrose (see section 4.4).

For the full list of excipients, see section 6.1.

3. Pharmaceutical form
Coated tablet. The tablets are white, biconvex, and round

4. Clinical particulars
4.1 Therapeutic indications
Contraception for women

4.2 Posology and method of administration
Posology
One tablet of Microlut daily without tablet-free breaks

Method of administration
The first tablet is removed from a blister pack well marked with the abbreviated day of the week for the start of tablet-taking. The tablets are taken continually for 35 days in the direction of the arrows, irrespective of whether bleeding occurs. The day after the tablets from one blister pack have been used up, the first tablet from a new blister pack is taken.

The tablets must be taken at about the same time every day with a sufficient amount of liquid. The interval between two consecutive tablets should be as close as possible to 24 hours. To avoid jeopardizing the contraceptive effect this time must not be exceeded by more than three hours at all events. The maximum reliability of Microlut can only be guaranteed if the time between tablet-taking is kept as close as possible to 24 hours.

Starting to take Microlut
• When not preceded by the taking of hormonal contraceptives (in the previous month) Tablet-taking is to start on the first day of the natural cycle (i.e. 1st day of menstruation). If the taking of Microlut starts later, an additional barrier method of contraception is to be used in the first seven days.
• Switching from a combined oral contraceptive (COC), a vaginal ring or

a transdermal patch If the user used the previous product correctly and consistently, she should start taking Microlut the day immediately after taking the last tablet of the previous hormone-free preparation and thus omit the hormone-free interval of this COC. The user must be instructed that if the contraceptive used previously also contained hormone-free tablets, such latter tablets are not to be taken. If a vaginal ring or transdermal patch was used correctly and consistently prior to the switch, the user should start taking Microlut on the day of removal of the last vaginal ring or transdermal patch of a cycle pack and thus omit the hormone-free interval. This approach ensures uninterrupted contraception.

• Switching from another progestogen-only pill (POP, injectable product, implant) If another oral progestogen-only pill (POP) was taken previously, the switchover can take place on any day without a tablet-free break.. If {the tablets} were taken correctly, no additional contraceptives measures need be applied. When switching from an implant, the taking of Microlut must start on the day of removal, and when switching from an injectable product tablet-taking must start at the time the next injection would have been due. When switching from an implant or injectable product an additional barrier method must be employed during the first seven days.

• After a first-trimester termination

The taking of Microlut can start immediately. During the first seven days an additional barrier method must be used.

• After a birth or abortion in the second trimester of pregnancy

Women who are not breast-feeding can start taking Microlut 21 days after a birth or second-trimester miscarriage. During the first seven days an additional barrier method must be used. If sexual intercourse has already taken place, pregnancy must be ruled out before you start taking Microlut, or the first menstrual bleeding must be waited for.

• See section 4.6 "Pregnancy and lactation" for use in the case of breastfeeding women.

What to do when tablets were forgotten

Even if only one tablet was taken late (i.e. if more than 27 hours have elapsed since the last tablet was taken) or if one tablet was forgotten, contraceptive protection may be impaired. The missed tablet should be taken as soon as possible, even if this means having to take two tablets at the same time. After this, tablet-taking is resumed at the normal time of day. In addition, a barrier method is to be used for the next seven days. If sexual intercourse has taken place in the previous seven days, the possibility that pregnancy may have occurred should be considered. The risk of pregnancy occurring increases with the number of tablets missed.

What to do in case of vomiting or severe diarrhea

If vomiting or diarrhea occurs within the first three to four hours of tablet-taking, the active substance may possibly not have been completely absorbed by the intestines. In such a case the same advice as given above for a missed tablet shall apply, i.e. an additional barrier

method must be used on the following seven days. Any replacement tablet(s) should be taken from the end of the current pack so that one retains an overview of daily tablet-taking from the days of the week shown on the blister pack.

Additional information for particular patient groups

Children and adolescents

Before the menarche there is no relevant indication for Microlut.

Elderly patients

Not applicable. There is no indication for Microlut after the menopause.

Patients with impaired hepatic function

Microlut is contraindicated in women with severe hepatic disorders (see section 4.3).

Patients with impaired renal function

Microlut has not been specifically investigated in patients with impaired renal function.

4.3 Contraindications

Microlut must not be used if any of the following disorders/risk factors apply. If any of these disorders/risk factors occur for the first time while Microlut is being taken, the drug must be stopped immediately.

Microlut must not be used in case of:

- hypersensitivity to the active substance or any other constituents listed in section 6.1,
- known or suspected pregnancy,
- present venous thromboembolic disorders (deep vein thrombosis, pulmonary embolism),
- past or present arterial and cardiovascular disorders (e.g. cerebrovascular attack, myocardial infarction) or prodromal signs (e.g. angina pectoris and transitory ischemic attack),
- diabetes mellitus with vascular changes,
- past or present severe hepatic disorders as long as liver function values have not returned to normal,
- past or present hepatic tumors (benign or malignant),
- known or suspected malignant disorders of the genital organs or breast, provided these are susceptible to sex hormone influence,
- unclarified vaginal hemorrhage.

4.4 Special warnings and precautions for use

Patients with the rare congenital fructose intolerance, congenital galactose intolerance, glucose/galactose malabsorption, sucrase-isomaltase deficiency or lactase deficiency should not take Microlut.

Medical examination/consultation

Before Microlut is prescribed for the first time or again at a later date a full medical history must be collected (including family history), and a physical checkup must be conducted based on the contraindications (see section 4.3) and warnings (see section 4.4).

Blood pressure should be measured and a pregnancy be ruled out. The user must also be advised to read the directions for use carefully and to follow them. The frequency and extent of checkups should be based on the applicable established practice guidelines and be adapted to the individual woman. The user should be advised that the taking of oral contraceptives does not protect against HIV infections (AIDS) and other sexually transmitted diseases.

Warnings

If any of the disorders/risk factors listed below is present, the benefit of Microlut should be weighed against the possible risks for the individual woman and should be discussed with her before she decides to start taking it. In case any of these disorders is exacerbated or occurs for the first time, or if risk factors arise, the woman must consult her physician. The latter will decide whether Microlut must be discontinued or not.

• Vascular disorders Epidemiological studies provide scarcely any evidence for a correlation between the use of hormonal contraceptives that contain a progestogen only and an enhanced risk of sustaining myocardial infarction and cerebral thromboembolism. The risk of sustaining cardiovascular and cerebral events is more closely associated with increasing age, high blood pressure and smoking. The risk of suffering a stroke might be slightly higher in women with high blood pressure taking oral contraceptives with a progestogen only.

The risk for venous thromboembolisms may be slightly, but not statistically significantly, increased. The taking of Microlut should be discontinued if a thrombosis occurs. One should also consider stopping Microlut in the case of immobilization due to surgery or illness. Women with a history of thromboembolic disorders should be advised of a possible reoccurrence.

The generally recognized risk factors for venous thromboembolism (VTE) include

- a personal or family history of the occurrence of VTE (in a sibling or parent at a relatively young age),
- advancing age,
- obesity (body mass index above 30 kg/m^2),
- prolonged immobilization, major surgery, any leg surgery or extensive injuries. In these situations it is advisable to stop taking the POP (in the case of elective surgery at least four weeks in advance) and to restart not earlier than two weeks after complete mobility has been restored. Thrombosis prophylaxis should be considered if the POP has not been stopped in time.

The enhanced risk of thromboembolism in the puerperium must also be taken into account.

Taking must be discontinued immediately any symptoms of an arterial or venous thrombosis occur or if this is suspected. Symptoms of venous or arterial thrombosis may be:

- unusual pain or swellings in a leg

- sudden severe pain in the chest, possibly radiating to the left arm
- suddenly occurring shortness of breath,
- a sudden coughing bout,
- unusually severe or persistent headache,
- sudden partial or complete loss of vision,
- diplopia,
- slurred speech or aphasia,
- vertigo,
- collapse with or without focal seizure,
- sudden weakness or marked numbness in one half or part of the body,
- disorders of the motor functions,
- “acute” abdomen.

• Tumor diseases

Breast

A metaanalysis involving 54 epidemiological studies pointed to a slightly enhanced relative risk (RR= 1.24) for breast cancer occurring in women currently taking combined oral contraceptives. The enhanced risk gradually declines over the 10 years after the combined oral contraceptives are no longer used.

Since breast cancer is rare in women below the age of 40, the number of additional cases of breast cancer diagnosed in current or previous users of combined oral contraceptives is low in comparison to the overall risk.

The risk of breast cancer being diagnosed in the users of progestogen-only preparations is probably of the same order of magnitude as that determined in connection with combined oral contraceptives. It must be borne in mind, however, that any indications in respect of progestogen-only preparations are based on a much smaller population of users and are therefore less conclusive than those concerning combined oral contraceptives. These studies do not provide any evidence of a causal link.

The findings may be due to a timelier diagnosis, the actual effects of the hormonal contraceptives, or a combination of both.

In women who took oral contraceptives it appears that the developmental stage of any breast cancer diagnosed was clinically less advanced than cancer diagnosed in nonusers.

Liver

In rare cases benign liver tumors, and even more rarely malignant liver tumors, were reported in women taking oral contraceptives. In isolated cases these tumors led to life-threatening hemorrhages in the abdominal cavity. Differential diagnosis should include hepatic tumors if severe upper abdominal pain, liver enlargement or signs of intraabdominal hemorrhage occur in women on oral contraceptives.

• Other diseases

In general progestogen-only preparations appear to have no effect on blood pressure in normotensive women. If, however, a persistent rise in blood pressure should develop during the use of Microlut, the

latter should be discontinued.
Likewise, a recurrence of cholestatic icterus and/or cholestasis-conditioned pruritus that occurred in a previous pregnancy or during earlier use of steroidal sex hormones make it necessary to stop using Microlut. Since Microlut may have an influence of peripheral insulin resistance and glucose tolerance, diabetics and any women who had diabetes mellitus during a past pregnancy must be closely monitored, especially in the initial period of use of this drug. Depressed mood and depression are well-known undesirable effects of hormonal contraceptive use (see section 4.8). Depression can be serious and is a wellknown risk factor for suicidal behaviour and suicide. Women should be advised to contact their doctor in the event of mood changes or depressive symptoms, including shortly after initiating treatment. Chloasma may occur on occasions, especially in women with a history of chloasma gravidarum. Women who are susceptible to this should therefore not expose themselves to direct sunlight or ultraviolet light when taking Microlut.
• Ectopic pregnancy
Ectopic pregnancies occur more frequently in users of Microlut than in users of combined oral contraceptives. For this reason Microlut should only be used by women with a history of extrauterine pregnancy or tubal deficiency (e.g. in the case of present or past salpingitis or if only one tube is present) after carefully analyzing the risks and benefits. If pain in the lower abdomen occurs with an irregular cycle (amenorrhea or amenorrhea followed by continuous bleeding), the possibility of an ectopic pregnancy must be considered.
• Persisting ovarian follicle
During the use of Microlut persisting ovarian follicles (often also called functional ovarian cysts) may occur. The majority of these follicles remain without symptoms, but some may be accompanied by pain in the lower abdomen or dyspareunia. In most cases these enlarged follicles disappear of their own accord during two to three months of observation.
Impaired efficacy
The efficacy of Microlut may be impaired, if
− one or several tablets are missed or taken late (see section 4.3)
− vomiting or severe diarrhea occurs (see section 4.4),
− if certain other drugs are taken at the same time (see section 4.5),
− If Microlut and preparations containing St-John's wort are taken at the same time (see section 4.5).

Cycle disturbances
In the majority of all cases bleeding is cyclical and at normal intervals, of normal duration and intensity. Nevertheless, shorter or longer intervals have also been observed.
For this reason the user should be informed before she starts taking the tablets that such changes in bleeding patterns are possible. The changes mainly occur in the initial months of use. Later on during

use the bleeding pattern settles down and in most cases an individual pattern is established. The user should be instructed to note all bleeding occurrences in a calendar.

• What to do in the case of intermenstrual bleeding
Intermenstrual bleeding of varying intensity can occur, especially in the initial months. From the medical point of view this is no reason to stop taking Microlut, provided organic reasons for such bleeding can be ruled out by suitable diagnostic means.
No attempt should be made to treat cyclical disturbances by administering additional estrogen. Such an approach would lead to a reversal of the changes in the cervical mucus brought about by Microlut, thus considerably jeopardizing contraceptive reliability.
• If cyclical bleeding fails to occur
In some women amenorrhea may occur, but in most cases this lasts only one or two cycles. In rare cases the amenorrhea may persist for longer periods.
If bleeding fails to occur again within six weeks from the last bleeding, pregnancy must be ruled out before further tablets are taken.

4.5 Interaction with other medicinal products and other forms of interaction

Please note: The information regarding prescribing the relevant medicinal products should be reviewed for possible interactions.

Influence of other medications on Microlut
There may be interactions with medicinal products inducing microsomal enzymes. This may result in an enhanced clearance of sexual hormones and breakthrough bleeding and/or loss of contraceptive efficacy.
Enzyme induction can already be observed after a few days of treatment. The maximum enzyme inducing effect is usually observed within a few weeks. After the end of therapy, the enzyme inducing effect may continue for up to 4 weeks.
Short-term treatment Women treated with liver enzyme inducing medicinal products should temporarily use a barrier method or another contraceptive method in addition to Microlut. The barrier method must be used for the entire duration of the concomitant use of the medicinal products and for up to 28 days after the end of treatment.
Long-term treatment For women receiving long-term treatment with liver enzyme inducing medicinal products, a different reliable non-hormonal contraception is recommended. Substances increasing the clearance of levonorgestrel (decreased efficacy of Microlut due to enzyme induction) such as:
Phenytoin, barbiturates, primidone, carbamazepine, rifampicin and possibly also oxcarbazepine, topiramate, felbamate, griseofulvin, and plant-based drugs containing St. John's wort (Hypericum perforatum).
Substances with different effects on the clearance of levonorgestrel
When co-administered with sexual hormones, many HIV/HCV protease inhibitors and non-nucleoside reverse-transcriptase inhibitors as well as

combinations of the two may increase or decrease plasma levels of the progestogen. The total effect of these changes may in some cases be clinically relevant. Therefore, the professional datasheets for the concomitantly prescribed HIV/HCV drugs should be reviewed for possible interactions and relevant recommendations. If in doubt, women should use an additional barrier method for contraception during therapy with protease inhibitors or non-nucleoside reversetranscriptase inhibitors.
Substances decreasing the clearance of levonorgestrel (enzyme inhibitors)
Potent and moderate CYP3A4 enzyme inhibitors such as azole antifungal drugs (e.g., fluconazole, itraconazole, ketoconazole, voriconazole), verapamil, macrolide antibiotics (e.g., clarithromycin, erythromycin) and grapefruit juice may increase the plasma concentration of levonorgestrel. The clinical relevance of potential interactions with enzyme inhibitors remains unclear.
Influence of Microlut on other medications
Oral contraceptives may influence the metabolism of specific other medicinal products. Consequently the plasma and tissue levels (e.g. of cyclosporin) can be impaired.

Note: You should refer to the professional datasheet of the respective concomitant medication for any possible interactions.
Other forms of interactions
Laboratory tests
The use of hormonal contraceptives may impair certain laboratory test findings, including biochemical parameters for hepatic, thyroid, adrenal and renal functions as well as plasma levels of (vector) proteins, e.g. of corticosteroid-binding globulin and of lipid/lipoprotein fractions, parameters for carbohydrate metabolism and coagulation and fibrinolysis parameters. These changes, however, generally remain within the normal range.

4.6 Pregnancy and Lactation

Pregnancy
Microlut is not indicated during pregnancy. If pregnancy occurs whilst taking Microlut, the drug product must be discontinued immediately. Data from a limited number of pregnancies exposed {to this drug} show no deleterious effects on the fetus for levonorgestrel on its own. Animal experimental studies have demonstrated reproduction toxicity (see section 5.3) Undesired hormonal effects on the development of urogenital tract cannot be completely ruled out, but most of the epidemiological studies carried out to date do not indicate any enhanced risk of deformities occurring in the offspring of mothers who took contraceptives prior to pregnancy, nor are there any indications of an embryotoxic or teratogenic effect coming about through accidental ingestion of progestogens at doses like those contained in Microlut during pregnancy.

Breast-feeding
During lactation hormonal contraceptives are not recommended as the

method of choice for contraception. After the nonhormonal methods progestogen-only preparations are regarded as the next best choice for contraception. If progestogen-only preparations are used six weeks after the birth, there appear to be no detrimental effects on the growth and development of the breastfed infant. There is no evidence to suggest that progestogen-only preparations impair either quality or quantity of breast milk, although small amounts of the active substance are excreted with the milk

4.7 Effects on ability to drive and use machines

Microlut has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

The most frequently reported side effects in association with taking Microlut are vaginal/uterine bleeding including spotting, menorrhagia and/or metrorrhagia and amenorrhea. They occur in > 10 % of users.

In the assessment of side effects the following frequency brackets are used: Very common (≥ 10 %)
Common (≥ 1 % and < 10 %)
Uncommon (≥ 0.1 % and < 1 %)
Rare (≥ 0.01 % and < 0.1 %)
Very rare (< 0.01 % or unknown)

The following side effects have been reported after the taking of Microlut.

	Incidence of side effect			
Body system	**Very common ≥ 10 %**	**Common ≥ 1 % - < 10 %**	**Uncommon ≥ 0.1 % - < 1 %**	**Rare ≥ 0,01 % - < 0,1 %**
Immune system disorders				hypersensitivity reactions
Psychiatric conditions		depressive moods, changes in libido		
Nervous system disorders		headache, dizziness, nervousness		
Ophthalmic conditions				poor tolerance of contact lenses
Gastrointestinal disorders		nausea, vomiting		

Skin and subcutaneous tissue disorders		acne	chloasma	hirsutism, skin diseases
Disorders of the sex organs and mammary gland	bleeding disturbances such as spotting, intermenstrual bleeding or amenorrhea	breast pain, breast tension, dysmenorrhea, vaginitis, menorrhagia*, metrorrhagia*		changes in vaginal secretion
General diseases			fluid retention in the tissues	
Checkups				changes in body weight

The most suitable MedDRA term has been used to describe a specific reaction, its symptoms and related conditions.
* applies generally to all progestogen-only preparations

See section 4.4 for further serious side effects, such as thromboembolic diseases, hepatic tumors, cervical and breast cancer.

Ectopic pregnancies occur more frequently in users of hormonal contraceptives that contain a progestogen only (so-called POPs) than in users of combined oral contraceptives (see section 4.2).
During the use of Microlut persisting ovarian follicles (often also called functional ovarian cysts) may occur (see section 4.2).

Reporting of suspected adverse reactions

Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS)
https://pv.pharmacyboardkenya.org

4.9 Overdose

There have been no reports of any serious damage to health caused by an overdose.
The symptoms that may occur in such a case include: nausea, vomiting and mild vaginal bleeding. There is no special antidote. Treatment should be symptomatic

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic category:
Progestogens, ATC code: G03AC03

Microlut contains the orally effective progestogen levonorgestrel at a very low dose.

The continuous daily ingestion of 30 µg levonorgestrel prevents conception by various separate mechanisms.

Microlut mainly acts via its peripheral progestogenic effect on cervical mucus, the tubes and the endometrium. This prevents ascension of the sperms as well as disturbing the transport and implantation of the ovum. Ovulation is inhibited in few women. Microlut impairs the gonadotropin peak in the middle of the cycle and the corpus luteum function, which can also contribute to the contraceptive effect.

POPs are particularly suitable for women in whom estrogens are contraindicated or not desired, and also for breastfeeding women starting six weeks after childbirth.

The contraceptive reliability of POPs is somewhat lower than with combined oral contraceptives. If taken properly, the risk of becoming pregnant is however very low, comparatively speaking.

In clinical studies in which 3,218 women took Microlut for up to two years, involving 28,000 menstrual cycles, 90 pregnancies occurred. Taking all these pregnancies into account, including those occasioned by incorrect tablet-taking, the Pearl Index for Microlut amounts to 4.14.

5.2 Pharmacokinetic properties

Absorption

Levonorgestrel is rapidly and almost completely absorbed on oral administration. A peak serum level of about 0.8 ng active substance per mL is reached about one hour after administration of 30 µg levonorgestrel (Microlut).
Absolute bioavailability of levonorgestrel from Microlut is 82 %.

Distribution

Levonorgestrel is bound to serum albumin and sex hormone binding globulin (SHBG). Only approx. 1.5 % of the total levonorgestrel serum concentration is in the form of free levonorgestrel; approx. 65 % is specifically bound to SHBG. The relative distribution of serum levonorgestrel (free, albumin-bound and SHBG- bound) depends on the actual level of SHBG. Upon ingestion of Microlut the serum level of SHBG may fall slightly, and this will have a slight effect on the relative distribution of levonorgestrel with respect to the two binding proteins.
The apparent volume of distribution of levonorgestrel is approx. 106 L.

Levonorgestrel passes into the mother's milk. About 0.1 % of the maternal dose can be transferred to the infant during breastfeeding.

Special patient groups
Serum levonorgestrel concentrations decrease with increasing body weight. According to a population pharmacokinetics analysis, mean levonorgestrel concentrations fell from approximately 288-379 ng/L at a body weight of 55 kg to values of 196-264 ng/L at a body weight of 80 kg, depending on baseline SHBG levels (range from 50 to 100 nmol/L).In women with a relatively high body weight, the mean levonorgestrel concentration fell still further: in women weighing 45 kg and women weighing 90 kg, there was an approximately two-fold difference in the levonorgestrel concentrations. In the absence of relevant data, the influence of reduced serum LNG on contraceptive efficacy currently cannot be quantified.

Biotransformation and elimination
Levonorgestrel is extensively metabolized. The most important biotransformation pathways are Δ4-3-oxo group reduction and hydroxylation at positions 2α, 1β and 16β, followed by conjugation. CYP3A4 is the principal enzyme involved in oxidative LNG metabolism. However, *in vitro* data indicate that CYP-dependent biotransformation reactions are less relevant for levonorgestrel than reduction and conjugation. There are no known pharmacologically active metabolites.
The metabolic clearance rate from serum is between 1 and 1.5 mL/min/kg.

Elimination
Levonorgestrel serum levels fall in two phases, characterized by half-lives of about one hour and 20 hours respectively.

Elimination of the metabolites is roughly equally shared between the urine and feces. Metabolite elimination half-life is about one day.

Steady-state conditions

After repeated daily ingestion of levonorgestrel serum levels roughly double and reach steady-state conditions after about five days. The pharmacokinetic properties of levonorgestrel are influenced by the serum levels of SHBG. A daily intake of 0.150 mg levonorgestrel (equivalent to five times the daily dose of Microlut) leads to a 50% drop in SHBG serum levels and to a 40% fall in the trough levels of levonorgestrel after two to three weeks.

5.3 Preclinical safety data

The toxicity profile of levonorgestrel is well known. In animal experiments levonorgestrel demonstrated an embryolethal effect and at high doses a virilization effect on female fetuses. Reproduction toxicological studies in rats, mice and rabbits showed no signs of a

teratogenic effect. On the strength of conventional studies into safety pharmacology, toxicity after repeated dosage, reproduction toxicology, genotoxicity and carcinogenic potential the preclinical findings reveal no special risk to humans aside from the information already listed in other sections. On the other hand it must be remembered that sex hormones can promote the growth of hormone-dependent tissue and tumors.

6. Pharmaceutical Particulars

6.1 List of Excipients

Tablet core:
lactose monohydrate,
Maize starch,
Polyvidone K 25,
Talc,
Magnesium stearate (Ph.Eur.)

Tablet coating:
Sucrose,
Povidone K 90,
Macrogol 6000,
Calcium carbonate,
Talc
Montanglycol wax

6.2 Incompatibilities

Not Applicable

6.3 Shelf-Life

5 Years

6.4 Special Precautions for storage

Do not store above 30°C.
Keep out of reach of children

6.5 Nature and Content of container

Blister pack (PVC/aluminum) containing 35 coated tablets in a

folding box. Pack containing three blister packs, each containing

35 coated tablets.

6.6 Special precautions for disposal and other handling

No special requirements

7. Marketing Authorization Holder

Bayer AG Physical address 13353 Berlin
Postal address 13342 Berlin Germany

8. Marketing Authorization Number

CTD18981

9. Date of first authorization/renewal of the authorization
February 2026

10. Date of revision of the text
02/02/2026