PROPOSED PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: **S3**

Carmadene 0,075 mg / 0,03 mg tablets

Gestodene / Ethinylestradiol

Contains sugar: each active white or off-white tablet contains 59,12 mg lactose monohydrate and each inactive green film-coated tablet contains 55,50 mg lactose monohydrate.

Read all of this leaflet carefully before you start taking CARMADENE

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other healthcare provider.
- CARMADENE has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What CARMADENE is and what it is used for

2. What you need to know before you take CARMADENE

3. How to take CARMADENE

4. Possible side effects

5. How to store CARMADENE

6. Contents of the pack and other information

1. What CARMADENE is and what it is used for

CARMADENE is used to prevent pregnancy.

Each of the 21 active hormonal tablets contains a small amount of two different female hormones, namely ethinylestradiol and gestodene.

Contraceptive pills such as CARMADENE that contain two hormones are called “combined” pills or “combined oral contraceptives”.

2. What you need to know before you take CARMADENE

Do not take CARMADENE:

if you are hypersensitive (allergic) to gestodene or ethinylestradiol, or any of the other ingredients of CARMADENE (listed in section 6).

Do not use CARMADENE if you have any of the conditions listed below. If any of these apply to you, tell your doctor before you start using CARMADENE. Your doctor may advise you to use a different type of Pill or an entirely different (non-hormonal) method of birth control.

- If you have, or have ever had a disorder affecting the blood circulation: in particular, those conditions relating to thrombosis (the formation of a blood clot) in the blood vessels of the legs (deep vein thrombosis), the lungs (pulmonary embolism), the heart (heart attack), or other parts of the body;
- if you have or have had a stroke (caused by a blood clot or a rupture of a blood vessel in the brain);
- if you have or have ever had a condition that may be a first sign of a heart attack (such as angina pectoris or chest pain) or stroke (such as transient ischaemic attack or small reversible stroke);
- if you have a history of migraine accompanied by e.g. visual symptoms, speech disability, or weakness or numbness in any part of your body;
- if you have diabetes mellitus with blood vessel damage;
- if you have or have had pancreatitis (an inflammation of the pancreas) associated with high levels of fatty substances in your blood;
- if you have or have had jaundice (yellowing of the skin) or liver disease;
- if you have or have had a cancer that may grow under the influence of sex hormones (e.g. of the breast or the genital organs);

- if you have or have had a benign or malignant liver tumour;
- if you have any unexplained vaginal bleeding;
- if you are pregnant or think you might be pregnant;
- if you have depression, which is not well controlled with treatment;
- if you have had depression with previous use of hormonal contraceptives.

If any of these conditions appear for the first time while using CARMADENE, stop taking it immediately and consult your doctor. In the meantime, use non-hormonal contraceptive measures.

Use in older women:

CARMADENE is not intended for use after menopause.

Warnings and precautions

Take special care with CARMADENE:

Before taking CARMADENE tell your doctor if:

- You have an inflammation of your veins (superficial phlebitis);
- you have varicose veins;
- anyone in your immediate family has had a thrombosis, a heart attack or a stroke;
- you have a heart valve disorder or a certain heart rhythm disorder;
- you suffer from migraine;
- you suffer from epilepsy;
- you smoke;
- you have diabetes;
- you are overweight;
- you have high blood pressure;
- you or someone in your immediate family has or has had high blood levels of cholesterol or triglycerides (fatty substances);
- anyone in your immediate family has had breast cancer;

- you have liver or gall bladder disease;
- you have Crohn's disease or ulcerative colitis (chronic inflammatory bowel disease);
- you have systemic lupus erythematosus (SLE; a disease affecting the skin all over the body);
- you have haemolytic uremic syndrome (HUS; a disorder of blood coagulation causing failure of the kidneys);
- you have sickle cell disease;
- you have a condition that occurred for the first time or worsened during pregnancy or previous use of sex hormones (e.g. hearing loss, a metabolic disease called porphyria, a skin disease called herpes gestationis, a neurological disease called Sydenham's chorea);
- you have or have had chloasma (yellowish-brown pigmentation patches on the skin, particularly of the face); if so, avoid too much exposure to the sun or ultraviolet radiation;
- you have hereditary angioedema; exogenous oestrogens may induce or exacerbate symptoms of angioedema. You should see your doctor immediately if you experience symptoms of angioedema such as swollen face, tongue and/or pharynx and/or difficulty swallowing or hives together with difficulty breathing;
- you are on treatment for depression;
- you have had depression with previous use of hormonal contraceptives;
- you have a substance abuse problem;
- you have an underlying psychiatric disorder such as post-traumatic stress disorder or bipolar disorder;
- you have a family history of mental disorders;
- you have a history of physical or sexual abuse.

Hormonal contraceptives including CARMADENE, may cause mood changes and depression, which may be severe. Severe depression is associated with a higher risk

of suicidal thoughts/behaviour (e.g. talking about suicide, withdrawing from social contact, having mood swings, being preoccupied with death or violence, feeling hopeless about a situation, increasing use of alcohol/drugs, doing self-destructive things, personality changes) and suicide. If you experience mood changes and depression, contact your doctor for advice.

If any of the above conditions appear for the first time, recur or worsen while using CARMADENE, you

should contact your doctor.

CARMADENE and thrombosis:

A thrombosis is the formation of a blood clot which may block a blood vessel.

A thrombosis sometimes occurs in the deep veins of the legs (deep venous thrombosis).

If this blood clot breaks away from the veins where it is formed, it may reach and block the arteries of the lungs, causing a so-called “pulmonary embolism”. Deep venous thrombosis is a rare occurrence. The risk for venous thromboembolism is highest during the first year a woman ever uses CARMADENE.

Overall, the risk for venous thromboembolism in users of low oestrogen dose (< 50 µg ethinylestradiol) pills, such as CARMADENE, is higher than for non-users of combined oral contraceptives.

Blood clots can also occur in the blood vessels of the heart (causing a heart attack) or the brain (causing a stroke). Extremely rarely blood clots can occur in the liver, gut, kidney or eye. Very occasionally thrombosis may cause serious permanent disabilities or may even be fatal.

When using CARMADENE you should stop smoking, especially if you are older than about 35 years of age.

If you develop high blood pressure while using CARMADENE, you may be told to stop using it. The risk of having deep venous thrombosis is temporarily increased as a result of an operation or immobilisation (for example, when you have your leg or legs in plaster or splints). In women who use CARMADENE, the risk may be yet higher. Tell your doctor you are using CARMADENE well in advance of any expected hospitalisation or surgery. Your doctor may tell you to stop taking CARMADENE several weeks before surgery or at the time of immobilisation. Your doctor will also tell you when you can start taking CARMADENE again after you are back on your feet. If you notice possible signs of a thrombosis, stop taking CARMADENE and consult your doctor immediately.

CARMADENE and cancer:

An increased risk of cervical cancer in long-term users of combined oral contraceptives, such as

CARMADENE, has been reported in epidemiological studies.

In rare cases benign liver tumours and even more rarely, malignant liver tumours have been reported in users of CARMADENE. These tumours may lead to internal bleeding. Contact your doctor immediately if you have severe pain in your abdomen.

Children and adolescents

CARMADENE is not for use in females whose periods have not yet started.

Other medicines and CARMADENE

Always tell your healthcare provider if you are taking any other medicine. (This includes all complementary or traditional medicines.)

If you are taking any of the following medicines please consult your healthcare professional: these include medicines used for the treatment of epilepsy (e.g. primidone, phenytoin, barbiturates, carbamazepine, oxcarbazepine, topiramate, felbamate); tuberculosis (e.g. rifampicin, rifabutin) and HIV infections (e.g. ritonavir, nevirapine); antibiotics (e.g. penicillins, tetracyclines, griseofulvin) for some other infectious diseases; and the herbal remedy St. John's wort (primarily used for the treatment of depressive moods).

During treatment with any of these medicines, a barrier method such as a condom should be temporarily used in addition to CARMADENE, or another method of contraception should be chosen if these medicines are going to be used for prolonged periods.

The barrier method should be used for the duration of the concomitant administration and for 28 days after discontinuation of the medicine. However, if you are taking an antibiotic (excluding rifampicin and griseofulvin), you should use the barrier method until 7 days after completing the course.

If the period during which the barrier method is used runs beyond the end of the active tablets in the CARMADENE pack, the inactive tables should be omitted and the next CARMADENE pack should be started.

The first tablet should be taken from the silver section of the calendar pack by selecting the tablet corresponding to the day of the week (e.g. "MO' for Monday). Then take 1 tablet every day following the directions shown by

the arrows.

CARMADENE may also interfere with the working of other medicines, e.g. medicines containing cyclosporin, or the anti-epileptic lamotrigine.

Laboratory tests

If you need a blood test, tell your doctor or the laboratory staff that you are taking CARMADENE, because oral contraceptives can affect the results of some tests.

Pregnancy and breastfeeding

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other healthcare provider for advice before taking this medicine.

CARMADENE and pregnancy:

CARMADENE must not be used by women who are pregnant, or who think they may be pregnant. If you suspect that you are pregnant while you are already using CARMADENE, you should consult your doctor as soon as possible.

CARMADENE and breastfeeding:

CARMADENE is not recommended for use during breastfeeding. If you wish to take CARMADENE while breastfeeding, please seek the advice of your doctor.

Driving and using machines

You should be aware of how you react to CARMADENE before you drive or operate machinery. If you feel dizzy or drowsy after taking CARMADENE, do not drive or operate machinery until these effects wear off.

CARMADENE contains lactose monohydrate

Lactose is a type of sugar. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking CARMADENE.

3. How to take CARMADENE

Do not share medicines prescribed for you with any other person.

Always take CARMADENE exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

CARMADENE, when taken correctly, has a failure rate of approximately 1 % per year. The failure rate may increase when pills are missed or taken incorrectly.

When and how to take the tablets:

The first tablet should be taken from the silver section of the calendar pack by selecting the tablet corresponding to the day of the week (e.g. “MO’ for Monday).

Take your tablet at about the same time each day, with some liquid if necessary. Follow the direction of the arrows until all 28 tablets have been taken.

Usually a period will start on day 2 to 3 after the last active CARMADENE tablet (i.e. while you are taking the green tablets from the bottom row of your pack). Do not leave a gap between packs, i.e. start taking your next pack on the day after you have finished the current one, even if your period continues. This means that you will always start new packs on the same day of the week, and also that you have your withdrawal bleed on about the same days, each month.

Starting your first pack of CARMADENE:

When no hormonal contraceptive has been used in the past month:

Start taking CARMADENE on the first day of your cycle, i.e. the first day of menstrual bleeding. The first tablet should be taken from the silver section of the calendar pack by selecting the tablet corresponding to the day of the week (e.g. “MO’ for Monday).

Then take 1 tablet every day following the directions shown by the arrows. You may also start on days 2 to 5 of your menstrual cycle, but in that case make sure you also use an additional contraceptive method (barrier method) for the first 7 days of tablet-taking in the first cycle.

When changing from a combined Pill, vaginal ring, or transdermal (contraceptive) patch:

You can start taking CARMADENE the day after you take the last tablet from your present Pill pack (this means no tablet-free break). If your present Pill pack also contains inactive tablets you can start CARMADENE on the day after taking the last **active** tablet (if you are not sure which this is, ask your doctor or pharmacist). You can also start later, but never later than the day following the tablet-free break of your present Pill (or the day after the last inactive tablet of your present Pill).

The first tablet should be taken from the silver section of the calendar pack by selecting the tablet corresponding to the day of the week (e.g. “MO’ for Monday). Then take 1 tablet every day following the directions shown by the arrows.

In case you have used a vaginal ring or transdermal patch, you should start using CARMADENE preferably on the day of removal, but at the latest when the next application would have been due.

The first tablet should be taken from the silver section of the calendar pack by selecting the tablet corresponding to the day of the week (e.g. “MO’ for Monday). Then take 1 tablet every day following the directions shown by the arrows.

If you follow these instructions, it is not necessary to use an additional contraceptive method.

When changing from a progestogen-only pill (minipill):

You can stop taking the minipill any day and start taking CARMADENE the next day, at the same time. But make sure you also use an additional contraceptive method (a barrier method) for the first 7 days of tablet-taking when having intercourse.

The first tablet should be taken from the silver section of the calendar pack by selecting the tablet corresponding to the day of the week (e.g. “MO’ for Monday). Then take 1 tablet every day following the directions shown by the arrows.

When changing from an injectable, an implant, or a progestogen-releasing intrauterine device (IUD):

Start using CARMADENE when your next injection is due or on the day that your implant or your IUD is removed. But make sure you also use an additional contraceptive method (a barrier method) for the first 7 days of tablet-taking when having intercourse.

The first tablet should be taken from the silver section of the calendar pack by selecting the tablet corresponding to the day of the week (e.g. “MO’ for Monday). Then take 1 tablet every day following the directions shown by the arrows.

After having a baby:

If you have just had a baby, your doctor may tell you to wait until after your first normal period before you start taking CARMADENE. Sometimes it is possible to start sooner. Your doctor will advise you. If you are breastfeeding and want to take CARMADENE, you should discuss this first with your doctor.

After a miscarriage or an abortion:

Your doctor will advise you.

For how long should you take CARMADENE:

CARMADENE must be taken for as long as you want to prevent pregnancy. You can stop taking CARMADENE at any time you want. If you stop because you want to get pregnant, it is generally recommended that you wait until you have had a natural period before trying to conceive. This helps you to work out when the baby will be due. If you do not want to become pregnant, ask your doctor about other methods of birth control.

If you have the impression that the effect of CARMADENE is too strong or too weak, tell your doctor or pharmacist.

If you take more CARMADENE than you should

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre.

Symptoms that may occur in case of taking an overdose are: nausea, vomiting and in young girls; slight vaginal bleeding. There have been no reports of serious effects from overdose noted.

If you forget to take CARMADENE

Management of missed tablets:

The green tablets are inactive tablets and missing these can be disregarded. However, they should be discarded to avoid unintentionally prolonging the inactive tablet phase. The following advice only refers to missed active tablets.

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

If she is **more than 12 hours** late in taking any active tablet, contraceptive protection may be reduced. 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. 7 days of uninterrupted active tablet-taking are required to attain adequate suppression of the hypothalamic-pituitary-ovarian-axis.

Accordingly, the following advice can be given in daily practice:

First 7 days of active tablet-taking:

The user should take the last missed tablet as soon as she remembers, even if this means taking two tablets at the same time. She then continues to take tablets at her usual time. In addition, a barrier method such as a condom 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 that are missed and the closer they are to the inactive tablet phase, the higher the risk of a pregnancy.

Second 7 days of active tablet-taking:

The user should take the last missed tablet as soon as she remembers, even if this means taking two tablets at the same time. She then continues to take tablets at her usual time. Provided that the woman has taken her tablets correctly in the 7 days preceding the first missed tablet, there is no need to use extra contraceptive precautions. However, if this is not the case, or if she missed more than 1 tablet, the woman should be advised to use extra precautions for 7 days.

Third 7 days of active tablet-taking:

The risk of reduced reliability is imminent because of the forthcoming inactive tablet phase. However, by adjusting the tablet-taking schedule, reduced contraceptive protection can still be prevented. If either of the following two options is adhered to, there is no need to use extra contraceptive precautions, provided that in the 7 days preceding the first missed tablet the woman has taken all tablets correctly. If this is not the case, the woman should be advised to follow the first of these two options, and also to use extra precautions for the next 7 days as well.

1. The user should take the last missed tablet as soon as she remembers, even if this means taking two tablets at the same time. She then continues to take tablets at her usual time until the active tablets are used up. The 7 inactive tablets must be discarded. The next pack must be started right away. The user is unlikely to have a withdrawal bleed until the end of the active tablets section of the second pack, but she may experience spotting or breakthrough bleeding on active tablet-taking days.

2. The woman may also be advised to discontinue active tablet-taking from the current pack. She should then have a tablet-free interval of up to 7 days, including the days she missed tablets, and subsequently continue with the next pack, starting in the silver section with the tablet for the appropriate day of the week.

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

If you stop taking CARMADENE

*Y*ou should always consult your doctor before deciding to interrupt the course of treatment or stop taking CARMADENE altogether.

4. Possible side effects

CARMADENE can have side effects.

Not all side effects reported for CARMADENE are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking CARMADENE, please consult your healthcare provider for advice.

If any of the following happens, stop taking / using CARMADENE and tell your doctor immediately or go to the casualty department at your nearest hospital:

- Swelling of the hands, feet, ankles, face, lips, mouth, tongue or throat, which may cause difficulty in swallowing or breathing, blueness of the skin;
- skin rash, lesions, itchiness of the skin, blistering or peeling of the skin or any other type of skin irritation; or
- chest tightness, difficulty breathing, feeling dizzy or fainting due to low blood pressure.

These are all very serious side effects. If you have them, you may have had a serious reaction to CARMADENE. You may need urgent medical attention or hospitalisation.

An increased risk of blood clots in your veins (venous thromboembolism (VTE)) or blood clots in your arteries (arterial thromboembolism (ATE)) is present for all women taking combined hormonal contraceptives. Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

Harmful blood clots in a vein or artery for example:

- In a leg or foot (i.e. Deep vein thrombosis - DVT);
- in a lung (i.e. Pulmonary embolism - PE);
- heart attack;
- stroke;
- mini-stroke or temporary stroke-like symptoms, known as a transient ischaemic attack (TIA);
- blood clots in the liver, stomach/intestine, kidneys or eye.

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:

Frequent side effects:

- Depressive or altered mood;
- headache;
- nausea;
- abdominal pain;
- sore or tender breasts;
- weight gain.

Less frequent side effects

- fluid retention;
- an increased or decreased interest in sex;
- migraine;
- poor tolerance of contact lenses;
- vomiting;
- diarrhoea;
- acne, skin rash and itchiness;
- changes in the shape of the breast;

- vaginal discharge;
- breast discharge;
- weight loss.

Side effects with unknown frequency:

- Swelling under the skin;
- excess lipids in the blood;
- changes in blood sugar control;
- worsening of a disease known as chorea characterised by irregular, sudden, involuntary movements;
- abnormal liver test results;
- possible aggravation of inflammatory bowel disease: symptoms include abdominal cramps and pain, diarrhoea (which may be bloody), weight loss;
- pigmentation disorders. This may happen even if you have been using CARMADENE for a number of months. This may be reduced by avoiding too much sunlight;
- bleeding and spotting between your periods can sometimes occur for the first few months but this usually stops once your body has adjusted to CARMADENE. If it continues, becomes heavy or starts again, contact your doctor;
- absence of menstruations;
- suicidal thoughts/behaviour and suicide.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on the SAHPRA website or to Cipla Medpro (Pty) Ltd. by e-mail: drugsafetysa@cipla.com or telephone: 080 222 6662 (toll free). By reporting side effects, you can help provide more information on the safety of CARMADENE.

5. How to store CARMADENE

Store at or below 25 °C in a cool, dry place.

Store the blisters in the outer carton to protect from light and moisture.

Store all medicines out of reach of children.

Do not refrigerate or freeze.

Do not use after the expiry date stated on the carton and blister strip.

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What CARMADENE contains

Active white or off-white tablets

The active substances are gestodene and ethinylestradiol.

Each active tablet contains gestodene 0,075 mg and ethinylestradiol 0,03 mg.

The other ingredients are lactose monohydrate, magnesium stearate, microcrystalline cellulose, polacrilin potassium, povidone K-30.

Inactive green film-coated tablets (placebo)

The inactive tablets are placebo and do not contain any active ingredients.

The tablet core consists of lactose monohydrate, magnesium stearate, maize starch, povidone K-30, silica colloidal anhydrous.

The tablet coat consists of FD&C blue 2 aluminium lake, hypromellose 2910, polysorbate 80, titanium dioxide, triacetin, yellow iron oxide.

What CARMADENE looks like and contents of the pack

Active tablets

21 round, white or off-white tablets, with a diameter of approximately 5,7 mm, debossed with ‘C’ on one side and ‘33’ on the other.

Inactive film-coated tablets (placebo)

7 round, green film-coated tablets.

The tablets are contained in PVC-PVDC/aluminium blisters. Aluminium foil is a foil of push-through aluminium with a lacquered dull side, and a heat sealable bright side lacquered for sealing to PVC.

The blisters are contained in an outer cardboard carton.

Pack size: The 28-day pack (Every-day calendar pack) contains 21 active hormonal white or off-white tablets plus 7 inactive non-hormonal (placebo) green film-coated tablets.

Holder of certificate of registration

CIPLA MEDPRO (PTY) LTD.

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To Be Confirmed

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