

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS:

S4

DIVA 35 (Tablets)

cyproterone acetate and ethinylestradiol

DIVA 35 contains sugar (lactose and saccharose)

Read all of this leaflet carefully before you start taking DIVA 35.

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- DIVA 35 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 DIVA 35 is and what it is used for
2. What you need to know before you take DIVA 35
3. How to take DIVA 35
4. Possible side effects
5. How to store DIVA 35
6. Contents of the pack and other information

1. What DIVA 35 is and what it is used for

DIVA 35 is used as an oral contraceptive which is known also as the Pill, OC's, or birth control pills. They usually contain two types of female hormones, estrogens and progestins.

When taken by mouth on a regular schedule, they change the hormone balance of the body, which prevents pregnancy.

Applicant/HCR: Unicorn Pharmaceuticals (Pty) Ltd

Product name, dosage form(s) and strength(s):

Diva 35, each hormonal tablet contains cyproterone acetate 2,00 mg and ethinylestradiol 0,035 mg

This medicine is also used in the treatment of other conditions that are helped by added hormones, such as androgen-dependent acne, androgen-dependent hair loss or abnormal hairiness.

This medicine is available only on your doctor's prescription.

2. What you need to know before you take DIVA 35

Important information about some of the ingredients of DIVA 35

DIVA 35 contains lactose. Patients with the rare hereditary conditions of lactose or galactose intolerance should not take DIVA 35.

Allergies - Tell your doctor if you have ever had any unusual or allergic reaction to estrogens or progestins. Also tell your doctor and pharmacist if you are allergic to any other substances, such as foods, preservatives, or dyes.

Pregnancy - This medicine is not recommended for use during pregnancy.

Do not take DIVA 35

- If you are hypersensitive (allergic) to *cyproterone acetate* OR *ethinylestradiol* or any of the other ingredients of DIVA 35 listed above.
- You have depression, which is not well controlled with treatment.
- You have had depression with previous use of hormonal contraceptives.
- If you have moderately impaired liver function or cholestasis, the Dubin-Johnson or Rotor- syndromes, hepatic adenomas, estrogen-dependent neoplasms (cancers) such as breast or endometrial cancer, cardiovascular disease including previous or current thrombo-embolic disorders, or high risk of them and arterial disease or multiple risk factors for it.
- *If you suffer from* - Disorders of fat metabolism, undiagnosed vaginal bleeding, jaundice with less flow of bile, involuntary movements of the limbs of facial muscles, herpes

(inflammatory skin disease caused by a virus (herpes simplex or varicella zoster), pemphigoid gestationis, or worsening hearing loss.

- *If you suffer from* - Severe or focal migraine, cerebrovascular conditions, advanced diabetes mellitus (high blood sugar) with vascular changes, sickle-cell disease (abnormal shaped red blood cells) and porphyria.
- If you are a male or a child

Other medicines and DIVA 35

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

Reduced DIVA 35 plasma levels have been obtained with concomitant use of certain antibiotics (e.g. ampicillin, tetracycline) and oral contraceptive failure may occur. Spotting and breakthrough bleeding are possible signs of diminished effectiveness. For maximal protection, additional non-hormonal contraception should be recommended for the duration of antibiotic therapy and for seven days afterwards. Those on long-term antibiotic therapy need only take extra precautions for the first two weeks of antibiotic therapy.

An impaired action of DIVA 35 is noted with enzyme inducers such as:

- anti-epileptic agents,
- griseofulvin
- barbiturates
- phenylbutazone and rifampicin.
- modafinil and some antiviral agents, such as nelvinavir, ritonavir and nevirapine.

Reduced effectiveness was observed when DIVA 35 was administered with:

- anticoagulants
- antidepressants

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- antidiabetics
- antihypertensives
- beta blockers and diuretics.

The plasma concentrations of cyclosporine and theophylline may be increased with concomitant use. Large supplements of vitamin C have been reported to increase serum ethinylestradiol concentrations. Withdrawal of high doses of vitamin C may lead to breakthrough bleeding.

Mild laxatives do not impair the action of DIVA 35.

Warnings and precautions

Tell your doctor before using DIVA 35:

- That you are on treatment for depression
- That you have had depression with previous use of hormonal contraceptives
- That you have a substance abuse problem
- You have underlying psychiatric disorder such as post-traumatic stress disorder or bipolar disorder
- That you have a family history of mental disorders
- That you have a history of physical or sexual abuse

Hormonal contraceptives including DIVA 35, may cause mood changes and depression, which may be severe.

Severe depression is associated with a higher risk of suicidal thoughts/behavior (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.

Other medical problems

The presence of other medical problems may affect the use of this medicine. Make sure you tell your doctor if you have any other medical problems, especially patients with a history of:

- gallbladder disease,
- conditions influenced by fluid retention,
- high blood pressure,
- varicose veins,
- a history of phlebitis,
- otosclerosis,
- multiple sclerosis,
- epilepsy,
- tetanus,
- chorea minor,
- asthma.

DIVA 35 should be stopped immediately if any of the following occur:

- Sudden severe chest pain, sudden breathlessness, or severe pain/swelling in calf of one leg (possibly indicative of thrombo-embolic complications). The medication should be discontinued at least 4 to 6 weeks before surgery of the type associated with an increased risk of thrombo-embolism, or during periods of prolonged immobilization.
- Unusual, severe, prolonged headache, sudden disturbances of vision or hearing or other perceptual disorders, collapse, marked numbness or weakness affecting one side of the body, or other signs and symptoms suggestive of cerebrovascular disease.
- Hepatitis, jaundice, generalised itching, liver enlargement, severe upper abdominal pain
- Onset of severe depression.
- Significant rise in blood pressure.

- Clear exacerbation of other conditions known to be capable of deteriorating during oral contraception or pregnancy.
- Increase in epileptic seizures.

Additional precautions while you are on DIVA 35 treatment

- Regular examinations are recommended at about 6-monthly intervals during the use of DIVA 35.

Regular blood pressure checks, including a pre-treatment level, are advisable.

- Prolonged amenorrhoea (absence of menstruation) following the use of DIVA 35 may occur. Caution is advised where oligomenorrhoea (little menstruation) or amenorrhoea (absence of menstruation) have occurred in the past.
- Irregular tablet-taking, vomiting or intestinal disorders with diarrhoea may decrease the efficacy of DIVA 35. Additional methods of contraception should be used at the time of such disorders in order to prevent a possible pregnancy, which would be a compelling reason for the discontinuation of DIVA 35 treatment.
- Surgery is more likely to be associated with an increased incidence of thrombotic (*clotting within a blood vessel*) side effects. Adequate precaution should be taken. Under no circumstances should DIVA 35 be stopped without having adopted a satisfactory alternative method for contraception.
- If an active tablet is either delayed or missed it should be taken as soon as possible. Contraceptive protection is maintained if the delayed tablet is taken within 12 hours of the usual administration time. If more than 12 hours elapse from the time the tablets are normally taken, and also in the case of vomiting or diarrhoea, the patient must continue to take the other tablets in the pack at the usual time in order to avoid a premature withdrawal bleeding during this cycle. At this same time, however, an additional non-hormonal method of contraception (with exception of the rhythm and temperature methods) must be employed in order to prevent a pregnancy.

- If an inter-menstrual bleeding occurs during the 3 weeks in which the active tablets are

being taken, their use should not be interrupted. A slight bleeding (spotting) will usually stop spontaneously. However, if the bleeding is heavy, similar to menstrual bleeding, then a thorough examination is indicated to exclude organic factors.

- If bleeding fails to occur while the tablets from the starter section are being taken, tablet-taking must provisionally be stopped and the doctor must be consulted.
- The incidence of disease of the circulatory system in women using DIVA 35 is significantly greater than those of controls, and the mortality is slightly increased. Increased mortality from myocardial infarction is much greater in women aged 35 years or over, particularly if they used the contraceptive for longer than 5 years and if they smoke. Other risk factors include a family history of arterial disease, hypercholesterolaemia, familial hyperlipoproteinaemia, diabetes mellitus, hypertension, obesity and migraine. Specific risk factors for venous thrombo-embolism include a family history of venous thrombo- embolism, varicose veins and, again, obesity. However, the risk of mortality due to DIVA 35 in women under 35 who are in the high-risk group is in general far less than the risk of mortality due to pregnancy.
- Benign and malignant liver tumours leading in isolated cases to life-threatening intra-abdominal haemorrhage, have been observed after the use of hormonal substances such as those contained in DIVA 35. If severe upper abdominal complaints, liver enlargement or signs of intra-abdominal haemorrhage occur, a liver tumour should be included in the differential-diagnostic considerations.

Cigarette smoking during the use of oral contraceptives has been found to increase the risk of serious side-effects affecting the heart and/or blood circulation, such as dangerous blood clots, heart attack or stroke. The risk increases as the age of the patient and the amount of smoking increase. This risk is greater in women age 35 and over. *To reduce the risk of serious side -effects do not smoke cigarettes while using oral contraceptives.*

Pregnancy, breastfeeding and fertility

If you are pregnant you should not take Diva 35. If you become pregnant while taking Diva 35 you should stop taking it immediately and contact your doctor. Taking Diva 35 while you are breastfeeding your baby is not recommended. If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other healthcare professional for advice before taking Diva.

3. How to take DIVA 35

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

Always take DIVA 35 exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Take this medicine only as directed by your doctor. This medicine must be taken exactly on schedule to prevent pregnancy. Try to take the medicine at the same time each day, not more than 24 hours apart to reduce the possibility of side-effects and to provide the best protection.

Initial course:

One tablet daily for 28 days, starting on the first day of the menstrual cycle (the first day of menstruation counting as Day 1).

Subsequent course:

After the last tablet has been taken from the first pack, tablet-taking is continued from a new pack the very next day.

Length of use:

The length of use depends on the severity of the clinical picture. In general, treatment should be carried out over several months. It is recommended that DIVA 35 be taken for at least another 3 to 4 cycles after the signs have subsided. Should there be a recurrence weeks or months after discontinuation, treatment with DIVA 35 may be resumed.

When changing from an oral contraceptive and relying on the contraceptive action of DIVA 35, the instructions given below should be followed:

Changing from 21-day combined oral contraceptives:

The first tablet of DIVA 35 should be taken on the first day immediately after the end of the previous oral contraceptive course. Additional contraceptive precautions are not required.

Changing from a combined Every Day Pill (28 day tablets):

The first DIVA 35 tablet should be taken the day after the last active tablet from the Every Day Pill pack. Additional contraceptive precautions are not then required.

Changing from a progesterone-only pill (POP):

The first tablet of DIVA 35 should be taken on the first day of bleeding, even if a POP has already been taken on that day. Additional contraceptive precautions are not required. The remaining progesterone-only pills should be discarded.

Other Precautions

- *It is very important that your doctor check your progress at regular visits to make sure this medicine does not cause unwanted effects. These visits will usually be every 6 to 12 months, but some doctors require them more often.*
- *When you begin to use oral contraceptives, your body will require at least 7 days to adjust before pregnancy will be prevented; therefore, you should use a second method of birth control for the first cycle (or 3 weeks) to ensure full protection.*
- *Tell the medical doctor or dentist in charge that you are taking this medicine before any kind of surgery (including dental surgery) or emergency treatment, since this medicine may cause serious blood clots, heart attack, or stroke.*
- *Certain medicines may reduce the effectiveness of this medicine. You should use a second method of birth control during each cycle in which any of the medicines listed under "What you need to know before you take DIVA 35" are used. Check with your*

doctor if you have any questions about this.

- Vaginal bleeding of various amounts may occur between your regular menstrual periods during the first 3 months of use. This is sometimes called spotting when slight, or breakthrough bleeding when heavier.

If this should occur:

- Continue with your regular dosing schedule.
- The bleeding usually stops within 1 week.
- Check with your doctor if the bleeding continues for more than 1 week.
- After you have been taking this medicine on schedule and for more than 3 months, check with your doctor.

Missed menstrual periods may occur:

- If you have not taken the medicine exactly as scheduled. Pregnancy must be considered a possibility.
- If the medicine is not properly adjusted for you needs.
- If you have taken oral contraceptives for a long time, usually 2 or more years, and stop their use.

Check with your doctor if you miss any menstrual periods so that the cause may be determined.

- Some people who take this medicine may become more sensitive to sunlight than they are normally. When you begin taking this medicine, avoid too much sun and do not use a sunlamp until you see how you react to the sun, especially if you tend to burn easily. If you have a severe reaction, check with your doctor. Some people may develop brown, blotchy spots on exposed areas. These spots usually disappear gradually when the medicine is stopped.
- If you wear contact lenses and notice a change in vision or are not able to wear them, check with your doctor.
- *If you suspect that you may have become pregnant, stop taking this medicine immediately and check with your doctor.*

- If you are scheduled for any laboratory tests, tell your doctor that you are taking birth control pills.

If you take more DIVA 35 than you should

Call your doctor, pharmacist, poison centre or go to the nearest hospital emergency unit immediately. Take your box of DIVA 35 capsules with you.

If you forget to take DIVA 35

Missed dose and special circumstances requiring additional contraception:

If a patient forgets to take her tablet at the usual time, she must take it within the next 12 hours at the latest. If more than 12 hours elapse from the time that she normally takes her tablet, and also in the case of vomiting or diarrhoea, she must continue to take the other tablets in the pack at the usual time in order to avoid premature withdrawal bleeding during the cycle. At the same time, however, an additional, non- hormonal method of contraception (with the exception of the rhythm and temperature methods) must be employed in order to prevent a pregnancy which would be a compelling reason for the discontinuation of DIVA 35.

If tablet(s) have been missed during the last 7 days of a pack, there should be no break before the next pack is started. In this situation, a withdrawal bleed should not be expected until the end of the second pack. Some breakthrough bleeding may occur on tablet taking days, but this is not clinically significant. If the patient does not have a withdrawal bleed during the tablet-free interval following the end of the second pack, the possibility of pregnancy must be ruled out before starting the next pack.

4. Possible side effects

DIVA 35 can have side effects.

Not all side effects reported for DIVA 35 are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking DIVA

35, please consult your health care provider for advice.

Cyproterone acetate:

Neoplasms (abnormal tissue growth) benign (not cancerous) and malignant (cancerous):

- Less frequent: *Liver cancer*

Blood and lymphatic system disorders:

- Less frequent: *Thrombosis (clotting within a blood vessel)*

Endocrine (internal or hormonal secretion of a ductless gland) disorders:

- Less frequent: *Weight gain*

Psychiatric disorders:

- More frequent: *Changes in conscious and unconscious sexual desire*
- Less frequent: *Depression*

Gastrointestinal disorders:

- Less frequent: *Nausea (inclination to vomit or feeling sick), vomiting (being sick)*

Hepato-biliary (Liver & gall) disorders:

- Less frequent: *Altered liver function, inflammation of the liver, jaundice, enlargement of the liver, liver failure, liver carcinoma, gall bladder disease*

Skin and subcutaneous tissue disorders:

- Less frequent: *loss of hair, abnormal sensitivity to light, allergic rash or skin eruption,*

Reproductive system and breast disorders:

- More frequent: *Breast tenderness*

Ethinylestradiol:

Infections and infestations:

- More frequent: *Vaginal candidiasis or yeast-like infection*

Blood and lymphatic system disorders:

- Less frequent: *Thromboembolic (clotting within blood vessel, resulting in a plug) disorders,*

thrombosis (clotting within a blood vessel)

Metabolic and nutritional disorders:

- Incidence unknown: *Reduced tolerance towards sugars, changes in fat metabolism*

Psychiatric disorders:

- More frequent: *Changes in appetite, depression*
- Less frequent: *Mood or mental changes, changes in conscious or unconscious sexual desire*

Nervous system disorders:

- More frequent: *Dizziness (mild), headache, migraine (severe complex type of headache together with other symptoms)*

Eye disorders:

- Less frequent: *Intolerance to contact lenses*

Vascular disorders:

- More frequent: *Water retention*
- Less frequent: *Hypertension/High blood pressure*

Gastrointestinal disorders:

- More frequent: *Gastrointestinal irritation, abdominal cramps, nausea (inclination to vomit or feeling sick)*
- Less frequent: *Vomiting (being sick)*

Hepato-biliary (Liver & gall) disorders:

- Less frequent: *Poor liver function, gall bladder disease, inflammation of the liver, jaundice with less flow of bile*

Skin and subcutaneous tissue disorders:

- More frequent: *itchy skin, skin rash*
- Incidence unknown: *pigmented facial patches, patchy pigmentation of sun-exposed skin, a breakout bleeding of the skin*

Reproductive system and breast disorders:

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- Incidence unknown: *Change in cervical secretions*

Ethinylestradiol/cyproterone cyclical:

Neoplasms (abnormal tissue growth) benign (not cancerous) and malignant (cancerous):

- Incidence unknown: *Increased risk of cervical or breast cancer*

Reproductive system and breast disorders:

- More frequent: *Menstrual irregularities, spotting (slight bleeding), breakthrough bleeding, amenorrhoea (absence of menstruation)*
- Incidence unknown: *Anovulation post-treatment (to treat the condition where the patient does not ovulate after being on DIVA-35 treatment)*

Reported post marketing:

Suicidal thoughts/behavior and suicide

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

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

<https://www.sahpra.org.za/Publications/Index/8>. Side effects can also be reported to Unicorn Pharmaceuticals (Pty) Ltd to vigilance@unicornpharma.co.za. By reporting side effects, you can help provide more information on the safety of DIVA 35.

5. How to store DIVA 35

Store in original packs below 25 °C.

Store all medicines out of reach of children.

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Store away from heat and direct light.

Do not store in bathroom, near the kitchen sink, or in other damp places. Heat or moisture may cause the medicine to break down.

Do not keep outdated or medicines no longer needed. Be sure that any discarded medicine is out of reach of children.

6. Contents of the pack and other information

What DIVA 35 contains

Active ingredients:

The 28-day pack (every day pack) contains 21 hormonal tablets each with 2 milligrams cyproterone acetate and 35 micrograms of ethinylestradiol. It also contains 7 non-hormonal tablets.

Inactive ingredients:

Tablet core: Lactose, Maize Starch, Povidone, Talcum, Magnesium stearate.

Tablet coating: Saccharose, Calcium carbonate, Talcum, Titanium dioxide, Povidone, Polyethylene glycol, Glycerol, Iron oxide pigment, Montan glycole wax.

What DIVA 35 looks like and contents of the pack

21 round, biconvex, yellow sugar-coated tablets with a 5,7 mm nominal diameter and 7 round, biconvex, white sugar-coated tablets with a 6,85 mm nominal diameter.

Each PVC/PVDC blister and aluminium foil contains 28 tablets. Each carton contains either 1 or 3 blister strips.

Holder of Certificate of Registration

Unicorn Pharmaceuticals (Pty) Ltd

Coner of Searle and Pontac Streets

Woodstock, Cape Town,

Applicant/HCR: Unicorn Pharmaceuticals (Pty) Ltd

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