

## DIANE® -35 BAYER MIDDLE EAST

0.035 mg/2 mg coated tablets

Active ingredients: Ethinylestradiol/Cyproterone acetate

### 1. WHAT DIANE-35 IS AND WHAT IT IS USED FOR

Diane-35 is a progestogen-oestrogen combination with anti-androgen action.

Diane-35 is used in cases of:

androgenization symptoms (symptoms caused by an increased effect of male sexual hormones) in women requiring hormonal treatment:

- acne: in pronounced form when accompanied by inflammation or node formation (Acne papulopustulosa, Acne nodulocystica) or if there is a danger of scarring for which local treatment alone would not guarantee success. The benefits of hormone treatment should be weighed against those of systemic antibiotics therapy.
- milder forms of unnaturally excessive facial and body hair (hirsutism);
- androgen-related hair loss (androgenetic alopecia).

#### Note:

Although Diane-35 also has a contraceptive effect, it should not be used exclusively for contraceptive purposes, but only by women who require therapy for the above-mentioned androgen-dependent clinical symptoms. (For further details see: «When to take special care with Diane-35», «Possible side-effects»; for details about the duration of treatment see: «How to take Diane-35»).

In almost all cases, the acne can generally be expected to completely disappear, often within just a few months. Particularly severe cases may, however, require treatment to be extended before the complete effectiveness of the medication becomes evident.

It is recommended that treatment be stopped 3 to 4 cycles after the complete disappearance of the symptoms; women should not continue to use Diane-35 for contraceptive purposes only.

If androgen-dependent clinical symptoms reappear, treatment with Diane-35 can be repeated.

### 2. WHAT YOU NEED TO KNOW BEFORE TAKING DIANE-35?

#### 2.1 When not to use Diane-35

- if you or someone in your family has a history of obstructed veins or a blood clot of unknown origin (known, idiopathic venous thromboembolism (VTE) (in cases where your family history of vein obstruction involves a sibling or parent at a relatively young age),
- if you have (or ever have had) a blood clot (thrombotic and thromboembolic diseases) in the veins (e.g. deep phlebothrombosis of the leg or pulmonary embolism),
- if you have (or ever have had) a blood clot in the arteries (thrombotic and thromboembolic events, e.g. heart attack) or preliminary stages of such diseases that are caused by blood clots in the arteries (e.g. episodic attacks of a sensation of chest constriction, so-called angina pectoris or episodic attacks of disturbed vision or muscle paralysis caused by insufficient perfusion of the brain),
- if you have a condition that increases the risk of blood clots (e.g. disorders of the coagulation system with tendency to blood clots (thrombosis), certain cardiac diseases),
- if you have ever had a stroke
- if you have a serious risk factor or several risk factors for blood clots in the veins or arteries (venous or arterial thromboses), which might also contraindicate use of this medication (see «When to take special care with Diane-35»),
- if you have diabetes mellitus involving changes in the blood vessels, a certain blood disease (sickle cell anaemia), or severe forms of high blood pressure,
- if you have (or ever have had) an inflammation of the pancreas, accompanied by a strong increase in blood lipids and/or other lipid metabolism disorders,

- if you have (or ever have had) severe liver function disorders (including excretion disorders such as Dubin-Johnson and Rotor's Syndrome), in cases where your liver function values have not yet returned to normal,
- if you have (or ever have had) benign or malignant liver tumours,
- vaginal bleeding whose origin has not been clarified by a physician
- migraine involving sensory perception and/or movement disorders (migraine accompagnée),
- if you smoke (see «When to take special care with Diane-35»),
- if you have (or ever 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 had? jaundice, persistent itching or herpes (herpes gestationis) during a previous pregnancy, or exacerbated hearing loss in women with middle ear deafness (otosclerosis) during a previous pregnancy,
- if you want to get pregnant, or if you are either currently pregnant or breastfeeding,
- if you have a hypersensitivity (allergy) to ethinylestradiol, cyproterone acetate or any of the other ingredients of Diane-35.

Diane-35 is not for use in men.

You must immediately stop taking the medication and contact your physician if any of the above-mentioned symptoms appear while taking Diane-35. In the meantime you should use a different, non-hormonal contraceptive method; for details see «General remarks».

## 2.2 When to take special care with Diane-35

### *General remarks*

Several situations are described in this leaflet that require you to stop using Diane-35 or that may negatively influence the reliability of Diane-35. In such situations you should either refrain from sexual intercourse or use extra nonhormonal contraceptive precautions, e.g. condoms or another barrier method. Do not use rhythm or temperature methods.

**Diane-35 does not protect against HIV infection (AIDS) or any other sexually transmitted disease.**

## 2.2.1 You should also immediately stop taking Diane-35

- if migraine-like headaches occur for the first time or if they occur more frequently than usual or are unusually painfully,
- if you experience acute vision or hearing disorders or movement disorders, particularly paralysis of any kind (a possible first sign of a cerebral stroke) or other perception disorders,
- at the first sign of vein inflammation with blood clots (thrombophlebitis) or thromboembolic symptoms (see Section 2.2.2 «Particularly close monitoring by a physician is required»),
- 6 weeks prior to any scheduled surgery (e.g. abdominal or orthopaedic operations), (see Section «Certain factors may increase the risk of obstruction of the veins or arteries»)
- if you have jaundice, liver inflammation or whole-body itching,
- if epileptic attacks increase,
- if your blood pressure increases significantly,
- if you suffer an onset of severe depression,
- if you have severe upper abdominal pain or an enlarged liver,
- if there is a clear worsening of diseases that are known to be aggravated during the use of hormonal contraceptives or pregnancy,
- if you suspect or know that you are pregnant. If you become pregnant you must immediately stop taking this medication; this is because the results of several studies indicate that there may be a slight increase in the risk of foetal malformation in cases where oral contraceptives are taken in early pregnancy.

Contact your physician if think you may be pregnant.

## 2.2.2 Particularly close monitoring by a physician is required

- if you are diabetic (diabetes mellitus),
- if your measured blood pressure is more than 140/90 mmHg (high blood pressure),
- if you have a tendency to inflammation of the superficial veins (phlebitis) or pronounced varicose veins,
- if you suffer from a particular form of hearing loss (otosclerosis),
- if you have epilepsy,

- if you suffer from a particular form of St. Vitus' dance (chorea minor Sydenham),
- if you suffer from a certain intermittent disorder of haemoglobin formation (porphyria) and if this reoccurs during Diane-35 use.
- if you are over the age of 40.

It should be noted that there is an increased risk of thromboembolic events occurring during puerperium (just after childbirth) (see «Precautions for pregnancy and breast-feeding»).

Other illnesses that may involve vascular complications include diabetes (diabetes mellitus), ovarian cysts (polycystic ovary syndrome, PCO syndrome), systemic lupus erythematosus (a particular disease of the immune system), a form of renal insufficiency (hemolytic-uremic syndrome), and chronic inflammatory intestinal disorders (Cohn's disease or ulcerative colitis).

Certain biochemical factors that may suggest you are predisposed to obstructive diseases of the blood vessels. Such factors include resistance to activated protein C (APC), hyperhomocysteinaemia, antithrombin-III deficiency, protein C deficiency, protein S deficiency, antiphospholipid antibodies (anticardiolipin antibodies, lupus anticoagulant).

The composition of Diane-35 resembles a hormonal contraceptive, i.e. an oral contraceptive (OC). Therefore, the following warnings related to the use of OCs also apply for Diane-35.

### 2.2.3 Oral contraceptives (OCs) and vascular disease

Use of an OC or Diane-35 involves an increased risk of deep vein obstruction by a blood clot (thrombosis), which under certain circumstances, may detach itself and pass into the lungs (so-called pulmonary embolism). The additional danger associated with vein thromboses and pulmonary embolisms (referred to together as venous thromboembolism or «VTE») is at its greatest during the first year of initial use of an OC. The risk of VTE among women who use an OC is, however, still less than it is during pregnancy (an estimated 60 cases of vein obstruction for every 100,000 pregnancies).

A thrombosis does not always heal completely and may sometimes result in lasting disabilities. The consequences of a thrombosis may even be fatal.

### Certain factors can increase the risk of a vein or artery obstruction, e.g.

- increasing age,
- if you are considerably overweight (body mass index in excess of 30 kg/m<sup>2</sup>),
- lipid metabolism disorders,
- a genetic predisposition to coagulation defects,
- you or an immediate family member have a history of vein obstruction, which was caused by a blood clot (thrombus) of unknown origin (i.e. vessel obstruction in a sibling or parent occurring at a relatively young, see «When to take special care with Diane-35»),
- in association with prolonged immobilization, major surgery, any surgery involving the legs or more extensive injuries. In these situations it is better to stop taking the oral contraceptive (you should stop at least four weeks before a planned surgery) and not start again until two weeks after you are back on your feet. In cases where an OC or Diane-35 cannot be stopped for the recommended period, prophylactic measures to treat thrombosis should be considered,
- there is no scientific consensus as regards the possible significance of varicose veins and superficial vein obstruction in cases involving the initial onset of, or progressive obstruction, of a vein due to a blood clot (thrombus)
- smoking (women over 30 years of age should not smoke if they are taking medications which contain hormones such as those in Diane-35 (women smokers have an increased <relative risk> for thromboembolism, particularly arterial thromboses), see section 2. «When not to use Diane-35»),
- cardiac valve diseases,
- irregular heart beat, e.g. atrial fibrillation,
- high blood pressure,
- diabetes,
- migraine.

### Please contact your physician without delay and stop taking the tablets immediately if you have complaints that might indicate a thrombosis or pulmonary embolism, e.g.

- unusual pain or swelling in one leg,
- pain and sensation of constriction in the chest, possible radiating to the left arm,

- sudden occurrence of breathing difficulties,
- non-specific coughing,
- unusual, severe or lasting headache,
- sudden partial or total loss of vision,
- double vision,
- unclear speech or speech disability,
- dizziness,
- collapse, possibly in connection with an epileptic seizure,
- sudden weakness or pronounced feeling of numbness on one side of the body or other part of the body,
- movement disorders (impaired motor function),
- severe, unbearable stomach-ache.

Epidemiological studies indicate that the frequency of vascular obstructions occurring in patients using Diane-35 is greater than in patients taking combination oral contraceptives with low oestrogen (<50 µg ethinylestradiol).

In rare cases, a vascular occlusion can also occur in an artery as the result of a blood clot (arterial thrombosis), e.g. in the coronary arteries or in the arteries supplying blood to the brain, thereby causing a heart attack or a cerebral stroke.

Epidemiological studies indicate a link between use of OCs and an increased risk of arterial thromboembolism. Such events occur only rarely.

Vessel obstruction can also occur in very rare instances in the blood vessels of the liver, abdominal cavity, kidneys or eyes.

It is not known to what extent Diane-35 influences the risk of a venous occlusion disease vis-à-vis the risks associated with OCs.

As regards women who use Diane-35 for the treatment of severe acne, milder forms of unnaturally excessive facial and body hair (hirsutism) or androgen-related hair loss (androgenetic alopecia), it is very probable that this also includes women who already have a natural tendency to an increased cardiovascular risk, e.g. in connection with the emergence of cysts in the ovaries (polycystic ovary syndrome).

#### **2.2.4 Oral contraceptives (OCs) and cancer**

Cervical cancer has been reported somewhat more frequently in women who take OCs for prolonged

periods. The extent to which this might also be explained by sexual behaviour (e.g. frequent change of partners) or factors other than «taking the pill» is unclear.

Breast cancer is diagnosed somewhat more frequently in women who take OCs, than it is in women of the same age who do not use OCs for contraceptive purposes. Breast cancer rates slowly normalise after an OC is stopped. After 10 years there is no difference between former OC users and other women. In view of the fact that breast cancer occurs relatively rarely in women under 40 years of age, the number of additional cases of breast cancer among former or current OC users is small, when compared with the overall risk of breast cancer. The studies are not conclusive as regards the underlying causes. The observed higher risk may be explained by the earlier detection of breast cancer among OC users, by the biological effects of an OC, or by a combination of the two.

Benign liver tumours have been diagnosed among OC users in rare cases, malignant tumours occur even more rarely. Such tumours have resulted in life-threatening internal bleeding in a few cases. If you experience sudden, severe stomach pain you should consult your physician immediately.

#### **2.2.5 Reduced efficacy**

The efficacy of Diane-35 may be reduced if, for instance, you forget to take a tablet (see section 3. «If you forget to take Diane-35»), or in connection with gastrointestinal disease or in association with certain medications you may be taking at the same time (see section 3. «What can reduce your contraceptive protection?»).

#### **2.2.6 Medical consultation/examination**

Before taking a hormone-containing medication such as Diane-35, you need to undergo a general physical examination (body weight, blood pressure, heart, legs and skin, urine test for sugar, and, if necessary special liver diagnostics), as well as a gynaecological examination (including the breast and a cervical smear); a detailed family case history (history of disease in your family) will also be compiled. The possibility of pregnancy should be ruled out

prior to taking Diane-35. Disorders of the coagulation system need to be ruled out in the event that any of your blood relatives had blood clots at an early age (thromboembolic diseases, e.g. deep venous thrombosis, cerebral stroke, heart attack). It is recommended that you come in for a check-up about every six-months while taking this medication.

### 2.3 Taking Diane-35 with other medications

Please inform your physician or your pharmacist if you are now using, or if you have recently used any oral or topical medications, even if they were obtained without a prescription.

Interactions between hormone preparations such as Diane-35 and other medications may cause spotting and/or may negatively impact its contraceptive efficacy.

The following medications can impair the effectiveness of Diane-35:

- medications for the treatment of epilepsy such as hydantoins (e.g. phenytoin), barbiturates (e.g. barbexalone), primidone, carbamazepine, oxcarbazepine, topiramate and felbamate
- medications for the treatment of tuberculosis (e.g. rifampicin)
- certain antibiotics prescribed for the treatment of certain infections (e.g. penicillin, tetracycline and griseofulvin)
- medications for the treatment of HIV infections (e.g. ritonavir, nevirapin)
- medicinal products containing St. John's Wort (Hypericum)

OCs can also influence the metabolism of other medications. For example, Diane-35 may impair the effectiveness or tolerance of cyclosporine (medication to suppress the immune system) or lamotrigine (epilepsy medication).

Women taking Diane-35, in addition to any of the medications from the abovementioned substance classes, should also use supplementary barrier methods of contraception during this period, i.e. as long as they take another medication and for 28 days thereafter.

Women taking antibiotics should also use supplementary barrier methods of contraception during this

period, i.e. as long as they are taking another medication and for 7 days thereafter.

If a supplementary barrier method is continued after the end of the pack, the next pack should be started immediately, without observing a seven-day waiting period.

The need for medications to treat diabetes (mellitus) may also change over time.

Please note that these guidelines may also apply for any other medications you have taken recently.

Note:

Diane-35 must should never be taken in combination other hormonal contraception medications; such medications must be stopped before beginning therapy with Diane-35 (for more information see «How to take Diane-35»).

### 2.4 Pregnancy and breastfeeding

Do not use Diane-35 if you are pregnant or if you suspect you may be pregnant.

If you become pregnant while taking Diane-35, stop taking it immediately and contact your doctor. Nevertheless, the past use of Diane-35 does not constitute grounds for terminating a pregnancy.

The use of Diane-35 is prohibited during breastfeeding, because it may reduce milk production and because small amounts of the active ingredient may pass into the breast milk.

Ask your physician or pharmacist for advice before taking any medications.

### 2.5 Effect on ability to drive and to use machinery

No special precautionary measures are required.

### 2.6 Important information about other ingredients contained in Diane-35

Each tablet of this medicinal product contains lactose and sucrose (sugar). If you are intolerant to certain types of sugar you should contact your doctor before taking Diane-35.

## 3. HOW TO TAKE DIANE-35

### When and how to take Diane-35

Diane-35 acts to suppress ovulation, which results in a contraceptive effect. Women taking Diane-35 should therefore not use another hormonal

contraceptive, because this would result in an overdose of hormones and is not required for effective contraception. For the same reason, women who wish to become pregnant should not use Diane-35.

Unless otherwise advised by your physician, you should take Diane-35 as described below. Please take as directed, otherwise Diane-35 may not provide the desired effect.

You should start taking Diane-35 on the first day of your menstruation cycle.

Only women who do not menstruate should begin therapy immediately and as prescribed by a physician, in this case the day the first tablet is taken is considered to be the first day of the cycle, after which treatment is continued in accordance with the following recommendations.

The first tablet is removed from a blister marked with the day of the week (e.g. "Mo" for Monday); it is then swallowed unchewed and with some liquid if necessary. If you start Diane-35 soon after childbirth or a miscarriage, you should ask your physician whether additional protective measures may be required during the first cycle in order to ensure effective contraception.

After that, another tablet is taken from the blister each day in the direction of the arrow until the calendar pack is empty. You should always take the tablet at the same time of day. After finishing the pack, you will not take any tablets for the next 7 days, during which your menstrual bleeding should start in about 2-4 days.

You will start taking the tablets again after this 7-day interval, regardless of whether or not the bleeding has stopped or still persists.

Note:

Contraceptive protection begins on the first day a tablet is taken; this protection also continues during the 7-day interval between packs. As a result, no further hormonal contraceptives are required during this time period.

### Starting your first pack of Diane-35

- If you did not use an OC during the previous month: Begin taking Diane-35 on the first day of your cycle, i.e. on the first day you menstruate. If you begin

taking the tablets between Days 2 and 5, to ensure contraceptive protection you will also need to use an additional barrier method (e.g. condoms).

- If you have been using either an oral contraceptive (containing two hormonal active ingredients, a so-called combined oral contraceptive), a vaginal ring or a transdermal patch:

It is best to begin taking Diane-35 on the day after you took the last tablet of your last medication containing an active ingredient (or after removal of the vaginal ring or the transdermal patch), but no later than the day after the usual tablet-free interval (ring-free, patch-free). If the last pack of your previous OC also contains tablets without active ingredient, you first need to finish these tablets, before then starting Diane-35 on the day after.

- If you have been using an OC that contains only one hormone (progestogen) (so-called "mini pill"):

You can stop taking the mini pill at any time and start taking Diane-35 on the following day. During the first 7 days you should use an additional barrier method (e.g. condom) to ensure contraceptive protection.

- Switching from an injection, an implant or IUD (coil): You should start to take Diane-35 on the day of your next scheduled injection or on the same day that the implant or the IUD is removed. During the first 7 days you should use an additional barrier method (e.g. condom) to ensure contraceptive protection.

- After having a baby:

If you have just had a baby, you should not begin taking Diane-35 earlier than 21 to 28 days after giving birth. If you start later, you should use a barrier method to ensure effective contraception during the first 7 days. If you have already had sexual intercourse before you start Diane-35 you should first make sure that you are not pregnant or wait for your first menstrual bleeding to occur.

- After a miscarriage or abortion: Please consult your physician.

### What can reduce your contraceptive protection?

Errors in pill-taking, vomiting or intestinal diseases accompanied by diarrhoea, extended intake of certain medications at the same time as Diane-35 (see

“Taking Diane-35 with other medications”) and very rare individual metabolic disorders may cancel out the contraceptive effect. Mild laxatives have no influence on contraceptive protection.

#### For how long should Diane-35 be used?

In the unlikely event that bleeding does not occur during the tablet-free interval, you should not take Diane-35 until you have contacted your physician.

You should not generally expect immediate results if you are being treated for androgenization symptoms. In some cases this may require therapy for a period of several months. It is recommended that treatment be stopped 3 to 4 cycles after the complete disappearance the related symptoms.

In cases where therapy of

- severe acne or seborrhoea lasting at least six months, or
- androgen-related hair loss (alopecia) and unnaturally excessive facial and body hair (hirsutism) lasting at least 12 months,

does not bring about the desired result, the combined application of Diane-35 and Androcur® 10 mg tablets or Androcur® 50 mg tablets and/or another therapy approach be considered.

As soon as your androgenization symptoms have disappeared, if you desire continued contraceptive protection you may switch to a low-dosage OC.

Treatment with Diane-35 can be repeated if the androgenetic symptoms reappear.

**If you have taken more Diane-35 tablets than you should have (overdose)** Possible indications of an overdose include nausea and vomiting (usually after 12 to 24 hours, possibly continuing for several days), as well as slight vaginal bleeding. If you take larger quantities you must consult a physician who will treat your symptoms.

#### If you forget to take Diane-35

- If you are **less than 12 hours late** in taking a tablet, the reliability of Diane-35 is maintained. Take the missed tablet as soon as you remember and then take the next tablets at the usual time.
- If you are **more than 12 hours late** in taking any tablet, the reliability of Diane-35 may be reduced. There is a particularly high risk of becoming pregnant

if you miss tablets from the beginning or from the end of the pack. For this reason you should follow the guidelines provided below (see scheme below).

#### **If you forget more than one tablet from your current blister pack:**

Ask your physician for advice.

#### **If you forget one tablet in Week 1:**

Take the missed tablet as soon as you remember (even if this means taking two tablets at the same time) and take the next tablets at the usual time.

Use extra contraceptive precautions (barrier method) for the next 7 days. You may be pregnant if you had sexual intercourse in the week before missing the tablet. In this case contact your doctor immediately.

#### **If you forget one tablet in Week 2:**

Take the missed tablet as soon as you remember (even if this means taking two tablets at the same time) and take the next tablets at the usual time.

The reliability of Diane-35 is maintained. You do not need to use extra contraceptive precautions.

#### **If you forget one tablet in Week 3:**

You may choose either of the following options:

1. Take the missed tablet as soon as you remember (even if this means taking two tablets at the same time) and take the next tablets at the usual time.

Start the next pack as soon as the current pack is finished so that no gap is left between packs. You may not experience withdrawal bleeding until the end of the second pack, but you may experience spotting or breakthrough bleeding while taking tablets from the second pack.

Or

2. You may immediately stop taking tablets from your current pack and then start a new pack within the tablet-free interval of not more than 7 days (including the day you missed your tablet). If you want to start the next pack on the same day of the week to which you were accustomed, you may reduce the tablet-free interval to less than 7 days.

- If you forget several tablets from a pack and menstrual bleeding does not start during the first normal tablet-free interval, you may be pregnant. Consult your doctor before starting the next pack.

**What to do**

**... if you suffer from vomiting or diarrhoea?**

If you vomit or have severe diarrhoea, the active ingredients of your Diane-35 tablet may not be completely absorbed and you will need to take additional contraceptive precautions.

If you vomit within 3 to 4 hours after taking your tablet, you should follow the instructions pertaining to missed tablets. If you do not wish to deviate from your usual intake schedule you must take a substitute tablet from another blister pack.

**... if unexpected bleeding occurs?**

Unexpected bleeding (spotting or breakthrough bleeding) may occur, particularly in the early months, however, you should not change your pill-taking schedule. These irregular bleeding episodes generally diminish after your first three cycle pack, i.e. until your body becomes accustomed to Diane-35. Still, you should consult your physician immediately if the bleeding either persists, becomes more severe or reappears.

**... if you miss your period?**

If you have taken all of your tablets as directed, you have not vomited or experienced severe diarrhoea and you have not taken any other drugs, then is very unlikely that you are pregnant. However, you should not start the next pack of Diane-35 until your doctor has checked you are not pregnant.

**If you want to stop taking Diane-35**

Consult your physician or pharmacist if you want to stop taking Diane-35.

**4. POSSIBLE SIDE-EFFECTS**

Like all medicines, Diane-35 can cause side-effects, although not everybody gets them.

All women who use Diane-35 are at a higher risk for venous and arterial thromboembolism (e.g. venous thromboembolism, pulmonary embolism, stroke, heart attack). For further information, see "When to take special care with Diane- 35" in the section "What you need to know before taking Diane-35".

This risk can be further increased by additional factors (smoking, high blood pressure, blood clotting or lipid metabolism disorders, significantly overweight, varicose veins, previous history of phlebitis and thromboses), see "What you need to know before taking Diane-35".

For information about other serious side-effects such as tumours of the liver, cancer of the breast or cervix, see "When to take special care with Diane-35".

The following frequency-of-occurrence definitions are used as the basis for assessing side-effects:

<b>Very common:</b>	Occurring in more than 1 in 10 treated patients
<b>Common:</b>	Occurring in fewer than 1 in 10, but more than 1 in 100 treated patients
<b>Uncommon:</b>	Occurring in fewer than 1 in 100, but more than 1 in 1000 treated patients
<b>Rare:</b>	Occurring in fewer than 1 in 1000, but more than 1 in 10,000 treated patients
<b>Very rare:</b>	Occurring in fewer than 1 in 10,000 treated patients, including isolated cases

The most common side-effects (>10%) associated with the use of an OC containing the active ingredients ethinylestradiol and levonorgestrel are: headache (including migraine), spotting and intermenstrual bleeding.

Frequency rates for side effects		
Common	Uncommon	Rare
<b>Organ system</b>		
<b>Eye disorders</b>		
		contact lens intolerance (dry eyes)
<b>Gastrointestinal disorders</b>		
Nausea, stomach-ache	Vomiting, diarrhea	
<b>Immune system disorders</b>		
		Hypersensitivity reaction
<b>Investigations</b>		
Weight gain	High blood pressure	Weight loss
<b>Metabolic and nutritional disorders</b>		
	Fluid retention in tissue	
<b>Diseases of the nervous system</b>		
Headache	Migraine	
<b>Psychiatric disorders</b>		
Depressive moods, mood swings	Decrease libido	
<b>Reproductive system and breast disorders</b>		
Sensitivity of the breast, breast pain, intermenstrual bleeding	Breast hypertrophy	Mammary gland secretion, changes in vaginal secretion (e.g. increased discharge)
<b>Skin and subcutaneous tissue disorders</b>		
	Skin rash, hives, Yellowish-brown spots on skin (chloasma)	Nodal fever (erythema nodosum), severe skin rash (erythema multiforme)

Sexual hormones influence mammary gland tissue, which can cause increased sensitivity to other factors that may promote the development of cancer.

Nonetheless, sexual hormones are only one of several other possible risk factors that are not associated with the use of hormonal contraceptives. Epidemiological studies investigating the possible link between hormonal contraceptives and breast cancer have not shown conclusive evidence as to whether this disease occurs more frequently in women who started taking an OC at an early age, and continued to do so until middle age.

Women with lipid metabolism disorders (hypertriglyceridaemia) or women with family histories of such diseases could be at increased risk for developing pancreatic inflammation while taking an OC.

Even though a slight increase in blood pressure has been reported for many women taking OCs, clinically relevant instances of high blood pressure remain rare. It is only in such rare cases that Diane-35 must be stopped immediately.

No connection between taking an OC and a clinically relevant increase in blood pressure has been established. However, women should stop taking Diane-35 in cases where therapy for their pre-existing high blood pressure is not successful during treatment with Diane-35. If appropriate, Diane-35 can be resumed after blood pressure measurements return to normal, as a result of treatment with antihypertensive medications.

The following diseases have been reported to occur and/or to worsen both during pregnancy and while using an OC, although no clear link with OC use has yet been established: jaundice and/or itching caused by bile congestion; gallstones; disruption in haemoglobin formation; a particular disorder of the immune system (systemic lupus erythematosus); a form of renal insufficiency (hemolyticuremic syndrome); a form of St. Vitus' Dance (Sydenham's chorea); herpes during pregnancy (herpes gestationis); middle ear deafness due to ossification.

If you suffer from hereditary angio-oedema (acute swelling of the subcutis and mucosa, particularly in the areas of the eyelids and lips, in throat mucosa and tongue), medications containing estrogens may

trigger or worsen the angiooedema symptoms. You should seek medical care immediately if typical angiooedema symptoms appear such as face swelling, tongue and/or throat and/or swallowing disorders, or skin rash in combination with breathing difficulties.

Acute or chronic liver function disorders require that Diane-35 treatment be stopped until the liver function markers normalize. The reappearance of jaundice and/or itching caused by bile congestion that occurred during an earlier pregnancy or previous regimen of sexual hormones also requires that Diane-35 treatment be stopped.

Although OCs may influence insulin and sugar metabolism, there are no indications that the dose needs to be modified for diabetic OC-users. However, diabetics should be closely monitored, particularly during the initial period of taking this kind of medication.

Exacerbation of existing depression, epilepsy and intestinal disorders such as Cohn's disease and ulcerative colitis have been reported in connection with OCs. Yellowish-brown pigment spots on the skin may appear occasionally, particularly in women who already had them during pregnancy. Women with this predisposition who take Diane-35 should not expose themselves to direct sunlight or to ultraviolet light (e.g. in a solarium).

If women with excessive body hair (hirsutism) notice a recent, significant worsening of these symptoms, a physician needs to clarify the underlying reasons (androgen-producing tumour, disorders of the enzymes of the adrenal cortex).

On the basis of its composition, Diane-35 ensures a contraceptive effect when taken as directed. Irregular intake of Diane-35 can cause menstrual cycle irregularities. It is very important that Diane-35 be taken as directed in order to prevent both cycle irregularities and pregnancy (due to the possible influence of cyproterone acetate on the developing foetus).

If any of the side effects becomes serious or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

**5. HOW TO STORE DIANE-35**

Keep all drugs out of the reach and sight of children. Do not use this medication after the expiration date printed on the folding box and blister pack "To be used before" or "Use before". The expiration date refers to the last day of the respective month.

Store below 30°C.

**6. FURTHER INFORMATION****What Diane-35 contains:**

1 coated tablet contains 0.035 mg ethinylestradiol and 2 mg cyproterone acetate.

**The other ingredients are**

Tablet core: lactose monohydrate, maize starch, povidone 25 000, talc and magnesium stearate,

Tablet coating: sucrose, povidone 700 000, macrogol 6000, calcium carbonate (E 170), talcum, glycerol 85% (E 422), titanium dioxide (E 171), ferric oxide pigment (yellow, E 172) and montanglycol wax.

**What Diane-35 looks like and content of the pack:**

The tablets are beige, round, and sugar-coated.

Diane-35 is presented as a blister pack containing 21 coated tablets, in packages of 3x21 coated tablets and 6x21 coated tablets.

**Pharmaceutical company****Manufacturer**

Bayer Schering Pharma AG  
D-13342 Berlin

**These Instructions for Use were last revised in February 2008**

**Properties**

The cyproterone acetate contained in Diane-35 inhibits the influence of male sexual hormones (androgens), which are also formed by the female organism. The intensified sebaceous gland function that plays an important role in the origin of acne and seborrhoea is reduced during treatment with Diane-35. This brings about a healing of the existing sources of acne - usually after 3 to 4 months of treatment. Excessively fatty hair and skin generally dissipate even earlier and the hair loss that accompa-

nies therapy also diminishes. For sexually mature women with mild forms of hirsutism, however, therapy cannot be expected to succeed until after several months of treatment.