GENERIC NAME: CYPROTERONE ACETATE + ETHINYL ESTRADIOL

	migraine and should be used with caution if other forms of migraine are present. **Use in pregnancy:** Prior to starting Althea, pregnancy must be ruled out. However, should a pregnancy occur while taking the tablet, the administration has to be withdrawn at once. **Use in lactation:** Women with newborn babies should not use the tablet when breastfeeding.
Special Precautions	Before taking hormonal contraceptives, undergo an appropriate medical examination and medical history carefully evaluated. Regular examination is recommended during use. The contraceptive effectiveness of hormonal contraceptives may be reduced during episodes of vomiting or diarrhea. During this period, to ensure the avoidance of pregnancy, using a condom is recommended for 7 days after recovery. Caution on use if there is a history of clinical depression, gallbladder disease, sickle-cell disease or conditions influenced by fluid retention. It should be used with caution by those with varicose veins. It should also be used with caution by those with risk factor for cardiovascular disease eg, diabetes mellitus, smoking, obesity, hypertension or a family history of cardiovascular disorders.
Side Effects	Some women may experience side effects eg, nausea, vomiting, chloasma (melasma) and other skin or hair changes, headache, water retention, slight weight change, breast tenderness and changes in libido. Menstrual irregularities eg, spotting, breakthrough bleeding or amenorrhea can occur during its use. Most of these side effects are mild and usually disappear after a few months of contraceptive use.
Storage	Store at a temperature not exceeding 30°C.
Description	Each tablet contains cyproterone acetate 2 mg and ethinyl estradiol 35 mcg.
Mechanism of Action	Oral contraceptive. Althea is a combined low-dose oral contraceptive pill with antiandrogenic properties. Each tablet contains cyproterone acetate, a progesterone with antiandrogenic and progestogenic properties and ethinyl estradiol, an estrogen. Oral Contraceptive: Althea stops ovulation, thins the lining of the uterus and thickens the cervical mucus. In combination, these actions prevent pregnancy. Antiandrogen: Althea contains cyproterone acetate that works as an antiandrogen. It competes at the receptor sites with androgens and reduces their effects. Cyproterone acetate inhibits the influence of the androgens produced in women. Althea reduces the development of acne and seborrhea. It heals existing acne efflorescence after 3-4 months therapy. It also reduces the greasiness of the hair and skin. When cyproterone acetate is given in combination with ethinyl estradiol, it is likely to reduce hair growth, lighten the hair color and decrease the hair thickness in hirsutic areas. **Pharmacokinetics:** Cyproterone acetate is slowly absorbed from the GIT with peak plasma concentrations being achieved in 3-4 hrs. It is about 96% bound to plasma proteins. The terminal elimination $t_{½}$ is about 38 hrs. Cyproterone is metabolized in the liver; about 35% of a dose is excreted in urine as free and conjugated metabolites, the remainder being excreted in the bile. The principal metabolite, 15β-hydroxycyproterone, has antiandrogenic activity. Ethinyl estradiol is absorbed well and rapidly by the GIT. The presence of an ethinyl group at the 17-position greatly reduces hepatic first-pass metabolism compared with estradiol, enabling the compound to be much more active if taken orally. There are some initial conjugation at the gut wall and the systemic bioavailability is only 40%. Ethinyl estradiol is highly protein bound, unlike naturally occurring estrogens, which are mainly bound to sex hormone-binding globulin; it is principally bound to albumin. It is metabolized in the liver and excreted in urine and feces. Metabolites undergo enterohepatic recycling.
MIMS Class	Acne Treatment Preparations / Oral Contraceptives
ATC Classification	G03CA53 - estradiol, combinations : Belongs to the class of natural and semisynthetic estrogens used in estrogenic hormone preparations.
Regulatory Classification	Rx
Presentation/Packing	Tab 21's.
Manufacturer	Pond's Chemical
Distributor	DKT

Likes 0

be carried out and the family medical history must be carefully researched before starting the treatment, which is subject to medical prescription only.
Disorder of blood coagulation system must also be excluded where family member suffered at a young age from the formation of blood clots (eg, deep vein thrombosis, stroke and heart attack).
Cybelle contains lactose. If the patient has intolerance to certain sugars, consult the doctor before taking this medication.
Effects on the Ability to Drive or Operate Machinery: It is unlikely that the patient will experience any side effects which will affect the ability to drive or operate machinery.

Adverse Drug Reactions

Like all medicines, Cybelle can cause adverse effects although not everybody gets them. Cybelle is generally well tolerated.
If any of the adverse effects get serious, or if the patient notices any adverse effects not listed, please tell the doctor or pharmacist.
Serious reactions associated with the use of Cybelle, as well as the related symptoms are described in Precautions.
The following adverse effects have been reported by users of Cybelle.

Close

System Organ Class	Common (≥1/100)	Uncommon (≥1/1000 and <1/100)	Rare (<1/1000)
Eye Disorders			Contact lens intolerance
Gastrointestinal Disorders	Nausea, abdominal pain	Vomiting, diarrhea	
Immune System Disorders			Hypersensitivity
Metabolism and Nutrition Disorders	Increased body weight	Fluid retention	Decreased body weight
Nervous System Disorders	Headache, depressive mood, altered mood	Migraine, decreased sexual drive	Increased sexual drive
Reproductive System and Breast Disorders	Breast tenderness, breast pain	Breast enlargement (hypertrophy)	Breast discharge, vaginal discharge
Skin and Subcutaneous Tissue Disorders		Rash	Erythema nodosum, erythema multiforme

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occur in the first fe
lessen with time.
If the patient suffe
trigger or exacerb

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View ADR Monitor

Drug Interactions

Some medicines
medicine used fo
barbiturates, carb
tuberculosis (eg,
efavirenz), some a
(griseofulvin) for s
containing St. John'
Cybelle may also
cyclosporine, lam
Inform the doctor or pharmacist if the patient is taking or have recently taken any other medicines or herbal products, even those not prescribed. Also tell any other doctor or dentist who prescribes another medicine (or the dispensing pharmacist) that the patient uses Cybelle. The doctor or pharmacist can tell if the patient needs to take additional contraceptive precautions and if so, for how long.

Storage

Store at temperatures not exceeding 30°C.

Description

Each tablet contains cyproterone acetate 2 mg and ethinyl estradiol 35 mcg.

Mechanism of Action

Cyproterone acetate is an anti-androgen. The ovaries produce androgens (male sex hormones) to change into estrogens (female sex hormones). Androgens can stimulate growth of hair on the face and body, and production of sebum (oil from the skin). If the skin produces too much oil, the pores of the skin will become blocked, which can lead to spots. Cyproterone acetate acts by reducing the amount of androgens released by the ovaries and by reducing the amount that can act in the body.
Ethinylestradiol is an estrogen (female sex hormone) which should be given in combination with cyproterone acetate.
Cybelle also acts like an oral contraceptive: by preventing the release of eggs, thickening the mucus in the neck of the womb to stop sperm passing through and making the lining of the womb unsuitable for an egg to grow on. The patient should not take another oral contraceptive while taking these tablets.

MIMS Class

Acne Treatment Preparations / Oral Contraceptives

ATC Classification

G03HB01 - cyproterone and estrogen. Belongs to the class of antiandrogen preparations in combination with estrogens. Used to counter androgenic activities.

Regulatory Classification

Rx

Presentation/Packing

FC tab (yellow orange, round and biconvex) 21's.

Manufacturer: Chemway Pharma

Distributor: Chemway Pharma

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examination and the patient's medical history should be carefully evaluated. Regular examination is recommended during use. The contraceptive effectiveness of hormonal contraceptives may be reduced during episodes of vomiting or diarrhea. To avoid pregnancy during this period, using a condom is recommended for 7 days after recovery.
Consult a healthcare provider if suffering from the following conditions: History of clinical depression, gallbladder disease, sickle-cell disease or conditions influenced by fluid retention. It should be used with caution by those with varicose veins. It should also be used with caution by those with a risk factor for cardiovascular disease eg, diabetes mellitus, smoking, obesity, hypertension or a family history of cardiovascular disorders.

Adverse Drug Reactions

The oral contraceptive is the most researched product in the history of medicine and its safety has long been established. Some women may experience side effects eg, nausea, vomiting, chloasma (melasma) and other skin or hair changes, headache, water retention, slight weight change, breast tenderness and changes in libido. Menstrual irregularities eg, spotting, breakthrough bleeding or amenorrhea can occur during its use.
View ADR Monitoring Website

Drug Interactions

Concurrent use of oral contraceptives and inducers of hepatic microsomal enzymes, including barbiturates eg, phenobarbital, primidone, carbamazepine, oxcarbazepine, felbamate and topiramate, griseofulvin, phenylbutazone, phenytoin, troglitazone, St. John's wort and rifampicin may decrease contraceptive efficacy and/or increase breakthrough bleeding.
Concurrent use of oral contraceptives and anti-infective agents eg, ampicillin, chloramphenicol, neomycin, nitrofurantoin, penicillin V, sulfonamides and tetracyclines may result in decreased efficacy of the contraceptives.
Concurrent use of oral contraceptives and troleandomycin may increase the risk of cholestatic jaundice, therefore, the drugs should be used together cautiously.
Concurrent use of oral contraceptives containing ethinyl estradiol and drugs or foods that inhibit cytochrome P-450 isoenzyme 3A4 (CYP3A4) eg, clarithromycin, erythromycin, grapefruit juice, itraconazole, ketoconazole, ritonavir may result in increased plasma concentrations of ethinyl estradiol and an increase in the incidence of adverse effects.
Analgesics, isoniazid, antimigraine drugs and tranquilizers may decrease the efficacy of oral contraceptives.
Alcohol may reduce the effectiveness of cyproterone acetate.

Storage

Store at temperatures not exceeding 30°C.
Shelf-Life: 36 months.

Description

Each Crimson tablet contains cyproterone acetate 2 mg and ethinyl estradiol 35 mcg.

Mechanism of Action

Crimson is a combined low-dose oral contraceptive pill with antiandrogenic properties. Each tablet contains cyproterone acetate, a progesterone with antiandrogenic and progestogenic properties and ethinyl estradiol, an estrogen.
Pharmacokinetics: Cyproterone acetate is slowly absorbed from the gastrointestinal tract with peak plasma concentrations being achieved in 3-4 hrs. It is about 96% bound to plasma proteins. The terminal elimination $t_{½}$ is about 38 hrs. Cyproterone is metabolized in the liver; about 35% of a dose is excreted in urine as free and conjugated metabolites, the remainder being excreted in the bile. The principal metabolite, 15β-hydroxycyproterone, has antiandrogenic activity.
Ethinyl estradiol is absorbed well and rapidly by the gastrointestinal tract. The presence of an ethinyl group at the 17-position greatly reduces hepatic first-pass metabolism compared with estradiol, enabling the compound to be much more active if taken orally. There are some initial conjugation at the gut wall and the systemic bioavailability is only 40%. Ethinyl estradiol is highly protein bound, unlike naturally occurring estrogens, which are mainly bound to sex hormone-binding globulin; it is principally bound to albumin. It is metabolized in the liver and excreted in urine and feces. Metabolites undergo enterohepatic recycling.

MIMS Class

Acne Treatment Preparations / Oral Contraceptives

ATC Classification

G03CA01 - ethinylestradiol . Belongs to the class of natural and semisynthetic estrogens used in estrogenic hormone preparations.

Regulatory Classification

Rx

Presentation/Packing

Tab 21's.

Manufacturer: Cyno Sure Healthcare

Distributor: Cyno Sure Healthcare

Estelle-35 ED and driving
Estelle-35 ED is not likely to impair your ability to drive or use machinery.

HOW TO TAKE ESTELLE-35 ED

Follow all directions given to you by your doctor or pharmacist carefully.
They may differ from the information contained in this leaflet.

If you do not understand the instructions on the label or in this leaflet, ask your doctor or pharmacist for help.

How to take it

Take one tablet daily at about the same time everyday. You must take Estelle-35 ED every day regardless of how often you have sex. It will also help you remember when to take it.

Swallow the tablet whole with water.
It does not matter if you take it before or after food. Each blister pack is marked with the day of the week.

Take your first tablet from the red area on the blister pack corresponding to the day of the week.
Follow the direction of the arrows on the blister pack until all the tablets have been taken.

Always start a new blister pack on the same day of the week as your previous pack.

Taking Estelle-35 ED for the first time

If you are starting Estelle-35 ED after a natural cycle, and you have not used a hormonal contraceptive in the past month, start on the first day of your period, i.e. on the first day of your menstrual bleeding.

You must also use additional barrier contraceptive precautions (e.g. condoms or a diaphragm) for the first 14 days of tablet-taking when having intercourse.

Your doctor will advise you when to start if you:

- are taking Estelle-35 ED after having a baby
- have had a miscarriage or an abortion.

Changing from another contraceptive

Changing from a combined oral contraceptive:
Start taking Estelle-35 ED on the day after taking the last active tablet in your previous Pill pack. Bleeding may not occur until the end of the first pack of Estelle-35 ED.

If you are not sure which were the active/inactive tablets were in your previous Pill pack, ask your doctor or pharmacist.
Your previous Pill pack may have different colour tablets to those of Estelle-35 ED.

Changing from a progestogen-only pill ('minipill'):
Stop taking the minipill on any day and start taking Estelle-35 ED at the same time the next day.

You must also use additional barrier contraceptive precautions (e.g. condoms or a diaphragm) for the first 14 days of tablet-taking when having intercourse.

Changing from a progestogen only injection, implant or intrauterine system (IUS):
Start taking Estelle-35 ED when your next injection is due, or on the day that your implant or IUS is removed.

You must also use additional barrier contraceptive precautions (e.g. condoms or a diaphragm) for the first 14 days of tablet-taking when having intercourse.

Stopping Estelle-35 ED

You can stop taking Estelle-35 ED at any time. If you are considering becoming pregnant, it is recommended that you begin taking a vitamin supplement containing folic acid. It is best that you start taking folic acid tablets before you stop taking Estelle-35 ED and not stop until your doctor advises this. Seek advice from your doctor or pharmacist about suitable supplements. It is both safe and recommended that you take folic acid during pregnancy.

If you forget to take it

If you miss a tablet and take the missing tablet within 12 hours of missing it, you will be protected against pregnancy. If you are more than 12 hours late follow these detailed instructions:

For Estelle-35 ED to be most effective, yellow active tablets need to be taken uninterrupted for 7 days.

If you have been taking the yellow active tablets for 7 uninterrupted days and miss a yellow active tablet, take the missed tablet as soon as you remember, then go back to taking your medicine as you would normally, even if this means taking two tablets in one day.
You will not need to use additional barrier contraceptive precautions.

The chance of pregnancy after missing a yellow active tablet depends on when you missed the tablet. **There is a higher risk of becoming pregnant if you miss a tablet at the beginning or end of a pack.**

If after taking your missed tablet you have less than 7 days of yellow active tablets left in a row, you should finish the active tablets in your pack but skip the white inactive tablets and start a new pack.
This is the best way to maintain contraceptive protection. However, you may not have a period until the end of the yellow active tablets of the second pack. You may have spotting or breakthrough bleeding on tablet-taking days.

If you have been taking the yellow active tablets for less than 7 days and miss a yellow active tablet, take the missed tablet as soon as you remember, then go back to taking your medicine as you would normally, even if this means taking two tablets in one day. In addition, you must also use additional barrier contraceptive precautions (e.g. condoms or a diaphragm) for the next 7 days.
If you have had sexual intercourse during that time, there is a possibility of pregnancy and you may need emergency contraception.

If you forget to take more than one yellow active tablet, seek advice from your doctor or pharmacist about what to do.
If you have had sexual intercourse in the week before missing your tablets, there is a possibility of becoming pregnant.

If you forget to take a white inactive tablet, take it as soon as you remember and take the next tablet at the usual time.
You are still protected against pregnancy because the white tablets do not contain any active ingredients.

Ask your doctor or pharmacist to answer any questions you may have.

If you take too much (overdose)

If you think that you or anyone else may have taken too much Estelle-35 ED, immediately telephone your doctor or the Poisons Information Centre (telephone 13 11 26 in Australia or 0800 poison or 0800 764 766 in New Zealand) for advice, or go to the Emergency Department at your nearest hospital. Do this even if there are no signs of discomfort or poisoning.
You may need medical attention.

WHILE YOU ARE TAKING ESTELLE-35 ED

Things you must do

Tell any other doctors, dentists, and pharmacists who treat you that you are taking this medicine.

If you are about to have any blood tests, tell your doctor that you are taking this medicine.
It may interfere with the results of some tests.

Have regular check ups with your doctor.
When you are taking the Pill, your doctor will tell you to return for regular check ups, including getting a pap smear test. Your doctor will advise how often you need a pap smear test. A pap smear test can detect abnormal cells lining the cervix. Sometimes abnormal cells can progress to cancer.

If you are about to start on any new medicine, remind your doctor and pharmacist that you are taking Estelle-35 ED.

Stop taking Estelle-35 ED and see your doctor immediately if you notice possible signs of thrombosis. These include:

- an unusual cough
- severe pain in the chest which may reach the left arm
- breathlessness
- any unusual, severe, or prolonged headache or migraine attack
- partial or complete loss of vision, or double vision
- slurring or speech disability
- sudden changes to your hearing, sense of smell, or taste
- dizziness or fainting
- weakness or numbness in any part of your body
- severe pain in your abdomen
- severe pain or swelling in either of your legs.

You must contact your doctor as soon as you can if:

- You experience changes in your personal health.
- A lump appears in your breasts.
- You start using other medicines including non-prescription medicines.
- You need surgery or are going to be kept immobile. Talk to your doctor at least four weeks before the surgery or immobilisation is planned.
- Abnormal, heavy bleeding occurs from your vagina.
- You missed taking active yellow tablets in the first week of any pack and had intercourse during the preceding 7 days.
- Your period doesn't occur twice in a row or you think you may be pregnant. Talk to your doctor before continuing with your next pack of Estelle-35 ED.

If you become pregnant while taking this medicine, tell your doctor immediately.

If you vomit within 3-4 hours or have severe diarrhoea after taking a yellow active tablet, the active ingredients may not have been completely absorbed. This is like missing a tablet. Follow the advice for missed tablets.

If you have unexpected bleeding and it continues, becomes heavy, or occurs again, tell your doctor.
When taking these tablets for the first few months, you can have irregular vaginal bleeding (spotting or breakthrough bleeding) between your periods. You may need to use sanitary protection, but continue to take your tablets as normal. Irregular vaginal bleeding usually stops once your body has adjusted to the Pill, usually after about 3 months.

If you have missed a period, but you have taken all your tablets, it is very unlikely that you are pregnant. Provided that:

- you have taken the yellow active tablets at the right time
- you have not been taking medicine(s) that may interfere with Estelle-35 ED.
- you have not vomited or had severe diarrhoea during this cycle.

If this is so, continue to take Estelle-35 ED as usual. If you have any concerns consult your doctor or pharmacist.

If you miss your period twice in a row, you may be pregnant and you should seek advice from your doctor. Do not start the next pack of Estelle-35 ED until your doctor has checked that you are not pregnant.

Estelle-35 ED will not protect you from HIV-AIDS or any other Sexually Transmitted Diseases (STDs), such as chlamydia, genital herpes, genital warts, gonorrhoea, hepatitis B, human papilloma virus and syphilis.
To protect yourself from STDs, you will need to use additional barrier contraceptives (e.g. condoms).

Things you must not do

Do not take Estelle-35 ED to treat any other conditions, unless your doctor tells you to.

Do not give your medicine to anyone else.

Do not stop taking your medicine or change the dosage without checking with your doctor.
You may become pregnant if you are not using any other contraceptive and you stop taking Estelle-35 ED, or do not take a tablet every day.

SIDE EFFECTS

Tell your doctor or pharmacist as soon as possible if you do not feel well while you are taking Estelle-35 ED. All medicines can have side effects. Sometimes they are serious, most of the time they are not. You may need medical treatment if you get some of the side effects.

Ask your doctor or pharmacist to answer any questions you may have.

Rarely, serious side effects may occur. If any of the symptoms listed in the section "While you are using Estelle-35 ED" develop, stop taking Estelle-35 ED and tell your doctor immediately or go to the Casualty Department at your nearest hospital.

Also, tell your doctor if you notice any skin rash or itchiness.

Other side effects listed below may also occur in some patients. Tell your pharmacist or doctor if you notice any of these effects.

- Tender and/or painful breasts with or without secretion
- Gastric upsets
- Headache
- Feeling depressed
- Libido changes
- Reduced tolerance to contact lenses
- Feeling or being sick
- Any change in normal secretion from the vagina including change in menstrual flow
- Rash, allergy, sensitivity to sunlight, itchiness
- Appetite and/or body weight changes including fluid retention

Do not be alarmed by this list of possible side effects. They do not occur often and you are unlikely to experience any of them.

AFTER TAKING ESTELLE-35 ED

Storage

Keep your tablets in the blister pack until it is time to take them.
If you take the tablets out of the pack they may not keep well.

Keep your tablets in a cool dry place where the temperature stays below 25°C.

Do not store it or any other medicine in the bathroom, near a sink, or on a window-sill.

Do not leave it in the car.
Heat and damp can destroy some medicines.

Keep Estelle-35 ED where children cannot reach it.
A locked cupboard at least one-and-a-half metres above the ground is a good place to store medicines.

Disposal

If your doctor tells you to stop taking this medicine or the expiry date has passed, ask your pharmacist what to do with any medicine that is left over.

Return any unused medicine to your pharmacist.

PRODUCT DESCRIPTION

What it looks like

Estelle-35 ED is a calendar pack containing 21 small yellow active tablets and 7 larger white non- active tablets per blister strip.

Available as packs of 28 tablets and 84 tablets.

Ingredients

The ingredients in Estelle-35 ED small yellow active tablets are cyproterone acetate, ethinyloestradiol, lactose, microcrystalline cellulose, povidone, croscarmellose sodium, magnesium stearate, Opadry white, Opadry buff, Opaglos white, Quinoline yellow, and sucrose.

The ingredients in Estelle-35 ED white non-active tablets are lactose, microcrystalline cellulose, and magnesium stearate.

Supplier

Ascent Pharma Pty Ltd
151-153 Clarendon Street
South Melbourne VIC 3205
www.ascentpharma.com.au

ascent

For further information please call 1800 554 414.

Australian Registration Number

AUST R 93607

Date of most recent amendment:
1 March 2013

Cyproterone acetate is a white to pale yellow crystalline powder. M.P. 206 - 213°C.

Cyproterone acetate is very soluble in chloroform and dioxane, freely soluble in acetone and benzene, soluble in ethanol, methanol and ethyl acetate, sparingly soluble in solvent hexane and almost insoluble in water.

Ethinyloestradiol is a white to slightly yellowish-white, crystalline powder. M.P. 181 - 185°C.

Ethinyloestradiol is practically insoluble in water, freely soluble in ethanol (96%) and ether, sparingly soluble in chloroform. It dissolves in dilute alkaline solutions.

As well as the active ingredients, Diane-35 ED tablets also contain the following excipients: lactose, maize starch, povidone, magnesium stearate, sucrose, macrogol 6000, calcium carbonate, purified talc, glycerol, titanium dioxide, iron oxide yellow, glycol montanate, purified water.

Each white placebo tablet contains: lactose, maize starch, povidone, magnesium stearate, sucrose, macrogol 6000, calcium carbonate, purified talc, glycol montanate.

PHARMACOLOGY

Pharmacodynamic properties

The substance cyproterone acetate contained in Diane-35 ED blocks the effect of endogenously produced and exogenously administered androgens at the target organs by means of competitive inhibition. This results in a gradual regression of signs of androgenisation, irrespective of whether increased androgen values or increased peripheral sensitivity, are the cause of the disorder. The decrease in androgen concentration at the target organs has an additional therapeutic effect.

While Diane-35 ED is being taken, the increased sebaceous gland function, which plays an important role in the development of acne and seborrhoea, is reduced. This leads - usually after 3 to 4 months of therapy - to the healing of existing acne efflorescences. The excessive greasiness of the hair and skin generally disappears earlier. The loss of hair which frequently accompanies seborrhoea likewise diminishes. Treatment with Diane-35 ED is indicated in women of child-bearing age who exhibit mild forms of hirsutism, and in particular in slightly increased facial hair; results do not, however, become apparent until after several months of use.

Apart from the described antiandrogen effect, cyproterone acetate has also a pronounced progestational action. The combination of ethinyloestradiol and cyproterone acetate prevents a possible pregnancy by the inhibition of ovulation, the inspissation of cervical mucus so as to constitute a barrier to sperm, and the rendering of the endometrium unreceptive to implantation.

As well as protection against pregnancy, combined oral contraceptives (COCs) have several positive properties which, next to the negative properties (see PRECAUTIONS, ADVERSE EFFECTS), can be useful in deciding on the method of birth control. For the majority of users, the cycle is more regular, the

- Presence or a history of venous or arterial thrombotic/thromboembolic events (e.g. deep venous thrombosis, pulmonary embolism, myocardial infarction) or of a cerebrovascular accident.
- Presence or history of prodromi of a thrombosis (e.g. transient ischaemic attack, angina pectoris).
- History of migraine with focal neurological symptoms.
- Diabetes mellitus with vascular involvement.
- The presence of a severe or multiple risk factor(s) for venous or arterial thrombosis may also constitute a contraindication (see PRECAUTIONS).
- Pancreatitis or a history thereof if associated with severe hypertriglyceridemia.
- Presence or history of severe hepatic disease as long as liver function values have not returned to normal.
- Presence or history of liver tumours (benign or malignant).
- Known or suspected sex-steroid influenced malignancies (e.g. of the genital organs or the breasts).
- Undiagnosed vaginal bleeding.
- Known or suspected pregnancy.
- Lactation.
- Hypersensitivity to any of the ingredients in Diane-35 ED.

Diane -35 ED is not for use in men.

The clinical and epidemiological experience with oestrogen/progestogen combinations like Diane-35 ED is predominantly based on combined oral contraceptives (COCs). Therefore, the following warnings related to the use of COCs apply also for Diane-35 ED.

PRECAUTIONS

If any of the conditions/risk factors mentioned below are present, the benefits of the use of Diane-35 ED should be weighed against the possible risks for each individual woman and discussed with the woman before she decides to start taking it. In the event of aggravation, exacerbation or first appearance of any of these conditions or risk factors, the woman should contact her doctor. The doctor should then decide on whether use of Diane-35 ED should be discontinued.

- **Circulatory Disorders**

Epidemiological studies have suggested an association between the use of COCs and an increased risk of arterial and venous thrombotic and thromboembolic diseases such as myocardial infarction, deep venous thrombosis, pulmonary embolism and of cerebrovascular accidents. These events occur rarely.

Venous thromboembolism (VTE), manifesting as deep venous thrombosis and/or pulmonary embolism, may occur during the use of all COCs. The risk of thromboembolism is highest during the first year a woman uses a COC.
This increased risk is present after initially starting a COC or restarting (following a 4 week or greater pill free interval) the same or a different COC. Data from a large, prospective 3-armed cohort study (EURAS[1] and LASS[2]) suggest that this increased risk is mainly present during the first 3 months.

A large, prospective 3-armed cohort study has shown that the incidence rate of VTE ranged from 8 to 10 per 10,000 woman years in low oestrogen dose (< 50 µg ethinyloestradiol) COC users. The most recent data suggest that the incidence rate of VTE is approximately 4.4 per 10,000 woman years in non-pregnant non-COC users, and ranged from 20 to 30 per 10,000 pregnant women or post partum.

Overall the risk of VTE in users of low oestrogen dose (< 50 µg ethinyloestradiol) COCs are two to threefold higher than for non-users of COCs who are not pregnant and remains lower than the risk associated with pregnancy and delivery.

VTE may be fatal (in 1-2% of the cases).

Extremely rarely, thrombosis has been reported to occur in other blood vessels, e.g. hepatic, mesenteric, renal, cerebral or retinal veins and arteries, in COC users. There is no consensus as to whether the occurrence of these events is associated with the use of COCs.

Symptoms of a venous (includes pulmonary embolism (PE) and deep venous thrombosis (DVT)) or arterial thrombotic/thromboembolic (includes myocardial infarction (MI), vascular occlusion and cerebrovascular accident) events can include: unilateral leg pain and/or swelling; pain or tenderness in the leg which may be felt only when standing or walking; increased warmth in the affected leg; red or discoloured skin on the leg; sudden severe pain in the chest which may increase with deep breathing; pain, discomfort, pressure, heaviness, sensation of squeezing or fullness in the chest, arm or below the breastbone; discomfort radiating to the back, jaw, throat, arm, stomach; rapid or irregular heartbeat; sudden onset of unexplained shortness of breath or rapid breathing; sudden onset of coughing which may bring up blood; sudden severe, prolonged headache with no known cause; sudden partial or complete loss of vision; diplopia; sense of anxiety; dizziness; slurred speech or aphasia; sudden confusion; vertigo; collapse with or without focal seizure; weakness or very marked numbness suddenly affecting one side or one part of the body; motor disturbances; "acute" abdomen; fullness, indigestion or choking feeling; sweating; nausea; vomiting.

Some of these symptoms (e.g. "shortness of breath", "coughing") are non-specific and might be misinterpreted as more common or less severe events (e.g. respiratory tract infections).

Arterial thromboembolic events may be fatal.

The risk of venous or arterial thrombotic/ thromboembolic events or of a cerebrovascular accident increases with:

- age;
- smoking (with heavier smoking and increasing age the risk further increases, especially in women over 35 years of age);
- a positive family history (i.e. venous or arterial thromboembolism ever in a sibling or parent at a relatively early age). If a hereditary predisposition is known or suspected, the woman should be referred to a specialist for advice before deciding about any COC use;
- obesity (body mass index over 30 kg/m^2);

- overweight;
- dyslipoproteinemia;
- hypertension;
- migraine;
- valvular heart disease;
- atrial fibrillation;
- prolonged immobilisation (e.g. long haul flights), major surgery, any surgery to the legs, or major trauma. In these situations it is advisable to discontinue COC use (in the case of elective surgery at least four weeks in advance) and not to resume until two weeks after complete remobilisation.

There is no consensus about the possible role of varicose veins and superficial thrombophlebitis in venous thromboembolism.

The increased risk of thromboembolism in the puerperium must be considered (see Use in Pregnancy).

Other medical conditions which have been associated with adverse circulatory events include diabetes mellitus, polycystic ovary syndrome, systemic lupus erythematosus, haemolytic uraemic syndrome, chronic inflammatory bowel disease (Crohn's disease or ulcerative colitis) and sickle cell disease.

An increase in frequency or severity of migraine during COC use (which may be prodromal of a cerebrovascular event) may be a reason for immediate discontinuation of the COC.

Biochemical factors that may be indicative of hereditary or acquired predisposition for venous or arterial thrombosis include Activated Protein C (APC) resistance, hyperhomocysteinemia, antithrombin-III deficiency, protein C deficiency, protein S deficiency, antiphospholipid antibodies (anticardiolipin antibodies, lupus anticoagulant).

When considering the risk/benefit, the doctor should take into account that adequate treatment of a condition may reduce the associated risk of thrombosis and that the risk associated with pregnancy is higher than that associated with low-dose COCs (<50 µg ethinyloestradiol).

- **Tumours**

The most important risk factor for cervical cancer is persistent HPV infection. Some epidemiological studies have indicated that long-term use of COCs may further contribute to this increased risk but there continues to be controversy about the extent to which this finding is attributable to confounding effects, e.g. cervical screening and sexual behaviour including use of barrier contraceptives.

A meta-analysis from 54 epidemiological studies reported that there is a slightly increased relative risk (RR = 1.24) of having breast cancer diagnosed in women who are currently taking COCs. The excess risk gradually disappears during the course of the 10 years after cessation of COC use. Because breast cancer is rare in women under 40 years of age, the excess number of breast cancer diagnoses in current and recent COC users is small in relation to the overall risk of breast cancer. These studies do not provide evidence for causation. The observed pattern of increased risk may be due to an earlier diagnosis of breast cancer in

COC users, the biological effects of COCs or a combination of both. The breast cancers diagnosed in ever-users tend to be less advanced clinically than the cancers diagnosed in never-users.

In rare cases, benign liver tumours, and even more rarely, malignant liver tumours have been reported in users of COCs. In isolated cases, these tumours have led to life-threatening intra-abdominal haemorrhages. A liver tumour should be considered in the differential diagnosis when severe upper abdominal pain, liver enlargement or signs of intra-abdominal haemorrhage occur in women taking COCs.

- **Other conditions**

Women with hypertriglyceridemia, or a family history thereof, may be at an increased risk of pancreatitis when taking COCs.

Although small increases in blood pressure have been reported in many women taking COCs, clinically relevant increases are rare. A relationship between COC use and clinical hypertension has not been established. However, if a sustained clinically significant hypertension develops during the use of a COC then it is prudent for the doctor to withdraw the COC and treat the hypertension. Where considered appropriate, COC use may be resumed if normotensive values can be achieved with antihypertensive therapy.

The following conditions have been reported to occur or deteriorate with both pregnancy and COC use, but the evidence of an association with COC use is inconclusive: jaundice and/or pruritus related to cholestasis; gallstone formation; porphyria; systemic lupus erythematosus; haemolytic uraemic syndrome; Sydenham's chorea; herpes gestationis, and otosclerosis-related hearing loss.

In women with hereditary angio-oedema exogenous oestrogens may induce or exacerbate symptoms of angio-oedema.

Acute or chronic disturbances of liver function may necessitate the discontinuation of COC use until markers of liver function return to normal. Recurrence of cholestatic jaundice which occurred first during pregnancy or previous use of sex steroids necessitates the discontinuation of COCs.

Although COCs may have an effect on peripheral insulin resistance and glucose tolerance, there is no evidence for a need to alter the therapeutic regimen in diabetics taking low-dose COCs (containing < 50 µg ethinyloestradiol). However, diabetic women should be carefully observed while taking COCs.
Crohn's disease and ulcerative colitis have been associated with COC use.

Chloasma may occasionally occur, especially in women with a history of chloasma gravidarum. Women with a tendency to chloasma should avoid exposure to the sun or ultraviolet radiation whilst taking COCs.

If in women suffering from hirsutism, symptoms have recently developed or increased substantially, the causes (androgen-producing tumour, adrenal enzyme defect) must be clarified by differential diagnosis.

Each beige active tablet contains 31.12 mg of lactose and each white placebo tablet contains 48.25 mg of lactose. Patients with rare hereditary problems of

galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption who are on a lactose free diet should take this amount into consideration.

Check the following before use:

- **Medical Examination/Consultation**

A complete medical history and physical examination should be taken prior to the initiation or reinstitution of Diane-35 ED, guided by the CONTRAINDICATIONS and PRECAUTIONS, and should be repeated periodically. In general, an annual examination is recommended. Periodic medical assessment is also of importance because contraindications (e.g. a transient ischaemic attack, etc.) or risk factors (e.g. a family history of venous or arterial thrombosis) may appear for the first time during the use of a COC. The frequency and nature of these assessments should be adapted to the individual woman but should generally include special reference to blood pressure, breasts, abdomen and pelvic organs, including cervical cytology, and relevant laboratory tests.

- **Sexually Transmitted Diseases including HIV infections and AIDS**

Diane-35 ED does not protect against sexually transmitted diseases (STDs), including HIV infections (AIDS). The woman should be advised that additional barrier contraceptive measures are needed to prevent transmission of STDs.

- **Reduced Efficacy**

The efficacy of COCs may be reduced in the event of missed beige active tablets, vomiting, or diarrhoea during active tablet taking or concomitant medication (see DOSAGE AND ADMINISTRATION).

- **Reduced Cycle Control**

With all COCs, irregular bleeding (spotting or breakthrough bleeding) may occur, especially during the first months of use. Therefore, the evaluation of any irregular bleeding is only meaningful after an adaptation interval of about three cycles.

If bleeding irregularities persist or occur after previously regular cycles, then non-hormonal causes should be considered and adequate diagnostic measures are indicated to exclude malignancy or pregnancy. These may include curettage.

In some women, withdrawal bleeding may not occur during the placebo tablet interval. If the COC has been taken according to the directions, it is unlikely that the woman is pregnant. However, if the COC has not been taken according to these directions prior to the first missed withdrawal bleed or if two withdrawal bleeds are missed, pregnancy must be ruled out before COC use is continued.

Use in Pregnancy

Pregnancy Category B3

- *Antibiotics (interference with enterohepatic circulation):*

Some clinical reports suggest that enterohepatic circulation of oestrogens may decrease when certain antibiotic agents (e.g. penicillins, tetracylines) are given which may reduce ethinyloestradiol concentrations.

Women prescribed antibiotics (except rifampicin and griseofulvin) should use the barrier method until 7 days after completing a course of antibiotics. If the period in which the barrier method is used runs beyond the end of the active tablets in the COC pack, the white placebo tablets should be omitted and the next COC pack started.

- *Influence of Diane-35 ED on other medication*

Oestrogen/progestogen preparations like Diane-35 ED may affect the metabolism of certain other medicines. Accordingly, plasma and tissue concentrations may either increase (e.g. cyclosporin) or decrease (e.g. lamotrigine).

Note: The product information of concomitant medications should be consulted to identify potential interactions.

Effect on Laboratory tests

The use of preparations like Diane-35 ED may influence the results of certain laboratory tests, including biochemical parameters of liver, thyroid, adrenal and renal function, plasma levels of carrier proteins, e.g. corticosteroid binding globulin and lipid/lipoprotein fractions, parameters of carbohydrate metabolism and parameters of coagulation and fibrinolysis. Changes generally remain within the normal laboratory range.

ADVERSE EFFECTS

Various adverse reactions have been associated with oral contraceptive use. The most serious reactions associated with the use of oral contraceptives are discussed under PRECAUTIONS.

In the event of aggravation, exacerbation or first appearance of any of these conditions or risk factors, the woman should contact her doctor. The doctor should then decide on whether its use should be discontinued.

System Organ Class	Common (≥ 1/100)	Uncommon (≥ 1/1000 and < 1/100)	Rare (≤ 1/1000)
Gastrointestinal disorders	Nausea, Abdominal pain	Vomiting, Diarrhoea	
Metabolism and nutrition disorders		Fluid retention	
Psychiatric disorders	Depressed mood, Altered mood	Decreased libido	Increased libido
Nervous system disorders	Headache	Migraine	
Skin and subcutaneous tissue disorders		Rash, Urticaria	Erythema nodosum, Erythema multiforme

Eye disorders			Contact lens intolerance
Reproductive system and breast disorders	Breast pain, Breast tenderness	Breast hypertrophy	Vaginal discharge, Breast discharge
Immune system disorders			Hypersensitivity
Investigations	Increased weight		Decreased weight

Other adverse reactions:

Eyes disorders: cataract.

DOSAGE AND ADMINISTRATION

Combined oral contraceptives, when taken correctly have a failure rate of approximately 1% per year.

Diane-35 ED is to be taken regularly in order to achieve therapeutic efficacy and the required contraceptive protection. Previously used hormonal contraception should be discontinued. The dose regimen of Diane-35 ED is similar to the usual regimen of most of the combined oral contraceptives. Thus, the same administration rules must be considered. The irregular intake of Diane-35 ED can lead to intermenstrual bleeding and could deteriorate the therapeutic and contraceptive reliability. Therapy should not be initiated unless pregnancy has been excluded.

How to take Diane-35 ED

One tablet is to be taken daily. The tablets must be taken in the order directed on the pack at about the same time every day, with some liquid as needed. Tablet taking should be continuous for 28 consecutive days, starting with a tablet corresponding to that day of the week from the red section of the Diane-35 ED pack.

If a woman starts on a Monday, Tuesday, Wednesday, Thursday or Friday, her first tablet is a white placebo tablet, while if she starts on a Saturday or Sunday her first tablet will be beige active tablet. Thereafter, one tablet is taken daily, following the arrows marked on the pack, until all tablets have been taken. Each subsequent pack is started the day after the last tablet of the previous pack.

Withdrawal bleeding should usually occur on day 2 to 3 after the last beige active tablet is taken and may not have finished before the next pack is started.

How to start Diane-35 ED

- **No preceding hormonal contraceptive use (in the past month)**

Tablet-taking has to start on day 1 of the woman's natural cycle (i.e. the first day of her menstrual bleeding). Starting on day 2 -5 of the menstrual cycle is allowed, but during the first cycle a barrier method is recommended in addition for the first 7 days of tablet-taking.

- **Changing from a combined hormonal contraceptive (combined oral**

Viewing: Philippines (Change Region)

Welcome, Nina Theresa

MIMS Philippines

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contraceptives

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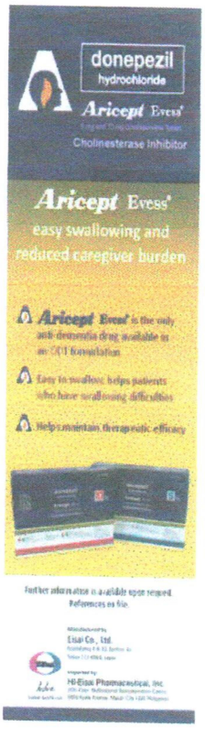

Further information is available upon request.
References on file.

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Concise Info Manufacturer Info

Concise Prescribing Information of:

Ancea

- Manufacturer
- Contents
- Dosage
- Contraindications
- Adverse Drug Reactions
- MIMS Class
- Regulatory Classification
- Distributor
- Indications
- Administration
- Special Precautions
- Drug Interactions
- ATC Classification
- Presentation/Packing

Related Information: Ancea Concise Info *Abbreviation Index*

Manufacturer	Unicure
Distributor	Endure Medical
Contents	Ethinyl estradiol 0.035 mg, cyproterone acetate 2 mg
Indications	Hormonal treatment of acne & hirsutism, seborrhea, androgenic alopecia & as OC in women.
Dosage	1 tab daily for 21 days starting on the 2nd day of the menstrual cycle, followed by 7 tab-free days. Discontinue after 3 or 4 cycles.
Administration	May be taken with or without food.
Contraindications	Impaired liver function or cholestasis, Dubin-Johnson or Rotor syndromes, hepatic adenoma, estrogen-dependent neoplasms eg breast or endometrial cancer, CV disease including thromboembolic disorders, arterial disease, disorder of lipid metabolism, undiagnosed vag bleeding, possible pregnancy or history during pregnancy of pruritus or cholestatic jaundice, chorea, herpes gestations, pemphigoid gestations or deteriorating otosclerosis, severe focal migraine.
Special Precautions	Other forms of migraine.
Adverse Drug Reactions	Change in menstrual bleeding; menstrual spotting or breakthrough bleeding; steepening of corneal curvature which may make contact lenses uncomfortable; blood clots in the blood vessels (eg DVT, pulmonary embolism, heart attack, stroke); headache, upset stomach, nausea, vomiting, breast tenderness, wt changes, decreased sex drive, depressed mood, fluid retention, candidiasis, chloasma, rise in BP, liver function disturbance, gallstones. View ADR Monitoring Website
Drug Interactions	Enzyme-inducing drugs: antiepileptics, griseofulvin, rifamycin, antibiotics, antivirals, modafinil, oral retinoids, analgesics, anticoagulants, antidepressants, antidiabetics, lamotrigine, antihypertensives, benzodiazepines, ciclosporin, clofibrate, corticosteroids, lidocaine, selegiline, levothyroxine, xanthines.
MIMS Class	Acne Treatment Preparations / Oral Contraceptives
ATC Classification	G03CA01 - ethinylestradiol : Belongs to the class of natural and semisynthetic estrogens used in estrogenic hormone preparations.
Regulatory Classification	Rx

Presentation/Packing

Form	Packing/Price
Ancea film-coated tab	21's

Manufacturer: Unicure

Distributor: Endure Medical

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JPOG PEER-REVIEWED JOURNAL FOR ASIAN CLINICIANS — Read JPOG

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gsk — Augmentin (amoxicillin, clavulanic acid, ...)

ALLERGAN — Cellufresh (carboxymethylcellulose sodium)

BAYER — Supraneuron (vitamin B1, vitamin B12, ...)

GX — Zyllohist (loratadine)

Question Of The Month

Please indicate how much you agree or disagree with the following statement about using MIMS.com when researching clinical information online: MIMS.com has made looking for information online easier