

FEMODENE[®] ED

Gestodene/Ethinylloestradiol Tablets

Presentation

FEMODENE ED: The memo-pack holds 21 white tablets, diameter 5.7 mm, containing 0.075 mg gestodene and 0.030 mg ethinylloestradiol and in addition, 7 larger white non-hormonal tablets diameter 6.8 mm.

All tablets have a lustrous sugar coating.

Uses

Actions

The contraceptive effect of FEMODENE ED is based on the interaction of various factors, the most important of which are seen as the inhibition of ovulation and the changes in the cervical secretion. When FEMODENE ED is taken according to instructions, the egg cells are prevented from maturing to the point at which they can be fertilised, the cervical mucus remains thick so as to constitute a barrier to sperm, and the endometrium is rendered unreceptive to implantation.

As well as protection against pregnancy, oestrogen/progestogen combinations have several positive properties which, next to the negative properties (see "*Warnings and Precautions*" and "*Adverse Effects*"), can be useful in deciding on the method of birth control.

With combined oral contraceptives (COCs) the cycle is more regular and menstruation is often less painful and bleeding is lighter. The latter may result in a decrease in the occurrence of iron deficiency. Apart from this there is evidence of a reduced risk of endometrial cancer and ovarian cancer. With the higher-dosed combined oral contraceptives containing 0.05 mg ethinylloestradiol, there is evidence of a reduced risk of fibrocystic tumors of the breasts, ovarian cysts, pelvic inflammatory disease and ectopic pregnancy. This may also apply to lower-dosed COCs.

Pharmacokinetics

- Gestodene

Absorption

Orally administered gestodene is rapidly and completely absorbed. Peak serum concentrations of 4 ng/mL are reached at about 1 hour after single ingestion. Bioavailability is about 99%.

Distribution

Gestodene is bound to serum albumin and to sex hormone binding globulin (SHBG). Only 1 - 2% of the total serum medicine concentrations are present as free steroid, 50 - 70% are specifically bound to SHBG. The ethinyloestradiol-induced threefold increase in SHBG influences the proportion of gestodene bound to the serum proteins, causing an increase of the SHBG-bound fraction and a decrease of the albumin-bound fraction. Following daily ingestion, drug serum levels increase about four-fold, reaching steady-state conditions during the second half of a treatment cycle. The apparent volume of distribution of gestodene is 0.7 L/kg.

Metabolism

Gestodene is completely metabolised by the known pathways of steroid metabolism. The metabolic clearance rate from serum is 0.8 mL/min/kg. No interaction was found when gestodene was acutely co-administered with ethinyloestradiol.

Elimination

Gestodene serum levels decrease in two phases. The terminal disposition phase is characterised by a half-life of 12 - 15 hours. Gestodene is not excreted in unchanged form. Its metabolites are excreted at a urinary to biliary ratio of about 6:4. The half-life of metabolite excretion is about 1 day.

Steady-State Conditions

Gestodene pharmacokinetics are influenced by SHBG levels, which are increased about threefold when co-administered with ethinyloestradiol. Following daily ingestion medicine serum levels increase about fourfold reaching steady-state conditions during the second half of a treatment cycle.

- Ethinyloestradiol

Absorption

Orally administered ethinyloestradiol is rapidly and completely absorbed. Peak serum concentrations of about 80 pg/mL are reached within 1 - 2 hours. During absorption and first-pass liver passage, ethinyloestradiol is metabolised extensively, resulting in a mean oral bioavailability of about 45% with a large interindividual variation of about 20 - 65%.

Distribution

Ethinyloestradiol is highly but non-specifically bound to serum albumin (approx. 98%), and induces an increase in the serum concentrations of SHBG. An apparent volume of distribution of about 2.8 - 8.6 L/kg was reported.

Metabolism

Ethinyloestradiol is subject to presystemic conjugation in both small bowel mucosa and the liver. Ethinyloestradiol is primarily metabolised by aromatic

hydroxylation but a wide variety of hydroxylated and methylated metabolites are formed, and these are present as free metabolites and as conjugates with glucuronides and sulfate. The metabolic clearance rate was reported to be 2.3 - 7 mL/min/kg.

Elimination

Ethinylloestradiol serum levels decrease in two disposition phases characterised by half-lives of about 1 hour and 10 - 20 hours, respectively. Unchanged medicine is not excreted, ethinylloestradiol metabolites are excreted at a urinary to biliary ratio of 4:6. The half-life of metabolite excretion is about 1 day.

Steady-state Conditions

According to the variable half-life of the terminal disposition phase from serum and the daily ingestion, steady-state serum levels of ethinylloestradiol will be reached after about one week.

Indications

Oral contraception

Dosage and Administration

Combined oral contraceptives, such as FEMODENE ED, when taken correctly, have a failure rate of approximately 1% per year. The failure rate may increase when pills are missed or taken incorrectly.

How to Take FEMODENE ED

Tablets must be taken in the order directed on the package every day at about the same time with some water as needed. Tablet-taking is continuous. One tablet is to be taken daily for ED consecutive days. Each subsequent pack is started the day after the last tablet of the previous pack following the directional arrows. Withdrawal bleeding usually occurs while taking the 7 non-hormonal tablets. This usually starts on day 2 - 3 after starting the non-hormonal tablets and may not have finished before the next pack is started.

How to Start FEMODENE ED

START WITH THE FIRST TABLET FROM THE GREEN SECTION MARKED WITH THAT DAY OF THE WEEK, in accordance with one of the following:

- 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 days 2 - 3 is allowed, but during the first cycle an additional barrier contraceptive method is recommended for the first 7 days of tablet taking.

- Changing from another combined oral contraceptive (COC), vaginal ring or transdermal patch

The woman should start with FEMODENE ED preferably on the day after the last hormonal tablet of her previous COC, but at the latest on the day following the usual tablet-free or non-hormonal tablet interval of her previous COC.

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

- Changing from a progestogen-only method (minipill, injection, implant) or progestogen-releasing intrauterine system (IUS)

The woman may switch any day from the minipill, from an implant or IUS on the day of its removal, or from an injectable when the next injection would be due. In all of these cases, the woman should be advised to additionally use a barrier contraceptive method for the first 7 days of tablet taking.

- Following first-trimester abortion

The woman may start immediately. When doing so, she need not take additional contraceptive measures.

- Following delivery or second-trimester abortion

The woman should be advised to start at day 21 to ED after delivery or second-trimester abortion. When starting later than this, the woman should be advised to additionally use a barrier contraceptive method for the first 7 days of tablet taking. However, if intercourse has already occurred, pregnancy should be excluded before starting FEMODENE ED or the woman has to wait for her first menstrual period.

Management of Missed Tablets

Errors in taking the non-hormonal tablets contained in FEMODENE ED can be ignored. However, they should be discarded to avoid unintentionally prolonging the placebo tablet phase. The following advice only refers to missed hormonal tablets:

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

If she is **more than 12 hours** late in taking any hormonal tablet, contraceptive protection may be reduced.

There is a particularly high risk of pregnancy if tablets are missed just before or immediately after taking the non-hormonal tablets. If tablets are missed in

the first week of taking hormonal tablets following the non-hormonal tablets and intercourse took place in the preceding 7 days, the possibility of pregnancy should be considered.

The management of missed tablets can be guided by the following two basic rules:

1. Tablet-taking must never be discontinued for longer than 7 days.
2. Seven days of uninterrupted tablet taking are required to attain adequate suppression of the hypothalamic-pituitary-ovarian axis.

These rules form the basis of the instructions to patients provided in the package insert.

Extra Contraceptive Precautions

When you need extra contraceptive precautions, either:

- don't have sex; or
- use a cap plus spermicide; or
- use a condom

Do not use the rhythm or temperature methods as extra contraceptive precautions. This is because oral contraceptives alter the usual menstrual cycle changes, such as changes in temperature and cervical mucus.

The 7 Day Rule

- Continue taking your Pills.
- You will not be protected from pregnancy until you have taken your daily small hormone Pill for the next 7 days in a row.
- Use another method of contraception (see "*Extra Contraceptive Precautions*") such as condoms or do not have sexual intercourse for these next 7 days.
- If there are fewer than 7 small hormone Pills left in the pack, or before the large white non-hormonal Pills in the pack, go straight on to the small hormone Pills in the green section of the next pack. This means that you miss out the large white non-hormonal Pills. You may not have a period until the end of the next pack. This is not harmful.

If the woman missed tablets and subsequently has no withdrawal bleed in the non-hormonal phase, the possibility of a pregnancy should be considered.

Advice in Case of Vomiting or severe Diarrhoea

If vomiting or severe diarrhoea occurs within 3 - 4 hours after hormonal tablet taking, absorption may not be complete and additional barrier contraceptive

measures should be used. In such an event, the advice concerning missed tablets is applicable. If the woman does not want to change her normal tablet-taking schedule, she has to take the extra tablet(s) needed from another pack.

How to Shift Periods or How to Delay a Period

To delay a period the woman should continue with hormonal tablets from another pack of FEMODENE ED without taking the non-hormonal tablets from her current pack. The extension can be carried on for as long as desired until the end of the hormonal tablets in the second pack. During the extension the woman may experience breakthrough bleeding or spotting. Regular intake of FEMODENE ED is then resumed after the non-hormonal tablet phase.

To shift her periods to another day of the week than the woman is used to with her current scheme, she can be advised to shorten her forthcoming non-hormonal tablet phase by as many days as she likes. The shorter the hormone-free interval, the higher the risk that she does not have a withdrawal bleed and will experience breakthrough-bleeding and spotting during the second pack (just as when delaying a period).

Contraindications

Combined oral contraceptives should not be used in the presence of any of the conditions listed below. Should any of the conditions appear for the first time during their use, the product should be stopped immediately.

- Presence or 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 ischemic attack, angina pectoris)
- Diabetes mellitus with vascular involvement
- Disturbed lipometabolism
- The presence of a severe or multiple risk factor(s) for venous or arterial thrombosis, including hereditary thrombophilia, may also constitute a contraindication (see also "*Warnings and Precautions for Use - Circulatory Disorders*").
- Pancreatitis or a history thereof if associated with severe hypertriglyceridemia
- Severe hepatic disease as long as liver function values have not returned to normal
- Presence or history of liver tumors (benign or malignant)

- Presence or history of migraine with focal neurological symptoms
- Known or suspected sex-steroid influenced malignancies (e.g. of the genital organs or the breasts)
- Undiagnosed vaginal bleeding
- Known or suspected pregnancy
- Hypersensitivity to any of the active substances or excipients of FEMODENE ED.

Warnings and Precautions

The clinical and epidemiological evidence for COCs like FEMODENE ED is predominantly based on experience with COCs in general. Therefore, the following warnings related to the use of COCs apply also to the use of FEMODENE ED.

If any of the conditions/risk factors mentioned below are present, the benefits of COC use should be weighed against the possible risks for each individual woman and discussed with the woman before she decides to start using it. In the event of aggravation, exacerbation or first appearance of any of these conditions or risk factors, the woman should contact her physician. The physician should then decide whether the COC 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 for venous 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 suggest that this increased risk is mainly present during the first 3 months.

Overall the risk of VTE in users of low oestrogen dose (< 50 µg ethinyloestradiol) COCs is 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.

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 venous or arterial thrombotic/thromboembolic events or of cerebrovascular accident can include: unilateral leg pain and/or swelling; sudden severe pain in the chest, whether or not it radiates to the left arm; sudden breathlessness; sudden onset of coughing; any unusual, severe, prolonged headache; sudden partial or complete loss of vision; diplopia; slurred speech or aphasia; 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.

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 suspected, the woman should be referred to a specialist for advice before deciding about any COC use.
- obesity (body mass index over 30 kg/m²)
- dyslipoproteinemia
- hypertension
- migraine
- valvular heart disease
- atrial fibrillation
- prolonged immobilisation, 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 also the "*Pregnancy and Lactation*" section).

Other medical conditions which have been associated with adverse circulatory events include diabetes mellitus, systemic lupus erythematosus, hemolytic

uremic syndrome, chronic inflammatory bowel disease (Crohn's disease or ulcerative colitis) and sickle cell disease.

An increase in frequency or severity of headaches during COC use, in particular the onset of migraine 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 risk/benefit, the physician 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 (< 0.05 mg ethinylloestradiol).

- **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 using 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, and even more rarely, malignant liver tumors have been reported in users of COCs. In isolated cases, these tumors have led to life-threatening intra-abdominal hemorrhages. A liver tumor should be considered in the differential diagnosis when severe upper abdominal pain, liver enlargement or signs of intra-abdominal hemorrhage occur in women taking COCs.

- **Other Conditions**

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

Although small increases in blood pressure have been reported in many women taking COCs, clinically relevant increases are rare. However, if a sustained clinically significant hypertension develops during the use of a COC, then it is prudent for the physician 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; hemolytic uremic syndrome; Sydenham's chorea; herpes gestationis; otosclerosis-related hearing loss.

In women with hereditary angioedema exogenous oestrogens may induce or exacerbate symptoms of angioedema.

Acute or chronic disturbances of liver or kidney function may necessitate the discontinuation of COC use until markers of liver or kidney 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 using low-dose COCs (containing < 0.05 mg 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.

Each white active tablet contains 37.43 mg of lactose and each white placebo tablets 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.

- **Medical Examination/Consultation**

A complete medical history and physical examination should be taken prior to the initiation or reinstatement of FEMODENE ED, guided by the "Contraindications" and "Warnings and Precautions" sections. This should be repeated at least annually during the use of FEMODENE ED. Periodic medical assessment is also of importance because contraindications (e.g. a transient ischemic 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 FEMODENE ED. 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**

Women should be advised that preparations like FEMODENE ED do not protect against HIV infections (AIDS) and other sexually transmissible diseases (STDs). The woman should be advised that additional barrier contraceptive measures are needed to prevent transmission of STDs.

- **Reduced Efficacy**

The efficacy of FEMODENE ED may be reduced in the event of missed hormonal tablets (see “*Management of Missed Tablets*”), vomiting or severe diarrhoea (see “*Advice in Case of Vomiting or Severe Diarrhoea*”) or concomitant medication (see “*Interactions*”).

- **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 while taking the 7 non-hormonal tablets. If the COC has been taken according to the directions described in the “*Dosage and Administration*” section, 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

The administration of FEMODENE ED is contraindicated during pregnancy. If pregnancy occurs during treatment with FEMODENE ED, further intake must be stopped.

Pregnancy (Category B3). (Accumulated evidence reports that inadvertent exposure to these agents in early pregnancy has not been associated with an increased risk of birth defects).

Extensive epidemiological studies have revealed neither an increased risk of birth defects in children born to women who used COCs prior to pregnancy,

nor a teratogenic effect when COCs were taken inadvertently during early pregnancy. See also “*Contraindications*”.

Use in Lactation

Lactation may be influenced by COCs as they may reduce the quantity and change the composition of breast milk. Therefore the use of COCs should generally not be recommended until the nursing mother has completely weaned her child. Small amounts of the contraceptive steroids and/or their metabolites may be excreted with the milk but there is no evidence that this adversely affects infant health.

Paediatric Use

FEMODENE ED is only indicated after menarche.

Use in the Elderly

FEMODENE ED is not indicated after menopause.

Patients with hepatic impairment

FEMODENE ED is contraindicated in women with severe hepatic diseases. See CONTRAINDICATIONS.

Patients with renal impairment

FEMODENE ED has not been specifically studied in renal impaired patients. There is no data suggesting the need for a dosage adjustment in patients with renal impairment.

Effects on Ability to Drive and Use Machines

No studies on the effects on the ability to drive and use machines have been performed. No effects on ability to drive and use machines have been observed in users of COCs.

Preclinical Safety Data

Preclinical data reveal no special risks for humans based on conventional studies of repeated dose toxicity, genotoxicity, carcinogenic potential and toxicity to reproduction. However, it should be borne in mind that sex steroids can promote the growth of certain hormone-dependent tissues and tumors.

Adverse Effects

Serious undesirable effects of FEMODENE ED have been referred to in the “*Contraindications*” and “*Warnings and Precautions*” sections.

In addition, the following undesirable effects have been reported in users of COCs such as FEMODENE ED, although the causal relationships have not been confirmed:

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, diarrhoea	
Immune System Disorders			Hypersensitivity
Investigations	Increased weight		Decreased weight
Metabolism and Nutrition Disorders		Fluid retention	
Nervous System Disorders	Headache	Migraine	
Psychiatric Disorders	Depressed mood, altered mood	Increased libido	Decreased libido
Reproductive System and Breast Disorders	Breast pain, breast tenderness	Breast hypertrophy	Vaginal discharge, breast discharge
Skin and Subcutaneous Tissue Disorders		Rash, urticaria	Erythema nodosum, erythema multiforme

In women with hereditary angioedema exogenous oestrogens may induce or exacerbate symptoms of angioedema.

Interactions

Interactions between oral contraceptives and other medicines which result in an increased clearance of sex hormones can lead to breakthrough bleeding and/or oral contraceptive failure. The following interactions have been reported in the literature.

Hepatic Metabolism: Interactions can occur with medicines that induce microsomal enzymes which can result in increased clearance of sex hormones (e.g. phenytoin, barbiturates, primidone, carbamazepine, rifampicin and possibly also oxcarbazepine, topiramate, felbamate, griseofulvin and products containing St John's Wort).

Also HIV protease (e.g. ritonavir) and the non-nucleoside reverse transcriptase inhibitors (e.g. nevirapine), and combinations of them, have been reported to potentially affect hepatic metabolism.

Interference with Enterohepatic Circulation: Some clinical reports suggest that the enterohepatic circulation of oestrogens may decrease when certain antibiotic agents are given, which may reduce ethinylestradiol concentrations (e.g. penicillins and tetracyclines).

Women on short-term treatment with any of the above-mentioned classes of medicines, or individual medicines, should temporarily use a barrier method in addition to taking hormonal FEMODENE ED tablets, i.e. during the time of concomitant medicine administration and for 7 days after their discontinuation. For women on rifampicin or other microsomal enzyme-inducing medicines, a barrier method should be used in addition to FEMODENE ED during the time of concomitant medicine administration and for ED days after its discontinuation. Women on treatment with antibiotics (except rifampicin and griseofulvin) should use a barrier method until 7 days after discontinuation. If the period during which the barrier method is used runs beyond the end of the hormonal tablets in the FEMODENE ED pack, the non-hormonal tablets should be omitted and the next FEMODENE ED pack should be started.

Oral contraceptives such as FEMODENE ED may interfere with the metabolism of other medicines. Accordingly, plasma and tissue concentrations may either increase (e.g. cyclosporin) or decrease (e.g. lamotrigine).

The prescribing information of concomitant medications should be consulted to identify potential interactions.

- **Laboratory Tests**

The use of preparations like FEMODENE 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.

Overdosage

There have been no reports of serious deleterious effects from overdose.

Symptoms

Symptoms that may occur in case of taking an overdose of active tablets are: nausea, vomiting and, in young girls, slight vaginal bleeding.

Treatment

There are no antidotes and further treatment should be symptomatic.

Pharmaceutical Precautions

Shelf life: 5 years

Special precautions for storage: Store below 25 °C

Medicine Classification

Prescription Medicine

Package Quantities

3 calendar-packs each containing ED tablets.

FEMODENE ED tablets are contained in blister packs consisting of transparent film made of polyvinyl chloride and metallic foils made of aluminium (mat side hot sealable).

Further Information

List of Excipients

Lactose monohydrate, maize starch, povidone, sodium calcium edetate, magnesium stearate, sucrose, macrogol 6000, calcium carbonate, purified talc, glycol montanate.

Instructions for Use/Handling

Store all medicines properly and keep them out of reach of children.

Name and Address

Bayer New Zealand Limited
3 Argus Place
Hillcrest
North Shore
AUCKLAND 0627

Free phone: 0800 233 988

Date of Preparation

25 February 2010.