Bayer HealthCare

SCHEDULING STATUS: S3

PROPRIETARY NAME AND DOSAGE FORM:

MELODENE

Tablets

COMPOSITION:

The 28-day pack (Every-Day pack) contains 21 hormonal tablets each with gestodene (17α-ethinyl-13-ethyl-17β-hydroxy-4,15-gonadiene-3-one) 0,075 mg and ethinyloestradiol (17α-ethinyl-estra-1,3,5(10)-triene-3,17β-diol) 0,02 mg, plus 7 non-hormonal tablets.

The inactive ingredients are: lactose, maize starch, povidone 25 000, magnesium stearate, purified water, sucrose, povidone 700 000, polyethylene glycol 6 000, calcium carbonate, talc, montanglycol wax (wax E), povidone 90, calcium carbonate, glycerol 85 % (w/w), titanium dioxide, red ferric oxide pigment and yellow ferric oxide.

PHARMACOLOGICAL CLASSIFICATION:

A 18.8 Ovulation controlling agents

PHARMACOLOGICAL ACTION:

Pharmacodynamic properties:

MELODENE is a combined low-dose monophasic oral contraceptive with estrogenic (ethinyloestradiol) and progestogenic (gestodene) peripheral effects.

The contraceptive effect of MELODENE 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.

Pharmacokinetic properties:

- Gestodene

Absorption:
Orally administered gestodene is rapidly and completely absorbed. Peak serum concentrations of 3,5 ng/ml are reached at about 1 hour after single dose ingestion. Bioavailability is about 99 %.

Distribution:
Gestodene is bound to serum albumin and to sex hormone binding globulin (SHBG). Only 1 to 2 % of the total serum gestodene concentrations are present as free steroid, 50 to 70 % are specifically bound to SHBG. The ethinyloestradiol-induced 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. 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 clearance rate from serum is 0,8 ml/min/kg. No interaction was found with the co-administered ethinyloestradiol.

Elimination:
Gestodene serum levels decrease in two phases. The terminal disposition phase is characterised by a half-life of approximately 12 hours. Gestodene is not excreted in its unchanged form. Its metabolites are excreted at a urinary to biliary ratio of about 6:4. The half-life of metabolite excretion is about 24 hours.

Steady-state conditions:
Gestodene pharmacokinetics are influenced by SHBG levels, which are increased about twofold when co-administered with ethinyloestradiol. Following daily ingestion, gestodene 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 65 pg/ml are reached at 1,7 hours. During absorption and first liver passage, ethinyloestradiol is metabolised extensively, resulting in a mean oral bioavailability of about 45 % with a large interindividual variation of about 20 to 65 %.

Distribution:
Ethinyloestradiol is highly but non-specifically bound to serum albumin (approximately 98 %) and induces an increase in the serum concentrations of SHBG. An apparent volume of distribution of about 2,8 to 8,6 l/kg was reported.

Metabolism:
Ethinyloestradiol is subject to presystemic conjugation in both the 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 sulphate. The clearance rate was reported to be 2,3 to 7 ml/min/kg.

Elimination:
Ethinyloestradiol serum levels decrease in two disposition phases characterised by half-lives of about 1 hour and 10 to 20 hours, respectively. Unchanged drug is not excreted; ethinyloestradiol metabolites are excreted at a urinary to biliary ratio of 4:6. The half-life of metabolite excretion is about 24 hours.

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 ethinyloestradiol will be reached after about 1 week.

INDICATIONS:

MELODENE is indicated for the prevention of pregnancy (oral contraception).

CONTRA-INDICATIONS:

MELODENE 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 MELODENE use, MELODENE should be stopped immediately.

- 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 prodromata 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 (such as e.g. hypertension, a family history of thromboembolic events, prolonged immobilisation – see further risk factors for thromboembolism under “Warnings - Circulatory disorders” below and “Side effects and special precautions”) may also constitute a contra-indication.
- Pancreatitis or a history thereof if associated with severe hypertriglyceridaemia.
- 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 (see “Pregnancy and lactation”).
- Hypersensitivity to the active substances or to any of the excipients of MELODENE.

WARNINGS:

If any of the conditions/risk factors mentioned below are present, the benefits of MELODENE 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 medical practitioner. The medical practitioner should then decide on whether its use should be discontinued.

Circulatory disorders:

Epidemiological studies have suggested an association between the use of combined oral contraceptives, such as MELODENE, and an increased risk of arterial and venous thrombotic and thromboembolic diseases such as myocardial infarction, stroke, deep venous thrombosis, and pulmonary embolism.

The risk of venous thromboembolism (VTE) is highest during the first year of use. This increased risk is present after initially starting combined oral contraceptives, such as MELODENE, or restarting (following a 4 week or greater pill free interval) the same or different combined oral contraceptives. 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 for venous thromboembolism (VTE) in users of low oestrogen dose (< 50 µg ethinyloestradiol) combined oral contraceptives, such as MELODENE, is higher than for non-users of combined oral contraceptives.
VTE may be fatal.
Venous thromboembolism, manifesting as deep venous thrombosis and/or pulmonary embolism, may occur during the use of combined oral contraceptives, such as MELODENE.

Thrombosis has been reported to occur in other blood vessels, e.g. hepatic, mesenteric, renal, cerebral or retinal veins and arteries, in combined oral contraceptive users, such as MELODENE.

Symptoms of venous or arterial thrombotic/thromboembolic events or of a 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 combined oral contraceptive use; obesity (body mass index over 30 kg/m^2);
- dyslipoproteinaemia;
- 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 MELODENE (in the case of elective surgery at least four weeks in advance) and not to resume until two weeks after complete remobilisation.

The increased risk of thromboembolism in the puerperium must be considered (see "Pregnancy and lactation"). Other medical conditions that have been associated with thrombotic incidents include diabetes mellitus, systemic lupus erythematosus, haemolytic uraemic syndrome, chronic inflammatory bowel disease (Crohn's disease or ulcerative colitis) and sickle cell disease.

The onset of, or increase in frequency or severity of migraine during MELODENE use (which may be prodromal of a cerebrovascular event) may be a reason for immediate discontinuation of MELODENE.

Biochemical factors that may be indicative of a hereditary or acquired predisposition for venous or arterial

thrombosis include Activated Protein C (APC) resistance, hyperhomocysteinaemia, antithrombin-III deficiency, protein C deficiency, protein S deficiency, antiphospholipid antibodies (anticardiolipin antibodies, lupus anticoagulant).

When considering risk/benefit, the medical practitioner 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 combined low-dose oral contraceptive use, such as MELODENE, (< 0,05 mg ethinyloestradiol).

Tumours:

An increased risk of cervical cancer in long-term users of combined oral contraceptives, such as MELODENE, has been reported in epidemiological studies.

A meta-analysis from epidemiological studies reported that there is an increased relative risk of having breast cancer diagnosed in women who are currently using MELODENE. 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 combined oral contraceptives.

Benign liver tumours, and rarely, malignant liver tumours have been reported in users of combined oral contraceptives. In isolated cases, these tumours have led to life-threatening intra-abdominal haemorrhages. A hepatic 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 MELODENE.

Other conditions:

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

Small increases in blood pressure have been reported in many women taking combined oral contraceptives, such as MELODENE; clinically relevant increases may occur. If a sustained clinically significant hypertension develops during the use of MELODENE, then it is prudent for the medical practitioner to withdraw MELODENE and treat the hypertension. Where considered appropriate, MELODENE use may be resumed if normotensive values can be achieved with antihypertensive therapy.

The following conditions have been reported to occur or deteriorate with combined oral contraceptive use: jaundice and/or pruritus related to cholestasis; gallstone formation; porphyria; systemic lupus erythematosus; haemolytic uraemic 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 function may necessitate the discontinuation of MELODENE use until markers of liver function return to normal. The recurrence of cholestatic jaundice that occurred first during pregnancy or previous use of sex steroids necessitates the discontinuation of MELODENE.

Although MELODENE 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 MELODENE. However, diabetic women should be carefully observed while taking MELODENE.

Crohn's disease and ulcerative colitis have been associated with combined oral contraceptives.

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 MELODENE.

INTERACTIONS:

Interactions between MELODENE and other medicines may lead to breakthrough bleeding and/or 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 an increased clearance of MELODENE (e.g. phenytoin, barbiturates, primidone, carbamazepine, rifampicin, and possibly also oxcarbazepine, topiramate, felbamate, ritonavir, griseofulvin and products containing St John's Wort).

Safety and efficacy of oral combined contraceptives, such as MELODENE, may be affected by HIV protease (e.g. ritonavir) and non-nucleoside reverse transcriptase inhibitors (e.g. nevirapine), and combinations of them, due to the hepatic metabolism. Other contraceptive mechanisms should be used.

Interference with enterohepatic circulation:

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

Women on treatment with any of these medicines should temporarily use a barrier method in addition to MELODENE, or choose another method of contraception. With microsomal enzyme-inducing medicines, the barrier method should be used during the time of concomitant medicine administration and for 28 days after their discontinuation. Women on treatment with antibiotics (except rifampicin and griseofulvin) should use the barrier method until 7 days after discontinuation. If the period during which the barrier method is used runs beyond the end of the active tablets in the MELODENE pack, the inactive tablets should be omitted and the next MELODENE pack should be started.

MELODENE may interfere with the metabolism of other medicines. Accordingly, plasma and tissue concentrations may either increase (e.g. cyclosporin and benzodiazepines) or decrease (e.g. lamotrigine).

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

Laboratory tests:

The use of MELODENE 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.

PREGNANCY AND LACTATION:

MELODENE is contra-indicated in pregnancy. If pregnancy occurs during treatment with MELODENE, further intake should be stopped.

Lactation may be influenced by MELODENE as it may reduce the quantity and change the composition of breast milk. Therefore, the use of MELODENE should generally not be recommended until the breast-feeding mother has completely weaned her child. Small amounts of the active ingredients of MELODENE and/or their metabolites may be excreted with the milk.

DOSAGE AND DIRECTIONS FOR USE:

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

How to take MELODENE:

Tablets must be taken in the order directed by the arrows on the pack, every day at about the same time with some liquid as needed. Tablet-taking is continuous. One tablet is to be taken daily for 28 consecutive days. The first tablet should be taken from the silver section of the calendar pack by selecting the appropriate tablet for that day of the week (e.g. "MO" for Monday). Each subsequent pack is started the day after the last tablet of the previous pack. Withdrawal bleeding usually starts 2 to 3 days after starting the inactive tablets and may not have finished before the next pack is started. If a patient starts MELODENE during the latter part of the week, the very first cycle may be slightly shortened.

How to start MELODENE:

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 to 5 is allowed, but during the first cycle an additional barrier method is recommended in addition for the first 7 days of tablet-taking.

Changing from a combined hormonal contraceptive/combined oral contraceptive (COC), (vaginal ring, or transdermal patch):
The woman should start with MELODENE preferably on the day after the last active tablet (the last tablet containing the active substance) of her previous combined oral contraceptive, but at the latest on the day following the usual placebo tablet interval of her previous combined oral contraceptive.
In case a vaginal ring or transdermal patch has been used, the woman should start using MELODENE 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 from a progestogen-releasing intrauterine system:
The woman may switch on any day from the minipill (from an implant or the intrauterine system on the day of its removal, from an injectable when the next injection would be due), but should in all of these cases be advised to additionally use a barrier 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:
For breastfeeding women see "Pregnancy and lactation". Women should be advised to start 21 to 28 days after delivery or second-trimester abortion. When starting later, the woman should be advised to additionally use a barrier method for the first 7 days of tablet-taking. However, if intercourse has already occurred, pregnancy should be excluded before the actual start of MELODENE use, or the woman must wait for her first menstrual period.

Management of missed tablets:

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

If the user is ***less than 12 hours*** late in taking any active tablet, contraceptive protection is not reduced. The woman should take the tablet as soon as she remembers and should take further tablets at the usual time.
If she is ***more than 12 hours*** late in taking any active tablet, contraceptive protection may be reduced. The management of missed tablets can be guided by the following two basic rules:

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

Accordingly the following advice can be given in daily practice:

First 7 days of active tablet-taking:
The user should take the last missed tablet as soon as she remembers, even if this means taking two tablets at the same time. She then continues to take tablets at her usual time. In addition, a barrier method such as a condom should be used for the next 7 days. If intercourse took place in the preceding 7 days, the possibility of a pregnancy should be considered. The more tablets that are missed and the closer they are to the inactive tablet phase, the higher the risk of a pregnancy.

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

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

1. The user should take the last missed tablet as soon as she remembers, even if this means taking two tablets at the same time. She then continues to take tablets at her usual time until the active tablets are used up. The 7 inactive tablets must be discarded. The next pack must be started right away. The user is unlikely to have a withdrawal bleed until the end of the active tablets section of the second pack, but she may experience spotting or breakthrough bleeding on active tablet-taking days.
2. The woman may also be advised to discontinue active tablet-taking from the current pack. She should then have a tablet-free interval of up to 7 days, including the days she missed tablets, and subsequently continue with the next pack, starting in the silver section with the tablet for the appropriate day of the week.

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

Advice in case of gastrointestinal disturbances:

In case of severe gastrointestinal disturbances, absorption may not be complete and additional contraceptive measures should be taken.

If vomiting occurs within 3 to 4 hours after active tablet-taking, the advice concerning missed tablets is applicable. If the woman does not want to change her normal tablet-taking schedule, she must take the extra tablet(s) needed from another pack.

How to delay a period:

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

Additional information on special populations:

Children and adolescents:
MELODENE is only indicated after menarche.

Geriatric patients:
Not applicable. MELODENE is not indicated after menopause.

Patients with hepatic impairment:
MELODENE is contra-indicated in women with severe hepatic diseases as long as liver function values have not returned to normal. See also section “Contra-indications”.

Patients with renal impairment:
MELODENE has not been specifically studied in renally impaired patients. Available data do not suggest a change in treatment in this patient population.

SIDE EFFECTS AND SPECIAL PRECAUTIONS:

Side effects:

The most serious undesirable effects associated with the use of MELODENE are listed under “Warnings”.

Other side effects that have been reported in users of combined oral contraceptives, such as MELODENE, but for which the association has been neither confirmed nor refuted are:

System Organ Class	Common (≥ 1/100 to < 1/10)	Uncommon (≥ 1/1000 and < 1/100)	Rare (≥ 1/10,000 to ≤ 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	decreased libido	increased 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

The following serious adverse events have been reported in women using COCs, which are discussed in section "Warnings":

- Venous thromboembolic disorders.
- Arterial thromboembolic disorders.
- Cerebrovascular accidents.
- Hypertension.
- Hypertriglyceridemia.
- Changes in glucose tolerance or effect on peripheral insulin resistance.
- Liver tumours (benign and malignant).
- Liver function disturbances.
- Chloasma.
- In women with hereditary angioedema exogenous estrogens may induce or exacerbate symptoms of angioedema.
- Occurrence or deterioration of conditions for which association with COC use is not conclusive: 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, Crohn's disease, ulcerative colitis, cervical cancer.

The frequency of diagnosis of breast cancer is very slightly increased among OC users. As breast cancer is rare in women under 40 years of age the excess number is small in relation to the overall risk of breast cancer. Causation with COC use is unknown. For further information, see sections "Contra-indications" and "Warnings".

Special precautions:

Medical examination/consultation:
A complete medical history and physical examination should be taken prior to the initiation or reinstitution of MELODENE use, guided by the "Contra-indications" and "Warnings", and should be repeated periodically. Periodic medical assessment is also of importance because contra-indications (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 MELODENE.
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.
Women should be advised that MELODENE does not protect against HIV infections (AIDS) and other sexually transmitted diseases.

Reduced efficacy:
The efficacy of MELODENE may be reduced in the event of e.g. missed active tablets, gastrointestinal disturbances during active tablet-taking (see "Dosage and Directions for Use"), or concomitant medication (see "Interactions").

Reduced cycle control:
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 inactive tablet phase. If MELODENE has been taken according to the directions described in "Dosage and Directions for Use", it is unlikely that the woman is pregnant. However, if MELODENE 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 MELODENE use is continued.
MELODENE contains lactose, patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption, should not take this medicine.

Effects on ability to drive and use machines:
No observed effects.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

There have been no reports of serious deleterious effects from overdose. Symptoms that may occur in case of taking an overdose of active tablets are: nausea; vomiting; and, in young girls, slight vaginal bleeding. There are no antidotes and further treatment should be symptomatic

IDENTIFICATION:

21 small white round coated hormonal tablets and 7 large pink round coated non-hormonal tablets.

PRESENTATION:

Cartons with one or three calendar blister packs each containing 28 tablets.

STORAGE INSTRUCTIONS:

Store in original packs at room temperature (at or below 30 °C).
Protect from light.
STORE ALL MEDICINES OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER:

31/18.8/0462

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

Bayer (Pty) Ltd
Reg. No.: 1968/011192/07
27 Wrench Road
ISANDO
1609

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