PROFESSIONAL INFORMATION LEAFLET: MARDESSA

SCHEDULING STATUS S3

1. NAME OF THE MEDICINE

MARDESSA Film-Coated Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

21 white film-coated tablets (active tablets):

Each film-coated tablet contains 0,15 mg desogestrel and 0,02 mg ethinylestradiol.

Excipient with known effect:

Each film-coated tablet contains 54,91 mg lactose (as monohydrate).

7 green placebo (inactive) film-coated tablets:

The tablet does not contain active substances.

Excipient with known effect:

Each film-coated tablet contains 55,50 mg lactose (as monohydrate).

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Film-coated tablet

21 Round, white (active) film-coated tablets with C and 5 debossed on opposite sides.

7 Round, green (inactive) film-coated tablets.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Oral contraception.

4.2 Posology and method of administration

For oral use.

Medical examination/consultation

Prior to the initiation or reinstitution of MARDESSA a complete medical history including family history should be taken, and physical examination should be taken prior to the initiation or reinstitution of combined oral contraceptive use, guided by the contraindications and warnings, and should be repeated at least annually during the use of MARDESSA. 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 MARDESSA.

The frequency and nature of these assessments should be based on established practice guidelines and 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.

How to take MARDESSA

Tablets must be taken in the order directed on the package every day at about the same time with some liquid as needed. 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 tablet corresponding to the day of the week (e.g. “MO’ for Monday). Following the directions shown by the arrows, one tablet must be taken daily until the pack is finished. Each subsequent pack is started the day after the last tablet of the current pack. During the placebo days a withdrawal bleed usually occurs. This usually starts on day 2 to 3 after the last active tablet and may not have finished before the next pack is started.

How to start MARDESSA

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). The first tablet should be taken from the silver section of the calendar pack by selecting the tablet corresponding to the day of the week (e.g. “MO’ for Monday). Then take 1 tablet every day following

the directions shown by the arrows. Starting on days 2 to 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 another combined oral contraceptive:

The women should start with MARDESSA on the day after the last active tablet of her previous combined oral contraceptive, but at the latest on the day following the usual inactive tablet phase of her previous combined oral contraceptive. The first tablet should be taken from the silver section of the calendar pack by selecting the tablet corresponding to the day of the week (e.g. “MO’ for Monday). Then take 1 tablet every day following the directions shown by the arrows.

Changing from a progestogen-only method (minipill, injection, implant):

The woman may switch any day from the minipill (from an implant on the day of its removal and 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.

The first tablet should be taken from the silver section of the calendar pack by selecting the tablet corresponding to the day of the week (e.g. “MO’ for Monday). Then take 1 tablet every day following the directions shown by the arrows.

Following first-trimester abortion:

The woman may start immediately. When doing so, she need not take additional contraceptive measures. The first tablet should be taken from the silver section of the calendar pack by selecting the tablet corresponding to the day of the week (e.g. “MO’ for Monday). Then take 1 tablet every day following the directions shown by the arrows.

Following delivery or second-trimester abortion:

Women should be advised to start at day 21 to 28 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 MARDESSA use, or the woman has to wait for her first menstrual period.

The first tablet should be taken from the silver section of the calendar pack by selecting the tablet corresponding to the day of the week (e.g. “MO’ for Monday). Then take 1 tablet every day following the directions shown by the arrows.

For breastfeeding women see “Pregnancy and lactation”.

Management of missed 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** 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.

Due to starting in the silver section, the first cycle of active tablets can be shorter than subsequent cycles. If tablets are missed in the first cycle of use, the medical practitioner is referred to the basic rules. In all other cases, in accordance with these rules, the following advice can be given in daily practice:

Day 1 – 7 /Week 1 (active tablets)

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.

Day 8 – 14 /Week 2 (active tablets)

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 the 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.

Day 15 – 21 /Week 3 (active tablets)

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 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. The next pack must be started as soon as the active tablets in the current pack are finished, i.e. no inactive tablets (green tablets) should be taken. 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 immediately continue with the inactive tablets.

The total number of missed tablets and inactive tablets must never exceed

7 tablets. Subsequently she should continue with the next pack.

Day 22 – 28 /Week 4 (inactive/placebo tablets)

Contraceptive protection is not reduced; the woman should take further tablets at the usual time.
If the woman missed active tablets and subsequently has no withdrawal bleed in the first normal inactive tablet phase, the possibility of a pregnancy should be considered.

Advice in case of gastrointestinal disturbances:

In case of severe gastrointestinal disturbances (vomiting, diarrhoea), 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, as given in the previous section 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 MARDESSA 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 MARDESSA is then resumed after the usual 7-day inactive tablet phase.
To shift her period to another day of the week than the woman is used to with her current scheme, she can be advised to shorten her forthcoming inactive tablet time by as many days as she likes. The shorter the 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).

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 MARDESSA has been taken according to the directions described above, it is unlikely that the woman is pregnant. However, if MARDESSA 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 MARDESSA use is continued.

Special Populations

Hepatic impairment:

Not recommended in women with or a history of severe hepatic disease as long as liver function values have not returned to normal (see sections 4.4 and 5.2).

Children and adolescents:

MARDESSA is only indicated after menarche.

Elderly:

MARDESSA is not indicated after menopause.

4.3 Contraindications

- MARDESSA is contraindicated in patients with a known hypersensitivity to desogestrel or ethinylestradiol or to any excipient listed under section 6.1.

Combined oral contraceptives (COCs) such as MARDESSA 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 MARDESSA use, the medicine 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 prodromata of a thrombosis (e.g. angina pectoris and transient ischaemic attack).
- Migraine or a history of this condition.
- 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 immobilization).
- 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.

4.4 Special warnings and precautions for use

If any of the conditions/risk factors mentioned below is present, the benefits of combined oral contraceptive 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 case 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 and an increased risk for arterial and venous thrombotic and thromboembolic diseases (e.g. myocardial infarction, stroke, deep venous thrombosis and pulmonary embolism).

Venous thromboembolism (VTE), manifesting as deep venous thrombosis and/or pulmonary embolism, may occur during the use of MARDESSA.

Thrombosis has been reported to occur in other blood vessels e.g. hepatic, mesenteric, renal or retinal veins and arteries, in combined oral contraceptive users. Symptoms of venous or arterial thrombosis 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 increases further, especially in women over 35 years of age);
- a positive family history (venous or arterial thromboembolism ever in a sibling or parent at 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 combined oral contraceptive use (in the case of elective surgery at least four weeks in advance) and not to resume until two weeks after complete remobilisation.

Other medical conditions which have been associated with adverse circulatory events 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 MARDESSA use (which may be prodromal of a cerebrovascular event) may be a reason for immediate discontinuation of MARDESSA.
Biochemical factors that may be indicative of a 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, plus anticoagulants).

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 oral contraceptive use.

Tumours

An increased risk of cervical cancer in long-term users of combined oral contraceptives has been reported in epidemiological studies.
A meta-analysis from epidemiological studies reports that there is an increased relative risk of having breast cancer diagnosed in women who are currently using COCs such as MARDESSA.
Benign liver tumours and, even more rarely, malignant liver tumours have been reported in users of COCs such as MARDESSA. 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 MARDESSA.

Mood changes and depressive symptoms

Depressed mood and depression are well-known undesirable effects of hormonal contraceptive use (see section 4.8). Depression can be serious and is a well-known risk factor for suicidal behaviour and suicide. Women should be advised to contact their healthcare professional in case of mood changes and depressive symptoms, including shortly after initiating the treatment.

Other conditions

Women with hypertriglyceridaemia, or a family history thereof, may be at an increased risk of pancreatitis when using combined oral contraceptives such as MARDESSA.

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

The occurrence or deterioration of the following conditions have been reported with the use of COCs such as MARDESSA: 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; hereditary angiooedema.

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

Although combined oral contraceptives 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 MARDESSA. However, diabetic women should be carefully observed while taking MARDESSA.

Crohn's disease and ulcerative colitis have -been associated with combined oral contraceptive 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 MARDESSA.

Respiratory: Asthma may deteriorate in women taking MARDESSA.

Women should be advised that MARDESSA does not protect against HIV infections (AIDS) and other sexually transmitted diseases (STDs). Women should be advised that additional barrier contraceptive measures are needed to prevent transmission of STDs and HIV infection.

Reduced efficacy

The efficacy of MARDESSA may be reduced in the event of missed active tablets, vomiting or concomitant medication.

Laboratory tests

The use of contraceptive steroids 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 metabolites and parameters of coagulation and fibrinolysis. Changes generally remain within the normal laboratory range.

Lactose

MARDESSA contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance e.g. galactosaemia, Lapp lactase deficiency or glucose-galactose malabsorption or fructose intolerance should not take MARDESSA.

4.5 Interaction with other medicines and other forms of interaction

Interactions that result in an increased clearance of sex hormones can lead to breakthrough bleeding and oral contraceptive failure. This has been established with hydantoins, barbiturates, primidone, carbamazepine and rifampicin; oxcarbamazepine, topiramate, felbamate, griseofulvin and medicines containing St. John's wort. The mechanism of this interaction appears to be based on the hepatic enzyme-inducing properties of these medicines. Maximal enzyme induction is generally not seen for 2 to 3 weeks, but may then be sustained for at least 4 weeks after the cessation of these medicines. Contraceptive failures have also been reported with antibiotics, such as ampicillins and tetracyclines. The mechanism of this effect has not been elucidated.

Women on short-term treatment with any of the above-mentioned classes of medicine or individual medicine should use a barrier method temporarily, in addition to the combined oral contraceptive i.e. during the time of concomitant administration and for 7 days after their discontinuation. For women on rifampicin, a barrier method should be used in addition to the combined oral contraceptive during the time of rifampicin administration and for 28 days after its discontinuation. If concomitant administration runs beyond the end of the tablets in the current oral contraceptive pack, the inactive tablets must be discarded and the next oral contraceptive pack should be started right away, with the active tablet in the silver section.

In women on long-term treatment with hepatic enzyme-inducing medicines, increased contraceptive steroid doses are recommended. If a high contraceptive dosage is not desirable or appears to be

unsatisfactory or unreliable e.g. in the case of irregular bleeding, another method of contraception should be advised.

Oral contraceptives may affect the metabolism of other medicines. Accordingly, plasma and tissue concentrations may be affected (e.g. benzodiazepines).

4.6 Fertility, pregnancy and lactation

Extensive epidemiological studies have revealed neither an increased risk of birth defects in children born to women who have used combined oral contraceptives prior to pregnancy, nor a teratogenic effect when combined oral contraceptives were taken inadvertently during early pregnancy. Feminisation of the male foetus may occur.

Breastfeeding

Breastfeeding may be influenced by combined oral contraceptives, as they may reduce the quantity and change the composition of breast milk, therefore the use of combined oral contraceptives 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.

Fertility

No data available.

4.7 Effects on ability to drive and use machines

No effects on ability to drive and use machines have been observed in users of combined oral contraceptives such as MARDESSA.

4.8 Undesirable effects

Table 1: Tabulated summary of adverse reactions

The following undesirable effects have been reported.

System Organ Class	**MARDESSA Tablets Side Effects**
Immune system disorders	
Less frequent:	Hypersensitivity
Metabolism and nutrition disorders	
Frequent:	Body weight changes (increased or decreased), fluid retention
Psychiatric disorders	
Frequent:	Depressive mood, mood altered
Less frequent:	changes in libido (increased or decreased)
Nervous system disorders	
Frequent:	Headache, migraine
Eyes disorders	
Less frequent:	Contact lens intolerance
Gastrointestinal disorders	
Frequent:	Nausea, vomiting, diarrhoea, abdominal pain
Skin and subcutaneous tissue disorders	
Frequent:	Rash, urticaria

Less frequent:	Erythema nodosum, erythema multiforme
Reproductive system and breast disorders	
Frequent:	Breast pain, breast tenderness, breast enlargement
Less frequent:	Breast discharge, vaginal discharge

Post-marketing reported side effects:

The following side effects have been reported with the post-marketing use of hormonal contraceptives:

Frequency unknown

- Severe depression with a higher risk of suicidal thoughts/behaviour and suicide

Reporting of suspected adverse reactions:

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the "6.04 Adverse Drug Reaction Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. In addition, suspected adverse reactions can be reported to Actor Pharma (Pty) Ltd via email: pharmacovigilance@ actorpharma.co.za or telephonically on 011 312 3812.

4.9 Overdose

There have been no reports of serious deleterious effects from overdose. Symptoms that may occur in this case are: Nausea, vomiting and possible slight vaginal bleeding in young girls. There are no antidotes and further treatment should be symptomatic.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

PHARMACOLOGICAL CLASSIFICATION:

A.18.8 Ovulation controlling agents

The contraceptive effect of MARDESSA 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 secretions.

5.2 Pharmacokinetic properties

Desogestrel

Absorption

Orally administered desogestrel is rapidly and completely absorbed and converted to etonogestrel. Peak serum concentrations of approximately 2 ng/ml are reached at about 1,5 hours after single ingestion. Bioavailability is 62 to 81 %.

Distribution

Etonogestrel is bound to serum albumin and to sex hormone binding globulin (SHBG). Only 2 to 4 % of the total serum drug concentrations are present as free steroid, 40 to 70 % are specifically bound to SHBG. The ethinylestradiol-induced increase in SHBG influences the distribution over 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 desogestrel is 1,5 litre/kg.

Metabolism

Etonogestrel is completely metabolised by the known pathways of steroid metabolism. The metabolic clearance rate from serum is about 2 ml/min/kg. No interaction was found with the co-administered ethinylestradiol.

Elimination

Etonogestrel serum levels decrease in two phases. The terminal disposition phase is characterised by a half-life of approximately 30 hours. Desogestrel and its metabolites are excreted at a urinary to biliary ratio of about 6:4.

Steady-state conditions

Etonogestrel pharmacokinetics are influenced by SHBG levels, which are increased threefold by ethinylestradiol. Following daily ingestion, drug serum levels increase about two- to threefold, reaching steady state conditions during the second half of the treatment cycle.

Ethinylestradiol

Absorption

Orally administered ethinylestradiol is absorbed rapidly and completely absorbed. Peak serum concentrations of about 80 pg/ml are reached within 1 to 2 hours. Absolute bioavailability as a result of pre-systemic conjugation and first-pass metabolism is approximately 60 %.

Distribution

Ethinylestradiol is highly but non-specifically bound to serum albumin (approximately 98,5 %) and induces an increase in the serum concentrations of SHBG. An apparent volume of distribution of about 5 l/kg was determined.

Metabolism

Ethinylestradiol is subject to pre-systemic conjugation in both the small bowel mucosa and the liver. Ethinylestradiol 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 metabolic clearance rate of ethinylestradiol is about 5 ml/min/kg.

Elimination

Ethinylestradiol serum levels decrease in two phases, the terminal disposition phase is characterised by a half-life of approximately 24 hours. Unchanged drug is not excreted, ethinylestradiol metabolites are excreted at a urinary to biliary ratio of 4:6. The half-life of metabolite excretion is about one day.

Steady-state conditions

Steady-state concentrations are reached after 3 to 4 days when serum drug levels are higher by 30 to 40 % as compared to single dose.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Active tablets

Tablet core:

lactose monohydrate

maize starch

povidone

RRR-α-Tocopherol

silica colloidal hydrated

silica colloidal anhydrous

stearic acid

Composition of coating system:

hypromellose

polyethylene glycol

titanium dioxide

Inactive tablets

Tablet core:

lactose monohydrate

maize starch

povidone

silica colloidal anhydrous

magnesium stearate

Composition of coating system:

hypromellose

triacetin

polysorbate 80

titanium dioxide

FD&C Blue 2 Aluminium Lake

yellow iron oxide

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years

6.4 Special precautions for storage

Store at or below 25 °C in the original package in order to protect from light.

6.5 Nature and contents of container

PVC-PVDC/Aluminium blisters enclosed in a carton.

Pack size: Each carton contains 28 (21+7) tablets.

6.6 Special precautions for disposal

No special requirement.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Actor Pharma (Pty) Ltd[1]

Royal Palm Business Estate

Unit 7, 646 Washington Street

Halfway House, Midrand, 1685

8. REGISTRATION NUMBER(S)

To be allocated

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

[1] Company Registration number.: 2008/008787/07