PROFESSIONAL INFORMATION

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

Novofem® film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each red film-coated tablet contains: estradiol hemihydrate equivalent to anhydrous estradiol 1 mg.

Each white film-coated tablet contains: estradiol hemihydrate equivalent to anhydrous estradiol 1 mg and norethisterone acetate 1 mg.

Excipients with known effect:

Contains sugar:

Each red film-coated tablet contains 37,3 mg lactose monohydrate.

Each white film-coated tablet contains 36,8 mg lactose monohydrate.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet.

Red film-coated, biconvex tablets engraved with NOVO 282.

White, film-coated, biconvex tablets engraved with NOVO 283.

4. CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

- Novofem® is indicated for the treatment of symptoms associated with estrogen deficiency in postmenopausal women with an intact uterus.
- To reduce the risk of bone loss in postmenopausal women.

The experience of treating women over 65 years is limited.

Novofem® has no contraceptive effect.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION

Novofem® is a continuous sequential preparation for hormone replacement therapy. The estrogen is dosed continuously. The progestagen is added for 12 days of every 28 day cycle, in a sequential manner.

Take one tablet daily, preferably at the same time each day, until all the 28 tablets have been taken. Begin by taking the red tablets for 16 days followed by the white tablets for 12 days. After intake of the last white tablet, treatment is continued with the first red tablet of a new pack on the next day.

In women who are not taking HRT or women transferring from a continuous combined HRT product, treatment may be started on any convenient day.

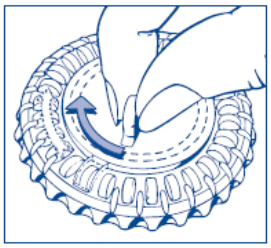
In women transferring from a sequential HRT regimen, treatment should begin the day following completion of the prior regimen.

A switch to a higher dose combination product could be indicated if the response after three months is insufficient for satisfactory symptom relief.

A menstruation-like bleeding usually occurs at the beginning of a new treatment cycle. If you forget to take one tablet, the forgotten tablet is to be discarded. Forgetting a dose may increase the likelihood of breakthrough bleeding and spotting.

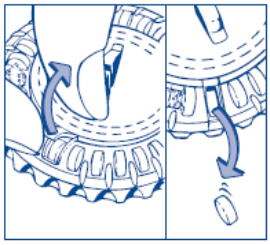
Instructions for use of the calendar dial pack

1. **Set the day reminder:**



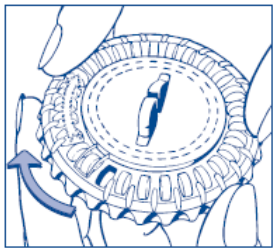
Turn the inner disc to set the selected day of the week opposite the little plastic tab.

2. **How to take the first tablet:**



Break the plastic tab and tip out the first tablet.

3. **Every day:**



Simply move the transparent dial clockwise one space as indicated by the arrow.

Tip out the next tablet.

The transparent dial can only be turned after the tablet in the opening has been removed.

4.3 CONTRAINDICATIONS

- Known hypersensitivity to estradiol, norethisterone acetate or to any of the excipients of Novofem® (see section 6.1)
- Known or suspected breast cancer or history (personal and/or family) of breast cancer
- Known, past or suspected estrogen-dependent malignant tumours (e.g., endometrial cancer)
- Undiagnosed genital bleeding
- Current or previous idiopathic venous thromboembolism (deep venous thrombosis, pulmonary embolism)
- Inherited thrombophilia or known thrombophilic disorders (e.g., protein C, protein S or antithrombin deficiency (see section 4.4)
- Active or recent arterial thromboembolic events (e.g., angina, myocardial infarction)
- Active liver disease. Acute liver disease or a history of liver disease, as long as liver function tests have failed to return to normal
- Porphyria
- Untreated endometrial hyperplasia
- Known or suspected pregnancy, and lactation (see section 4.6)
- Patients with known inherited genetic mutations: BRCA1 and BRCA2 genes
- Early menstrual periods (before the age of 12 years)

- History of non-cancerous breast diseases (atypical hyperplasia or lobular carcinoma *in situ*)
- Previous treatment using radiation therapy to the chest or breast
- Previous exposure to diethylstilbestrol (DES)

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

For the treatment of post-menopausal symptoms, Novofem® should only be initiated for symptoms that adversely affect quality of life. In all cases, a careful appraisal of the risks and benefits should be undertaken at least annually and HRT Novofem® should only be continued as long as the benefit outweighs the risk.

Evidence regarding the risks associated with HRT in the treatment of premature menopause is limited. Due to the low level of absolute risk in younger women, however, the balance of benefits and risks for these women may be more favourable than in older women.

Endometrial hyperplasia and carcinoma

In women with an intact uterus, the use of estrogens is associated with an increased incidence of endometrial hyperplasia and carcinoma, when estrogens are administered alone for prolonged periods. The reported increase in endometrial cancer risk among estrogen-only users varies from 2- to 12-fold greater compared with non-users, depending on the duration of treatment and estrogen dose (see section 4.8). After stopping treatment, the risk may remain elevated for at least 10 years.

The addition of progestagen for at least 12 days per cycle in non-hysterectomised women reduces this risk.

Breakthrough bleeding and spotting may occur during the first months of treatment. If breakthrough bleeding or spotting appears after some time on therapy, or continues after treatment has been discontinued, the reason should be investigated, which may include endometrial biopsy to exclude endometrial malignancy.

Coronary artery disease (CAD)

There is no evidence from randomised controlled trials of protection against myocardial infarction in women with or without existing CAD who received combined estrogen-progestagen or estrogen-only HRT.

The relative risk of CAD during use of combined estrogen-progestagen HRT is slightly increased. As the baseline absolute risk of CAD is strongly dependent on age, the number of extra cases of CAD due to estrogen-progestagen use is very low in healthy women close to menopause, but will rise with more advanced age.

Stroke

Combined estrogen-progestagen and estrogen-only therapy are associated with an up to 1,5-fold increase in risk of ischaemic stroke. The relative risk does not change with age or time since menopause. However, as the baseline risk of stroke is strongly age-dependent, the overall risk of stroke in women who use HRT will increase with age (see section 4.8).

Ovarian cancer

Ovarian cancer is much rarer than breast cancer. Epidemiological evidence from a large meta-analysis suggests a slightly increased risk in women taking estrogen-

only or combined estrogen-progestagen HRT, which becomes apparent within 5 years of use and diminishes over time after stopping.

Some other studies, including the WHI trial, suggest that use of combined HRTs may be associated with a similar or slightly smaller risk (see section 4.8).

Hypothyroidism

Patients who require thyroid hormone replacement therapy should have their thyroid function monitored regularly while on Novofem® to ensure that thyroid hormone levels remain in an acceptable range.

Angioedema

Estrogens may induce or exacerbate symptoms of angioedema, in particular in women with hereditary angioedema.

Other conditions

Estrogens such as Novofem® may cause fluid retention and, therefore, patients with cardiac or renal dysfunction should be carefully observed.

Women with pre-existing/familial hypertriglyceridaemia should be followed closely during estrogen replacement or hormone replacement therapy, since rare cases of large increases of plasma triglycerides leading to pancreatitis and other complications have been reported with estrogen therapy in this condition.

Estrogens increase thyroid binding globulin (TBG), leading to increased circulating total thyroid hormone, as measured by protein-bound iodine (PBI), T4 levels (by column or by radio-immunoassay) or T3 levels (by radio-immunoassay). T3 resin uptake is decreased, reflecting the elevated TBG. Free T4 and free T3

concentrations are unaltered. Other binding proteins may be elevated in serum, i.e., corticoid binding globulins (CBG), sex-hormone-binding globulin (SHBG) leading to increased circulating corticosteroids and sex steroids, respectively. Free or biological active hormone concentrations are unchanged. Other plasma proteins may be increased (angiotensinogen/renin substrate, alpha-I-antitrypsin and ceruloplasmin).

HRT use does not improve cognitive function. There is some evidence of increased risk of probable dementia in women who start using continuous combined or estrogen-only HRT after the age of 65. It is unknown whether the findings apply to younger post-menopausal women or other HRT products.

Patients with advanced renal impairment should be closely monitored as it might be expected that the circulating levels of the active components of Novofem® would be increased. In case of aggravation of asthma, epilepsy or diabetes mellitus Novofem® should be reconsidered.

An increase in the risk of surgically confirmed gallbladder disease in postmenopausal women receiving estrogens has been reported.

The use of estrogen may influence the results of certain endocrine tests and liver enzymes.

The requirement of insulin or oral anti diabetics can be increased as a consequence of reduced glucose tolerance.

Medical examination/follow-up

Before initiating or reinstituting Novofem® a complete personal and family history should be taken. Physical (including pelvic and breast) examinations should be guided by this and contraindications and warnings for use (see section 4.3 and 4.4). During treatment, periodic check-ups are recommended.
A careful appraisal of the risks and benefits should be undertaken at least annually and treatment with Novofem® should not exceed a period of 5 years. Women should be advised what changes in their breasts should be reported to their doctor or nurse.

Investigations, including appropriate imaging tools, e.g., mammography, should be carried out in accordance with currently accepted screening practices and modified to the clinical needs of the individual. Regular breast examination and, where appropriate, mammography should be carried out in women on Novofem®.

Breakthrough bleeding and spotting may occur during the first months of treatment. If breakthrough bleeding or spotting appears after some time on therapy with Novofem®, or continues after treatment has been discontinued, the cause should be investigated.

Conditions which need supervision

If any of the following conditions are present, have occurred previously and/or have aggravated during pregnancy or previous hormone treatment, the patient should be closely supervised, as these conditions may recur or be aggravated during treatment with Novofem®:

- Leiomyoma (uterine fibroids), endometriosis, endometrial hyperplasia
- Risk factors for thromboembolic disorders (see section 4.3)

- Risk factors for estrogen dependent tumours, e.g., 1st degree heredity for breast cancer
- Hypertension
- Liver disorders (e.g., liver adenoma, icterus) (see section 4.3)
- Diabetes mellitus with or without vascular involvement
- Cholelithiasis
- Sudden hearing loss
- Migraine or (severe) headache
- Systemic lupus erythematosus
- A history of endometrial hyperplasia
- Epilepsy
- Asthma
- Otosclerosis.

Reasons for immediate withdrawal of therapy:

- Venous or arterial thromboembolic disorders;
- Arterial disease;
- Jaundice or deterioration in liver function;
- Significant increase in blood pressure;
- Sudden partial or complete loss of vision or a sudden onset of proptosis or diplopia;
- New onset of migraine-type headache;
- Pregnancy.

Venous thromboembolism (see section 4.3)

In women with risk factors for venous thromboembolism (VTE), the benefits of treatment with Novofem® need to be carefully weighed against risks (see section

4.3). Novofem® is associated with a higher relative risk of developing venous thromboembolism (VTE), i.e., deep vein thrombosis or pulmonary embolism.

One randomised controlled trial and epidemiological studies found a two - to three - fold higher risk for users of HRT compared with non-users. For non-users it is estimated that the number of cases of VTE that will occur over a 5 year period is about 3 per 1 000 women aged 50 - 59 years and 8 per 1 000 women aged between 60 - 69 years. It is estimated that in healthy women who use HRT for 5 years, the number of additional cases of VTE over a 5 year period will be between 2 and 6 (best estimate = 4) per 1 000 women aged 50 - 59 years and between 5 and 15 (best estimate = 9) per 1 000 women aged 60 - 69 years. The occurrence of such an event is more likely in the first year of HRT than later.

Patients with known thrombophilic states have an increased risk of VTE and HRT may add to this risk. HRT is therefore contraindicated in these patients (see section 4.3).

Generally recognised risk factors for VTE include use of estrogens, older age, a personal history or family history, severe obesity (body mass index > 30 kg/m^2), pregnancy/postpartum period, cancer and systemic lupus erythematosus (SLE). There is no consensus about the possible role of varicose veins in VTE.

Women already on anticoagulant treatment require careful consideration of the benefit-risk of Novofem®.

The risk of VTE may be temporarily increased with prolonged immobilisation, major trauma or major surgery. Scrupulous attention should be given to prophylactic

measures to prevent VTE following surgery. Where prolonged immobilisation is liable to follow elective surgery, particularly abdominal or orthopaedic surgery to the lower limbs, consideration should be given to temporarily stopping Novofem® 4 to 6 weeks earlier. Treatment should not be restarted until the woman is completely mobilised.

In women with no personal history of VTE but with a first degree relative with a history of venous thromboembolism at a young age, screening may be offered after careful counselling regarding its limitations (only a proportion of thrombophilic defects are identified by screening).

If a thrombophilic defect is identified which segregates with venous thromboembolism in family members or if the defect is 'severe' (e.g., antithrombin, protein S, or protein C deficiencies or a combination of defects), HRT is contraindicated.

If VTE develops after initiating therapy, Novofem® should be discontinued. Patients should be told to contact their doctors immediately when they are aware of a potential thromboembolic symptom (e.g., painful swelling of a leg, sudden pain in the chest, dyspnoea).

Depressed mood, depression and risk of suicidality

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 medical practitioner in case of mood changes and depressive symptoms including shortly after initiating the treatment.

Breast cancer

Hormone replacement therapy, including Novofem®, contains estrogen and progestagen which, on prolonged use, may increase the risk of developing breast cancer. A meta-analysis of prospective epidemiological studies from 1992 to 2018 reported a significant increase in the risk of developing breast cancer in 55 575 women 40 – 59 years of age who used menopausal hormone therapy (MHT). The risk increased steadily with duration of use and was slightly greater for estrogen-progestagen than estrogen-only preparations, and the risk persisted for more than 10 years after stopping the treatment. The relative risk (RR) to develop breast cancer for estrogen-progestagen preparations was 1,60 at 1 – 4 years and RR = 2,08 at 5 – 14 years, while that for estrogen-only preparations were 1,17 at 1 – 4 years and 1,33 at 5 – 14 years. There was no risk to develop breast cancer in women who started MHT at 60 years of age.

All women on Novofem® should receive yearly breast examinations by a health care provider and perform monthly breast self-examinations. Mammography evaluations should be done based on patient age, risk factors, and prior mammogram results.

HRT, especially estrogen-progestagen combined treatment, increases the density of mammographic images which may adversely affect the radiological detection of breast cancer.

Endometrial cancer

In women with an intact uterus, the risk of endometrial hyperplasia and endometrial cancer increases with increasing duration of use of unopposed estrogens. According to data from epidemiological studies, the best estimate of the risk is that

for women not using HRT, about 5 in every 1 000 are expected to have endometrial cancer diagnosed between the ages of 50 and 65.

Depending on the duration of treatment and estrogen dose, the reported increase in endometrial cancer risk among unopposed estrogen users varies from 2- to 12-fold greater compared with non-users. Adding a progestagen to estrogen-only therapy greatly reduces this increased risk.

Novofem® tablets contain lactose monohydrate.

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency, or glucose-galactose malabsorption should not take Novofem®.

4.5 Interaction with other medicines and other forms of interaction

The metabolism of Novofem® may be increased by concomitant use of substances known to induce medicine-metabolising enzymes, specifically cytochrome P450 enzymes such as anticonvulsants (e.g., phenobarbitone, phenytoin, carbamazepine) and anti-infectives (e.g., rifampicin, rifabutin, nevirapine, efavirenz).

Ritonavir, telaprevir and nelfinavir, although known as strong inhibitors, by contrast exhibit inducing properties when used concomitantly with steroid hormones. Herbal preparations containing St John's wort (*Hypericum perforatum*) may induce the metabolism of Novofem®.

Clinically, an increased metabolism of Novofem® may lead to decreased effect and changes in the uterine bleeding profile.

Novofem® can enhance the effects of imipramine.

If ciclosporin is given concomitantly, there may be increased blood levels of ciclosporin, creatinine and transferases due to the decreased hepatic excretion of ciclosporin.

The requirement of treatment with oral antidiabetic medicines or with insulin may change due to the estrogen effect on glucose tolerance (will be decreased) and the response to insulin, i.e., the requirement of insulin or oral antidiabetics can be increased as a consequence of reduced glucose tolerance.

Some laboratory tests may be influenced by estrogen therapy, such as tests for glucose tolerance or thyroid function.

Medicines that inhibit the activity of hepatic microsomal medicine-metabolising enzymes, e.g., ketoconazole, may increase circulating levels of the active substances in Novofem®.

Hormone contraceptives containing oestrogens have been shown to significantly decrease plasma concentrations of lamotrigine when co-administered due to induction of lamotrigine glucuronidation. This may reduce seizure control. Although the potential interaction between hormone replacement therapy and lamotrigine has not been studied, it is expected that a similar interaction exists, which may lead to a reduction in seizure control among women taking both medicinal products together.

4.6 FERTILITY, PREGNANCY AND LACTATION

Novofem® is contraindicated during pregnancy (see section 4.3).

If pregnancy occurs during medication with Novofem®, treatment should be withdrawn immediately.

Data on exposed pregnancies indicate adverse effects of norethisterone on the foetus. Masculinisation of female foetuses was observed.

Lactation

Novofem® is contraindicated during lactation (see section 4.3).

Mothers on Novofem® should not breastfeed.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Novofem® can cause side effects, such as dizziness, that may interfere with the ability to drive and use machines (see section 4.8). Caution is advised until the effects of Novofem® are known.

4.8 UNDESIRABLE EFFECTS

The most frequently reported side effects during treatment in clinical trials conducted with an HRT product similar to Novofem® were breast tenderness and headache.

The side effects listed below may occur during Novofem ® treatment.

System organ class	Frequent	Less frequent
Infections and infestations	Vaginal candidiasis	
Immune system disorders		Allergic reaction
Psychiatric disorders		Nervousness
Nervous system disorders	Headache Dizziness Insomnia	Migraine Libido disorder Vertigo

	Depression	
Vascular disorders	Increased blood pressure; Aggravated hypertension	Venous thromboembolism Peripheral embolism and thrombosis
Gastrointestinal disorders	Dyspepsia Abdominal pain Flatulence Nausea	Vomiting Diarrhoea Bloating
Hepatobiliary disorders		Gallbladder Disease; Gallstones
Skin and subcutaneous tissue disorders	Rash Pruritus	Alopecia Acne
Musculoskeletal and connective tissue disorders		Muscle cramps
Reproductive system and breast disorders	Breast tenderness Vaginal haemorrhage Uterine fibroids aggravated	Uterine fibroids
General disorders and administration site conditions	Oedema	
Investigations	Weight increased	

Post- marketing side effects

In addition to the above-mentioned side effects, those presented below have been spontaneously reported:

- Neoplasms benign and malignant (including cysts and polyps): Endometrial cancer
- Immune system disorders: Generalised hypersensitivity reactions (e.g., anaphylactic reaction/shock)
- Psychiatric disorders: Anxiety
- Nervous system disorders: Stroke
- Eye disorders: Visual disturbances
- Cardiac disorders: Myocardial infarction
- Reproductive system and breast disorder: Hyperplasia of endometrium, vulvovaginal pruritus
- Skin and subcutaneous tissue disorders: Seborrhoea, angioedema, hirsutism
- Investigations: Body mass decreased.

Other side effects have been reported in association with Novofem® treatment:

- Venous thromboembolism, i.e., deep leg or pelvic venous thrombosis and pulmonary embolism, is more frequent among hormone replacement therapy users than among non-users.
- Skin and subcutaneous disorders: Chloasma, erythema multiforme, erythema nodosum, haemorrhagic eruption, vascular purpura
- Probable dementia over the age of 65 (see section 4.4)
- Gall bladder disease
- Dry eyes
- Tear film composition changes

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

Ovarian cancer

Use of estrogen-only or combined estrogen-progestagen HRT has been associated with a slightly increased risk of having ovarian cancer diagnosed (see section 4.4). A meta-analysis from 52 epidemiological studies reported an increased risk of ovarian cancer in women currently using HRT compared to women who have never used HRT (RR 1,43, 95 % CI 1,31 - 1,56). For women aged 50 to 54 years taking 5 years of HRT, this results in about 1 extra case per 2 000 users. In women aged 50 to 54 who are not taking HRT, about 2 women in 2 000 will be diagnosed with ovarian cancer over a 5-year period.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of Novofem® is important. It allows continued monitoring of the benefit/risk balance of Novofem®. Healthcare providers are requested to report any suspected adverse reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

4.9 OVERDOSE

In overdose, side effects will be exacerbated & exaggerated (see section 4.8). Symptoms of over dosage with oral estrogens are breast tenderness, nausea, vomiting and/or metrorrhagia.

Overdosage of progestagens may lead to a depressive mood, fatigue, acne and hirsutism.

Treatment should be symptomatic.

5. PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Category and class: A 21.8.2 Progesterones with estrogens

Pharmacotherapeutic group: Progestagens and estrogens, sequential preparations

ATC code: G03FB05

The estrogen component of Novofem®, 17β-estradiol, substitutes for the loss of estrogen production in postmenopausal women. The progestagen component of Novofem®, norethisterone acetate, reduces the estrogen-induced endometrial hyperplasia in non-hysterectomised women.

Estrogen deficiency at menopause is associated with an increased bone turnover and decline in bone mass. The effect of estrogens on the bone mineral density is dose-dependent. After discontinuation of HRT, bone mass is lost at a rate similar to that in untreated women.

5.2 PHARMACOKINETIC PROPERTIES

Following oral administration of 17β-estradiol (E2) in micronised form, rapid absorption from the gastrointestinal tract occurs. It undergoes extensive first-pass metabolism in the liver and other enteric organs. After single dose administration, E2 reaches a peak plasma concentration of approximately 28 pg/mL (range 13 - 40 pg/mL) within 5 - 8 hours. The half-life of E2 is about 12 - 14 hours. It circulates bound to sex hormone binding globulin (37 %) and to albumin (61 %), while only approximately 1 - 2 % is unbound. Metabolism of E2 occurs mainly in the liver and the gut but also in target organs and involves the formation of less active or

inactive metabolites, including estrone, catecholestrogens and several estrogen sulphates and glucuronides.

Estrogens are excreted with the bile, where they are hydrolysed and reabsorbed (enterohepatic circulation), and mainly in urine in biologically inactive form.
After oral administration norethisterone acetate is rapidly absorbed and transformed to norethisterone (NET). It undergoes first-pass metabolism in the liver and other enteric organs. After single dose administration, NET reaches a peak plasma concentration of approximately 9 ng/mL (range 6 - 11 ng/mL) within 0,5 – 1,5 hours. The terminal half-life of NET is about 8 - 11 hours. NET binds to Sex Hormone Binding Globulin (36 %) and to albumin (61 %). The most important metabolites are isomers of 5α-dihydro-NET and of tetrahydro-NET, which are excreted mainly in the urine as sulphate or glucuronide conjugates.
The pharmacokinetics of estradiol is not influenced by norethisterone acetate.
The pharmacokinetics in the elderly has not been studied.

5.3 PRECLINICAL SAFETY DATA

Animal studies with estradiol and norethisterone acetate have shown estrogenic and progestagenic effects as expected. Both compounds induced adverse effects in preclinical reproductive toxicity studies, in particular embryotoxic effects and anomalies in urogenital tract development. Concerning other preclinic effects, the toxicity profiles of estradiol and norethisterone acetate are well-known and reveal no particular human risks beyond those discussed in other sections of the Profession Information and which generally apply to hormone substitution therapy.

6. PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Both the white and the red film-coated tablets contain:

Hydroxypropylcellulose,

Lactose monohydrate,

Magnesium stearate (E572),

Maize starch and

Talc (E553b).

Red film-coated tablets also contain:

Hypromellose,

Propylene glycol,

Red iron oxide (E172),

Talc (E553b) and

Titanium dioxide (E171).

White film-coated tablets also contain:

Hypromellose,

Talc (E553b) and

Triacetin (E1518).

6.2 INCOMPATIBILITIES

Not applicable.

6.3 SHELF LIFE

48 months.

Store at or below 25 ˚C.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store in a dry place, protected from light.

Do not refrigerate.

Keep the container in the outer carton until required for use.

Do not use this product after the expiration date marked on the label of the calendar dial pack and/or carton.

6.5 NATURE AND CONTENTS OF CONTAINER

Novofem® is supplied in a calendar dial pack with 28 tablets.

The calendar dial pack consists of the following three parts:

- The base of coloured non-transparent polypropylene;
- The ring-shaped lid made of transparent polystyrene;
- The centre dial made of coloured non-transparent polystyrene.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING

None.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Novo Nordisk (Pty) Ltd.

90 Grayston Drive

Sandown

Sandton

2031, Gauteng

Tel: +27 011 202 0500

8. REGISTRATION NUMBER

37/21.8.2/0297

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

29 July 2005

10. DATE OF REVISION OF THE TEXT

26 August 2025