

PROFESSIONAL INFORMATION

NATIVA COMPLEX® MENOPAUSE SUPPORT capsules

- Complementary Medicine.
- D33.7 Complementary Medicine: Discipline-Specific Traditional Claims – Combination Product.
- This unregistered medicine has not been evaluated by the SAHPRA for its quality, safety or intended use.

SCHEDULING STATUS

[S0]

1. NAME OF THE MEDICINE

NATIVA COMPLEX® MENOPAUSE SUPPORT (capsules)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains:

Active ingredient	Per capsule	Per maximum daily dosage (2 capsules)	%NRV* per maximum daily dosage (2 capsules)
<i>Panax ginseng</i> C.A. Meyer (Korean ginseng) [root extract, 5:1 extract providing 250 mg dried herb equivalent]	50 mg	100 mg	*
<i>Tribolium pretense</i> L. (Red clover) [aerial extract] Providing Isoflavones	50 mg 20 mg ALE**	100 mg 40 mg ALE**	*
<i>Glycine max</i> L. (Soybean) [bean extract 40 %] Providing Soy isoflavones of which Genistein	38 mg 15,2 mg 9,5 mg ALE**	76 mg 30,4 mg 19 mg ALE**	*
<i>Angelica sinensis</i> (Oliv.) Diels (Dong quai) [root extract, 20:1 extract standardised to liguistilde 5 % providing 400 mg dried herb equivalent]	20 mg	40 mg	*
Thiamine hydrochloride (Vitamin B1)	1,1 mg	2,2 mg	183 %
Riboflavin (Vitamin B2)	1,1 mg	2,2 mg	169 %
Nicotinamide (Vitamin B3)	12,5 mg	25 mg	156 %
Calcium-D pantothenic acid (Vitamin B5)	6 mg	12 mg	240 %
Pyridoxine hydrochloride (Vitamin B6)	12,5 mg	25 mg	1471 %
Folic acid (Vitamin B9)	200 µg	400 µg	100 %
Cyanocobalamin (Vitamin B12)	4 µg	8 µg	333 %
Cholecalciferol (Vitamin D3)	240 IU (6 µg)	480 IU (12 µg)	80 %
Tocopherol acetate (Vitamin E)	9,4 IU (6,32 mg TE***)	18,8 IU (12,64 mg TE****)	84 %

*Nutrient reference values for adults and children older than 4years. *NRV not established. **Aglycone isoflavone equivalent. ***D-alpha-Tocopherol Equivalents.

Nativa Complex® Menopause Support capsules is sugar and preservative free.

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Capsule, hard gelatine. Nativa Complex® Menopause Support capsules are light grey capsules.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Nativa Complex® Menopause Support capsules is a supplement which contains herbal extracts, phytoestrogens and vitamins to help improve overall well-being during menopause. It can help the body to counter symptoms of menopause such as hot flushes and night sweats. The body's need for certain nutrients may increase during menopause and Nativa Complex® Menopause Support can supplement nutrient deficiencies and offer additional nutritional support. Nativa Complex® Menopause Support can also support a healthy metabolism and improve energy levels. For a diagnosis or if symptoms persist, consult a medical practitioner. Efficacy of support may vary between users.

4.2 Posology and method of administration

The recommended daily dosage is

Women 18 years and older:

One (1) capsule in the morning and one (1) capsule in the evening, after a meal, with a glass of water.

Advise patients to consult a healthcare provider for use beyond three (3) months. Advise patients to use for a minimum of two (2) weeks to see beneficial effects. Advise the patient to not take dosage at the same time as other prescribed medications (minimum two (2) hours before or two (2) hours after taking Nativa Complex® Menopause Support).

4.3 Contraindications

- Hypersensitivity to any of the ingredients of Nativa Complex® Menopause Support (see section 6.1 List of excipients). Patients should be advised to consult their medical practitioner if in doubt.
- Must not be given to patients with a cobalamin or cobalt hypersensitivity as Nativa Complex® Menopause Support contains vitamin B12.
- Must not be given to patients who have breast cancer or a history of breast cancer or a predisposition to breast cancer, as indicated by an abnormal mammogram and/or biopsy, or family history of breast cancer as the product contains red clover and soybean (isoflavones).
- Must not be given to patients with diarrhoea or haemorrhagic disorders (including protein S deficiency) as Nativa Complex® Menopause Support contains dong quai.
- Must not be given to patients who are pregnant or breastfeeding or have hypermenorrhoea/profuse menstrual flow/heavy periods as Nativa Complex® Menopause Support contains dong quai (see 4.6).
- This product is formulated for women only and is not suitable for use in men, children or adolescents.
- Patients taking any chronic medication should not use this product without consulting their medical practitioner.

4.4 Special warnings and precautions for use

- Ensure patients are up to date on appointed clinical tests such as mammograms and endometrial ultrasounds or biopsies before using this product as it contains red clover and soybean (isoflavones).
- Nativa Complex® Menopause Support capsules may cause endometrial proliferation when given without progestogens to patients with an intact uterus.
- Advise patients to consult a healthcare provider or doctor prior to use if they have a history of hormonal or gynaecological disorders (e.g., endometriosis, uterine fibroids) as Nativa Complex® Menopause Support contains red clover and soybean (isoflavones).
- Advise patients to consult a healthcare provider or doctor prior to use if they are taking birth control pills or hormone replacement therapy, including thyroid replacement therapy (see 4.5).
- Advise patients to consult a healthcare provider or doctor prior to use if they have a liver disorder or develop liver-related symptoms (e.g., abdominal pain, jaundice, dark urine) as Nativa Complex® Menopause Support contains soybean.
- Advise patients to consult a healthcare provider or doctor prior to use if they have a cardiovascular disorder or are taking QT interval-prolonging medication (see 4.5) as Nativa Complex® Menopause Support contains Korean ginseng.
- Advise patients to consult a healthcare provider or doctor prior to use if they are taking anticoagulants or antiplatelet medication (see 4.5).
- Patients with blood pressure disorders should use this product with caution as dong quai and Korean ginseng can exhibit blood pressure raising or lowering effects.
- Patients with diabetes (or hypoglycaemia) should use this product with caution as Korean ginseng may lower blood glucose levels.
- Korean ginseng can result in false elevated digoxin levels on some serum assays.
- Advise patients to stop use and consult a healthcare provider or doctor if they experience delayed or absent menstruation or increased menstrual bleeding time.
- Patients, in particular postmenopausal women, should stop use and consult a healthcare provider or doctor if they experience breast pain, discomfort, soreness and/or tenderness, abnormal uterine bleeding including spotting and/or recurrence of menstruation.
- Patients experiencing the worsening of hot flashes and/or night sweats should stop use and consult a healthcare provider.
- Advise patients to discontinue use at least 2 weeks before elective surgery due to the influence of this product on bleeding time, blood sugar levels and blood pressure.
- Advise patients not to exceed the daily recommended dose.
- Advise patients to exercise caution with extended use.
- Advise patients taking other supplements not to exceed the nutrient reference values provided for vitamin D and E (see section 2. QUALITATIVE AND QUANTITATIVE COMPOSITION); due allowance should always be made for intake of vitamins and minerals from other sources.
- Advise patients not to use after the date of expiry.
- Products containing herbal ingredients may interact with some medication.

Porphyria

Safety has not been established.

4.5 Interaction with other medicinal products and other forms of interactions

No interaction studies have been performed on Nativa Complex® Menopause Support, see below interactions with individual ingredients.

Active ingredient	Medicine	Description
Korean ginseng	Antidiabetic medication	May lower blood glucose levels, increasing the risk of hypoglycaemia.
Korean ginseng, red clover, dong quai, vitamin B3 and vitamin E	Blood thinners (anticoagulant or anti-platelet medication) e.g., warfarin	May have a blood thinning effect, increasing the risk of bleeding.
Korean ginseng, red clover and soybean and dong quai	Hormone replacement therapy, oral contraceptives, thyroid medication	May interfere with therapy due to competition for oestrogen receptors; may increase the risk of venous thromboembolism; may lower thyroxine available in active form.
Korean ginseng	Immuno-suppressants	Korean ginseng might have immune system stimulating properties; concomitant use may interfere with immune-suppressive therapy.
Korean ginseng	Monamine oxidase inhibitors (MAOIs)	Concomitant use may increase sides effects of MAOIs.
Korean ginseng	QT interval-prolonging medication	Korean ginseng can have an additive effect with medication that prolong the QT interval, potentially increasing the risk of ventricular arrhythmias.
Korean ginseng	Stimulants (e.g., caffeine, ephedrine, pseudoephedrine)	Concomitant use might increase the risk of adverse stimulant effects.

4.6 Fertility, pregnancy and lactation

Pregnancy

Safety of most of the ingredients for use during pregnancy has not been established. Dong quai is specifically contraindicated, therefore this product should not be used in patients who are pregnant.

Breastfeeding

Safety of most of the ingredients for use during lactation (breastfeeding) has not been established. Dong quai is specifically contraindicated, therefore this product should not be used if patients are lactating (breastfeeding).

Fertility

There are no known effects of Nativa Complex® Menopause Support on fertility.

4.7 Effects on the ability to drive and use machines.

Based on the side effect profile, Nativa Complex® Menopause Support should not affect the ability to drive or operate machinery.

4.8 Undesirable effects

Nativa Complex® Menopause Support capsules are generally well tolerated with the occurrence of adverse events unknown. Patients experiencing any side effects or sensitivity to any of the ingredients, should discontinue use. Adverse reactions reported in the literature are listed below, by system organ class and frequency. Frequencies are defined as:

- very common (≥1/10)
- common (≥1/100 to <1/10)
- uncommon (≥1/1,000 to <1/100)
- rare (≥1/10,000 to <1/1,000)
- very rare (<1/10,000)
- not known (cannot be estimated from the available data).

System Organ Class	Frequency	Adverse Event
Immune system disorders	Not known	Hypersensitivity reactions or anaphylaxis, symptoms include: difficulty breathing or swallowing, angioedema, itchy throat, urticaria and itching.
Nervous system disorders	Not known	Insomnia, anxiety and headaches.
Gastrointestinal disorders	Not known	Abdominal cramps, constipation, diarrhoea, dyspepsia, heartburn, nausea and vomiting.
Reproductive system and breast disorders	Not known	Breast pain, discomfort and/or tenderness.

If symptoms persist, or if any adverse reactions occur, advise the patient to consult a healthcare provider.

Reporting of suspected adverse reactions

Reporting of suspected adverse reactions after authorisation of the medicinal product 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 "6JA Adverse Drug Reactions Reporting Form", found online under SAHPRA's publications: <https://www.sahpra.org.za/Publications/Index/8>.

4.9 Overdose

See 4.8 Undesirable effects

In overdose, side effects can be precipitated and/or be of increased severity. There is no evidence that this product can lead to an overdose when used as recommended.

Treatment

If an accidental overdose occurs, treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

D33.7 Complementary Medicine: Discipline Specific Traditional Claims – Combination Product

Pharmacotherapeutic classification: Vitamins and other combinations

ATC code: A11J0C

Panax ginseng (Korean ginseng)

Korean ginseng contains several active constituents including triterpenoid saponins, which are referred to collectively as ginsenosides or panaxosides. In animal models where ovaries have been removed, Korean ginseng extract increased serum ceruloplasmin oxidase activity (a measure of oestrogenic activity in the liver). In vitro research has shown that the constituent, ginsenoside-Rb1, acts as a phytoestrogen, possibly by binding and activating the oestrogen receptor. Korean ginseng, alone or in combination with other ingredients, seems to improve sexual arousal in postmenopausal females with sexual dysfunction. In clinical research, Korean ginseng has demonstrated anti-fatigue effects, speculated to be partially due to its antioxidant effects. Korean ginseng has shown to decrease serum reactive oxygen species and measurements of oxidation and increase antioxidant status.

Tribolium pratense (red clover)

Red clover contains isoflavones, also called phytoestrogens, which are structurally similar to oestrogens. It also contains flavonoids (apigenin, luteolin), biokinin A, flavanones, coumestrol, coumarin, glycitein, phenolic acids, saponins, and cyanogenic glycosides (lotaustrian and linamarin). Red clover also contains a volatile oil consisting of benzyl alcohol, 2-phenylethanol, ornats, acetates, methyl salicylate and methyl anthranilate. Red clover has shown affinity for both mu- and delta-opioid receptors which regulate temperature, mood and hormonal levels and actions which may explain the beneficial effect red clover has on menopausal symptoms. Red clover phytoestrogens also have affinity for oestradiol-alpha (found in the ovaries, breasts, uterus, and adrenal glands) and oestradiol-beta receptors (found in the vascular endothelium, brain, bone and heart), with preferential binding to oestrogen receptor-beta.

Soy isoflavones

Soy isoflavones are heterocyclic phenols with structural similarity to selective oestrogen-receptor modulators (SERMs) and oestradiol. As with red clover phytoestrogens, they have a higher affinity for the beta-oestrogen receptor. In postmenopausal women with low endogenous oestrogens, soy phytoestrogens have a weak oestrogenic effect. The beneficial effect of soy on menopausal symptoms such as hot flashes is speculated to be due to the constituent, genistein. Some other research suggests that the synergistic effect of the phytoestrogens and other constituents present in soy may be responsible for these effects.

Angelica sinensis (dong quai)

Dong quai contains several active constituents including angelic acid, ferulic acid, liguistilde, brefeldin A, succinic acid butylphthalide, nicotinic acid, angelica polysaccharide and phytosterols such as beta-sitosterol. Some clinical research shows that dong quai improves menopausal symptoms when used in combination with other constituents. Dong quai extract is speculated to competitively inhibit oestradiol from binding to oestrogen receptors and may induce transcription activity in oestrogen-responsive cells.

B Vitamins

The B vitamins have integral roles in cellular functioning, acting as co-enzymes in a vast array of catabolic and anabolic enzymatic reactions. Their combined effects are particularly prevalent to numerous aspects of brain function, including energy production, DNA/RNA synthesis/repair, genomic and non-genomic methylation, and the synthesis of numerous neurochemicals and signalling molecules. They prevent infections and helps support or promote many physiological processes including hormone and cholesterol production and cardiovascular health. During menopause, vitamin B supplementation requirements are increased. Deficiencies in B vitamins may contribute to adverse health outcomes in menopause and may increase the incidence of stroke, cognitive decline and lower bone mineral density.

Vitamin D3

The primary function of vitamin D is to regulate serum calcium and phosphorus concentrations. Vitamin D increases the efficiency of the intestinal absorption of calcium, primarily in the jejunum and duodenum, and phosphorus, particularly in the jejunum and ileum. The supplementation of low dose vitamin D (200 IU) has shown to improve the quality of life in symptomatic menopausal women, suggested to be due to its beneficial effects in preventing osteoporosis, cardiovascular disease, diabetes, cancer, infections and neurodegenerative diseases.

Vitamin E

Vitamin E functions as a chain-breaking antioxidant, thereby preventing the formation of free radicals and protecting cells from oxidative damage. In a placebo double blind-controlled trial, vitamin E supplementation (400 IU daily) significantly reduced the hot flashes severity score compared to the control.

5.2 Pharmacokinetic properties

Panax ginseng (Korean ginseng)

Absorption: After oral administration in humans, compound K, a constituent of Korean ginseng, was absorbed over 24 hours, with T_{max} occurring at 10,76 hours. The maximum concentration was 27,89 ng/ml and the area under the curve was 221,96 µg/h/ml.

Elimination: Limited information available.

Tribolium pratense (red clover)

Distribution: Metabolites of red clover isoflavones such as genistein, daidzein and equol have been detected in plasma, saliva, prostatic fluid and breast aspirate after oral intake. Metabolism: The isoflavones, formononetin and biochanin A, are demethylated in the liver and intestine by cytochrome P450 enzymes to daidzein and genistein, respectively. Daidzein is further broken down to form the oestrogenic metabolite, equol, and the less oestrogenic, O-desmethylangolensin (O-DMA).

Excretion: Red clover isoflavones and their metabolites are detected in the urine with excretion of the metabolites generally occurring within 24 hours after short-term administration. The half-life of daidzein and genistein is approximately 8 hours. With chronic administration of supplemental red clover isoflavones, the half-life is extended to 13 to 16 hours.

Soy isoflavones

Absorption: In the gastrointestinal tract, the soy isoflavones genistein and daidzein are hydrolysed by beta-glucosidases in the jejunum, releasing the isoflavone aglycone forms of genistein and daidzein which are absorbed from the human gut with about 85 % of soy isoflavones degraded in the intestines following ingestion.

Distribution: Genistein and daidzein are widely distributed in the body and undergo enterhepatic recycling with peak concentrations 4 to 8 hours after dietary intake, and excretion is within 24 hours.

Metabolism: Isoflavonoid glycosides are converted to hormone-like compounds by intestinal bacteria.

Elimination: Soy isoflavones are primarily excreted in the urine.

Angelica sinensis (dong quai)

Insufficient reliable information available.

Vitamins and minerals

The combination of vitamins and minerals is typical of the normal diet. Therefore, the pharmacological metabolism and fate of Nativa Complex® Menopause Support is anticipated to be similar.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Colloidal silicon dioxide
Magnesium stearate
Tapioca starch
Gelatine capsule (capsule constituents: bovine gelatine, colourants, titanium dioxide)

6.2 Incompatibilities

None known

6.3 Shelf life

24 months

6.4 Special precautions for storage

- Store in a dry place at or below 25 °C.
- Protect from light and moisture.
- Do not use after the expiry date printed on the carton.

6.5 Nature and contents of container

Nativa Complex® Menopause Support are light grey, hard gelatine capsules. Nativa Complex® Menopause Support capsules are available in a white, high density polyethylene container with a pink polypropylene flip-top cap. It contains 60 capsules and includes a patient information leaflet in a printed unit carton.

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Nativa (Pty) Ltd
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8. REGISTRATION NUMBER(S)

To be allocated

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

To be allocated

10. DATE OF REVISION OF THE TEXT

November 2022