

Side Effects

Tell your doctor or pharmacist as soon as possible if you do not feel well while you are using NATRAGEN®.

All medicines can have side effects in some people. Sometimes they are serious: most of the time they are not. Some side effects may need medical treatment.

Tell your doctor if you notice any of the following that are troublesome or ongoing:

- Skin irritation, for example rash or slight redness and itching of the skin where the cream has been applied. Any irritation will usually disappear within a few days. If it persists contact your doctor or pharmacist.
- Breast tenderness
- Bloating
- Headache or migraine
- Nausea, sickness, dizziness
- Palpitations (rapid beating of the heart)
- Breakthrough vaginal bleeding or spotting
- Weight gain
- Depression
- Fatigue
- Irritability
- Increased blood pressure
- Increased appetite
- Tinnitus (ringing of the ears)

Rarely reported events associated with oestrogen supplementation include:

- Increased incidence of blood clotting
- Changes to the tissue of the breast and endometrium (uterus)

Tell your doctor if you observe any other effects not listed above.

Do not be alarmed by this list of possible side effects. You most likely will not experience any of them. Check with your doctor or pharmacist if you have any questions with regards potential side effects.

If you use too much (overdose)

Because of the way NATRAGEN® is used, an unintentional overdose is unlikely.

If you think that you or anyone else may have used too much NATRAGEN®, immediately telephone your doctor or the Poisons Information Centre (telephone 13 11 26) for advice or go to the Accident and Emergency Department at your nearest hospital. Do this even if there are no signs of discomfort or poisoning.

If NATRAGEN® is accidentally swallowed or eaten contact a doctor.

After using NATRAGEN®

Storage

Keep the tube sealed until time for use.

Replace cap firmly on the tube once opened.

Do not transfer the cream out of the original tube into another container.

Keep the tube in a cool dry place where the temperature stays below 30°C.

Do not leave it in the car on a hot day or on window sills.

DO NOT FREEZE.

Once opened, the content of the tube should be used within 12 weeks.

Keep medicines out of reach of children.

Disposal

If your doctor tells you to stop using NATRAGEN® ask your pharmacist what to do with any cream that is left over.

Sponsor

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NATRAGEN® is a registered trademark.

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NATRAGEN® Cream

Oestradiol (es-tra-diol) 0.2% w/w cream



Consumer Medicine Information

Product description

What it looks like

NATRAGEN® cream is a white opaque odourless cream in a white laminated tube. The crimp at the base of the tube has the batch number and expiry date imprinted on it.

The tube is boxed and in the box is a consumer information sheet and plastic graduated applicator.

Ingredients

Each 50 gram tube contains 100 milligrams (100mg) of oestradiol. Each 2 unit (1 gram) dose delivers approximately 2mg of oestradiol.

Other ingredients in the cream include cetomacrogol 1000, cetostearyl alcohol, almond oil, macadamia nut oil, dl- α -tocopherol acetate (Vitamin E acetate), butylated hydroxytoluene, anhydrous citric acid, triethanolamine, Carbomer 940, B&J Phenonip, hydroxybenzoates, phenoxyethanol and purified water.

NATRAGEN® contains no animal products.

NATRAGEN® is available in a 50 gram sealed laminated tube.

What is in this leaflet?

This leaflet answers some of the common questions about NATRAGEN®. It does not contain all the available information. It does not take the place of talking to your doctor or pharmacist.

All medicines have risks and benefits. Your doctor has weighed the possible risks of you using NATRAGEN® against the benefits it can have for you.

If you have any concerns about using NATRAGEN® talk to your doctor or pharmacist.

Keep this leaflet with the medicine. You may need to read it again.

What NATRAGEN® is used for?

NATRAGEN® contains the active ingredient oestradiol.

Oestradiol is a naturally occurring hormone produced by the ovaries in women. It is one of a number of hormones classed as oestrogens. The amount of oestradiol produced throughout the menstrual cycle varies through the month. At the beginning of the cycle levels are low and build to a peak around day 12 and remain at an elevated level until day 26 of the cycle.

Levels fall dramatically if pregnancy does not result and the cycle starts over again.

Oestradiol is one of the three naturally occurring oestrogens the body makes – the others being oestrone and oestriol.

From puberty until old age oestrogens play a vital role in the female body.

Oestrogens control development and maintenance of the reproductive organs and breasts. Secondary sex characteristics including hair distribution, emotion, metabolism and fat distribution are controlled directly and indirectly by oestrogens.

Oestradiol is the most active oestrogen produced by the ovary.

Oestradiol production decreases with the menopause. This decline is frequently associated with hot flushes, night sweats and vaginal dryness. NATRAGEN® can relieve these symptoms.

Surgical removal of the ovaries and some forms of chemotherapy and/or radiotherapy will also result in menopausal symptoms.

The skin absorbs oestradiol and NATRAGEN® is a simple and effective means of getting oestradiol into the bloodstream.

Relief from symptoms will start within a few weeks of commencing NATRAGEN®. Best results are obtained after three months use.

If you have **not** had a hysterectomy your doctor will probably combine your treatment with another hormone called a progestogen. This will most likely be for 10-14 days.

Oestradiol for pharmaceutical purposes is manufactured in a laboratory from raw materials which include soya and wild yam. NATRAGEN®'s oestradiol is made through this same synthetic process with the end product being identical to the ovarian produced oestradiol and is termed 'natural' oestrogen.

Natural hormones including oestradiol are well absorbed from the gut, but are immediately broken down by the liver to make them clinically ineffective. For this reason tablets and capsules are not a good means of administration for naturally occurring hormones. Synthetic oestrogens are orally active, but do not always act identically to the natural hormones.

Prior to using NATRAGEN®

NATRAGEN® is only for use in women.

NATRAGEN® cream should not be used if you are allergic to oestradiol, NATRAGEN® or any of the ingredients contained within NATRAGEN®. These are listed at the top of this leaflet.

NATRAGEN® contains *almond oil* and *macadamia nut oil*.

Prior to using NATRAGEN® your doctor must be aware of any pre-existing medical conditions you may have.

It is important that your doctor knows of any history of cancer (especially cancer of the breast, ovary or uterus), endometriosis, heart disease or heart problems, thrombosis or blood clots, unexpected vaginal bleeding, liver disease, diabetes, high blood pressure, epilepsy or uterine fibroids.

NATRAGEN® may reduce the effectiveness of some medications such as oral hypoglycaemics (drugs that lower blood sugar), antihypertensives (drugs which lower blood pressure), anti-coagulants (drugs which "thin" the blood) or other hormone treatments.

Do not use NATRAGEN® if you are pregnant, thinking of becoming pregnant or breast feeding.

Breast Cancer: Before commencing on hormone therapy your doctor will undertake a full general and gynaecological examination. This will include an examination of your breasts. There is evidence indicating that hormone therapy is associated with a very small increase in the risk of developing breast cancer. While this risk is small and has only been associated with tableted forms of oestrogen it is important to be aware of this increased risk.

It is important that you discuss any concerns with your doctor.

Thrombosis (blood clots): Oestrogen use has been associated with a small increased risk of developing blood clots in the veins of the leg, lung or other parts of the body. Like breast cancer this risk is very small, but important to be aware of.

Risk factors that increase the likelihood of clots regardless of whether you use hormones or not include:

- being overweight
- a previous history of clots
- history of blood clots
- inability to move for long periods of time such as after major surgery or illness
- varicose veins
- systemic lupus erythematosus (SLE)
- increasing age

It is important that you discuss any concerns with your doctor.

Check with your doctor or pharmacist if you are unsure about whether you have any of these conditions before starting NATRAGEN®.

If you are taking other medications check with your doctor or pharmacist before starting NATRAGEN®.

Do not use NATRAGEN® after the expiry date which is printed on the base (crimp) of the tube.

If you use this medicine after the expiry date has passed, it may not work as well.

Do not use NATRAGEN® if the tamper proof seal at the top of the tube is damaged or broken. NATRAGEN® is not indicated for use in children.

How to use NATRAGEN®

Your doctor or pharmacist will explain how to apply NATRAGEN®.

Follow all directions exactly as they are explained. If you are unclear talk to your doctor.

The dose of NATRAGEN® will be determined for you by your doctor. This dose is specific to your condition and should not be varied unless directed to do so by your doctor. You will need to return to your doctor at regular intervals so that the dose can be checked to make sure it is right for you.

If you do not understand the instructions on the label, ask your doctor or pharmacist for help.

Opening the tube

To open the tube remove the cap and turn it upside down. Fit the triangle onto the top of the tube.

Twist to open. Dispose of the broken seal and replace the cap firmly after using the cream.

Measuring the correct dose of NATRAGEN® Cream

A small plastic applicator with one unit graduations is provided inside the NATRAGEN® box.

Your doctor will have determined what dose is appropriate for you.

The usual starting dose of NATRAGEN® is one or two units of cream applied once daily.

Squeeze the tube so that the prescribed dose of cream covers the applicators graduated guidelines.

Use immediately.

For example: if the dose required is 1 unit squeeze the NATRAGEN® tube so that 1 unit of cream is extruded on to the applicator. The principle is exactly the same as applying toothpaste to a toothbrush.

Each 1gram of NATRAGEN® cream provides 2mg of oestradiol. A 2 unit application of cream approximates to 2mg of oestradiol.

Where to apply NATRAGEN® cream

Always apply NATRAGEN® cream to clean dry flat areas of skin.

The area of application should be no more than two times the size of the hand (approximately 200cm²). Spreading over a larger area will dilute the efficacy of NATRAGEN®.

NATRAGEN® is generally used once daily. It is best to apply NATRAGEN® to the torso (abdomen) or the thigh as shown on the diagram.

Application of NATRAGEN® is usually once daily.

Check with your doctor or pharmacist if unsure of how much to use.

No perfume, deodorant or moisturising creams or gels should be used on the area because this may interfere with the absorption of NATRAGEN®.

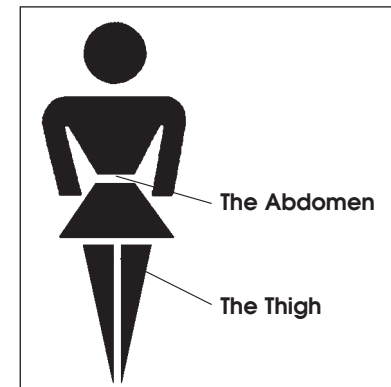
Never apply the cream to broken or damaged skin.

Do not use NATRAGEN® on the genital area.

NATRAGEN® cream should be applied at approximately the same time each day.

It is recommended that patients do not swim or shower until at least one hour after application of NATRAGEN® cream.

Close skin contact with the area of application within an hour of application by a partner should be avoided. This may result in the partner absorbing some oestradiol through the skin contact.



If you miss a dose

If you forget to apply your cream, you should apply it as soon as you remember provided this is within 12 hours of your usual time of application.

Otherwise do not apply the cream until the next application time. Missing a dose will not create an undue disruption to your treatment.

During NATRAGEN® use

Do's

Inform your doctor or pharmacist that you are using NATRAGEN® before starting any other prescribed medicine. Some medicines interact with other medications.

Tell all doctors, dentists and pharmacists who are treating you that you are using NATRAGEN®.

Have your breasts examined regularly by your doctor. A mammography (scan of the breast) should be conducted yearly.

Dont's

Do not give NATRAGEN® to anyone else, even if they have the same symptoms or condition as you.

Observe care when driving or operating machinery at the start of treatment using NATRAGEN® until you know how NATRAGEN® affects you. There is no evidence that NATRAGEN® will affect your ability to drive or to operate machinery.

Do not use NATRAGEN® if you are pregnant or planning on becoming pregnant in the near future. Women who are of reproductive age who may be prescribed NATRAGEN® are encouraged to use contraception prior to commencing use.

NATRAGEN® should not be used by lactating women.