FDA-Approved Patient Labeling
Divigel®
(estradiol gel) 0.1%

Read this PATIENT INFORMATION leaflet before you start using Divigel and read what you get each time you refill your Divigel prescription. There may be new information. This information does not take the place of talking to your healthcare provider about your menopausal symptoms or your treatment.

WHAT IS THE MOST IMPORTANT INFORMATION I SHOULD KNOW ABOUT Divigel (AN ESTROGEN HORMONE)?

- Using estrogen-alone increases your chance of getting cancer of the uterus (womb)
  Report any unusual vaginal bleeding right away while you are using Divigel. Vaginal bleeding after menopause may be a warning sign of cancer of the uterus (womb). Your healthcare provider should check any unusual vaginal bleeding to find out the cause.
- Do not use estrogen-alone to prevent heart disease, heart attacks, strokes or dementia (decline of brain function)
- Using estrogen-alone may increase your chances of getting strokes or blood clots
- Using estrogen-alone may increase your chance of getting dementia, based on a study of women 65 years of age or older
- Do not use estrogens with progestins to prevent heart disease, heart attacks, strokes or dementia
- Using estrogens with progestins may increase your chances of getting heart attacks, strokes, breast cancer, or blood clots
- Using estrogens with progestins may increase your chance of getting dementia, based on a study of women 65 years of age or older
- You and your healthcare provider should talk regularly about whether you still need treatment with Divigel

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What is Divigel?

Divigel is a medicine that contains the estrogen hormone estradiol, which is the same hormone made by a woman's ovaries. Divigel is a clear, colorless, smooth gel that is odorless when dry. When applied to the skin, estradiol is absorbed through the skin into the bloodstream.

What is Divigel used for?

Divigel is used after menopause to:

- **Reduce moderate to severe hot flashes**

Estrogens are hormones made by a woman's ovaries. The ovaries normally stop making estrogens when a woman is between 45 to 55 years old. This drop in body estrogen levels causes the "change of life" or menopause (the end of monthly menstrual periods). Sometimes, both ovaries are removed during an operation before natural menopause takes place. The sudden drop in estrogen levels causes "surgical menopause."

When the estrogen levels begin dropping, some women develop very uncomfortable symptoms, such as feelings of warmth in the face, neck, and chest, or sudden strong feelings of heat and sweating ("hot flashes" or "hot flushes"). In some women, the symptoms are mild, and they will not need estrogens. In other women, symptoms can be more severe. You and your healthcare provider should talk regularly about whether you still need treatment with Divigel.

Who should not use Divigel?

Do not start using Divigel if you:

- **Have unusual vaginal bleeding**
- **Currently have or have had certain cancers**
  Estrogens may increase the chances of getting certain types of cancers, including cancer of the breast or uterus. If you have or have had cancer, talk with your healthcare provider about whether you should use Divigel.
- **Had a stroke or heart attack**
- **Currently have or have had blood clots**
- **Currently have or have had liver problems**
- **Have been diagnosed with a bleeding disorder**
- **Are allergic to Divigel or any of its ingredients**
  See the list of ingredients in Divigel at the end of this leaflet.
- **Think you may be pregnant**

TELL YOUR HEALTHCARE PROVIDER:

- **If you have any unusual vaginal bleeding**
  Vaginal bleeding after menopause may be a warning sign of cancer of the uterus (womb). Your healthcare provider should check any vaginal bleeding to find out the cause.
- **About all of your medical problems**
  Your healthcare provider may need to check you more carefully if you have certain conditions, such as asthma (wheezing), epilepsy (seizures), diabetes, migraine; endometriosis, lupus, problems with your heart, liver, thyroid, kidneys, or have high calcium levels in your blood.
- **About all the medicines you take**
  This includes prescription and nonprescription medicines, vitamins, and herbal supplements. Some medicines may affect how Divigel works. Divigel may also affect how your other medicines work.
- **If you are going to have surgery or will be on bedrest**
  You may need to stop using Divigel.
- **If you are breastfeeding**
  The hormone in Divigel can pass into your breast milk.

How should I use Divigel?

- Divigel should be used once daily.
- Take the dose recommended by your healthcare provider and talk to him or her about how well that dose is working for you.
- Estrogens should be used at the lowest dose possible for your treatment and only as long as needed.

You and your healthcare provider should talk regularly (for example, every 3 to 6 months) about the dose you are taking and whether you still need treatment with Divigel.

How should Divigel be applied?

- Divigel should be applied once a day, around the same time each day
- Apply Divigel to clean, dry, and unbroken (without cuts or scrapes) skin. If you take a bath or shower, be sure to apply your Divigel after your skin is dry. The application site should be completely dry before dressing or swimming
- Apply Divigel to either your left or right upper thigh. Change between your left and right upper thigh each day to help prevent skin irritation

TO APPLY:

Step 1: Wash and dry your hands thoroughly.

Step 2: Sit in a comfortable position.

Step 3: Cut or tear the Divigel packet as shown in Figure A.

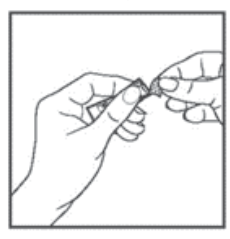

Figure A

Step 4: Using your thumb and index finger, squeeze the entire contents of the packet onto the skin of the upper thigh as shown in Figure B.

Figure B

Step 5: Gently spread the gel in a thin layer on your upper thigh over an area of about 5 by 7 inches, or two palm prints as shown in Figure C. It is not necessary to massage or rub in Divigel.

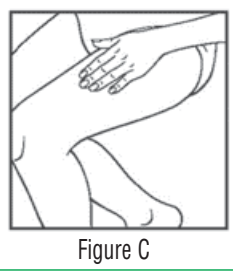

Figure C

Step 6: Allow the gel to dry completely before dressing.

Step 7: Dispose of the empty Divigel packet in the trash.

Step 8: Wash your hands with soap and water immediately after applying Divigel to remove any remaining gel and reduce the chance of transferring Divigel to other people.

Important things to remember when using Divigel

- **Wash your hands with soap and water after applying the gel to reduce the chance that the medicine will be spread from your hands to other people**
- Allow the gel to dry before dressing. Try to keep the area dry for as long as possible
- Do not allow others to come in contact with the area of skin where you applied the gel for at least one hour after you apply Divigel
- You should not allow others to apply the gel for you. However, if this is necessary, the individual should wear a disposable plastic glove to avoid direct contact with Divigel
- Do not apply Divigel to your face, breast, or irritated skin
- Never apply Divigel in or around the vagina
- **Divigel contains alcohol. Alcohol based gels are flammable. Avoid fire, flame or smoking until the gel has dried**

What should I do if I miss a dose?

If you miss a dose, do not double the dose on the next day to catch up. If your next dose is less than 12 hours away, it is best just to wait and apply your normal dose the next day. If it is more than 12 hours until the next dose, apply the dose you missed and resume your normal dosing the next day. Do not apply Divigel more than once each day. If you accidentally spill some of the contents of a Divigel packet, do not open a new packet. Wait and apply your normal dose the next day.

What should I do if someone else is exposed to Divigel?

Once you have applied Divigel, it has dried, and you have washed your hands, there is little risk of transfer to another person. If someone else is exposed to Divigel by direct contact with the wet gel, that person should wash the area of contact with soap and water as soon as possible. This is especially important for men and children. The longer the gel is in contact with the skin before washing, the chance is greater that the other person will absorb some of the estrogen hormone.

What should I do if I get Divigel in my eyes?

If you get Divigel in your eyes, flush your eyes right away with lukewarm tap water. If you have concerns, contact your healthcare provider.

What are the possible side effects of Divigel?

Side effects are grouped by how serious they are and how often they happen when you are treated.

Serious, but less common side effects include:

- Heart attack
- Stroke
- Blood clots
- Dementia
- Breast cancer
- Cancer of the lining of the uterus (womb)
- Cancer of the ovary
- High blood pressure
- High blood sugar
- Gallbladder disease
- Liver problems
- Enlargement of benign tumors of the uterus (“fibroids”)

Call your healthcare provider right away if you get any of the following warning signs or any other unusual symptoms that concern you:

- New breast lumps
- Unusual vaginal bleeding
- Changes in vision or speech
- Sudden new severe headaches
- Severe pains in your chest or legs with or without shortness of breath, weakness and fatigue

Less serious, but common, side effects include:

- Headache
- Breast pain
- Irregular vaginal bleeding or spotting
- Stomach or abdominal cramps, bloating
- Nausea and vomiting
- Hair loss
- Fluid retention
- Vaginal yeast infection

These are not all the possible side effects of Divigel. For more information, ask your healthcare provider or pharmacist for advice about side effects. You may report side effects to **Vertical Pharmaceuticals, LLC** at **1-877-95-VERTI (1-877-958-3784) or to FDA at 1-800-FDA-1088**.

What can I do to lower my chances of a serious side effect with Divigel?

- Talk with your healthcare provider regularly about whether you should continue using Divigel.
- If you have a uterus, talk to your healthcare provider about whether the addition of a progestin is right for you.

  The addition of a progestin is generally recommended for a woman with a uterus to reduce the chance of getting cancer of the uterus. See your healthcare provider right away if you get vaginal bleeding while using Divigel.
- Have a pelvic exam, breast exam and mammogram (breast X-ray) every year unless your healthcare provider tells you something else.

  If members of your family have had breast cancer or if you have ever had breast lumps or an abnormal mammogram, you may need to have breast exams more often.
- If you have high blood pressure, high cholesterol (fat in the blood), diabetes, are overweight, or if you use tobacco, you may have higher chances of getting heart disease.

  Ask your healthcare provider for ways to lower your chances of getting heart disease.

General information about safe and effective use of Divigel

Medicines are sometimes prescribed for conditions that are not mentioned in patient information leaflets. Do not use Divigel for conditions for which it was not prescribed. Do not give Divigel to other people, even if they have the same symptoms you have. It may harm them.

Keep Divigel out of the reach of children.

This leaflet provides a summary of the most important information about Divigel. If you would like more information, talk with your healthcare provider or pharmacist. You can ask for information about Divigel that is written for health professionals. You can get more information by calling the toll free number Customer Service: 1-866-600-4799.

What are the ingredients in Divigel?

The active ingredient in Divigel is estradiol.

The inactive ingredients are carbomer, ethanol, propylene glycol, purified water, and triethanolamine.

How is Divigel Supplied?

Divigel is supplied in individual foil packets, each one containing a single day’s dose.

Store Divigel packets at 20 to 25°C (68 to 77°F). Excursions permitted to 15 to 30°C (59 to 86°F). [See USP Controlled Room Temperature.]

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Patient Information: 10 pt.

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Black