**PRODUCT INFORMATION**

**NUVA-RING**

**[ethinyl estradiol]®**

**Pharmacology**

Ethinyl estradiol is a progestogen used as a component of contraceptive regimens. It is absorbed through the vaginal mucosa and is conjugated in the liver. The main metabolites are 16α-hydroxy-estrone and 16α-hydroxy-estradiol, which are excreted in the urine. Bioavailability of ethinyl estradiol after vaginal administration is approximately 55.6%.

**Bioavailability**

<table>
<thead>
<tr>
<th>Product</th>
<th>Mean (SD)</th>
<th>Median (SD)</th>
<th>Mean (SD)</th>
<th>Median (SD)</th>
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</thead>
<tbody>
<tr>
<td>Ethinyl Estradiol</td>
<td>34.7 (17.5)</td>
<td>59.3 (67.5)</td>
<td>44.7 (28.8)</td>
<td>34.8 (11.6)</td>
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</tbody>
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**Pharmacokinetics**

The pharmacokinetics of NuvaRing have not been studied in detail. However, it is known that ethinyl estradiol is rapidly absorbed from the vaginal mucosa and is conjugated in the liver. The main metabolites are 16α-hydroxy-estrone and 16α-hydroxy-estradiol, which are excreted in the urine.

**Clinical Considerations**

- **Contraceptive Effect:** NuvaRing provides a reliable method of contraception. Like oral contraceptives, NuvaRing is consistently and correctly used. The percentage who experience an accidental pregnancy during the first year if used properly is less than 1%.

**Contraindications**

- **Hypersensitivity**
- **Liver Disease**
- **Coronary Artery Disease**
- **Thromboembolism**
- **Hepatic Neoplasia**
- **Obesity**
- **Type 2 Diabetes**
- **Liver Tumors**
- **Hepatic Adenomas**
- **Severe Anemia**

**Warnings**

- **Increased Risk of Vascular Disease**
- **Cerebrovascular Events**
- **Cardiovascular Events**
- **Hepatitis**
- **Cholestasis**
- **Malignancy**

**Precautions**

- **Infection**
- **Sexually Transmitted Diseases**
- **Tuberculosis**
- **Cancer**
- **Hypertension**
- **Hyperlipidemia**
- **Obesity**
- **Diabetes**

**Special Considerations**

- **Weight Loss**
- **Osteoporosis**
- **Depression**
- **Migraine**
- **Premenstrual Syndrome**

**Interactions**

- **Drugs Metabolized by CYP450**
- **Drugs Active in Breast Milk**
- **Anticonvulsants**
- **Anticoagulants**

**Additional Information**

- **Teratogenesis**
- **Transaminase Elevations**
- **Osteoporosis**
- **Cholestasis**

**Pharmacokinetics**

- **Bioavailability:** The bioavailability of ethinyl estradiol after vaginal administration is approximately 55.6%.

**Dosage and Administration**

- **NuvaRing®**: The NuvaRing® is a flexible ring made of polyethylene that is inserted into the vagina once a month. It provides a continuous source of ethinyl estradiol for up to 3 weeks. The ring is typically inserted on the first day of the menstrual cycle or on the first day of a breakthrough bleed. To ensure consistent and effective contraception, the ring should be replaced at the same time and day of the week each month.

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How do I insert NuvaRing®?

1. Clench your right fist and place the ring between your thumb and index finger (Figure 2a) and press the sides together.

2. Use your left thumb and index finger to pinch the ring at the fold (Figure 2b).

3. Gently push the folded ring into your vagina (Figures 3a, 3b, and 3c). The exact position of the ring is not critical. However, it is important that the ring is in the vagina, and not in your rectum. If you are not sure the ring is in your vagina, it may have slipped into your rectum. Check the position of the ring by pushing gently on its fold with your index finger. If the ring is in your rectum, gently push it back into the vagina (Figures 2c and 2d).

4. NuvaRing® is placed three times a year: once during the first week of the woman’s menstrual period, once about 10:00 PM, after the one-week break you should insert a new ring on a Sunday at about 10:00 PM, and at that time you should remove the first NuvaRing® and insert a new one.

When can I start using NuvaRing®?

• an allergic reaction to any of the components of NuvaRing®

• disease of the heart valves with complications

• yellowing of the whites of the eyes or of the skin (jaundice) during pregnancy or after delivery

• diabetes with complications of the kidneys, eyes, nerves, or blood vessels

• anemia

• an infection of the uterus or fallopian tubes

• a history of frequent miscarriages or stillbirths

• a history of blood clots in your legs or arms

• an allergic reaction to female hormones

If you are pregnant or breast feeding, do not use NuvaRing®. If you become pregnant while using NuvaRing® or if you breast feed, stop using NuvaRing®. If you think you may be pregnant, talk to your healthcare provider right away.

Precautions

• you are allergic to any of the components of NuvaRing®

• you have had a blood clot in your legs or arms

• you have had a blood clot in your lungs

• you have had a stroke

• you have had a heart attack

• you have ever had breast cancer

• you have ever had a severe allergic reaction to any medication

• you have a history of blood clots

• you have a history of blood vessel disease

• you are immunocompromised

If you have any of the conditions listed above, talk to your healthcare provider before using NuvaRing®.

Use of NuvaRing® with other contraceptives

If you use NuvaRing® with other contraceptives, such as backup methods, talk to your healthcare provider about how to use them together.

Who should not use NuvaRing®?

• you have had a blood clot in your legs or arms

• you have had a blood clot in your lungs

• you have had a stroke

• you have had a heart attack

• you have ever had breast cancer

• you have ever had a severe allergic reaction to any medication

• you have a history of blood clots

• you have a history of blood vessel disease

• you are immunocompromised

If you have any of the conditions listed above, talk to your healthcare provider before using NuvaRing®.

If you are pregnant or breast feeding, do not use NuvaRing®. If you become pregnant while using NuvaRing® or if you breast feed, stop using NuvaRing®. If you think you may be pregnant, talk to your healthcare provider right away.

How long can I use NuvaRing®?

NuvaRing® is a hormonal contraceptive. It should be used for no more than 3 years, such as 1 year for the first year, 1 year for the second year, and 1 year for the third year. If you continue to use NuvaRing® after 3 years, talk to your healthcare provider.

When should I start NuvaRing®?

NuvaRing® is used during the second half of a woman’s menstrual cycle. If you start using NuvaRing® during the first week of your menstrual period, you must use an extra method of birth control, such as male condoms or spermicide, for the first seven days after starting NuvaRing®. If you start using NuvaRing® during the second week of your menstrual period, you must use an extra method of birth control, such as male condoms or spermicide, for the first three days after starting NuvaRing®. If you start using NuvaRing® during the third week of your menstrual period, you must use an extra method of birth control, such as male condoms or spermicide, for the first two days after starting NuvaRing®. If you start using NuvaRing® during the fourth week of your menstrual period, you must use an extra method of birth control, such as male condoms or spermicide, for the first day after starting NuvaRing®.

If you start using NuvaRing® during the sixth week of your menstrual period, you must use an extra method of birth control, such as male condoms or spermicide, for the first two weeks after starting NuvaRing®.

If you start using NuvaRing® during the eighth week of your menstrual period, you must use an extra method of birth control, such as male condoms or spermicide, for the first four weeks after starting NuvaRing®.

If you start using NuvaRing® during the tenth week of your menstrual period, you must use an extra method of birth control, such as male condoms or spermicide, for the first five weeks after starting NuvaRing®.

If you start using NuvaRing® during the twelfth week of your menstrual period, you must use an extra method of birth control, such as male condoms or spermicide, for the first six weeks after starting NuvaRing®.

If you start using NuvaRing® during the fourteenth week of your menstrual period, you must use an extra method of birth control, such as male condoms or spermicide, for the first seven weeks after starting NuvaRing®.

If you start using NuvaRing® during the sixteenth week of your menstrual period, you must use an extra method of birth control, such as male condoms or spermicide, for the first eight weeks after starting NuvaRing®.

If you start using NuvaRing® during the eighteenth week of your menstrual period, you must use an extra method of birth control, such as male condoms or spermicide, for the first nine weeks after starting NuvaRing®.

If you start using NuvaRing® during the twentieth week of your menstrual period, you must use an extra method of birth control, such as male condoms or spermicide, for the first ten weeks after starting NuvaRing®.

If you start using NuvaRing® during the twenty-second week of your menstrual period, you must use an extra method of birth control, such as male condoms or spermicide, for the first eleven weeks after starting NuvaRing®.

If you start using NuvaRing® during the twenty-fourth week of your menstrual period, you must use an extra method of birth control, such as male condoms or spermicide, for the first twelve weeks after starting NuvaRing®.

If you start using NuvaRing® during the twenty-sixth week of your menstrual period, you must use an extra method of birth control, such as male condoms or spermicide, for the first thirteen weeks after starting NuvaRing®.

If you start using NuvaRing® during the twenty-eighth week of your menstrual period, you must use an extra method of birth control, such as male condoms or spermicide, for the first fourteen weeks after starting NuvaRing®.

If you start using NuvaRing® during the thirty-week week of your menstrual period, you must use an extra method of birth control, such as male condoms or spermicide, for the first fifteen weeks after starting NuvaRing®.

If you start using NuvaRing® during the thirty-two week week of your menstrual period, you must use an extra method of birth control, such as male condoms or spermicide, for the first sixteen weeks after starting NuvaRing®.

If you start using NuvaRing® during the thirty-four week week of your menstrual period, you must use an extra method of birth control, such as male condoms or spermicide, for the first seventeen weeks after starting NuvaRing®.

If you start using NuvaRing® during the thirty-six week week of your menstrual period, you must use an extra method of birth control, such as male condoms or spermicide, for the first eighteen weeks after starting NuvaRing®.

If you start using NuvaRing® during the thirty-eight week week of your menstrual period, you must use an extra method of birth control, such as male condoms or spermicide, for the first nineteen weeks after starting NuvaRing®.

If you start using NuvaRing® during the forty-week week of your menstrual period, you must use an extra method of birth control, such as male condoms or spermicide, for the first twenty weeks after starting NuvaRing®.

If you start using NuvaRing® during the forty-two week week of your menstrual period, you must use an extra method of birth control, such as male condoms or spermicide, for the first twenty-one weeks after starting NuvaRing®.

If you start using NuvaRing® during the forty-four week week of your menstrual period, you must use an extra method of birth control, such as male condoms or spermicide, for the first twenty-two weeks after starting NuvaRing®.

If you start using NuvaRing® during the forty-six week week of your menstrual period, you must use an extra method of birth control, such as male condoms or spermicide, for the first twenty-three weeks after starting NuvaRing®.

If you start using NuvaRing® during the forty-eight week week of your menstrual period, you must use an extra method of birth control, such as male condoms or spermicide, for the first twenty-four weeks after starting NuvaRing®.

If you start using NuvaRing® during the fifty-week week of your menstrual period, you must use an extra method of birth control, such as male condoms or spermicide, for the first twenty-five weeks after starting NuvaRing®.

If you start using NuvaRing® during the fifty-two week week of your menstrual period, you must use an extra method of birth control, such as male condoms or spermicide, for the first twenty-six weeks after starting NuvaRing®.

If you start using NuvaRing® during the fifty-four week week of your menstrual period, you must use an extra method of birth control, such as male condoms or spermicide, for the first twenty-seven weeks after starting NuvaRing®.

If you start using NuvaRing® during the fifty-six week week of your menstrual period, you must use an extra method of birth control, such as male condoms or spermicide, for the first twenty-eight weeks after starting NuvaRing®.

If you start using NuvaRing® during the fifty-eight week week of your menstrual period, you must use an extra method of birth control, such as male condoms or spermicide, for the first twenty-nine weeks after starting NuvaRing®.

If you start using NuvaRing® during the sixty-week week of your menstrual period, you must use an extra method of birth control, such as male condoms or spermicide, for the first thirty weeks after starting NuvaRing®.

If you start using NuvaRing® during the sixty-two week week of your menstrual period, you must use an extra method of birth control, such as male condoms or spermicide, for the first thirty-one weeks after starting NuvaRing®.

If you start using NuvaRing® during the sixty-four week week of your menstrual period, you must use an extra method of birth control, such as male condoms or spermicide, for the first thirty-two weeks after starting NuvaRing®.

If you start using NuvaRing® during the sixty-six week week of your menstrual period, you must use an extra method of birth control, such as male condoms or spermicide, for the first thirty-three weeks after starting NuvaRing®.

If you start using NuvaRing® during the sixty-eight week week of your menstrual period, you must use an extra method of birth control, such as male condoms or spermicide, for the first thirty-four weeks after starting NuvaRing®.

If you start using NuvaRing® during the seventy-week week of your menstrual period, you must use an extra method of birth control, such as male condoms or spermicide, for the first thirty-five weeks after starting NuvaRing®.

If you start using NuvaRing® during the seventy-two week week of your menstrual period, you must use an extra method of birth control, such as male condoms or spermicide, for the first thirty-six weeks after starting NuvaRing®.

If you start using NuvaRing® during the seventy-four week week of your menstrual period, you must use an extra method of birth control, such as male condoms or spermicide, for the first thirty-seven weeks after starting NuvaRing®.