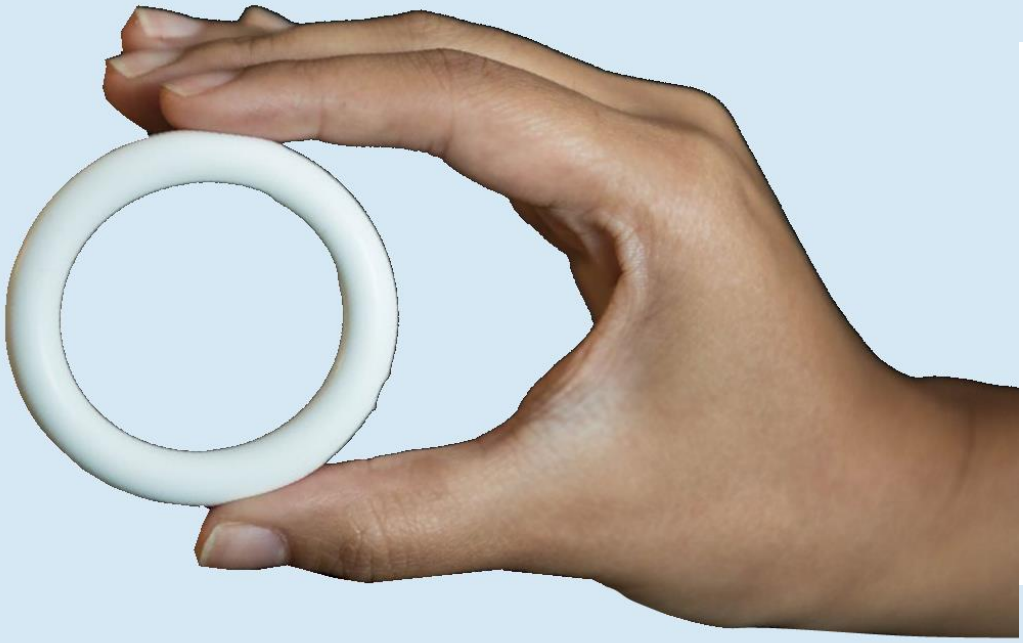
Annovera (segesterone acetate, ethinyl estradiol)



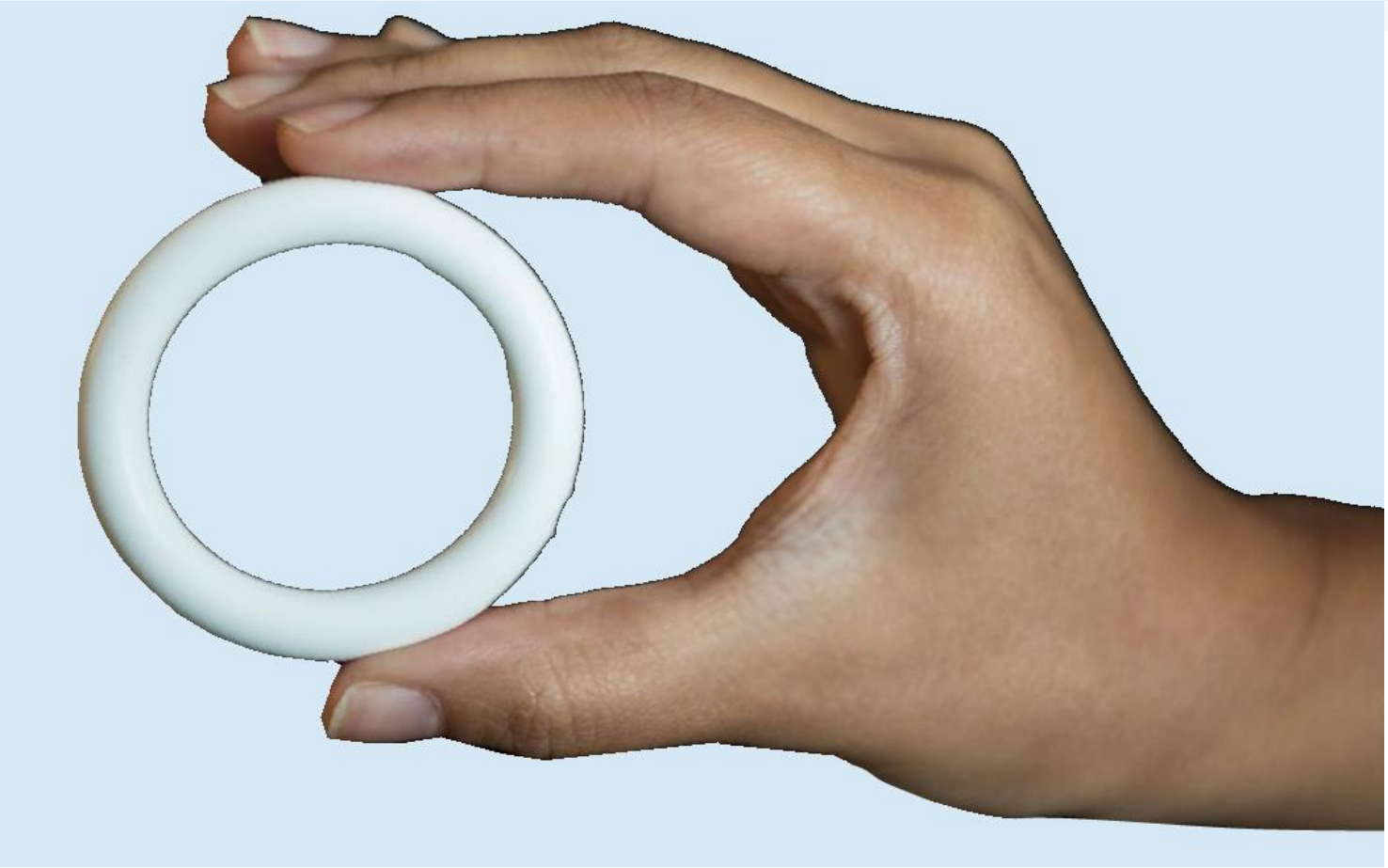
NEW PRODUCT SLIDESHOW

MPR

Introduction

- **Brand name:** Annovera
- **Generic name:** Segesterone acetate, ethinyl estradiol
- **Pharmacological class:** Progestin + estrogen
- **Strength and Formulation:** 103mg/17.4mg; vaginal ring system
- **Manufacturer:** TherapeuticsMD, Inc.
- **How supplied:** Vaginal system—1
- **Legal Classification:** Rx

Annovera



Indication

- Prevention of pregnancy for up to 1 year (13 cycles)

Limitation of Use

- Annovera has not been adequately studied in females with a BMI >29kg/m^2

Dosage & Administration

- **Insert vaginally** as directed; vaginal system should remain in the vagina continuously for 21 days (3 complete weeks), then removed for 1 week (during this time a withdrawal bleed usually occurs)
- The day and time of insertion should be noted so that the vaginal system can be removed 3 weeks later on the same day and at about the same time
- The removed vaginal system should be cleaned with mild soap and warm water, patted dry with a clean cloth towel or paper towel, and placed in its case during the 1-week dose-free interval; it should be cleaned again prior to reinsertion
- Repeat cycle for **up to 13 cycles**

Dosage & Administration

How to Start Annovera (see labeling for full description)

- **No hormonal contraceptive use in the preceding cycle and after copper IUD removal:** insert between days 2 and 5 of regular menstrual bleeding
- **Switching from combination hormonal contraceptives (CHC):** may switch on any day of the CHC cycle (Day 1-28)
- **Switching from progestin-only method:**
  - Pills: begin at the time scheduled to take next pill
  - Injection: begin at the time next scheduled for injection
  - Implant or IUS: begin at the time of removal

Dosage & Administration

How to Start Annovera (see labeling for full description)

- **Use after abortion or miscarriage:** may be initiated within the first 5 days following complete first trimester abortion or miscarriage; if more than 5 days have elapsed follow instructions for “No hormonal contraceptive use in the preceding cycle”
  - Should not be started earlier than 4 weeks after second trimester abortion or miscarriage due to increased risk of thromboembolism
- **Following childbirth:** should not be started sooner than 4 weeks postpartum and only in females who choose not to breastfeed
  - Females who are breastfeeding should not use Annovera until after weaning

Dosage & Administration

Deviations from Recommended Regimen (see labeling for full description)

- **Inadvertent removal or expulsion:** if expelled once during the 21 days and is replaced within 2 hours, efficacy should not be reduced; if out of the vagina for >2 hours, back-up contraception necessary until system has been in the vagina for 7 consecutive days
- **Prolonged vaginal system free interval:** consider possibility of pregnancy and use back-up contraception until system has been in vagina for 7 consecutive days
- **Prolonged use of Annovera:** if left in vagina for >21 days, remove for 7 days, then reinsert for 21 days to resume 21/7 schedule

Considerations for Special Populations

- **Pregnancy:** discontinue if occurs
- **Nursing mothers**: use another contraceptive method until breastfeeding discontinued
- **Pediatric**: use before menarche is not indicated
- **Geriatric:** not indicated
- **Renal impairment**: not recommended
- **Hepatic impairment**: steroid hormones may be poorly metabolized in patients with impairment; may necessitate discontinuation until liver function returns to normal

Contraindications

- High risk of **arterial or venous thrombotic disease** (eg, smokers or migraineurs over age 35, history of DVT or thromboembolism, cerebrovascular or coronary artery disease, thrombogenic valvular disease, atrial fibrillation, subacute bacterial endocarditis, hypercoagulopathies, uncontrolled hypertension, diabetes with hypertension or vascular disease, headaches with focal neurologic symptoms)
- Breast or other estrogen or progestin-sensitive cancer
- Undiagnosed abnormal uterine bleeding
- Liver tumors, acute hepatitis or severe cirrhosis
- Concomitant ombitasvir/paritaprevir/ritonavir, with or without dasabuvir

Boxed Warning

- **Cigarette smoking** increases risk of serious cardiovascular events
- Females >35 years old who smoke should not use Annovera

Warnings/Precautions

- Evaluate for **history of thrombotic or thromboembolic disorders** prior to initiation
- Increased risk of cardiovascular events (eg, stroke, MI) esp. in smokers, females (>35yrs of age)
- Discontinue if thrombotic event, unexplained visual changes, or jaundice occurs, and at least 4 weeks before through 2 weeks after surgery associated with increased risk of thromboembolism, and during prolonged immobilization

Warnings/Precautions

- Gallbladder disease
- Diabetes
- Prediabetes
- Uncontrolled dyslipidemias; consider alternative therapy
- Obesity
- Hypertriglyceridemia
- Pregnancy-related cholestasis
- Depression

Warnings/Precautions

- Evaluate if significant changes in headaches (consider discontinuation), irregular uterine bleeding, amenorrhea
- Monitor BP routinely; discontinue if significant increase
- Hereditary angioedema
- History of chloasma gravidarum; avoid sun or UV radiation exposure

Interactions

- See Contraindications
- **ALT elevations** with HCV regimen ombitasvir/paritaprevir/ritonavir, with or without dasabuvir; discontinue Annovera prior to starting HCV regimen and restart 2 weeks after completion
- May be **antagonized by CYP3A4** or other enzyme inducers (eg, aprepitant, barbiturates, bosentan, carbamazepine, efavirenz, felbamate, griseofulvin, oxcarbazepine, phenytoin, rifampin, rifabutin, rufinamide, topiramate, St. John’s wort); use an alternative method or a backup contraception

Interactions

- May be **potentiated by** atorvastatin, rosuvastatin, acetaminophen, ascorbic acid, itraconazole, voriconazole, fluconazole, ketoconazole, grapefruit juice, vaginal miconazole (oil-based)
- May be **affected by** HIV/HCV protease inhibitors, NNRTIs
- **May antagonize** lamotrigine, acetaminophen, morphine, salicylic acid, temazepam

Interactions

- **May potentiate** cyclosporine, prednisolone, theophylline, tizanidine, voriconazole
- May need **dose adjustment** of thyroid hormones
- May **affect lab tests** (eg, coagulation factors, lipids, glucose tolerance, binding proteins)
- **Avoid** concurrent oil-based vaginal lubricants, suppositories

Adverse Reactions

- **Most common (≥5%)**: headache/migraine, nausea/vomiting, vulvovaginal mycotic infection/candidiasis, abdominal pain lower/upper, dysmenorrhea, vaginal discharge, urinary tract infection, breast tenderness/pain/discomfort, bleeding irregularities including metrorrhagia, diarrhea, genital pruritus

- **Others:** toxic shock syndrome, cholasma, serious CV events, liver disease, VTEs, psychiatric events, hypersensitivity, spontaneous abortions

Mechanism of Action

- Annovera is a toroidal-shaped (ring), nonbiodegradable, flexible, opaque white vaginal system containing 2 active components, a progestin, segesterone acetate, and an estrogen, ethinyl estradiol
- When placed in the vagina, each Annovera releases an approximate average 0.15mg/day of segesterone acetate and 0.013mg/day of ethinyl estradiol over the 21 days in-use period of each cycle for up to 13 cycles (total of 273 days)
- The product lowers the risk of becoming pregnant primarily by suppressing ovulation

Clinical Trials

- The efficacy of Annovera was evaluated in two 1-year multicenter trials enrolling 2265 females, age 18–40 years, who were healthy and sexually active with regular menstrual cycles
- Mean age was 26.7 years and the mean BMI was 24.1 (16.0, 41.5) kg/m^2
- Based on pooled data from the 2 trials, 2111 females ≤35 years of age completed 17,427 evaluable 28-day cycles (cycles in which no back-up contraception was used)

Clinical Trials

- The pooled pregnancy rate, evaluated by the Pearl Index (PI), was 2.98 (95% [CI: 2.13, 4.06]) per 100 woman-years of Annovera use

- Return to fertility was assessed in 290 of the patients in the 2 trials who either desired pregnancy or switched to a nonhormonal method after the trials, and all 290 patients reported a return to fertility during the 6-month follow-up period (defined as a return of menses or pregnancy)

New Product Monograph

- For more information view the product monograph available at:

  https://www.empr.com/drug/annovera/