Segmented Intravaginal Rings: Opportunities for Multiple Indications

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Daré Segmented Intravaginal Rings

• Originally developed by Bob Langer (MIT) and Bill Crowley (MGH) to deliver one or more drugs in the vagina over extended periods of time
• Two or more segments in the ring are composed in ethylene vinylacetate (EVA) copolymers
• Drug is dispersed homogeneously in the polymer matrix and released primarily by diffusion
• Development of IVRs at Daré is focused on the sustained release of bioidentical estradiol (E₂) and/or bioidentical progesterone (P)
• These IVRs are capable of drug release for two or four weeks depending on target indication
E₂/P IVRs

- Designed to release E₂ at rates ranging from 80 to 160 µg/d and P at rate from 4 to 8 mg/d
E₂/P IVRs

In Vitro Release of E₂ and P from 160/4 E₂/P and 160/8 E₂/P IVRs¹

E₂/P IVRs

In Vivo Pharmacokinetics of E₂ from 160/4 and 160/8 E₂/P IVRs in Ovariectomized Female Sheep

P IVRs

In Vitro Release of P and Pharmacokinetics from 4, 8, and 12 mg/d P IVRs

E₂/P IVRs: Target Indications

• Treatment of moderate to severe vasomotor symptoms associated with menopause
  • Vasomotor symptoms are commonly known as hot flushes or hot flashes
  • Generally defined clinically as mild, moderate (sensation of heat with sweating, able to continue activity), and severe (sensation of heat with sweating, causing cessation of activity)
  • Commonly treated with E₂ or E₂ with P

• Treatment of moderate to severe symptoms of vulvar and vaginal atrophy associated with menopause
  • Vaginal dryness (none, mild, moderate, or severe)
  • Vaginal and/or vulvar irritation/itching
  • Dysuria (none, mild, moderate or severe)
  • Vaginal pain associated with sexual activity (none, mild, moderate, or severe)
  • Vaginal bleeding associated with sexual activity (presence vs. absence)
P IVRs: Target Indications

- Prevention of preterm birth (PTB) in singleton pregnancies in women with a prior PTB or a women with a short cervix (<25 mm)
  - One product approved for PTB (Makena®, AMAG Pharmaceuticals), a once-weekly injection of 17α-hydroxyprogesterone caproate
  - Not indicated for women with a short cervix
  - Generic
  - Progesterone (vaginal or systemic) used off label

- Luteal phase support during advanced reproductive technology cycles
  - Vaginal progesterone (Endometrin®, Ferring Pharmaceuticals) is used to enhance clinical pregnancy and successful deliveries
  - Other progesterone products are administered vaginally (Prometrium®, Solvay Pharmaceuticals and Crinone®, Allergan USA, Inc.) but use is off-label
  - Progesterone is also administered i.m. (off-label)

References: