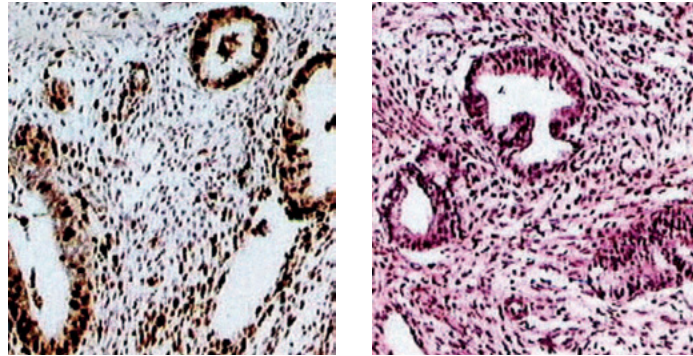


Pentravan[®]

Pentravan[®] in fertility

- Preliminary study conducted in 10 women following a IVF-ET process with estradiol 3 mg/ml in Pentravan[®] intravaginal administration, showed increased endometrial proliferation by 20% in 10 days and 60-70% in 20 days^a
- Estradiol and progesterone are administered with Pentravan[®] before the embryo transfer. Maintenance of 3 months in case of gestation



Proliferative endometrium after the use of estradiol (3mg/ml) in Pentravan[®] with intravaginal administration

Formulations

Rx/

Endometrial preparation

Estradiol 3 mg
in Pentravan[®] c.s.p. 1 g
Apply 1 g/day intravaginally.*
(BUD 3 months)

Rx/

Pre-transfer and maintenance

Estradiol 3 mg
Progesterone 300 mg
in Pentravan[®] c.s.p. 1 g
Apply 1 g/12 hours during days prior to embryo transfer** and for a 3 months period in case of gestation.*
Treatment for half a month
(BUD 3 months)

* For application 1 time/day the total amount to be prepared for monthly treatment is 40 g (5 dose applicators) due to compounding losses.
** For application 2 times/day the total amount to be prepared for half month treatment is 40 g (5 dose applicators) due to compounding losses.

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2. Maia H Jr, Haddad C, dos Santos Junior WSD, Pinheiro N, Silva Santos A and Coutinho A. Clinical Experience with Vaginal Gestrinone in Pentravan[®] in the Treatment of Endometriosis Pain. *Austin J Reprod Med Infertil*. 2015; 2(4): 1021.
3. Maia H Jr, Haddad C, Moura Hirsch MCD, Saback W, Casoy J (2014) Treatment of Refractory Endometriosis-Related Pain with Vaginal Gestrinone in Pentravan Associated with Pinus Pinaster Extract and Resveratrol: A Preliminary Study. *Gynecol/Obstet (Sunnyvale)* 4: 246. doi:10.4172/2161-0932.1000246
4. Hugo Maia Jr., Clarice Haddad, Wilson Saback Jr. Combined treatment of gestrinone with histone deacetylase inhibitors for the treatment of deep endometriosis-associated pain. Symposium SEUD congress 2017.
5. Keia Hobbs, MD Lara Handler, MSLS. Which treatments help women with reduced libido? *J Fam Pract*. 2013 February;62(2):102-103.
6. H. Maia Jr., C. Haddad, R. Maia, C.E. França and J. Casoy. Pulsatile administration of testosterone by the vaginal route using Pentravan[®]. November 8-11, 2012 Lisbon, Portugal.
7. Hugo Maia Jr. Vaginal administration of testosterone in Pentravan[®] and its effect on inflammatory and metabolic parameters in menopausal women with sexual dysfunction. International Conference on Women's Health, Gynecology & Obstetrics. July 08-10, 2014. DoubleTree by Hilton Hotel Chicago-North Shore Conference Center, USA.
8. Preliminary study.

Pentravan[®]

Pentravan[®], customized solutions for each patient

- Vehicle of high penetration
- Prevents first pass effect and RA saturation
- Direct effect in action point
- Proved effectiveness based on clinical studies

- **Endometriosis**
- **Menopause**
- **Fertility**



FagronLab™ jar 20 ml, 50 ml



Dose applicator 8 ml

Fagron Hellas
12 km N.R. Trikala - Larisa
P.C. 42100, P.O. Box 32
Trikala, Greece

T +30 24310 83633-5
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Pentravan[®]

High penetration through
vaginal mucosa



Essentials

Fagron
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medicine

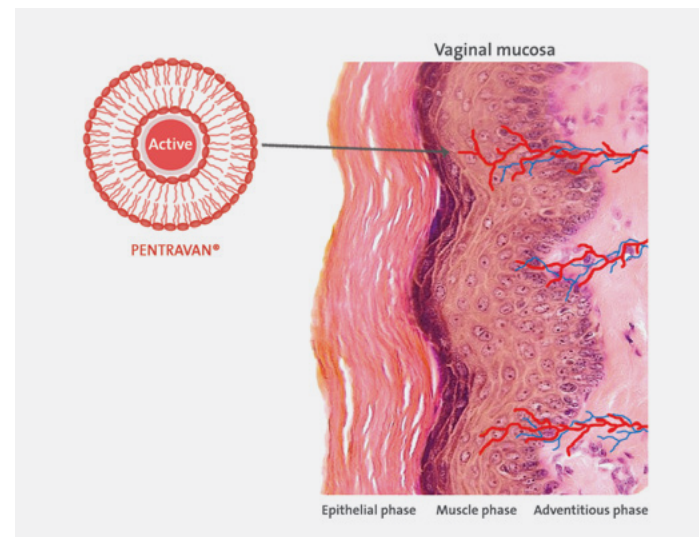
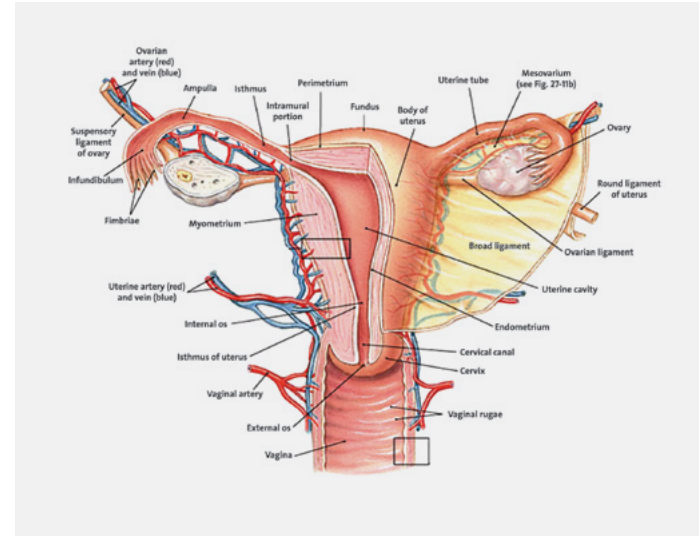
Pentravan[®]

High penetration of vaginal mucosa

Pentravan[®] is a vehicle formed by bilayer phospholipid nanosomes forming a liposomal space (matrix - assuring), and achieving high levels of penetration to the vaginal and uterine blood vessels.

Advantages of vaginal route of administration

- **Orally**
 - First pass effect
- **Transdermal**
 - Constant release that can saturate androgen receptors
- **Vaginal**
 - Decreased side effects
 - Dual effect: Systemic action and concentration in target tissue



16 studies demonstrate the permeability of Pentravan[®] in Franz cells

API	% Permeability 24 h
Progesterone	42.9 %
Testosterone	44.1 %
Gestrinone	61.4 %
Resveratrol	89.2 %

Free of parabens, propylene glycol, alcohol, petrolatums, irritating or allergenic ingredients.

Pentravan[®]

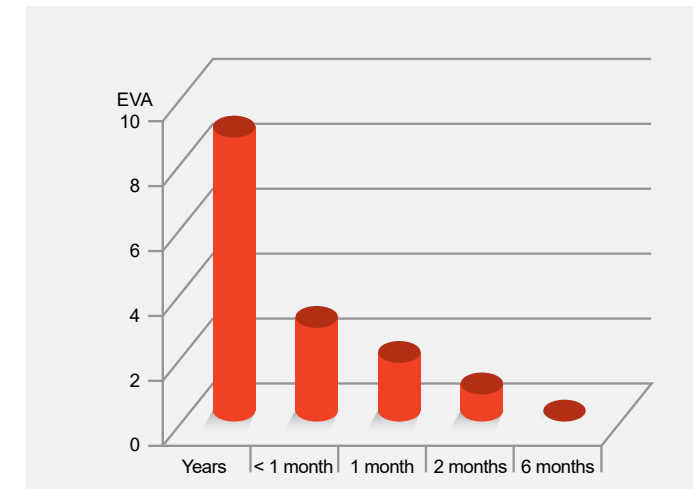
Pentravan[®] in endometriosis

- Endometriosis affects 2-10% of reproductive-age women and 50% with infertility¹
- Gestrinone inhibits aromatase producing an antiestrogenic effect

Clinical evidence

- 2 studies conducted in 15 and 47 women with deep endometriosis and pain not responding to oral contraceptives, treated with 5 mg gestrinone in Pentravan[®] vaginally 3 times a week and oral phytotherapy daily.^{2,3}
- Disappearance of pain in 85% of patients in 2 months and 100% in 3 months' time²
 - Decreased pain intensity from 9 to 3 during the 1st month and 0.5 by the 2nd month³
 - Significant decrease in uterine volume and endometriotic ovarian cysts ($p = 0.04$ and $p = 0.009$ respectively)^{2,3}
 - Stop bleeding in 90-100% of women during the second month^{2,3}

- Another study conducted in 33 women with sever endometriosis not responding to progestogens showed that gestrinone in Pentravan[®] combined with resveratrol and vitamin D3 applied topically showed potential reduction of pain⁴
- Resveratrol has an anti-inflammatory action
 - Vitamin D3 inhibits histone deacetylase, an enzyme that inhibits genes promoting endometriosis



Decreasing pain levels according to visual analog scale (VAS)

Formulations

Rx/
Gestrinone 5 mg
in Pentravan[®] c.s.p. 1 g
Apply 1 g intravaginally, 2-3 times/week.*
Treatment 2-5 months. (BUD 3 months)

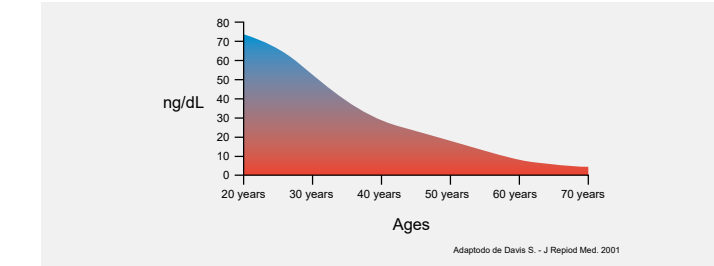
Rx/
Gestrinone 5 mg
Vitamin D3 5.000 U.I.
Resveratrol 100 mg
in Pentravan[®] c.s.p. 1 g
Apply 1 g intravaginally, 2-3 times/week.*
Treatment 2-5 months. (BUD 3 months)

* For application 3 times/week the total amount to be prepared for monthly treatment is 16 g (2 dose applicators) due to compounding losses.

Pentravan[®]

Pentravan[®] in menopause

During menopause, testosterone deficit occurs leading to a chronic inflammation process, causing to female sexual arousal/hypoactive sexual desire disorder, fatigue, sarcopenia, and depression.

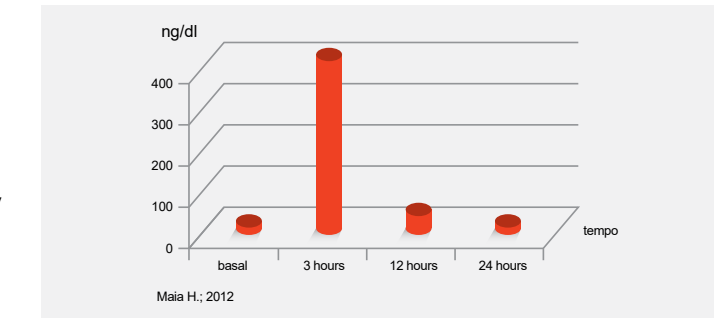


Decreasing levels of female testosterone

Clinical evidence

Double-blind study vs placebo in 814 postmenopausal women with 300-150 mcg transdermal testosterone for 1 year, showed a significant improvement of sexual function in those women.⁵

- 2 studies conducted in 26 and 42 postmenopausal women with decreased sexual desire who were given testosterone 3 mg/ml in Pentravan[®] vaginally
- 88-95% showed improvement of sexual function without androgenic adverse effects^{6,7}
 - Blood testosterone levels increased and decreased rapidly imitating physiological secretion^{6,7}



Serum levels of testosterone

Formulations

Rx/
Testosterone 2 - 3 mg
in Pentravan[®] c.s.p. 1 g
Apply 1 g/day intravaginally for the first 3 months,
then diminish at 2 times/week.** (BUD 3 months)

Rx/
Testosterone 2 - 3 mg
Vitamin D3 5.000 U. I.
Resveratrol 100 mg
in Pentravan[®] c.s.p. 1 g
Apply 1 g/day intravaginally for the first 3 months, then diminish at 2 times/week.** (BUD 3 months)

** For application 1 time/day the total amount to be prepared for monthly treatment is 40 g (5 dose applicators) due to compounding losses.