BlueCross BlueShield of Kansas City

An Independent Licensee of the Blue Cross and Blue Shield Association

# Implanted Hormone Pellets

**Policy Number:** 5.02.500
**Origination:** 11/2002
**Last Review:** 11/2014
**Next Review:** 11/2015

## Policy

Blue Cross and Blue Shield of Kansas City will provide coverage for Implanted Hormone Pellets when it is determined to be medically necessary because the criteria shown below are met.

## When Policy Topic is covered

Testopel® Pellets (testosterone pellets) are considered medically necessary as a second-line testosterone replacement therapy in males with congenital or acquired endogenous androgen absence or deficiency associated with primary or secondary hypogonadism (decreased function of sex organs) after oral and IM testosterone therapies have failed. Testopel® Pellets are also approved for treatment of delayed male puberty.

## When Policy Topic is not covered

Compounded hormone replacement therapy pellets for treatment of menopausal symptoms are considered investigational.

Testopel® Pellets are not approved for treatment of menopause symptoms and therefore are considered investigational for this indication.

## Considerations

This Blue Cross and Blue Shield of Kansas City policy Statement was developed using available resources such as, but not limited to: Hayes Medical Technology Directory, Food and Drug Administration (FDA) approvals, Facts and Comparisons, National specialty guidelines, Local medical policies of other health plans, Medicare (CMS), Local providers

## Description of Procedure or Service

Hormone replacement therapy (HRT) is used to decrease menopause symptoms, such as hot flashes and vaginal dryness.

In women with an intact uterus, HRT commonly consists of the combination of estrogen and a progestin to prevent endometrial hyperplasia or endometrial cancer. In the absence of a uterus, a progestin is unnecessary. There are many commercially available estrogen, progestin, and combination therapies.

Hormone pellets are a compounded substance where each pellet consists of a hard crystal of estradiol, which gradually releases estrogen into the blood stream.

There are currently no FDA-approved, commercially available formulations of implantable estradiol pellets available in the United States. These compounded formulations of estradiol have been shown to produce unpredictable and fluctuating levels of estrogens in the body.

Commercially prepared therapies are governed by strict guidelines enforced by the Food and Drug Administration. Because custom compounded medications are not governed by such laws, there may

be a lack of appropriate procedures in place at the compounding pharmacy to assure quality control-batch records, or precursor analysis-post manufacture review of potency and consistency.

Testosterone pellets (Testopel® Pellets) are FDA-approved for indications described under “Policy”.

## Rationale

While implantable estradiol pellets have been suggested as treatment for symptoms of menopause, there are no FDA-approved, commercially available formulations of implantable estradiol pellets available in the United States. These formulations of estradiol have been shown to produce unpredictable and fluctuating serum concentrations of estrogen.

The U.S. Food and Drug Administration's Fertility and Maternal Health Drugs Advisory Committee unanimously agreed to terminate compassionate investigative new drug (IND) programs for estrogen pellets as a last-resort treatment of menopausal disorder. The Committee noted “the risk of bleeding and infection, the lack of information on release rates, difficulty in reversibility of the drug, increased feasibility of over-dosage of the drug, and increased risk of non-compliance with safety measures [such as] the addition of progestin.”

Advocates of hormone implant therapy (HRT) for female menopause report that relief of short-term symptoms and long term prophylaxis against cardiovascular disease and osteoporosis during menopause are significant when HRT is delivered subcutaneously based on avoidance of first-pass metabolism through the liver.

There are several randomized controlled studies and uncontrolled prospective clinical trials evaluating subcutaneous HRT. Subcutaneous HRT therapy was compared with placebo and with oral and transdermal therapy. The studies had relatively few numbers of subjects considering the large number of women that are candidates for HRT. None of the studies were completely blinded. Symptom relief was largely based on subjective and patient reported results. These studies could be subject to bias based on placebo effect. Only 3 studies measured estrogen implant effect on bone density, which provided objective measurement. There have been relatively few studies in which delivery of estrogen replacement therapy using implants was directly compared with other methods of estrogen administration.

HRT for menopause has been the subject of debate. The benefit of HRT therapy as a whole, is not clearly defined. Additional research is needed to determine the optimal dosage and treatment interval.

Testosterone pellets (Testopel® Pellets), on the other hand, are FDA approved and are considered medically necessary as a second-line testosterone replacement therapy in males with congenital or acquired endogenous androgen absence or deficiency associated with primary or secondary hypogonadism (decreased function of sex organs) after oral and IM testosterone therapies have failed. Testopel® Pellets are also approved for treatment of delayed male puberty.

References:


1 Thom MH, Studd JW. Procedures in practice. Hormone implantation. Br Med J. 1980;280(6217):848-850.
2 Carmichael JM. Postmenopausal hormone replacement. US Pharmacist. 1992;:8-13.
3 Stumpf PG. Pharmacokinetics of estrogen. Obstet Gynecol. 1990;75(4)Suppl:9S-17S.
4 Kapetanakis E, Dmowski WP, Auletta F, et al. Endocrine and clinical effects of estradiol and testosterone pellets used in long-term replacement therapy. Int J Gynaecol Obstet. 1982;20(5):387-399.
5 Handelsman DJ, Conway AJ, Boylan LM. Pharmacokinetics and pharmacodynamics of testosterone pellets in man. J Clin Endocrinol Metab. 1990;71:216-222.

6 Garnett T, Studd J, Watson N. et al. A cross-sectional study of the effects of long-term percutaneous hormone replacement therapy on bone density. Obstet Gynecol. 1991;78(6):1002-1007.
7 Basaria S, Dobs AS. Hypogonadism and androgen replacement therapy in elderly men. Am J Med. 2001;110(7):563-572.
8 F-D-C- Reports Inc. Estrogen pellets availability under compassionate INDs should be discontinued as a last resort treatment for menopausal symptoms -- FDA advisory committee. The Pink Sheet. 1988 Jan 25;50(4).
9 Alexander JL, Kotz K, Dennerstein L, et al. The effects of postmenopausal hormone therapies on female sexual functioning: A review of double-blind, randomized controlled trials. Menopause. 2004;11(6 Pt 2):749-765.
10 Anderson RA, Wallace AM, Sattar N, et al. Evidence for tissue selectivity of the synthetic androgen 7 alpha-methyl-19-nortestosterone in hypogonadal men. J Clin Endocrinol Metab. 2003; 88(6):2784-93.
11 File SE, Heard JE, Rymer J. Trough oestradiol levels associated with cognitive impairment in post-menopausal women after 10 years of oestradiol implants. Psychopharmacology (Berl). 2002 Apr; 161(1): 107-12.
12 Vogelvang TE et al. Neither long-term treatment with raloxifene nor hormone replacement therapy modulate cardiac function in healthy postmenopausal women: Two randomized, placebo-controlled, 2-year studies. Am J Obstet Gynecol. 2002 Apr; 186(4): 729-736.
13 Kelleher S, Conway AJ, Handelsman DJ. Influence of implantation site and track geometry on the extrusion rate and pharmacology of testosterone implants. Clin Endocrinol (Oxf). 2001 Oct;55(4):531-6.
14 del Carmen Cravioto M, Larrea F, Delgado NE, et al. Pharmacokinetics and pharmacodynamics of 25-mg estradiol implants in postmenopausal Mexican women. Menopause. 2001 Sep-Oct; 8(5): 353-60.
15 Kenemans P, van Unnik GA, Mijatovic V, van der Mooren MJ. Perspectives in hormone replacement therapy. Maturitas. 2001 Jun 15; 38 Suppl 1:S41-8.
16 Howell S, Shalet S. Testosterone deficiency and replacement. Horm Res. 2001;56 Suppl 1:86-92.
17 Hayes, Inc. Estrogen Pellet Implants. Feb, 2000. Updated 3/22/04.
18 Stanczyk FZ, Shoupe D, Nunez V, et al. A randomized comparison of nonoral estradiol delivery in postmenopausal women. Am J Obstet Gynecol. 1988;159:1540-1546.
19 Studd JWW, Holland EFN, Leather AT, Smith RNJ. The dose-response of percutaneous oestradiol implants on the skeletons of postmenopausal women. Br J Obstet Gynaecol. 1994;101:787-791.
20 Studd JWW, Smith RNJ. Oestradiol and testosterone implants. Baillière's Clin Endocrinol Metabol. 1993;7:203-223.
21 Suhonen SP, Allonen HO, Lähteenmäki P. Sustained-release estradiol implants and a levonorgestrel-releasing intrauterine device in hormone replacement therapy. Am J Obstet Gynecol. 1995;172:562-567.
22 Templeman C, Quinn D, Hansen R, et al. An audit of oestrogen implant hormone replacement therapy. Aust NZ J Obstet Gynaecol. 1998;38:455-460.

## Billing Coding/Physician Documentation Information

11980 Subcutaneous hormone pellet implantation (implantation of estradiol and/or testosterone pellets beneath the skin)
S0189 Testosterone pellet, 75mg

## Additional Policy Key Words

N/A

## Related Topics

N/A

## Policy Implementation/Update Information

11/2002 Origination date
11/2003 Reviewed – No changes made
11/2004 Reviewed – No changes made
11/2005 Reviewed – No changes made

11/2006 Reviewed – No changes made
11/2007 Reviewed – No changes made
11/2008 Reviewed – No changes made
06/2009 Revised – Removed statement “Testosterone pellets require prior authorization through pharmacy services.”
11/2009 Reviewed – No changes made
11/2010 Reviewed – No changes made
11/2011 Reviewed – No changes made
11/2014 Reviewed – no changes made

---