Medical Policy Reference Manual
Medical Policy

2.01.053 Implantable Hormone Replacement Pellets

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Description

Hormone replacement therapy (HRT) using formulas in subcutaneously implantable pellet form is an alternative to hormone therapy by injection or oral ingestion. Pellets are surgically implanted in the physician's office and release their contents over a period of months.

Policy

Subcutaneous testosterone pellets are considered **medically necessary** for (1) treatment of patients with conditions related to primary or secondary hypogonadism and (2) treatment of delayed patient puberty.

Subcutaneous testosterone pellets for all other indications are considered **experimental / investigational** as they do not meet TEC criteria # 1 - 5.

Subcutaneous pellets composed of estradiol, estrogen, or estrogen in combination with testosterone are considered **experimental / investigational** as they do not meet TEC criteria # 1 or 5.

Policy Guidelines

Experimental / Investigational

The term "experimental/investigational" describes services or supplies that are in the developmental stage and are in the process of human or animal testing. Services or supplies that do not meet all 5 of the criteria listed below adopted by the BlueCross BlueShield Association Technology Evaluation Center (TEC) are deemed to be experimental/investigational:

1. The technology* must have final approval from the appropriate U.S. government regulatory bodies; and
2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes; and
3. The technology must improve the net health outcome; and
4. The technology must be as beneficial as any established alternatives; and
5. The improvement must be attainable outside the investigational settings.

* *Technology* includes drugs, devices, processes, systems, or techniques

Rationale:

1. The technology* must have final approval from the appropriate U.S. government regulatory bodies.

Testosterone pellets (example: Testopel® pellets), are FDA approved for androgen deficiency due to primary or secondary hypogonadism in males. Testosterone pellets are not labeled for use as a treatment for menopausal symptoms or reduced libido, and the pharmaceutical references and published literature do not substantiate an off-label indication for these purposes.

Subcutaneous implantable pellets made up of estradiol, estrogen, or testosterone in combination with estrogen or estradiol have been custom compounded by pharmacists according to physician specifications, but none of these are FDA approved for U.S. distribution; and their safety and efficacy has not been adequately demonstrated in well-

designed clinical trials. Compounded pellets continue to show unpredictability with fluctuating serum concentrations and as such, the FDA and Maternal Health Drugs Advisory Committee terminated compassionate investigative new drug (IND) programs for estrogen pellets as a last-resort treatment of menopausal disorder. Compounded drugs are not FDA-approved. (NAMS, 2022). Cleveland Clinic Journal of Medicine (CCJM) reports that the FDA has not approved testosterone therapy for patients with menopausal symptoms or reduced libido (Smith, T., & Batur, P. (2021).

2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes.

Inadequate research and unavailability of high quality pharmacokinetic data on safety and efficacy of compounded bioidentical implantable hormone therapy pellets for the treatment of menopause prevents conclusions concerning the effect of the technology on health outcomes. Safety concerns include lack of FDA oversight, dosing disparities, and insufficient health risk identification. (NAMS, 2022).

3. The technology must improve the net health outcome.

Testosterone therapy for menopausal women continues to have insufficient research. High quality RCTs that are well formed are necessary to confirm long-term safety, efficacy, and appropriate dosing of testosterone therapy in menopausal patients. Available research advises against testosterone pellet therapies which may have adverse effects related to lengthy hormone exposure and labile dosing. (Smith, T., & Batur, P. (2021).

4. The technology must be as beneficial as any established alternatives.

There is a lack of research comparing subcutaneous implantable pellets (estradiol, estrogen, or estrogen in combination with testosterone) with established alternatives. Additionally, there is a dearth of research comparing subcutaneous testosterone pellets as a treatment for patients with menopausal symptoms and/or reduced libido to established alternatives. Therefore, it is not possible to determine whether either is as effective as established alternatives for the treatment of these conditions.

5. The improvement must be attainable outside the investigational settings.

A net health outcomes improvement has not been demonstrated in the investigational settings for subcutaneous implantable pellets (estradiol, estrogen, or estrogen in combination with testosterone) and subcutaneous testosterone pellets as a treatment for patients with menopausal symptoms and/or reduced libido. Therefore, it is not possible to determine whether an improvement outside of the investigational setting can be expected for either indication.

Update 2022:
A search of the peer-reviewed literature was performed from the period of January 2020 through October 2022. Findings in the recent literature do not change the conclusions regarding the use of implantable hormone pellets for conditions other than those medically necessary indications listed in the policy section of this document. Therefore, the policy statements are unchanged.

Update 2020:
A search of the peer-reviewed literature was performed from the period of January 2018 through January 2020. Findings in the recent literature do not change the conclusions regarding the use of implantable hormone pellets for conditions other than those medically necessary indications listed in the policy section of this document. Therefore, the policy statements are unchanged.

Update 2017:
A search of the peer-reviewed literature was performed for the period of December 2015 through December 2017. Findings in the recent literature do not change the conclusions on the use of implantable hormone pellets for conditions other than those medically necessary indications listed in the policy section of this document. Therefore, the policy statements are unchanged.

Update 2015:
A search of the peer-reviewed literature was performed for the period of November 2013 through November 2015. Custom compounded pellets containing estradiol, estrogen, or estrogen combined with testosterone as a treatment for menopause have not been approved by the FDA. There are no FDA-approved commercially available implantable estradiol pellets available in the U.S. Therefore, the policy statements remain unchanged.

Update 2013:

A search of the peer-reviewed literature was performed for the period of September 2011 through October 2013. The policy statement has been modified to include *delay in male puberty* as a medically necessary indication for the use subcutaneous testosterone pellets. Subcutaneous testosterone pellets and subcutaneous pellets composed of estradiol, estrogen, or estrogen in combination with testosterone for women remain experimental / investigational. There are no FDA-approved, commercially available products for implantable estradiol pellets available in the U.S.

Update 2011:
A search of the peer-reviewed literature was performed for the period of September 2009 through August 2011. Findings in the recent literature do not change the conclusions on the use of implantable hormone pellets for conditions other than those medically necessary indications listed in the policy section of this document. Therefore, the policy statements are unchanged.

Update 2009:
A search of the peer-reviewed literature was performed for the period of August 2007 through August 2009. Findings in the literature do not change the conclusions regarding the use of implantable hormone pellets. The FDA has not approved testosterone pellets for conditions other than androgen deficiency due to primary or secondary hypogonadism in males, and the literature does not support an off-label indication. Custom compounded pellets made up of estradiol, estrogen, or estrogen in combination with testosterone as a treatment for menopause have not been approved by the FDA for U.S. distribution. Therefore, the policy remains unchanged.

Update 2007:
A search of the peer-reviewed literature was performed for the period of July 2005 through July 2007. Findings in the recent literature do not change the conclusions on the use of implantable hormone pellets for conditions other than those medically necessary indications listed in the Policy section of this document. Therefore, the policy statements are unchanged.

Benefit Applications
There are no Benefit Application guidelines for this Medical Policy.

Provider Guidelines
There are no Provider Guidelines for this medical policy.

Cross References to Related Policy and Procedures
There are no Related Policies for this Medical Policy.

References
The following were among the resources reviewed and considered in developing this policy. By reviewing and considering the resources, CareFirst does not in any way endorse the contents thereof nor assume any liability or responsibility in connection therewith. The opinions and conclusions of the authors of these resources are their own and may or may not be in agreement with those of CareFirst.

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