MEDICAL POLICY

POLICY TITLE	SUBCUTANEOUS HORMONE PELLET IMPLANTS
POLICY NUMBER	2.345

CLINICAL BENEFIT	☒ MINIMIZE SAFETY RISK OR CONCERN. ☒ MINIMIZE HARMFUL OR INEFFECTIVE INTERVENTIONS. ☐ ASSURE APPROPRIATE LEVEL OF CARE. ☐ ASSURE APPROPRIATE DURATION OF SERVICE FOR INTERVENTIONS. ☐ ASSURE THAT RECOMMENDED MEDICAL PREREQUISITES HAVE BEEN MET. ☐ ASSURE APPROPRIATE SITE OF TREATMENT OR SERVICE.
Effective Date:	**2/1/2024**

I. POLICY

Subcutaneous estradiol pellets are considered **investigational**, as there is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with this procedure.

Subcutaneous implantable testosterone pellets (Testopel pellets) may be considered **medically necessary** for any of the following indications:

- Delayed male puberty; **OR**
- Hypogonadotropic hypogonadism (congenital or acquired) with low serum testosterone*: idiopathic gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation; **OR**
- Primary hypogonadism (congenital or acquired) with low serum testosterone*: testicular failure due to conditions such as, but not limited to, cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy (also called orchidectomy), Klinefelter syndrome, chemotherapy/radiation or toxic damage from heavy metals; **OR**
- Female to male gender reassignment (see MP 1.144 Gender Affirming Surgery for specific guidance on surgery)

*Testosterone deficiency is indicated by at least two total serum testosterone levels that are below either the testing laboratory's normal reference range or 300 ng/dL. Two early morning total serum testosterone levels obtained on different days are required to determine medical necessity of testosterone replacement. One early morning total serum testosterone level is sufficient for persons with severe deficiency (less than 150 ng/dL).

As per The Endocrine Society Clinical Practice Guidelines (2018), if total serum testosterone levels are normal or borderline, a free testosterone level may be obtained. Free testosterone (FT) should be measured by an equilibrium dialysis method or estimated from total testosterone,

SHBG (Sex Hormone Binding Globulin), and albumin using a formula that accurately reflects FT by equilibrium dialysis. A harmonized reference range for FT has not been established, so reference ranges may vary considerably depending on the specific equilibrium dialysis method or the algorithm used to calculate FT. Therefore, until a harmonized reference range is established, the lower limits established by the laboratory may be used.

The diagnosis of testosterone deficiency must include the presence of signs and/or symptoms associated with low testosterone in combination with documented low total testosterone levels. Signs and/or symptoms of testosterone include, but are not limited to, reduced energy, reduced lean muscle mass, loss of body hair, gynecomastia, obesity (BMI ≥30 or increased waist circumference of >40 inches), poor memory, irritability, etc. Testosterone levels should not be measured during acute or subacute illness.

Other uses of implantable testosterone pellets are considered **investigational** including, but not limited to, their use in the treatment of sexual dysfunction in both men (e.g., erectile dysfunction) and women (e.g., decreased libido), hypogonadism due to aging, pain management in women, post-menopausal symptoms, depression and for the enhancement of athletic performance. There is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with this procedure.

Cross-reference:

MP 1.144 Gender Affirming Surgery
MP 2.016 Erectile Dysfunction

II. PRODUCT VARIATIONS TOP

This policy is only applicable to certain programs and products administered by Capital BlueCross and subject to benefit variations as discussed in Section VI. Please see additional information below.

FEP PPO - Refer to FEP Medical Policy Manual. The FEP Medical Policy manual can be found at: https://www.fepblue.org/benefit-plans/medical-policies-and-utilization-management-guidelines/medical-policies.

III. DESCRIPTION/BACKGROUND TOP

Hormone therapy can be delivered subcutaneously by implantation of the drug in pellet form in the lower abdomen or buttocks. The procedure is done in a physician's office with the use of a local anesthetic and a small incision for insertion. The release of the drug continues over a 3-6 month period, eliminating individual compliance with dosing schedules. Since the drug bypasses the gastrointestinal system and most liver metabolism, bioavailability can be increased. Sustained release can mimic endogenous production achieving therapeutic blood levels.

Menopause occurs when the ovaries no longer produce estrogen, causing the reproductive system to shut down and female is free of menses for one year. The normal aging process is

the usual reason for menopause. However, the loss of estrogen production may also be due to the surgical removal of the ovaries or as a result of treatment with chemotherapy.

While implantable estradiol pellets have been suggested as treatment for symptoms of menopause, there are no United States Food and Drug Administration (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 FDA'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."

Testosterone is an endogenous androgen. Androgens are responsible for normal growth and development of male sex organs. Testosterone is involved in the growth and maturation of the prostate, seminal vesicles, penis, and scrotum; development of male hair distribution (e.g., beard, pubic, chest and axillary hair); laryngeal enlargement, vocal cord thickening, and alterations in body musculature and fat distribution. Low serum testosterone concentrations due to inadequate secretion of testosterone is associated with male hypogonadism. Symptoms include decreased sexual desire with or without impotence, fatigue, and mood disturbances.

Implantable testosterone pellets may be indicated as second-line testosterone replacement therapy for males. Testosterone implants (Testopel Pellets) are commercially available in the United States. Testopel (testosterone) is indicated for replacement therapy in males for conditions associated with a deficiency or absence of endogenous testosterone.

Repeat pellet administration may be medically necessary to achieve adequate levels of testosterone. According to the American Urological Association (2018), "Patients on short-acting intramuscular (IM) or short-acting subcutaneous (SQ) pellets (testosterone cypionate or enanthate) should have their testosterone measured after several cycles such that testosterone level equilibration has been achieved. The Panel recommends that this be completed no earlier than three to four cycles. While no data exist on the optimal timing of the blood draw within a cycle, it has historically been recommended that blood draws be conducted mid-cycle. The main driving force behind such a strategy is convenience for patients and clinicians, although such timing has no ability to define peak and trough levels." The Endocrine Society indicates that "patients who are on long-acting SQ pellets require two separate assessments of testosterone to determine the dose and frequency required. The first testosterone measurement should be obtained two to four weeks after initial implant to determine if the number of inserted pellets needs to be increased or decreased to achieve the appropriate therapeutic level. Patients should then be tested after 10-12 weeks."

Pellets doses are between 600 – 1200 mg, dependent mostly on BMI, age, and pretreatment testosterone levels. As per the American Urological Association, the FDA recommends 2- 6 pellets every 3-6 months, noting that "These recommendations, however, are not based on

current testosterone pellet formulations and contrast with pharmacokinetic data available. Definitive dosing protocols have not been described." The number of pellets/dosing is adjusted to maintain serum testosterone concentrations in the "mid-normal" range. Most men require another administration after 4 months, with studies showing almost all men needed re-dosing at 6 months. Subsequent testosterone levels should be assessed around three months after implantation and re-checked every two to four weeks thereafter if persistently therapeutic levels are found. Although no consensus exists, it is reasonable to perform re-implantation when total testosterone levels are <400 ng/dL. Due to variations within the same individual, it is recommended to obtain end-of-cycle testosterone measurements prior to implantation to ensure that levels are sub-therapeutic.

Androgens are primarily indicated in males as replacement therapy when congenital or acquired endogenous androgen absence or deficiency is associated with primary or secondary hypogonadism. Primary hypogonadism includes conditions such as: testicular failure due to cryptorchidism, bilateral torsion, orchitis, or vanishing testis syndrome; inborn errors in testosterone biosynthesis; or bilateral orchidectomy. Hypogonadotropic hypogonadism (secondary hypogonadism conditions include gonadotropin-releasing hormone (GnRH) deficiency or pituitary-hypothalamic injury as a result of surgery, tumors, trauma, or radiation, and are the most common forms of hypogonadism seen in older adults.

IV. RATIONALE

TOP

Testosterone is available as Testopel in 77mg pellets (75mg testosterone) for subcutaneous implantation. If testosterone implants are to be used for treatment of androgen deficiency due to primary or secondary hypogonadism, the usual adult dosage is 150 to 450 mg subcutaneously every 3 to 4 months, or, in some cases, as long as 6 months. Dosage adjustment is needed to accommodate individual clinical requirements for such life changes as induction of puberty, development of secondary sexual characteristics, impotence due to testicular failure, or infertility due to oligospermia.

For treatment of delayed male puberty, a 6-month or shorter course of androgen is indicated for induction of puberty in patients with familial delayed puberty, a condition characterized by spontaneous, non-pathologic, late-onset puberty, if the patient does not respond to psychological treatment. If subcutaneous testosterone implants are to be used, the usual dosage is in the lower range of that listed above. Low doses are used initially and increased gradually as puberty progresses.

Testosterone is FDA-approved as replacement therapy only for men who have low testosterone levels due to disorders of the testicles, pituitary gland, or brain that cause hypogonadism (FDA, 2015). However, the FDA has become aware that testosterone is being used extensively in attempts to relieve symptoms in men who have low testosterone for no apparent reason other than aging. The benefits and safety of this use have not been established (FDA, 2015).

The FDA advises that health care professionals should prescribe testosterone therapy only for men with low testosterone levels caused by certain medical conditions and confirmed by laboratory tests (FDA, 2015). Health care professionals should make patients aware of the

possible increased cardiovascular risk when deciding whether to start or continue a patient on testosterone therapy.

The FDA is requiring that the manufacturers of all approved prescription testosterone products change their labeling to clarify the approved uses of these medications (FDA, 2015). The FDA is also requiring these manufacturers to add information to the labeling about a possible increased risk of heart attacks and strokes in patients taking testosterone. The FDA cautions that prescription testosterone products are approved only for men who have low testosterone levels caused by certain medical conditions. The benefit and safety of these medications have not been established for the treatment of low testosterone levels due to aging, even if a man's symptoms seem related to low testosterone (FDA, 2015).

Based on the available evidence from studies and expert input from an FDA Advisory Committee meeting, the FDA has concluded that there is a possible increased cardiovascular risk associated with testosterone use (FDA, 2015). These studies included aging men treated with testosterone. Some studies reported an increased risk of heart attack, stroke, or death associated with testosterone treatment, while others did not (FDA, 2015).

Pellet implantation is much less flexible for dosage adjustment than is oral administration, intramuscular injections of oil solutions, or aqueous suspensions and, therefore, great care should be used when estimating the amount of testosterone needed.

The number of pellets to be implanted depends upon the minimal daily requirements of testosterone propionate determined by a gradual reduction of the amount administered parenterally. The usual dosage is as follows: implant two 75 mg pellets for each 25 mg testosterone propionate required weekly. Thus when a patient requires injections of 75 mg per week, it is usually necessary to implant 450 mg (6 pellets). With injections of 50 mg per week, implantation of 300 mg (4 pellets) may suffice for approximately three months. With lower requirements by injection, correspondingly lower amounts may be implanted. It has been found that approximately one-third of the material is absorbed in the first month, one fourth in the second month, and one sixth in the third month. Adequate effect of the pellets ordinarily continues for three to four months, sometimes as long as six months.

Filho et al (2007) retrospectively reviewed the medical records of 258 post-menopausal patients using estradiol and testosterone implants as combined hormone therapy to evaluate the effects of testosterone on the endometrium after 2 years of continuous use. Endometrial thickness was measured by ultrasonography. Histology was performed on samples of thickened endometria obtained during hysteroscopy with biopsy. In the 44 patients in whom endometrial thickening was greater than 5 mm at the end of the second year of implant use, the most frequent finding at hysteroscopy was polypoid lesion in 61.3 % of cases, followed by normal uterine cavity in 31.8 % of cases and submucous myoma in 6.8 %. Histology of the endometrial samples confirmed endometrial polyp in 38.6 % of cases, a histologically normal endometrium in 31.8 % of cases, simple endometrial hyperplasia in 20.4 % of cases, and myoma and atrophic endometrium in 4.5 %. It is possible that testosterone may exert its anti-proliferative effects on the endometrium but not on polyps in an action similar to that exerted by combined

estrogen/progestin therapies. A greater incidence of simple, low-grade endometrial hyperplasia was found in this study compared with studies using continuous estrogen/progestin regimens. The use of progestins as the ideal endometrial protection should therefore be re-considered.

Fennell and colleagues (2010) compared the 2 long-acting depot testosterone (T) products -- subdermal T implants (TI) and injectable T undecanoate (TU) -- for maintenance of testosterone replacement therapy (TRT). Men with organic androgen deficiency (n = 38) undergoing regular TRT were recruited for a 2-period, randomized sequence, cross-over clinical trial without intervening wash-out period of TRT maintenance. For both depot T products, their pharmacokinetics and pharmacodynamics were evaluated using a range of androgen sensitive clinical, laboratory and quality of life measures as well as preference for ongoing treatment after experience of both products. The 2 depot T products had distinct pharmacokinetics and were not bioequivalent. However, there were no consistent clinical differences in a comprehensive range of pharmacodynamic measures reflecting androgen effects on biochemistry and hematology, muscle mass and strength, and quality of life, mood and sexual function. The majority (91 %) of subjects chose TU over TI at study completion. The authors concluded that despite significant pharmacokinetic differences, the 2 depot T products are clinically interchangeable allowing for choice dependent on patient and physician delivery preference in practice; but most patients preferred the injectable over the implantable form.

Reis and Abdo (2014) stated that with advancing age, there is an increase in the complaints of a lack of a libido in women and erectile dysfunction in men. The effectiveness of phosphodiesterase type 5 inhibitors (PDE5i), together with their minimal side effects and ease of administration, revolutionized the treatment of erectile dysfunction. For women, testosterone administration is the principal treatment for hypoactive sexual desire disorder. These investigators evaluated the use of androgens in the treatment of a lack of libido in women, comparing 2 periods, i.e., before and after the advent of the PDE5i. These researchers also analyzed the risks and benefits of androgen administration. They searched the Latin-American and Caribbean Health Sciences Literature, Cochrane Library, Excerpta Medica, Scientific Electronic Library Online, and Medline (PubMed) databases using the search terms disfunção sexual feminina/female sexual dysfunction, desejo sexual hipoativo/female hypoactive sexual desire disorder, testosterona/testosterone, terapia androgênica em mulheres/androgen therapy in women, and sexualidade/sexuality as well as combinations thereof. They selected articles written in English, Portuguese, or Spanish. The authors concluded that after the advent of PDE5i, there was a significant increase in the number of studies aimed at evaluating the use of testosterone in women with hypoactive sexual desire disorder. However, they stated that the risks and benefits of testosterone administration have yet to be clarified.

Corona et al (2014) noted that the role of testosterone supplementation (TS) as a treatment for male sexual dysfunction remains questionable. These researchers attempted a meta-analysis on the effect of TS on male sexual function and its synergism with the use of PDE5i. An extensive Medline, Embase, and Cochrane search was performed. All randomized controlled trials (RCTs) comparing the effect of TS versus placebo or the effect of TS as add on to PDE5is on sexual function were included. Data extraction was performed independently by 2 of the authors, and conflicts resolved by the third investigator. Out of 1,702 retrieved articles, 41 were

included in the study. In particular, 29 compared TS versus placebo, whereas 12 trials evaluated the effect of TS as add on to PDE5is. Testosterone supplementation is able to significantly ameliorate erectile function and to improve other aspects of male sexual response in hypogonadal patients. However, the presence of possible publication bias was detected. After applying "trim and fill" method, the positive effect of TS on erectile function and libido components retained significance only in RCTs partially or completely supported by pharmaceutical companies (confidence interval [CI]: 0.04 to 0.53 and 0.12 to 0.52, respectively). In addition, these researchers reported that TS could be associated with an improvement in PDE5i outcome. These results were not confirmed in placebo-controlled studies. The majority of studies, however, included mixed eugonadal/hypogonadal subjects, thus imparting uncertainty to the statistical analyses. The authors concluded that TS plays positive effects on male sexual function in hypogonadal subjects. The role of TS is uncertain in men who are not clearly hypogonadal. The apparent difference between industry-supported and independent studies could depend on trial design more than on publication bias. They stated that new RCTs exploring the effect of TS in selected cases of PDE5i failure that persistently retain low testosterone levels are advisable.

Fui et al (2014) stated that with increasing modernization and urbanization of Asia, much of the future focus of the obesity epidemic will be in the Asian region. Low testosterone levels are frequently encountered in obese men who do not otherwise have a recognizable hypothalamic-pituitary-testicular (HPT) axis pathology. Moderate obesity predominantly decreases total testosterone due to insulin resistance-associated reductions in sex hormone binding globulin. More severe obesity is additionally associated with reductions in free testosterone levels due to suppression of the HPT axis. Low testosterone by itself leads to increasing adiposity, creating a self-perpetuating cycle of metabolic complications. Obesity-associated hypotestosteronemia is a functional, non-permanent state, which can be reversible, but this requires substantial weight loss. While TRT can lead to moderate reductions in fat mass, obesity by itself, in the absence of symptomatic androgen deficiency, is not an established indication for TRT. The authors concluded that TRT may lead to a worsening of untreated sleep apnea and compromise fertility.

V. DEFINITIONS

TOP

ANDROGEN: A general term for any male sex hormone.

ENDOGENOUS: Developing or originating within the body.

HYPOGONADISM: An inadequate gonadal function, marked by deficiencies in the secretion of gonadal hormones and spermatogenesis.

MENOPAUSE: Cessation of menstruation in the female.

ORCHIECTOMY: Excision of one or both testes, done when a testis is seriously injured or diseased (as in testicular cancer).

SUBCUTANEOUS: Under the skin.

VI. BENEFIT VARIATIONS

TOP

The existence of this medical policy does not mean that this service is a covered benefit under the member's health benefit plan. Benefit determinations should be based in all cases on the applicable health benefit plan language. Medical policies do not constitute a description of benefits. A member's health benefit plan governs which services are covered, which are excluded, which are subject to benefit limits and which require preauthorization. There are different benefit plan designs in each product administered by Capital BlueCross. Members and providers should consult the member's health benefit plan for information or contact Capital BlueCross for benefit information.

VII. DISCLAIMER

TOP

Capital BlueCross's medical policies are developed to assist in administering a member's benefits, do not constitute medical advice and are subject to change. Treating providers are solely responsible for medical advice and treatment of members. Members should discuss any medical policy related to their coverage or condition with their provider and consult their benefit information to determine if the service is covered. If there is a discrepancy between this medical policy and a member's benefit information, the benefit information will govern. If a provider or a member has a question concerning the application of this medical policy to a specific member's plan of benefits, please contact Capital BlueCross' Provider Services or Member Services. Capital BlueCross considers the information contained in this medical policy to be proprietary and it may only be disseminated as permitted by law.

VIII. CODING INFORMATION

TOP

Note: This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.

Subcutaneous estradiol pellets are considered investigational; therefore, not covered:

Procedure Codes								
11980	J3490							

Subcutaneous implantable testosterone pellets (Testopel pellets) are covered when medically necessary:

Procedure Codes								
11980	S0189							

ICD-10-CM Diagnosis Codes	Description
E23.0	Hypopituitarism [hypothalamic hypogonadism] [not covered for androgen deficiency due to aging or idiopathic hypogonadism not due to disorders of the testicles, pituitary gland or brain]

POLICY TITLE	SUBCUTANEOUS HORMONE PELLET IMPLANTS
POLICY NUMBER	2.345

ICD-10-CM Diagnosis Codes	Description
E29.1	Testicular hypofunction [primary] [not covered for androgen deficiency due to aging or idiopathic hypogonadism not due to disorders of the testicles, pituitary gland or brain]
E30.0	Delayed puberty [congenital or acquired endogenous androgen absence or deficiency]
E89.5	Postprocedural testicular hypofunction
F64.0	Transsexualism
Z87.890	Personal history of sex reassignment

IX. REFERENCES

TOP

1. *Bhasin S, Cunningham G, Hayes F, et al. Testosterone Therapy in Men with Hypogonadisn: An Endocrine Society Clinical Practice* Guideline. *Journal of Clinical Endocrinology & Metabolism 2018 103(5):1715-1744*
2. *Corona G, Isidori AM, Buvat J, et al. Testosterone supplementation and sexual function: A meta-analysis study. J Sex Med. 2014;11(6):1577-1592*
3. *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; 50(4)*
4. *Fennell C, Sartorius G, Ly LP, et al. Randomized cross-over clinical trial of injectable vs. implantable depot testosterone for maintenance of testosterone replacement therapy in androgen deficient men. Clin Endocrinol (Oxf). 2010; 73(1):102-109*
5. *Filho AM, Barbosa IC, Maia H Jr, et al. Effects of subdermal implants of estradiol and testosterone on the endometrium of postmenopausal women. Gynecol Endocrinol. 2007; 23(9):511-517*
6. *Fui MN, Dupuis P, Grossmann M. Lowered testosterone in male obesity: Mechanisms, morbidity and management. Asian J Androl. 2014; 16(2):223-231*
7. *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*
8. *Mulhall JP, Trost LW, Brannigan RE et al: Evaluation and management of testosterone deficiency: AUA guideline. J Urol 2018; 200: 423*
9. *Nieschlag E, Behre HM, Bouchard P, et al. Testosterone replacement therapy: Current trends and future directions. Hum Reprod Update. 2004; 10(5):409-419*
10. *Ponce OJ, Spencer-Bonilla G, Alvarez-Villalobos N, et al. The efficacy and adverse events of testosterone replacement therapy in hypogonadal men: A systematic review and meta-analysis of randomized, placebo-controlled trials. J Clin Endocrinol Metab. 2018;103(5):1745-1754. PMID 29562341*

11. *Reis SL, Abdo CH. Benefits and risks of testosterone treatment for hypoactive sexual desire disorder in women: A critical review of studies published in the decades preceding and succeeding the advent of phosphodiesterase type 5 inhibitors. Clinics (Sao Paulo). 2014;69(4):294-303*
12. *Rivas AM, Mulkey Z, Lado-Abeal J, Yarbrough S. Diagnosing and managing low serum testosterone. Proc (Bayl Univ Med Cent). 2014;27(4):321-324. PMID 11929145*
13. *Santen RJ, Allred DC, Ardoin SP, et al. Postmenopausal Hormone Therapy: An Endocrine Society Scientific Statement. The Journal of Clinical Endocrinology & Metabolism. 2010; 95(Supp 1):S1-S66.*
14. *Seftel A. Testosterone replacement therapy for male hypogonadism: Part III. Pharmacologic and clinical profiles, monitoring, safety issues, and potential future agents. Int J Impot Res. 2007; 19(1):2-24*
15. *Snyder P, Matsumoto A and Martin K. Clinical features and diagnosis of male hypogonadism. In: UpToDate Online Journal [serial online]. Waltham, MA; UpToDate: updated March 5, 2022. Literature review current through September 2023*
16. *Testopel. [Product Information]. Malvern, PA, Auxilium Pharmaceuticals. May 2015.*
17. *U.S. Food and Drug Administration (FDA). FDA cautions about using testosterone products for low testosterone due to aging; Requires labeling change to inform of possible increased risk of heart attack and stroke. Testosterone Products: Drug Safety Communication. Silver Spring, MD: FDA; March 3, 2015*
18. *Wierman ME, Wiebke A, Basson R, et al. Androgen Therapy in Women: A Reappraisal: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab Oct 2014:99; 3489-3510*
19. *Xu L, Freeman G, Cowling BJ, Schooling CM (2013). Testosterone therapy and cardiovascular events among men: a systematic review and meta-analysis of placebo-controlled randomized trials. BMC Med. 2013;11:108. PMID: 23597181*

X. POLICY HISTORY

TOP

MP 2.345	**8/13/2020 Consensus review.** No change to policy statement. Rationale and References updated. FEP policy site updated.
	08/27/2021 Minor review. Expanded indications for treatment of primary hypogonadism to include Klinefelter syndrome, chemotherapy/radiation and toxic damage from heavy metals. Added “not limited to” the list of diagnoses. Reference added for MP 1.144 Gender Affirming Surgery for specific guidance for female to male gender reassignment. Androgen deficiency changed to Testosterone Deficiency to be consistent throughout the policy as well as verbiage used within various practice guidelines. Removed "consecutive" requirement for testing and changed to “obtained on different days”. Clarified usage of free testosterone. Changed fasting to early morning testing. Added requirement of signs/symptoms for diagnosis and treatment of testosterone deficiency.

POLICY TITLE	SUBCUTANEOUS HORMONE PELLET IMPLANTS
POLICY NUMBER	2.345

	12/6/2022 Consensus review. No change to policy statement. Policy variation and FEP language revised. References updated.
	10/2/2023 Consensus review. No change to policy statement. Rationale and References updated.

TOP