FirstCarolinaCare Insurance Company, Inc. is a wholly-owned subsidiary of FirstHealth, Inc.
Testosterone is an androgen hormone responsible for normal growth and development of male sex characteristics. In certain medical conditions such as hypogonadism, the endogenous level of testosterone falls below normal levels. Primary hypogonadism includes conditions such as testicular failure due to cryptorchidism, bilateral torsion, orchitis, or vanishing testis syndrome; bilateral orchidectomy; and inborn errors in the biosynthesis of testosterone. Secondary hypogonadism, also called hypogonadotropic hypogonadism includes conditions such as gonadotropin-releasing hormone (GnRH) deficiency or pituitary-hypothalamic injury resulting from tumors, trauma, surgery, or radiation.

Testosterone hormone replacement can be delivered by mouth, intramuscular injection, topically or subcutaneously by testosterone pellets. Testosterone pellets have been approved by the U.S. Food and Drug Administration for the treatment of congenital or acquired androgen deficiency as a result of primary or secondary hypogonadism.

Although secondary or tertiary hormonal treatments with androgens are indicated for palliation therapy in post-menopausal women with metastatic breast cancer, subcutaneous testosterone implants are not indicated for these uses and should not be used by females.

**Estrogen**

Estrogen is a hormone that occurs naturally, or is manufactured as a synthetic steroidal or nonsteroidal compound with estrogenic activity. Estrogen is used to treat moderate to severe symptoms of female menopause. Estrogen replacement therapy (ERT) indicates the use of estrogen hormone as a single agent. Estrogen in combination with progestin is called hormone replacement therapy (HRT).

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.”

Several studies (Studd, 1994; Holland, 1995; Wahab, 1997) 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.

There are several randomized controlled studies and uncontrolled prospective clinical trials evaluating subcutaneous HRT. Subcutaneous HRT was compared with placebo and with oral and transdermal therapy. The studies had relatively few subjects considering the large number of women candidates for HRT. None of the studies were completely blinded. Symptom relief was largely based on subjective and participant reported results. These studies could be subject to bias based on placebo effect. Reported problems with subcutaneous HRT therapy include:

- Problems with pellet removal if the therapy has to be discontinued;
- Infection, extrusion and/or discomfort at the insertion site;
- Fluctuating blood levels of estrogen;
- Dosing is not easily adjusted;
- Compliance with cyclical progesterone therapy in hysterectomized women; and
Cumulative effect of 2-3 times higher estrogen blood levels over several years not seen with the oral route.

HRT for menopause has been the subject of debate. Additional research is needed to determine the optimal dosage, treatment interval and benefit to risk ratio of hormone replacement therapy as a treatment for menopause. Estrogen compounded with testosterone for subcutaneous HRT is not FDA approved. The published literature does not demonstrate safety and utility in short and long term therapy.

**Background/Overview**
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.

According to the American Association of Clinical Endocrinologists (AACE, 2002), men with decreased testosterone levels may experience a higher incidence of osteoporosis, sexual dysfunction, fatigue, cardiovascular disease and disturbances in mood.

Menopause occurs when the ovaries no longer produce estrogen, causing the reproductive system to shut down. 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.

According to the AACE (2006), although many women are asymptomatic in menopause, other women in the hypoestrogenic state may experience symptoms that may be severe and have a negative impact on quality of life. Symptoms of estrogen deficiency include hot flashes, sweating, insomnia, and vaginal dryness and discomfort. Hormone replacement therapy goals are to alleviate menopause symptoms, and include estrogen alone or estrogen in combination with testosterone. However, there are currently no implantable hormone pellets approved by the FDA for treatment of symptoms of menopause.

**References:**


Government Agency, Medical Society, and Other Authoritative Publications:


Websites for additional information:


Estrogen and Testosterone Subcutaneous Hormone Implants
Hormone Implants
Testosterone Subcutaneous Hormone Implants

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