A permeation-enhanced non-scrotal testosterone transdermal system for the treatment of male hypogonadism

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14.1 Introduction

Male hypogonadism (testosterone deficiency) is a relatively common disorder in clinical practice and may present with a variety of clinical symptoms, including sexual dysfunction, fatigue, depressed mood, and the absence or regression of secondary sexual characteristics. Testosterone deficiency may occur as the result of Leydig cell dysfunction from primary disease of the testes or inadequate luteinizing hormone secretion from diseases of the pituitary or impaired gonadotropin-releasing hormone (Gn-RH) secretion by the hypothalamus (Griffin and Wilson 1992; Santen 1991). Infertility may be observed in men with testosterone deficiency, seminiferous tubule disease, or hypogonadotropin hypogonadism.

Some causes of hypogonadism are relatively common, while others are rare. Klinefelter's syndrome is a primary testicular disorder occurring in about 1 in 500 men and resulting in both androgen deficiency and infertility (Luciani and Guichaoua 1985; Nielsen and Wohlert 1991; Tunte and Niermann 1968). Infertility in men with primary testicular disease is irreversible, but those with gonadotropin deficiency and infertility can often be treated successfully (Huang and Huang 1994; McClure 1987; Nachtigall et al. 1997). Men with primary gonadal failure usually have azoospermia or oligospermia and testosterone deficiency. When successful fertility is improbable or not desired, testosterone replacement therapy is offered to men with androgen deficiency.

When selecting testosterone replacement therapy, a safe general principle is to mimic the normal concentrations of testosterone (350–1050 ng/dl) and its active metabolites (Behre et al. 1990; Cantrill et al. 1984; Meikle et al. 1992, 1996b; Matsumoto 1994, 1995). This will minimize unphysiologically high testosterone serum concentrations to prevent possible side-effects or low concentrations to prevent androgen deficiency. While it is known that