



Natural Therapies & Prescriptions That Enhance Life.™

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## Compounding for UROLOGY

*At ClearSpring Pharmacy, we compound sterile preparations according to USP<797> standards, the most stringent in the industry. We will work together with each physician to customize doses and combinations of medications to meet the specific needs of each patient.*

### Customized Therapy for Erectile Dysfunction

Erectile dysfunction (ED) is a common condition in aging men, with a prevalence of 52% in men aged 40 to 70 years. It is frequently associated with several comorbid conditions, including metabolic syndrome, cardiovascular disease and testosterone deficiency.<sup>1,2</sup> However, ED has many treatable causes, and does not need to be an inevitable consequence of aging. While oral phosphodiesterase type 5 (PDE-5) inhibitors (Viagra™, Cialis™, and Levitra™) are very popular, some patients are unable to take these medications because of drug interactions (ie, sildenafil and nitroglycerin) or a lack of response. In addition, PDE-5 inhibitors are associated with adverse effects and are not as effective in patients who have undergone radical prostatectomy or who have severe vascular disease, which is a common complication of advanced diabetes. Consequently, PDE-5 inhibitor therapy is associated with a high rate of discontinuation.

Self-injection (intracavernosal injection; ICI) is a well-accepted and popular therapy for ED from many causes, and is considered “the most effective medical therapy for diabetic erectile dysfunction.”<sup>3</sup> Tri-mix is a combination of medications (papaverine/phentolamine/prostaglandin) that produce an erection using various mechanisms of action. Men with ED who used tri-mix by self-injection and who changed to oral sildenafil (Viagra™) found they had a greater preference than expected for triple therapy and the erection quality was better with trimix than with sildenafil in 89%.<sup>4</sup> Fear of pain with self-injection therapy may discourage some men. Yet, in the majority of ED patients, findings from a Cleveland Clinic study show that discomfort is minimal, which may help to alleviate the fear of injection in those who may benefit from this therapy.<sup>5</sup> Early intracavernosal injections following radical prostatectomy facilitate early sexual intercourse, patient satisfaction and potentially earlier return of natural erections, according to a study from the Glickman Urological Institute, Cleveland Clinic Foundation.<sup>6</sup>

To assess the effectiveness of a progressive treatment program for erectile dysfunction in patients with cardiovascular diseases, 453 men aged 36 to 91 years were studied. Therapy in all patients was begun with sildenafil citrate 25 to 100 mg. Those with contraindications, drug adverse effects, or a negative response (erection insufficient for vaginal penetration) were given intracavernous injections of a combination of vasoactive drugs (bimix, trimix, or quadmix), followed by the addition of sildenafil citrate to the trimix in case of failure. Of 248 patients who received intracavernous injections: 135 (54.4%) had a positive response to bimix, 85 (75.2%) to the trimix, and 16 (57.1%) to the quadmix. At the 2-year follow-up of 447 patients, 131 (29.3%) were successfully treated with sildenafil citrate, 92 (20.6%) with dimix, 122 (27.3%) with trimix, 12 (2.7%) with quadmix, and 2 (0.4%) with sildenafil citrate + trimix. This progressive treatment program for erectile dysfunction had a high success rate in patients with cardiovascular disease: Overall, 98.7% achieved an erection sufficient for vaginal penetration immediately after the trial and 92.2% on follow-up; 10.7% achieved spontaneous erections.<sup>7</sup>

**Examples of preparations that can be prescribed and compounded for treatment of Erectile Dysfunction:**

BiMix	Papaverine 30 mg/mL, Phentolamine 1.0 mg/mL
TriMix	Papaverine 30mg/mL, Phentolamine 1.0 mg/mL, Alprostadil (PGE1) 10mcg/mL
QuadMix	Papaverine 30 mg/mL, Phentolamine 1.0 mg/mL, Alprostadil (PGE1) 10mcg/mL, Atropine 0.15 mg/mL

## Treatment for “Andropause”

Hypogonadism (low serum testosterone; “andropause”) is commonly associated with erectile dysfunction (ED). Testosterone replacement therapy (TRT) may be the best treatment for men with ED when the presentation includes diminished libido or other sexual symptoms or when non-sexual symptoms such as depressed mood, decreased sense of vitality, and increased fatigue also exist. Addition of testosterone may improve the action of PDE-5 inhibitors in men with low or low-normal testosterone levels and erectile dysfunction who have not responded to PDE-5 inhibitors alone.<sup>8,9</sup>

The health benefits of TRT also include improvements in body composition, bone density, cognition, and sense of well-being. Thus, there may be good reasons to use TRT as first-line therapy for the man with ED. Concerns regarding prostatic and cardiovascular risks of TRT have not been supported by the literature. Nevertheless, men receiving TRT must be monitored at regular intervals with digital rectal examination and blood testing for prostate-specific antigen. Hematocrit or hemoglobin also should be obtained regularly due to the risk of erythrocytosis.<sup>10</sup>

### Examples of preparation that can be prescribed and compounded for the treatment of low serum testosterone:

Testosterone 20% cream

Apply \_\_\_ mL topically once daily.

Disp: \_\_\_ grams (1 month supply)

\_\_\_ refills

## Anastrozole - Use of Customized Doses to Maintain a Healthy Androgen: Estrogen Balance

Anastrozole is a potent inhibitor of aromatase, the enzyme that is responsible for the conversion of testosterone to estradiol and androstenedione to estrone. The commercial product Arimidex™ (anastrozole 1 mg) has been used to treat postmenopausal women with hormone receptor-positive breast cancer. However, at lower doses, aromatase inhibitors can be used to effectively control estradiol levels and maintain a healthy androgen:estrogen balance without reducing estradiol to such low levels that adverse effects such as osteoporosis and hot flashes become a concern.

High estradiol levels can suppress testosterone production, and play a role in Metabolic Syndrome. Aromatase inhibitors such as anastrozole can reduce estradiol and increase serum bioavailable and total testosterone levels to the youthful normal range in older men with mild hypogonadism. ***Suppression of estradiol in men using low-dose anastrozole has been shown to have a positive effect on testosterone production without adverse effects during short term administration.***<sup>11</sup>

### Case Study: Anastrozole Used to Restore Fertility in Obese Male

A morbidly obese 29-year-old man presented to the Division of Metabolism, Endocrinology and Nutrition, University of Washington School of Medicine, Seattle, with a low sperm count. The patient and his healthy 32-year-old wife had been unable to conceive after more than 1 year of unprotected intercourse. The patient had been seen by an outside physician and had been diagnosed as having hypogonadism with a low sperm concentration of 2 million/ml (normal concentration  $\geq 20$  million/ml). At that time he was started on testosterone enantate 200 mg IM every 2 weeks, for hypogonadism. While the patient was on testosterone therapy, a repeat sperm collection showed a complete absence of sperm.

At the time of evaluation at the clinic, the patient had ceased testosterone therapy for 2 months, and said he had been overweight his entire life. Physical exam revealed normal vital signs, weight 154 kg, height 168 cm, and BMI 54.5 kg/m<sup>2</sup>. Notable findings on examination were the presence of stage IV gynecomastia and morbid central obesity as well as subnormal testicular volumes, low total and calculated free testosterone levels, and normal levels of sex hormone-binding globulin. Luteinizing hormone (LH) levels were suppressed and follicle stimulating hormone (FSH) levels were low. Serum estradiol was within the normal range. Obesity was felt to be the possible cause of secondary hypogonadism and associated infertility in the patient. Aromatase, which converts testosterone to estradiol, is highly expressed in peripheral fat tissue and increased aromatase activity is thought to result in increased estradiol production, which inhibits secretion of LH and FSH from the pituitary. Reduced levels of LH and FSH lead to a reduction in testosterone synthesis and sperm production, and to infertility. When fertility is desired in men with hypogonadism, treatment with testosterone is not appropriate because exogenous testosterone further inhibits gonadotropin secretion and impairs spermatogenesis in men. ***To counteract the physiologic effects of elevated estradiol in the described patient, treatment with anastrozole was initiated. This treatment normalized his serum testosterone levels and spermatogenesis, and after 6 months of therapy his wife became pregnant.*** Once the couple achieved a pregnancy, the therapeutic plan was to discontinue anastrozole as there are limited long-term safety data on the use of this agent in men, and to restart anastrozole if another pregnancy is desired in the future.<sup>12</sup>

### Examples of anastrozole preparations that can be prescribed and compounded:

Anastrozole 0.5 mg

Take 1 capsule by mouth three times weekly

Disp: 12 capsules (1 month supply)

\_\_\_ refills

### References:

<sup>1</sup> Postgrad Med. 2010 Nov;122(6):165-75.

<sup>2</sup> Med Clin North Am. 2011 Jan;95(1):213-21.

<sup>3</sup> Expert Opin Pharmacother. 2008 Feb;9(2):257-66.

<sup>4</sup> BJU Int. 2003 Aug;92(3):277-80

<sup>5</sup> J Sex Med. 2005 May;2(3):428-31

<sup>6</sup> Int J Impot Res. 2006 Sep-Oct;18(5):446-51.