

## Hypogonadism Treatment Chart

Formulation	Dosage <sup>a</sup>	Details and Pharmacokinetics	Adverse Effects
<b>Injectable</b>			
Testosterone cypionate, testosterone enanthate <sup>1,2</sup>	50-400 mg every 2-4 wk <sup>1,2</sup>	Slow-release, oil-based vehicles achieve testosterone levels in the supraphysiologic range within 72 h, and levels decrease slowly into the hypogonadal range by the end of the dosing interval. <sup>3-7</sup> Frequent intramuscular injections (once every 1, 2, or 3 wk or once a month) are required, and the wide variations in serum testosterone levels can lead to a roller-coaster effect characterized by undesirable swings in mood, energy, libido, and sexual function, which some patients find disagreeable. <sup>3,4,5,7</sup>	<ul style="list-style-type: none"> <li>Mood fluctuations<sup>4,5</sup></li> <li>Changes in libido<sup>4,5</sup></li> <li>Pain at injection site<sup>4</sup></li> <li>Erythrocytosis<sup>4</sup></li> </ul>
Testosterone undecanoate (in development in the United States) <sup>8</sup>	750 mg at baseline, 4 wk, and every 10 wk thereafter <sup>8</sup>	Long-acting formulation achieves eugonadal physiologic testosterone levels with fewer injections compared to other intramuscular formulations. <sup>6,8</sup> A 1000-mg formulation is available in more than 80 countries, and a 750-mg depot formulation is in development in the United States. <sup>8</sup> Long-term safety and efficacy of the 1000-mg formulation has been demonstrated in hypogonadal men treated for more than 7 y. <sup>9</sup> In the United States, a 24-wk trial with 130 hypogonadal men found that intramuscular injection of 750 mg at 0, 4, and 14 wk resulted in normal serum testosterone levels during weeks 14-24 in 94% of patients. <sup>8</sup> More than 92% of patients had a maximum concentration below 1500 ng/dL during treatment <sup>8</sup>	<ul style="list-style-type: none"> <li>Pain at injection site<sup>4</sup></li> </ul>
<b>Implantable</b>			
Testosterone pellets <sup>10</sup>	150-450 mg (2-6 pellets) every 3-6 mo <sup>10</sup>	Approximately one third of testosterone pellet material is absorbed in the first month, one fourth in the second month, and one sixth in the third month. <sup>10</sup> Insertion and removal of the pellets requires minor surgery, with the potential adverse effects of infection, bleeding, and extrusion. <sup>5,6,11</sup> The estimate of the required amount of testosterone must be precise, because pellets are a much less flexible delivery method in terms of dosage adjustment than oral medication or intramuscular injection <sup>10</sup>	<ul style="list-style-type: none"> <li>Infection<sup>4,5</sup></li> <li>Expulsion<sup>4,5</sup></li> <li>Newer formulation may have lower expulsion rate<sup>11</sup></li> </ul>
<b>Topical</b>			
Topical gel (available in 1% concentration <sup>12,13</sup> ; higher concentrations in development in the United States <sup>14,15</sup> )	50-100 mg daily <sup>12,13</sup>	Applied once daily to nongenital skin, gel provides serum testosterone levels in the physiologic range over the 24-h dosing period for most men. <sup>3,4,13</sup> The two available testosterone gel formulations in hydroalcoholic base are not bioequivalent, varying in bioavailability, with one providing significantly greater peak serum concentrations of total testosterone and free testosterone. <sup>16</sup> Another concern with testosterone gel is direct skin-to-skin transfer to another person who does not require testosterone therapy (eg, a partner or a child). <sup>4</sup> The US Food and Drug Administration has required a labeling change because of this (black box warning). <sup>17</sup> Some men experience skin irritation at the application site <sup>3,4</sup>	<ul style="list-style-type: none"> <li>Skin-to-skin transfer<sup>3,4</sup></li> <li>Localized skin irritation<sup>3,4</sup></li> </ul>
Transdermal patch <sup>18</sup>	5 mg daily <sup>18</sup>	Nongenital testosterone patches are applied daily (evening) to the skin of the back, thigh, or upper arm away from pressure areas. <sup>3,4</sup> One patch delivers 5 mg testosterone. <sup>3,4</sup> Some patients require 2 patches to achieve adequate serum testosterone levels. <sup>4</sup> This formulation generally achieves serum testosterone levels within the normal range. <sup>3,4</sup> Some men experience skin irritation at the application site <sup>3,4</sup>	<ul style="list-style-type: none"> <li>Localized skin irritation<sup>3,4</sup></li> <li>Skin irritation is much greater with patches than with gels<sup>6</sup></li> </ul>
<b>Transmucosal</b>			
Buccal bioadhesive tablet <sup>19</sup>	30 mg every 12 h <sup>19</sup>	Adheres to gum or inner cheek and releases a controlled, sustained amount of testosterone through the buccal mucosa as the system gradually hydrates. <sup>19</sup> In one trial, 16% of hypogonadal men using the buccal bioadhesive tablet reported gum-related adverse events, including edema, gingivitis, inflammation, and blistering <sup>20</sup>	<ul style="list-style-type: none"> <li>Alterations in taste<sup>4,5</sup></li> <li>Irritation of gums and oral mucosa<sup>4,5</sup></li> </ul>

<sup>a</sup>Dosage refers to amount of testosterone administered. Please refer to the prescribing information for specific dosing instructions.

### References

- Depo-Testosterone [package insert]. Kalamazoo, MI: Pharmacia Corporation; 2002.
- Delatestryl [package insert]. Lexington, MA: Indevus Pharmaceuticals Inc; 2005.
- AAACE Hypogonadism Task Force. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the evaluation and treatment of hypogonadism in adult male patients—2002 update. *Endocr Pract*. 2002;8(6):439-456.
- Bhasin S, Cunningham GR, Hayes FJ, et al. Testosterone therapy in adult men with androgen deficiency syndromes: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2006;91(6):1995-2010.
- Gooren LJG, Bunck MCM. Androgen replacement therapy: present and future [review]. *Drugs*. 2004;64(17):1861-1891.
- Harle L, Basaria S, Dobs AS. Nebido: a long-acting injectable testosterone for the treatment of male hypogonadism. *Expert Opin Pharmacother*. 2005;6(10):1751-1759.
- Rhoden EL, Morgentaler A. Risks of testosterone-replacement therapy and recommendations for monitoring [review]. *N Engl J Med*. 2004;350(5):482-492.
- Morgentaler A, Dobs AS, Kaufman JM, et al. Long acting testosterone undecanoate therapy in men with hypogonadism: results of a pharmacokinetic clinical study. *J Urol*. 2008;180(6):2307-2313.
- Schubert M, Zitzmann M, Yassin A. Intramuscular testosterone undecanoate for the treatment of male hypogonadism—review of recent data. *J Mens Health Gen*. 2006;3(4):356-362.
- Testopel [package insert]. Rye, NY: Barta Pharmaceutical Co Inc; 2007.
- Cavender RK, Fairall M. Subcutaneous testosterone pellet implant (Testopel) therapy for men with testosterone deficiency syndrome: a single-site retrospective safety analysis. *J Sex Med*. 2009;6(11):3177-3192.
- AndroGel [package insert]. Marietta, GA: Solvay Pharmaceuticals Inc; 2004.
- Testim [package insert]. Malvern, PA: Auxilium Pharmaceuticals Inc; 2006.
- A Study of Fortigel Testosterone Gel 2% in Males With Low Testosterone. Clinical Trials website. <http://clinicaltrials.gov/ct2/show/NCT00522431>. Accessed March 11, 2010.
- Testosterone Treatment for Hypogonadal Men. Clinical Trials website. <http://clinicaltrials.gov/ct2/show/NCT00433199>. Accessed March 11, 2010.
- Marbury T, Hamill E, Bachand R, Sebree T, Smith T. Evaluation of the pharmacokinetic profiles of the new testosterone topical gel formulation, Testim™, compared to AndroGel®. *Biopharm Drug Dispos*. 2003;24(3):115-120.
- Voelker R. Children's exposure to testosterone gel spurs FDA to order boxed label warning. *JAMA*. 2009;301(23):2428.
- Androderm [package insert]. Corona, CA: Watson Pharma Inc; 2005.
- Striant [package insert]. Livingston, NJ: Columbia Laboratories Inc; 2003.
- Wang C, Swerdloff R, Kipnes M, et al. New testosterone buccal system (Striant) delivers physiological testosterone levels: pharmacokinetics study in hypogonadal men. *J Clin Endocrinol Metab*. 2004;89(8):3821-3829.