

## Therapeutic Class Overview Growth Hormone

### Therapeutic Class

**Overview/Summary:** Growth hormone (GH) affects many of the metabolic processes carried out by somatic cells, most notably increasing body mass. Overall growth is stimulated by GH therapy; however, the effects are not evenly distributed among protein, lipid and carbohydrate compartments. Specifically, body protein content and bone mass increase, total body fat content decreases and there is an increase in plasma and liver lipid content due to the mobilization of free fatty acids from peripheral fat stores. Other physiological effects of GH include stimulation of cartilage growth.<sup>1</sup> In pediatric patients, once a diagnosis of growth hormone deficiency (GHD) is confirmed, GH therapy should be initiated immediately and continued at least until linear growth is nearly complete (e.g., decreased to 2.5 cm/year). Therapy should be initiated as soon as possible as evidence demonstrates that growth response is more robust when GH therapy is started at a younger age. Once adult height is achieved, patients should be retested to determine if GH treatment will be required during adulthood.<sup>1</sup> The role of GH therapy in adult patients with GHD is less clear. There is evidence to demonstrate that when used in adult patients with GHD, GH therapy increases muscle mass and decreases body fat. Evidence of other potential beneficial effects of GH therapy in adults are not as established, including improvement in bone mineral density, sense of well-being, muscle strength and lipid profile.<sup>2</sup> Included in this review are the various GH preparations. Specifically, all preparations contain somatotropin; otherwise known as recombinant human GH.<sup>3-12</sup> The various preparations are Food and Drug Administration (FDA)-approved for use in a variety of pediatric conditions associated with a failure in growth, including chronic kidney disease, Turner syndrome, being born small for gestational age, Prader-Willi syndrome, mutations in the Short Stature Homeobox gene and Noonan syndrome, as well as for idiopathic short stature.<sup>3-10</sup> The majority of preparations are also indicated for the treatment of GHD in adults as well.<sup>3-9</sup> Of note, Serostim® (somatotropin) is only FDA-approved for the treatment of human immunodeficiency virus-associated wasting or cachexia in adults.<sup>11</sup> In addition, Zorbtive® (somatotropin) is the only agent indicated by the FDA to treat short bowel syndrome.<sup>12</sup> All of the available GH preparations are available for subcutaneous injection and there are currently no generics available within the class.<sup>3-12</sup> Treatment guidelines support the use of GH in FDA-approved indications and they do not distinguish among the various preparations.<sup>13-22</sup>

**Table 1. Current Medications Available in Class<sup>3-11</sup>**

Generic (Trade Name)	Food and Drug Administration Approved Indications	Dosage Form/Strength	Generic Availability
Somatropin (Genotropin®)	Pediatric indications: growth failure associated with Prader-Willi syndrome, growth failure associated with Turner syndrome, growth failure in children born small for gestational age*, growth hormone deficiency, and idiopathic short stature <sup>‡</sup>  Adult indications: growth hormone deficiency <sup>  </sup>	Cartridge, powder for reconstitution: 5 mg 12 mg  Cartridge, powder for reconstitution (preservative-free): 0.2 mg 0.4 mg 0.6 mg 0.8 mg 1.0 mg 1.2 mg 1.4 mg 1.6 mg 1.8 mg 2.0 mg	-
Somatropin (Humatrope®)	Pediatric indications: growth failure associated with short-stature homeobox-containing gene	Cartridge, powder for reconstitution: 6 mg	-

Generic (Trade Name)	Food and Drug Administration Approved Indications	Dosage Form/Strength	Generic Availability
	deficiency, growth failure associated with Turner syndrome, growth failure in children born small for gestational age <sup>†</sup> , growth hormone deficiency, and idiopathic short stature <sup>‡</sup>  Adult indications: growth hormone deficiency <sup>  </sup>	12 mg 24 mg  Vial, powder for reconstitution: 5 mg	
Somatropin (Norditropin <sup>®</sup> )	Pediatric indications: growth failure associated with Noonan syndrome, growth failure associated with Turner syndrome, growth failure in children born small for gestational age <sup>†</sup> , and growth hormone deficiency  Adult indications: growth hormone deficiency <sup>  </sup>	Prefilled pen (Norditropin <sup>®</sup> FlexPro <sup>®</sup> ): 5 mg/1.5 mL 10 mg/1.5 mL 15 mg/1.5 mL	-
Somatropin (Nutropin <sup>®</sup> )	Pediatric indications: growth failure associated with chronic renal insufficiency before renal transplant <sup>§</sup> , growth failure associated with Turner syndrome <sup>#</sup> , growth hormone deficiency <sup>#</sup> , and idiopathic short stature <sup>‡, #</sup>  Adult indications: growth hormone deficiency <sup>  </sup>	Prefilled cartridge (Nutropin AQ NuSpin <sup>®</sup> ): 5 mg/2 mL 10 mg/2 mL 20 mg/2 mL  Prefilled pen cartridge (Nutropin AQ <sup>®</sup> ): 10 mg/2 mL 20 mg/2 mL	-
Somatropin (Omnitrope <sup>®</sup> )	Pediatric indications: growth failure associated with Prader-Willi syndrome, growth failure associated with Turner syndrome, growth failure in children born small for gestational age, growth hormone deficiency, and idiopathic short stature <sup>‡</sup>  Adult indications: growth hormone deficiency <sup>  </sup>	Prefilled cartridge: 5 mg/1.5 mL 10 mg/1.5 mL  Vial, powder for reconstitution: 5.8 mg/vial	-
Somatropin (Saizen <sup>®</sup> )	Pediatric indications: growth hormone deficiency  Adult indications: growth hormone deficiency <sup>  </sup>	Cartridge, powder for reconstitution: 8.8 mg  Vial, powder for reconstitution: 5 mg (15 IU) 8.8 mg (26.4 IU)	-
Somatropin (Serostim <sup>®</sup> )	Adult indications: human immunodeficiency virus-associated wasting or cachexia	Vial, powder for reconstitution: 4 mg (12 IU)  Vial, powder for reconstitution (preservative-free): 5 mg (15 IU) 6 mg (18 IU)	-
Somatropin (Zomacton <sup>®</sup> )	Pediatric indications: growth hormone deficiency	Vial, powder for reconstitution: 5 mg	-

Generic (Trade Name)	Food and Drug Administration Approved Indications	Dosage Form/Strength	Generic Availability
		10 mg	
Somatropin (Zorbtive®)	Adult indications: treatment of short bowel syndrome in patients receiving specialized nutritional support	Vial, powder for reconstitution: 8.8 mg	-

IU=International units

\*For patients that fail to manifest catch-up growth by age two years.

†For patients that fail to manifest catch-up growth by age two to four years.

‡Defined by height standard deviation score  $\leq -2.25$ , and associated with growth rates unlikely to permit attainment of adult height in the normal range, in pediatric patients whose epiphyses are not closed and for whom diagnostic evaluation excludes other causes associated with short stature that should be observed or treated by other means.

§Nutropin® should be used in conjunction with optimal management of CKD.

#Indicated for long-term treatment.

¶Zorbtive® should be used in conjunction with optimal management of Short Bowel Syndrome.

|| For patients who meet either adult-onset criteria (patients who have GH deficiency, either alone or associated with multiple hormone deficiencies (hypopituitarism), as a result of pituitary disease, hypothalamic disease, surgery, radiation therapy, or trauma) or childhood-onset criteria (Patients who were GH deficient during childhood as a result of congenital, genetic, acquired, or idiopathic causes).

### Evidence-based Medicine

- The evidence demonstrating the safety and efficacy of growth hormone (GH) in Food and Drug Administration approved indications is well established. Overall, treatment with GH is consistently “superior” to no treatment and/or placebo and data suggests that not one specific dosing regimen for each indication is preferred over another. Treatment with GH should be individualized based on growth response and tolerability.
- Of note, limited head-to-head clinical trials exist; therefore, it is difficult to determine if one specific preparation of GH (i.e., somatropin) is “superior” to another.<sup>23-153</sup> Treatment guidelines do not distinguish among the various preparations.<sup>12-22</sup>

### Key Points within the Medication Class

- According to Current Clinical Guidelines:
  - Among pediatric patients, growth hormone (GH) (somatropin) is recommended as a treatment option for children with growth failure associated with any of the following: growth hormone deficiency (GHD), Turner syndrome, Prader Willi syndrome, chronic renal insufficiency, born small for gestational age with subsequent growth failure at four years of age or later and short stature homeobox-containing gene deficiency.<sup>13,14,17-19</sup> GH is also a treatment option for pediatric patients with Noonan syndrome.<sup>15,16</sup>
    - The choice of preparation should be individualized after informed discussion between the responsible clinician and the patient and/or caretaker about the advantages or disadvantages of available preparations, taking into consideration therapeutic need and likelihood of adherence to treatment. If more than one preparation is suitable, the least costly should be chosen.
  - Among adult patients, GH is recommended for the approved uses of the preparation in patients with clinical features suggestive of adult GHD and biochemically proven evidence of GHD.<sup>21,22</sup>
- Other Key Facts:
  - No agents in the class are currently available generically.

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10. Zomacton® [package insert]. Parsippany (NJ): Ferring Pharmaceuticals Inc.; 2016 Feb.
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