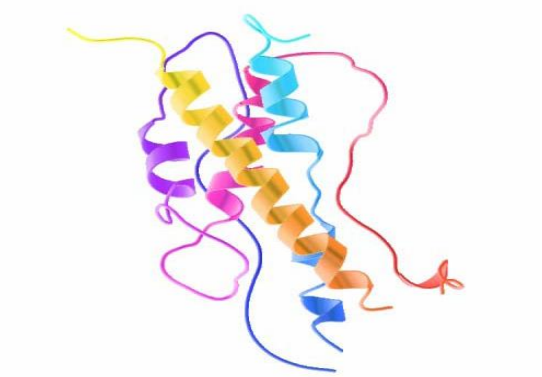
DAEWOONG PHARMACEUTICAL CO.,LTD.

Caretropin™

Daewoong Recombinant Human Growth Hormone



Active ingredient	**Somatropin**
Host cell	**Recombinant *Escherichia coli***
Indication	**Growth hormone deficiency**
Formulation	**1. Lyophilized powder in vial** **2. Liquid form in cartridge**
Administration	**Subcutaneous(s.c.) injection**

General Information

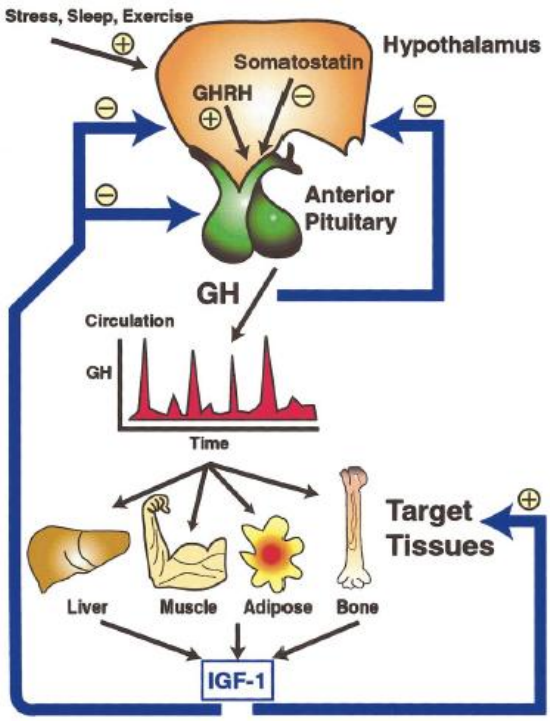
1. What is growth hormone?

Growth hormone (GH) is a single polypeptide hormone secreted from the cells of the pituitary gland. GHs in human are present as isomers of 27, 22, 20, 17, and 5 kDa. GH of 22 kDa, called somatropin, is the major component of GHs produced by human pituitary and used for the therapy. This kind of GH is composed of 191 amino acids and contains four α-helices arranged in a left-handed bundle orientation. Two disulfide bridges are located at Cys53-Cys165 and Cys182-Cys189 in GH, and the Cys residues make up the loop structure of the GH molecule.

The main effect of GH is to promote postnatal longitudinal growth. Hyposecretion of GH can lead to dwarfism. The growth-promoting effects of GH result from GH's diverse and pleiotropic effects on cellular metabolism and differentiation. GH is known to regulate the lipid, carbohydrate, nitrogen, and mineral metabolism within a cell. Many of GH actions are mediated by the activation of insulin-like growth factor I (IGF-1).

GH produced using recombinant DNA technology was approved by FDA for the treatment of children in short status in 1980s. Only the recombinant human GH (rhGH) has been used for the therapy since 1985, following the reports of Creutsfeldt-Jakob disease in four patients administered with pituitary-derived hGH. GH is also used for the treatment of adults with GH deficiency (GHD).

2. Mechanism of Action



- ► Secreted from a pituitary gland
- ► Binds to target tissues and activates their metabolism
  - → Promote bone-growth
  - → Facilitate IGF-1 synthesis
  - → Increase protein synthesis
  - → Decrease glucose level in blood
  - → Facilitate degradation of fat, etc.

Caretropin™ Products

1. Caretropin™ Lyophilized Powder (4 IU, 16 IU)

► Current status
- 16 IU: Approved in 2007 by Korean FDA
- 4 IU: Expected to be approved in 2011 by Korean FDA

► Stability
- 16 IU: Stable for 24 months (Stability test will be conducted at 30 and 36 months)
- 4 IU: Stable for 12 months (Stability test will be conducted at 18, 24, 30 and 36 months)

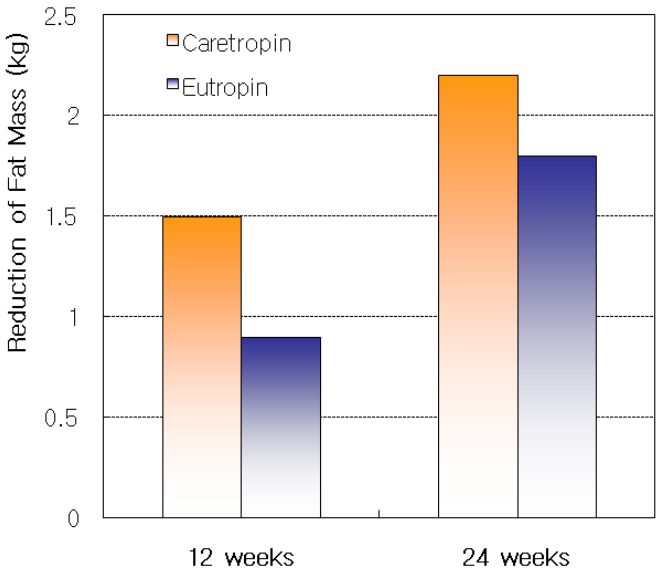
2. Caretropin™ Liquid Cartridge with Pen-type Syringe (22 IU)

► Pen-type syringe
- Type: reusable, multidose, dose dialing
- Injection method: push type
- 1.5 mL cartridge: ISO 11608-3 compatible

► Current status
- Approved in Dec. 2010 by Korean FDA

► Stability
- Stable for 18 months (Stability test will be conducted at 24, 30 and 36 months)

Phase 3 comparative study results of Caretropin™ are superior to Eutropin™



► Indication: Growth hormone deficiency in adults

► Methodology: Open, controlled study, therapeutic confirmatory study, randomized comparative method, multi-center trial

► Primary endpoint: Reduction of fat mass

► Secondary endpoint: LBM (Lean body mass)
WHR (Waist to hip ratio)
QoL (Quality of life)
IGF-1 (Insulin growth factor-1)
BMD (Bone mass density), etc.

► Conclusion

We evaluated the efficacy and safety of Caretropin™ in comparison with reference (Eutropin™). As a result of PP analysis on primary endpoint, change of fat mass had no significant difference and not shown the inferiority between two groups. Also, on PP analysis of secondary endpoint, no significant difference was observed. On evaluating the safety, an unusual and new adverse effect was not shown. The laboratory test results showed no difference among the groups. According to the results, we concluded that Caretropin™ and Eutropin™ had no difference on the efficacy and safety.

Quality of Caretropin™ Liquid Cartridge

1. GMP

Manufacturing plant in which Caretropin™ is produced conforms to KGMP (Korea Good Manufacturing Practice) as recommended by WHO guidance.

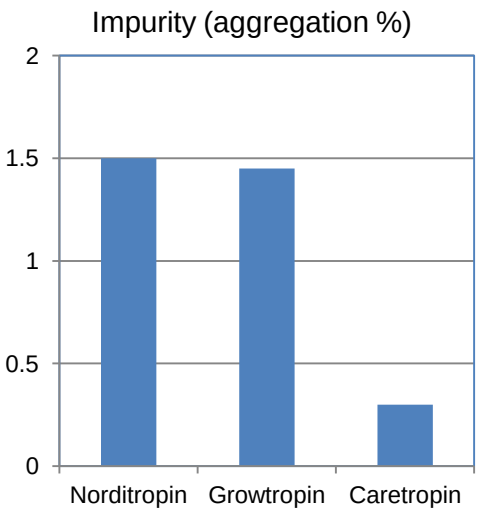
Stability of Caretropin™ Liquid Cartridge

1. Accelerated test

After 2 week in stress condition 40℃, 75% RH, Caretropin™ Liquid Cartridge showed higher stability than others in accelerated test. In the liquid formulation, the stability is very important for patient to use it in their home.

Product	Stability and Storage
Norditropin Cartridges	Be stored in the pen **in the refrigerator (2-8℃) and used within 4 weeks**
	May be stored for up to 3 weeks at not more than 25℃ (unused portion)
Nutropin AQ	Contents are stable for 28 days after initial use when stored at 2-8℃ (under refrigeration)
	There is no stability information at 25℃.
Accretropin	Be stored in the refrigerator (2-8℃).
	Once opened, Accretropin may be stored up to 14 days when refrigerated (2-8℃)
	There is no stability information at 25℃.

(Ref.: www.rxlist.com)



Patent Status

1. Manufacturing Process

"Novel human growth hormone releasing factor(hGRF)-human epidermal growth factor fusion gene, and its expression vector and manufacturing process of hGRF"

- Registered: Korea (KR 1999-0009995)

2. Liquid Formulation

"A stable liquid formulation of human growth hormone"

- Registered: Korea (KR 2005-0046381)
- Pending: PCT, China, Europe, Japan, USA, Brazil, India, Russia

3. Pen-type Syringe

"Medicines injectors"

- A patent is being processed for application in Korea, and Taiwan.

Key Benefits and Features

1. Convenience of Administration

- Liquid formulation with pen-type syringe
- Various dosage: 4 IU, 16 IU, 22 IU

2. Proven Efficacy

- The efficacy of Caretropin™ is superior to Eutropin™ (LGLS)
- Effective for the reduction of abdominal obesity in adults

3. High Quality & Competitive Price

- Compliance with European Pharmacopoeia standards
- High production yield using patent vector system

Product Information

[Components]

In 1 vial

■ Active ingredient: Recombinant human growth hormone ---------- 16 IU (5.3 mg)

■ Solvent: Water for injection (KP) ---------- 1 mL

In 1 cartridge

■ Active ingredient: Recombinant human growth hormone ---------- 22 IU (7.5 mg)

[Appearance]

Caretropin™ Lyophilized Powder

■ Active ingredient: White powder filled in a vial

Clear and colourless liquid when it is solved in solvent

■ Solvent: A colourless, transparent liquid filled in a vial

Caretropin™ Liquid Cartridge

■ Active ingredient: Colourless and transparent liquid in colourless and transparent cartridge

[Indication and usage]

Adult patients: Treatment of adults with either childhood-onset or adult-onset growth hormone deficiency.

[Dosage and administration]

Adult GH deficiency: A starting dose of 0.125 IU (0.04 mg)/kg of body weight (given in divided doses 6 to 7 times per week) is administered subcutaneously. The dose may be increased gradually to a maximum of 0.25 IU (0.08 mg)/kg of body weight per a week. Dose increase is adjusted based on the adverse event and serum IGF-1 concentrations according to age and gender. The minimum effective dose should be used.

In case of continuous edema or severe dysaesthesia, the dose should be decreased to avoid carpal tunnel syndrome.

[Storage]

Store Caretropin™ Lyophilized Powder or Liquid Cartridge in the refrigerator at 2-8℃ protecting from light.

[Expiring date]

■ Caretropin™ Lyophilized Powder: 24 months

■ Caretropin™ Liquid Cartridge: 18 months

Release Date : 2011.03.16

http://www.daewoong.com

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