Therapeutic Class Review[SM]

Hormones – Insulin Growth Factor -1
Mecasermin (Increlex®)

February 2006

New Product for Review:

Mecasermin (Increlex)

[also known as recombinant insulin growth factor- 1 (rhIGF-1)]

Dossier Provided by Manufacturer:

Dossier Evaluation: Requested 12/6/05; Not available.

Executive Summary

- The FDA approved mecasermin (Increlex) as an orphan drug in the treatment of extreme short stature for severe cases of IGF-1 deficiency or growth hormone resistance.
- The target population for which mecasermin (Increlex) is intended is rare and has no other treatment option.
  - Approximately 60,000 children world-wide have IGF-1 deficiency.
  - Less than 12,000 of these children have a severe deficiency.
- Tercica licensed rights to develop, manufacture and commercialize mecasermin (Increlex) from Genentech, Inc.
- Mecasermin (Increlex) has been studied in many other conditions and has large potential for off-label use in short stature due to other causes and/or endocrine/metabolic diseases.

Evidence:

- The FDA approved mecasermin (Increlex) based on a small open-label trial in recognition that:
  - Primary IGF-1 deficiency is a rare condition.
  - Large scale trials with robust study designs are unlikely.
- There is no useful evidence supporting mecasermin (Increlex) in treatment of short stature due to IGF-1 deficiency or that treatment allows children to achieve adult heights that will improve their ability to perform activities of daily living, ability to function, or cognitive thinking.
- Mecasermin (Increlex) has no proven benefit in the following:

- Milder forms of short stature from IGF-1 deficiency
- Short stature due to unknown cause (idiopathic short stature) or other underlying conditions (such as growth hormone deficiency, Prader Willi, or Turner's syndrome).
- Amyotrophic lateral sclerosis
- Type 1 Diabetes/Insulin Resistance (Phase III trials in diabetes and development efforts were suspended by the previous manufacturer, Genentech, for continued exploration of other intended uses).
- AIDS-wasting
- Cystic fibrosis

Caution is urged regarding the use of uncertain evidence trials in making health care decisions.

- Harms data is unreliable to evaluate the long-term benefit versus risks of mecasermin (Increlex).

Decision

Maintain mecasermin (Increlex) as non-preferred/non-formulary because there is no useful evidence to base long-term benefits or harms in the treatment of conditions which mecasermin (Increlex) has been studied in.

I. Products

Drug Product	FDA approval	FDA approved indications	Usual Dose/Route	Potential Off-label Uses[2,12,14-16]
mecasermin (Increlex®)	8/30/05	Long-term treatment of growth failure in children with severe primary IGF-1 deficiency or growth hormone gene deletion with neutralizing antibodies.	0.04 – 0.08mg/kg (40 to 80 mcg/kg) SQ twice daily.	Amyotrophic lateral sclerosis Diabetes mellitus, Mild-moderate primary IGF-1 deficiency, Short stature; HIV infection

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