



Therapeutic Class ReviewSM

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.

Available Therapeutic Alternatives: none

Reason for Review:

Determine preferred/formulary status for mecasermin (Increlex). Mecasermin is the synthetic version of human insulin-like growth factor-1 (IGF-1) given as a twice daily subcutaneous injection to improve height in children with extreme short stature due to IGF-1 deficiency and/or growth hormone resistance.

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.
 - Tercica predicts treatment of primary IGF-1 deficiency in children to be:
 - a \$200 million marketing opportunity with mecasermin (Increlex) as a treatment for the severe form of this condition.
 - a \$1 billion world-wide market with future plans to expand the labeling to a broader pediatric population with milder IGF-1 deficiency and short stature.

- Tercica will likely have future competition in late 2006 from another pipeline IGF-1 product combined with an IGF-1 binding protein (made by Insmed) and designed for once daily SQ administration.
- 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).

Conclusion

There is no useful evidence by which to gauge the long-term benefits or harms of the treatment of conditions in which mecasermin (Increlex) has been studied. However, because of the lack of preferred/formulary options that exist for the small population affected by these conditions, mecasermin (Increlex) is a preferred/formulary medication.

Products

| Drug Product | FDA approval | FDA approved indications | Usual Dose/Route | Cost ^a | 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. | 10mg/ml 4ml vial = \$562.50 per vial | Amyotrophic lateral sclerosis Diabetes mellitus, Mild-moderate primary IGF-1 deficiency, Short stature; HIV infection |

^a Cost estimate based on AWP (average wholesale price) listed in First Data Bank or MAC (maximum allowable cost) as of December 2005 for 1 month of therapy.

References

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