Mecasermin

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Approved indication: primary insulin-like growth factor-1 deficiency

Increlex (Ipsen)
vials containing 10 mg/mL solution

Some children fail to grow as expected because of an insensitivity to growth hormone. One cause is a deficiency of insulin-like growth factor-1 (IGF-1), as in Laron syndrome. In affected children, there is an abnormality in the growth hormone receptor. As a result, growth hormone fails to stimulate the synthesis of IGF-1 in the liver. This leads to slow growth and very short stature. In untreated patients the final height can be 4–10 standard deviations below the mean.

Genetic engineering has enabled the production of mecasermin, a recombinant human IGF-1. It has been available overseas for more than 10 years. Mecasermin is given twice daily by subcutaneous injection. It should be given shortly before or after a meal to reduce the risk of hypoglycaemia. The half-life of mecasermin is about six hours. It is metabolised in the liver and kidneys, but there is no information about how impairment of these organs might affect the drug's pharmacokinetics. Doses are based on body weight and adjusted according to adverse reactions and growth. Treatment continues until epiphyseal fusion.

Primary IGF-1 deficiency is a very rare condition. Clinical trials have therefore been small and mostly open label.

One open-label trial of mecasermin has followed 76 children with severe IGF-1 deficiency for up to 12 years. In the first year of treatment, growth increased from a baseline of 2.8 cm/year to 8 cm/year. The higher the dose, the faster the growth. Growth velocities remained above baseline for up to eight years of follow-up.[1] There were 21 children, treated for an average of 10 years, who reached an adult or new-adult height. They were an average of 13.4 cm taller than they would have been without treatment.[2]

Some of the adverse effects of an insulin-like growth factor are related to its mechanism of action. For example, some children will have seizures related to hypoglycaemia.[1] Blood glucose monitoring is recommended when the dose is changed and when a child is unwell or has reduced oral intake.

Giving a growth factor can cause hypertrophy of some tissues. The growth of lymphoid tissue in the tonsils and adenoids[1] can lead to chronic middle ear effusions, snoring and sleep apnoea. IGF-1 may have a role in cancer so children treated with mecasermin could have an increased risk of benign and malignant neoplasia.

Headache is a common adverse effect, but can be a symptom of intracranial hypertension. Fundoscopy is recommended particularly if there are other symptoms such as vomiting or altered vision.

An echocardiogram is recommended before treatment. Valve incompetence and cardiomegaly are uncommon adverse effects.

A European database of children being treated with IGF-1 therapy contained a safety population of 188 patients. The most frequent serious adverse events recorded in the database were hypoglycaemia, adeno-tonsillar hypertrophy and injection-site reactions.[3]

The approval of mecasermin in Australia is restricted to children who have the most severe manifestations of primary IGF-1 deficiency. Other causes of the deficiency must be excluded before beginning treatment. Mecasermin is not intended for secondary forms of IGF-1 deficiency such as hypopituitarism, malnutrition or chronic steroid therapy.

REFERENCES

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At the time the comment was prepared, information about this drug was available on the websites of the Food and Drug Administration in the USA, the European Medicines Agency and the Therapeutic Goods Administration.