

Intracranial hypertension (increased pressure around the brain)

High pressure in fluid around the brain (intracranial hypertension) can occur in some patients receiving Increlex treatment. Increased pressure in the brain may be caused by one of several factors other than treatment with Increlex. Therefore, if your child experiences symptoms of increased pressure in the brain, which include severe headache, pain behind the eyes or visual changes such as blurred vision with nausea and vomiting, it is important to determine the reason for these symptoms.

It is important to tell your doctor if your child has an unexplained, severe, persistent headache or visual disturbance. By examining your child's eyes, your doctor can confirm whether or not your child has increased pressure in their brain. Your doctor may then perform further tests to determine the cause of these symptoms and may adjust the dose of Increlex or stop treatment if necessary. It may be possible to restart treatment after the symptoms disappear.

Allergic (hypersensitivity) reactions

Increlex should not be given if your child is allergic (hypersensitive) to mecasecamin or any of the other ingredients of Increlex.

Allergic reactions have been reported in a few patients receiving Increlex treatment and can occur at the site of the injection (local reaction) or affect the whole body (systemic reaction). Allergic reactions at the injection site include itching (pruritus), redness and hives (urticaria) and these types of localised reactions usually do not require any further action.

Systemic allergic reactions affect the whole body, with swelling of the face especially around the mouth and tongue (angioedema), hives over the whole body (generalised urticaria), or swelling of the throat causing difficulty in breathing (dyspnoea). This medical condition could be life-threatening and may require admission to hospital.

It is important to take special care if your child has a systemic allergic reaction with Increlex. You should stop the treatment and get immediate medical help if your child gets a generalised rash or hives on the body located away from the injection site, develops trouble with their breathing, faintness, collapse or feels generally unwell.

Other side effects

You should consult your doctor if your child feels unwell or displays any of the following clinical symptoms:

- ✿ New or worsening snoring, breathing problems during sleep, ear pain, hearing problems or a feeling of fullness in the ears (these may be because treatment with Increlex has caused your child's tonsils and/or adenoids to get bigger)
- ✿ Worsening of a curved spine (scoliosis)
- ✿ Limp, difficulty walking or complains of hip or knee pain

Reporting of side effects

Increlex[®] is subject to additional monitoring as a condition of the licence allowing it to be sold in Europe. This will allow quick identification of new safety information. You can help by reporting any side effects your child gets. If your child gets any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet.

You can also report side effects directly via the Yellow Card Scheme at www.mhra.gov.uk/yellowcard.

By reporting side effects you can help provide more information on the safety of this medicine.

Further information

If you have any other questions or concerns about your child's condition or Increlex treatment, please speak to your doctor or nurse.

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Important Risk Minimisation Information for Patients

Patient Educational Information about Severe Primary IGF-1 Deficiency and how Increlex[®] can help

Introduction

As a parent or caregiver, your biggest concern is for your child's welfare. So, when you are told that there is a medical reason why your child is shorter than other children their age, you would naturally want to know as much detail as possible about the condition and the treatment that has been prescribed.

This booklet has been prepared to help you better understand the medical condition and prescribed treatment. It includes a questions and answer section that you and your child can read and discuss together.

What is Severe Primary IGF-1 Deficiency?

Severe primary IGF-1 deficiency (SPIGF-D) is one of the causes of short stature and children with this condition are much shorter than other children of the same age. Children with SPIGF-D have low levels of a hormone called IGF-1 in their blood but have normal levels of another hormone called growth hormone.

IGF-1 is insulin-like growth factor-1, a naturally occurring hormone that plays an important role in a child's growth. IGF-1 deficiency or IGFD is a term that describes lower than expected levels of IGF-1 in the blood. When IGF-1 levels are low, growth does not occur as it should. This clinical condition is known as severe primary IGF-1 deficiency or SPIGF-D.

The term 'severe' is used by doctors for the purpose of classification of the IGF-1 levels; the term 'primary' means that the IGF-1 deficiency does not result from other medical conditions.

Parents, patients and caregivers – answers to your questions

What is Increlex?

Increlex contains a recombinant (man-made) form of IGF-1, and is also called mecasermin. It has the same chemical structure and acts in the same way as naturally produced IGF-1.

Increlex is used to treat children who have growth problems because they have low levels of IGF-1 in their blood.

How is Increlex administered?

Increlex is given as an injection just under the skin (subcutaneous), twice each day. It must be given shortly before or just after a meal. This is because it has effects similar to insulin and therefore reduces the level of sugar in the blood.

Lipohypertrophy (small lump under the skin at injection site)

Increlex must be given using a different site at every injection, usually the stomach, thigh, buttocks or upper arm, to avoid an increase in fat tissue, also known as lipohypertrophy, around the area you inject. It is very important to be careful to rotate the sites, as lipohypertrophy will stop Increlex being absorbed into the body, and it will therefore not be effective.

The prescribed dose and frequency of Increlex injection should not be exceeded.

What are the possible side effects?

The possible side effects and ways of avoiding these side effects are described below.

Cancerous and non-cancerous tumours

The risk of developing cancerous or non-cancerous growths may be higher in patients who are receiving Increlex. It is important that your child does not receive this medicine if they have (or are suspected of having) any abnormal growths (tumours, cysts etc.) or any symptoms of cancer.

The risk of developing cancerous or non-cancerous growths may also be higher in patients who receive Increlex in a manner different to what is described on the package label, for example if they receive Increlex at a dose higher than that stated on the packaging or if they receive Increlex for a medical condition other than SPIGFD. Your doctor should discuss the potential benefits and risks of Increlex treatment with you. They may measure your child's IGF-1 level prior to treatment. You will also receive guidance on how to recognise the signs and symptoms of cancer, so that it may be found early if it does occur, and medical

treatment started as soon as possible.

Hypoglycaemia (low level of blood sugar)

The most common side effect is hypoglycaemia, an abnormally low level of blood sugar. The risk of hypoglycaemia is highest at the start of treatment, before the best dose of Increlex for your child has been found.

The symptoms and signs of hypoglycaemia may include some or all of the following: shaking, sweating or clamminess, feeling anxious, restless or confused, poor concentration, fast or irregular heart rate, excessive hunger, headache, feeling faint or dizzy, blurred vision, nausea or vomiting, tiredness, seizures, loss of consciousness.

The occurrence of hypoglycaemia can usually be avoided by giving each injection shortly before or immediately after a meal (within 20 minutes). Your child should always have a source of sugar such as orange juice, glucose gel or sweets available in case symptoms of hypoglycaemia occur. It is important that your child has a well-balanced diet including protein and fat such as meat and cheese in addition to sugar-containing foods.

In cases of severe hypoglycaemia, when symptoms do not get better or get worse even after eating or drinking a source of sugar, or if it is not possible for your child to drink sugar-containing fluids, medical attention should be obtained urgently as your child may require an injection of glucagon to increase their blood sugar level. Glucagon raises the blood sugar when it is injected. The clinical team at your hospital may teach you how to use glucagon, in case you need to give it to your child.

Increlex must not be given if your child is unable to eat for any reason. The dose of Increlex should not be increased to make up for one or more missed doses.

As a precaution, your child should avoid any high-risk activities such as intensive physical activity within 2-3 hours after the injection until a well-tolerated dose of Increlex has been established. This is particularly true at the start of Increlex treatment or if the dose of Increlex has been increased for any reason. **Your child should be monitored at fingertip for blood sugar (glucose) before each meal at treatment initiation and until a well-tolerated dose of Increlex is established.**

If frequent symptoms of hypoglycaemia or severe hypoglycaemia occur, blood sugar monitoring should continue regardless of eating condition and if possible, at the time of the event.