Package leaflet: Information for the user

INCRELEX 10 mg/ml solution for injection
Mecasermin

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects, you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What INCRELEX is and what it is used for

- INCRELEX is a liquid that contains mecasermin which is a man-made insulin-like growth factor-1 (IGF-1), which is similar to the IGF-1 made by your body.
- It is used to treat children and adolescents from 2 to 18 years old who are very short for their age because their bodies do not make enough IGF-1. This condition is called primary IGF-1 deficiency.

2. What you need to know before you use INCRELEX

Do not use INCRELEX
- If you currently have any tumour or growth, either cancerous or non-cancerous
- if you have had cancer in the past
- if you have any conditions which may increase the risk of cancer
- if you are allergic to mecasermin or any of the other ingredients of this medicine (listed in section 6)
- in premature babies or neonates because it contains benzyl alcohol

Warnings and precautions
There is an increased risk of tumours and growths (both cancerous and non-cancerous) in children and adolescents treated with INCRELEX. If any new growth, skin lesion or any unexpected symptom occurs during treatment or after treatment, see your doctor immediately since mecasermin may play a role in cancer development.

Talk to your doctor or pharmacist before using INCRELEX
- if you have a curved spine (scoliosis). You should be monitored for progression of scoliosis.
- if you develop a limp or hip or knee pain.
- if you have enlarged tonsils (tonsillar hypertrophy). You should have examinations periodically.
- if you have symptoms of increased pressure in the brain (intracranial hypertension), such as visual changes, headache, nausea and/or vomiting, contact the doctor for advice.
- if you have a localised reaction at the injection site or generalised allergic reaction with INCRELEX. Call the doctor as soon as possible if you get a localised rash. Get medical help immediately if you have

a generalised allergic reaction (hives, trouble breathing, faintness or collapse and feeling generally unwell).
- if you have finished growing (the bone growth plates are closed). In this case INCRELEX cannot help you grow and should not be used.

Children under 2 years old

The use of this medicine has not been studied in children under 2 years of age and is therefore not recommended.

Other medicines and INCRELEX

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Especially tell the doctor if you take insulin or other anti-diabetes medicines. A dose adjustment may be needed for these medicines.

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before using this medicine.

A negative pregnancy test is recommended for all women of child bearing potential prior to treatment with mecasermin. It is also recommended that all women of childbearing potential use adequate contraception during treatment.

Mecasermin therapy should be discontinued if pregnancy occurs.

Mecasermin should not be administered to a breast-feeding mother.

Driving and using machines

Mecasermin may cause hypoglycaemia (very common side effect, see section 4) that may impair your ability to drive and use machines because your ability to concentrate or react may be reduced.

You should avoid engaging in any high-risk activities (e.g., driving, etc.) within 2-3 hours after dosing, particularly at the start of INCRELEX treatment, until a dose of INCRELEX has been found which does not cause side effects that make these activities risky.

INCRELEX contains benzyl alcohol and sodium

INCRELEX contains benzyl alcohol as a preservative which may cause toxic reactions and allergic reactions in infants and children up to 3 years old.

This medicine contains less than 1 mmol sodium (23 mg) per vial, that is to say essentially ‘sodium-free’.

3. How to use INCRELEX

Always use this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

The typical dose is 0.04 to 0.12 mg/kg of patient weight administered twice a day. See the ‘Instructions for Use’ at the end of this leaflet.

Inject INCRELEX just under your skin shortly before or after a meal or snack because it may have insulin-like hypoglycaemic effects and so it may decrease blood sugar levels (see hypoglycaemia in section 4). Do

not inject your dose of INCRELEX if you cannot eat for any reason. Do not make up the missed dose by giving two doses the next time. The next dose should be taken as usual, with a meal or snack.

Inject INCRELEX just below the skin in your upper arm, upper leg (thigh), stomach area (abdomen), or buttocks. Change the injection site for each injection. Never inject it into a vein or muscle.

Only use INCRELEX that is clear and colourless.

Treatment with mecasermin is a long-term therapy. For further information ask the doctor.

If you use more INCRELEX than you should

Mecasermin, like insulin, may lower blood sugar levels (see hypoglycaemia in section 4).

If more INCRELEX than recommended was injected, contact your doctor immediately.

Acute overdose could lead to hypoglycaemia (low blood sugar).

Treatment of acute overdose of mecasermin should be directed at reversing hypoglycaemia. Sugar-containing fluids or food should be consumed. If the patient is not awake or alert enough to drink sugar-containing fluids, an injection of glucagon into the muscle may be necessary to reverse the low blood sugar. Your doctor or nurse will instruct you how to give the injection of glucagon.

Long-term overdose may result in enlargement of certain body parts (e.g., hands, feet, parts of the face) or excessive growth of the whole body. If you suspect long-term overdose, contact your doctor immediately.

If you forget to use INCRELEX

Do not use a double dose to make up for a forgotten dose.
If a dose is skipped, the next dose should not be made larger to compensate. The next dose should be taken as usual, with a meal or snack.

If you stop using INCRELEX

A disruption or early ending of treatment with mecasermin may impair the success of the growth therapy. Please ask the doctor for advice before stopping the treatment.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

The most frequently occurring side effects with mecasermin are: low blood sugar (hypoglycemia), vomiting, injection site reactions, headache and middle ear infections. Serious allergic reactions have also been reported with INCRELEX. If you develop any of these events, please follow the advice given for each event in the sections below.

Frequency not known (frequency cannot be estimated from the available data)
Cancerous and non-cancerous tumours
An increase in both cancerous and non-cancerous tumours has been reported in patients treated with INCRELEX. The risk of such tumours may be higher if INCRELEX is used for condition other than what is stated in Section 1 or used at higher than recommended dose as per Section 3.

Serious allergic reactions (anaphylaxis)

Generalised hives, difficulty in breathing, dizziness, swelling of the face and/or throat have been reported following mecasermin use. Stop INCRELEX immediately and seek urgent medical advice if you develop a serious allergic reaction.
Local allergic reactions at the injection site (itching, hives) have also been reported.

Hair loss (alopecia)
Hair loss has also been reported following mecasermin use.

Very common (may affect more than 1 in 10 people)
Low blood sugar (hypoglycaemia)
Mecasermin may lower blood sugar levels. Signs of low blood sugar are: dizziness, tiredness, restlessness, hunger, irritability, trouble concentrating, sweating, nausea and fast or irregular heartbeats.

Severe hypoglycaemia may cause unconsciousness, seizures/fits or death. Stop INCRELEX immediately and seek urgent medical advice if you develop seizures/fits or become unconscious.

If you take INCRELEX, you should avoid participating in high risk activities (such as vigorous physical activity) within 2 to 3 hours after INCRELEX injection, especially at the beginning of INCRELEX treatment.

Before beginning treatment with INCRELEX the doctor or nurse will explain to you how to treat hypoglycaemia. You should always have a source of sugar such as orange juice, glucose gel, sweets, or milk available in case symptoms of hypoglycaemia occur. For severe hypoglycaemia, if you are not responsive and cannot drink sugar-containing fluids, you should give an injection of glucagon. The doctor or nurse will instruct you how to give the injection. Glucagon raises the blood sugar when it is injected. It is important that you have a well-balanced diet including protein and fat such as meat and cheese in addition to sugar-containing foods.

You should be monitored at fingertip for blood sugar (glucose) before each meal at treatment initiation and until a well-tolerated dose 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.

Injection site hypertrophy (tissue at injection site increases in size) and bruising
These can be avoided by changing the injection site at each injection (injection site rotation).

Digestive system
Vomiting and pain in the upper belly have occurred with mecasermin treatment.

Infections
Infections of the middle ear have been observed in children with mecasermin treatment.

Musculoskeletal system
Joint pains and pains in the limbs have occurred with mecasermin treatment.

Nervous system
Headache has occurred with mecasermin treatment.

Common (may affect up to 1 in 10 people)
Seizures
Seizures (fits) have been observed with mecasermin treatment.
Dizziness and tremor have also been reported with mecasermin treatment.

Heart abnormalities
A fast heart rate and abnormal heart sounds have been reported with mecasermin treatment.

Increased blood sugar (hyperglycaemia)
Increased blood sugar has also been observed with mecasermin treatment.

Enlarged tonsils/adenoids
Mecasermin may enlarge your tonsils/adenoids. Some signs of enlarged tonsils/adenoids include: snoring, difficulty breathing or swallowing, sleep apnoea (a condition where breathing stops briefly during sleep), or fluid in the middle ear, as well as infections of the ear. Sleep apnoea can cause excessive daytime sleepiness. Call the doctor should these symptoms bother you. The doctor should regularly examine your tonsils/adenoids.

Enlarged thymus
An enlarged thymus (a specialised organ of the immune system) has been observed with mecasermin treatment.

Papilloedema
A swelling at the back of the eye (due to increased pressure within the brain) may be observed by a doctor or optician during mecasermin treatment.

Hypoacusis (hearing loss)
Hypoacusis (hearing loss), ear pain and fluid in the middle ear have been observed with mecasermin treatment. Tell the doctor if you develop hearing problems.

Worsened scoliosis (caused by rapid growth)
If you have scoliosis, you will need to be checked often for an increase in the curve of the spine.
Pain in muscles has also been seen with mecasermin treatment.

Reproductive system
Breast enlargement has been observed with mecasermin treatment.

Digestive system
Pain in the belly has occurred with mecasermin treatment.

Skin and hair changes
Skin thickening, moles and abnormal hair texture have been seen with mecasermin treatment.

Reactions at the injection site
Reactions including pain, irritation, bleeding, bruising, redness and hardening have been reported with INCRELEX treatment. Injection site reactions can be avoided by changing the injection site at each injection (injection site rotation).

Uncommon (may affect up to 1 in 100 people)
Increased pressure in the brain (intracranial hypertension)
INCRELEX can sometimes cause a temporary increase in pressure within the brain. The symptoms of intracranial hypertension can include visual changes, headache, nausea and/or vomiting. Tell the doctor immediately if you have any of these symptoms. Your doctor can check to see if intracranial hypertension is present. If it is present, your doctor may decide to temporarily reduce or discontinue mecasermin therapy. Mecasermin may be started again after the episode is over.

Heart abnormalities
In some patients treated with mecasermin, an ultrasound examination of the heart (echocardiogram) showed an increased size of the heart muscle and abnormalities of heart valve function. Your doctor may perform an echocardiogram before, during and after mecasermin treatment.

Reactions at the injection site
Reactions including rash, swelling and fatty lumps have been reported with INCRELEX treatment. Injection site reactions can be avoided by changing the injection site at each injection (injection site rotation).

Weight increase
Weight increase has been observed with mecasermin treatment.

Other uncommon side effects seen with mecasermin treatment include depression, nervousness.

Reporting of side effects
If you get 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 national reporting system (see details below). By reporting side effects, you can help provide more information on the safety of this medicine.

United Kingdom (Great Britain)
Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

5. How to store INCRELEX

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and label after EXP. The expiry date refers to the last day of the month.

Store in a refrigerator (2°C - 8°C). Do not freeze.
Keep the vial in the outer carton in order to protect from light.
After first use, the vial may be stored for up to 30 days at 2°C to 8ºC.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What INCRELEX contains
- The active substance is mecasermin. One ml contains 10 mg of mecasermin. Each vial contains 40 mg of mecasermin.
- The other ingredients are: benzyl alcohol, sodium chloride, polysorbate 20, glacial acetic acid, sodium acetate and water for injections (see section 2 "INCRELEX contains benzyl alcohol and sodium").

What INCRELEX looks like and contents of the pack

INCRELEX is a colourless to slightly yellow and clear to slightly opalescent solution for injection (injection) supplied in a glass vial closed with a stopper and a seal. The vial contains 4 ml of solution.

Pack size of 1 vial.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:
Ipsen Pharma
65, quai Georges Gorse
92100 Boulogne-Billancourt
France

Manufacturer:
Beaufour Ipsen Industrie
Rue Ethé Virton

28100 Dreux
France

Tjoapack Netherlands B.V.
Nieuwe Donk 9
4879 AC Etten-Leur
The Netherlands

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

United Kingdom (Great Britain)
Ipsen Limited.
Tel: + 44 (0) 1753 627777

This leaflet was last revised in May 2023.

This medicine has been authorised under ‘exceptional circumstances’. This means that because of the rarity of this disease it has been impossible to get complete information on this medicine.
The European Medicines Agency will review any new information on this medicine every year and this leaflet will be updated as necessary.

Other sources of information

Is this leaflet hard to see or read? Please phone +44 (0) 1753 627777 and ask for help.

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INSTRUCTIONS FOR USE

INCRELEX should be administered using sterile disposable syringes and injection needles which could be provided by your doctor, pharmacist or nurse. The syringes should be of small enough volume that the prescribed dose can be withdrawn from the vial with reasonable accuracy.

Preparing the dose

1. Wash your hands before getting INCRELEX ready for your injection.

2. Use a new disposable needle and syringe every time you give a dose. Use syringes and needles only once. Throw them away properly in a sharps container (such as a biohazard container), hard plastic container (such as a detergent bottle), or metal container (such as an empty coffee can). **Never** share needles and syringes.

3. Check the liquid to make sure it is clear and colourless. Do not use after the expiry date (which is stated on the label after EXP and it refers to the last day of the month) or if it is cloudy or if you see bits. If a vial freezes, dispose appropriately. Ask your pharmacist how to throw away medicines you no longer use.

4. If you are using a new vial, remove the protective cap. Do not remove the rubber stopper.

5. Wipe the rubber stopper of the vial with an alcohol swab to prevent contamination of the vial by germs that may be introduced by repeated needle insertions (see Figure 1).

Figure 1: Wipe top with alcohol

6. Before putting the needle into the vial, pull back on plunger to draw air into the syringe equal to the prescribed dose. Put the needle through the rubber top of the vial and push the plunger to inject air into the vial (see Figure 2).

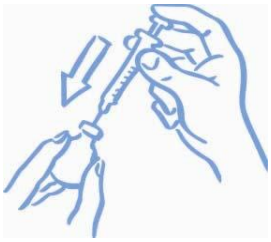


Figure 2: Inject air into vial

7. Leave the syringe in the vial and turn both upside down. Hold the syringe and vial firmly (see Figure 3).

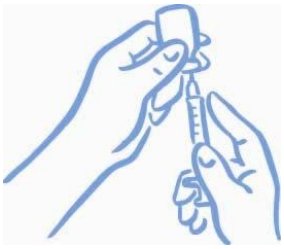


Figure 3: Prepare for extraction

8. Make sure the tip of the needle is in the liquid (see Figure 4). Pull the plunger to withdraw the correct dose into the syringe (see Figure 5).

Figure 4: Tip in liquid

Figure 5: Extract correct dose

9. Before you take the needle out of the vial, check the syringe for air bubbles. If bubbles are in the syringe, hold the vial and syringe with needle straight up and tap the side of the syringe until the bubbles float to the top. Push the bubbles out with the plunger and draw liquid back in until you have the correct dose (see Figure 6).

Figure 6: Remove air bubbles and refill syringe

10. Remove the needle from the vial and replace the protective cap. Do not let the needle touch anything. You are now ready to inject (see Figure 7).

Figure 7: Ready to inject

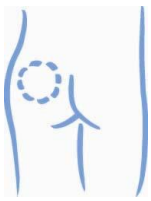
Injecting the dose:

Inject INCRELEX as instructed by the doctor.
Do not give the injection if you are unable to eat shortly before or after the injection.

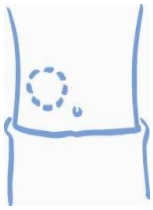
1. Decide on an injection area – upper arm, thigh, buttock, or abdomen (see below). The injection site should be changed for each injection (rotate the injection site) to avoid formation of a lump of fatty tissue under your skin (lipohypertrophy) caused by repeated injections in the same place.

Upper arm

Thigh



Buttock



Abdomen

2. Use alcohol or soap and water to clean the skin where you are going to inject you. The injection site should be dry before you inject.

3. Lightly pinch the skin. Insert the needle in the way the doctor showed you. Release the skin (see Figure A).

Figure A: Lightly pinch the skin and inject as instructed

4. Slowly push in the plunger of the syringe all the way, making sure you have injected all the liquid. Pull the needle straight out and gently press on the spot where you injected you with gauze or a cotton ball for a few seconds. **Do not rub the area** (see Figure B).

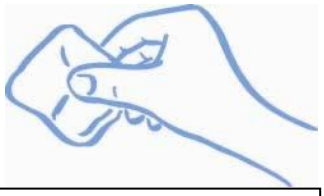


Figure B: Press (don't rub) with gauze or cotton

5. Follow the doctor's instructions for throwing away the needle and syringe. Do not recap the syringe. Used needle and syringe should be placed in a sharps container (such as a biohazard container), hard plastic container (such as a detergent bottle), or metal container (such as an empty coffee can). Such containers should be sealed and disposed of properly in the way your doctor described.