

Package leaflet: Information for the user
INCRELEX 10 mg/ml solution for injection
Mecasermin

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.

What is in this leaflet

1. What INCRELEX is and what it is used for
2. What you need to know before you use INCRELEX
3. How to use INCRELEX
4. Possible side effects
5. How to store INCRELEX
6. Contents of the pack and other information

1. What INCRELEX is and what it is used for

- INCRELEX is a liquid that contains mecasecamin which is a man-made insulin-like growth factor-1 (IGF-1), which is similar to the IGF-1 made by your body.
- INCRELEX 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 are allergic to mecasecamin or any of the other ingredients of this medicine (listed in section 6).
- if you have cancer.
- in premature babies or neonates because it contains benzyl alcohol.

Warnings and precautions

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, has 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

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

INCRELEX therapy should be discontinued if pregnancy occurs.

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

Driving and using machines

INCRELEX may cause hypoglycaemia (very common side effect) 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

INCRELEX contains 9 mg per ml of benzyl alcohol as a preservative.

Benzyl alcohol may cause toxic reactions and allergic reactions in infants and children up to 3 years old.

This medicinal product contains less than 1 mmol sodium (23 mg) per vial, i.e. 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. Never inject it into a vein or muscle. Change the injection site for each injection.

Only use INCRELEX that is clear and colourless.

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

If you use more INCRELEX than you should

INCRELEX, 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). 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.

Treatment of acute overdose of INCRELEX 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.

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 INCRELEX 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 INCRELEX are: low blood sugar (hypoglycemia), injection site reaction, snoring, hearing loss, headache and enlarged tonsils. 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)

Serious allergic reactions (anaphylaxis)

Can cause generalised hives, difficulty in breathing, dizziness, swelling of the face and/or throat have been reported. 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 INCRELEX use.

Very common (may affect more than 1 in 10 people)

Low blood sugar (hypoglycaemia)

INCRELEX 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.

Enlarged tonsils/adenoids

INCRELEX may enlarge your tonsils/adenoids. Some signs of enlarged tonsils/adenoids include: snoring, difficulty breathing or swallowing, sleep apnea (a condition where breathing stops briefly during sleep), or fluid in the middle ear, as well as infections of the ear. Sleep apnea can cause excessive daytime sleepiness. Call the doctor should these symptoms bother you. An infection of the tonsils has also been observed. The doctor should regularly examine your tonsils/adenoids. Swelling inside the nose, enlarged thymus and lymph nodes have been seen with INCRELEX treatment

Hypoaacusis (hearing loss)

Tell the doctor if you develop hearing problems.

Injection site hypertrophy (tissue at injection site increases in size)

These can be avoided by changing the injection site at each injection (injection site rotation).

Common (may affect up to 1 in 10 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 INCRELEX therapy. INCRELEX may be started again after the episode is over.

Heart abnormalities

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

Also, a racing pulse and heart valve abnormalities have been reported with INCRELEX treatment.

Seizures/fits associated with a high temperature (Febrile seizures)

Febrile seizures/fits have been observed with INCRELEX treatment.

Increased blood sugar (hyperglycaemia)

Increased blood sugar has also been observed with INCRELEX treatment.

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 and stiffness in muscles or joints, as well as jaw malformations, have also been seen with INCRELEX treatment.

Infections

Infections of the mouth, throat and the upper airways have been observed in children with INCRELEX treatment. Such infections may be associated with fever.

Kidney disorders

Kidney stones have been reported, as well as associated pain and kidney swelling.

Reproductive system

Breast enlargement, as well as cysts in the ovaries, have been observed.

Digestive system

Stomach-ache, difficulties swallowing, retching and vomiting have occurred with INCRELEX treatment. Weight gain/obesity have also been reported, as have increases in blood fat and in liver enzyme values.

Skin and hair changes

Skin thickening, moles, skin tags, and abnormal hair texture have been seen with INCRELEX treatment.

Reactions at the injection site

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

Other common side effects seen with INCRELEX treatment include restless legs, chest pain, depression, sleep terror, nervousness, abnormal behaviour and disorientation.

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 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 to 8°C.

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.

What INCRELEX looks like and contents of the pack

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

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 d'Ethe Virton
28100 Dreux
France

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

**België/Belgique/Belgien,
Luxembourg/Luxemburg**
Ipsen NV
Guldensporenpark 87
B-9820 Merelbeke
België /Belgique/Belgien
Tél/Tel: + 32 9 243 96 00

Italia
Ipsen SpA
Via A. Figino, 16
I-20156 Milano
Tel: + 39 - 02 - 39 22 41

România, България
Ipsen Pharma
Str. Grigore Alexandrescu nr. 59, clădirea HQ
Sector 1, 010623, București,
România
Tel/Тел.: + 40 (021) 231 27 20

Latvija
Ipsen Pharma
Bauskas 58
Riga LV 1004
Tel: +371 67622233

Česká republika

Ipsen Pharma, o.s.
Evropská 136/810
CZ-160 00 Praha 6
Tel: + 420 242 481 821

Danmark, Norge, Suomi/Finland, Sverige, Ísland

Institut Produits Synthèse (IPSEN) AB
Kista Science Tower
Färögatan 33
SE- 164 51 Kista
Sverige/Ruotsi/Svíþjóð
Tlf/Puh/Tel/Simi: +46 8 451 60 00

Deutschland, Österreich

Ipsen Pharma GmbH
Willy-Brandt-Str. 3
D-76275 Ettlingen
Tel: + 49 7243 184-80

Eesti

ESTOBIIN OÜ
Udeselja 4-4
EE-11913 Tallinn
Tel: +372 51 55 810

Ελλάδα, Κύπρος, Malta

Ipsen EΠE
Αγ. Δημητρίου 63
Άλιμος
GR-17456 Αθήνα
Ελλάδα
Τηλ: + 30 - 210 - 984 3324

España

Ipsen Pharma S.A.
Torre Realía, Plaza de Europa, 41-43
08908 L'Hospitalet de Llobregat
Barcelona
Tel: + 34 - 936 - 858 100

France

Ipsen Pharma
65 quai Georges Gorse
F-92100 Boulogne-Billancourt
Tél: + 33 - 1 - 58 33 50 00

Ireland

Ipsen Pharmaceuticals Ltd.
7 Upper Leeson Street
IRL-Dublin 4
Tel: + 353 - 1 - 668 1377

Lietuva

Ipsen Pharma Lietuvos filialas
Betygalos g. 2
LT-47183 Kaunas
Tel. + 370 37 337854

Magyarország

Ipsen Pharma SAS Magyarországi
Kereskedelmi Képviselő
Árbóc utca 6.
H-1133 Budapest
Tel.: + 36 1 555 5930

Nederland

Ipsen Farmaceutica B.V.
Taurusavenue 33 B
NL-2132 LS Hoofddorp
Tel: + 31 23 55 41 600

Polska

Ipsen Poland Sp. z o.o.
Al. Jana Pawła II 29
PL-00-867 Warszawa
Tel.: + 48 (0) 22 653 68 00

Portugal

Ipsen Portugal - Produtos Farmacêuticos S.A.
Alameda Fernão Lopes, nº 16-11º, Mirafleres
P-1495 - 190 Algés
Tel: + 351 - 21 - 412 3550

Slovenija

PharmaSwiss d.o.o.
Dolenjska cesta 242c
SI-1000 Ljubljana
Tel: + 386 1 236 47 00

United Kingdom

Ipsen Ltd.
190 Bath Road
Slough, Berkshire
SL1 3XE
Tel: + 44 - (0)1753 - 62 77 00

Slovenská republika

Liek s.r.o.
Hviezdoslavova 19
SK-90301 Senec
Tel: + 421 245 646 322

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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

Detailed information on this medicine is available on the European Medicines Agency web site: <http://www.ema.europa.eu>. There are also links to other websites about rare diseases and treatments.



INSTRUCTIONS FOR USE

INCRELEX should be administered using sterile disposable syringes and injection needles which could be provided by physician / pharmacist / 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).

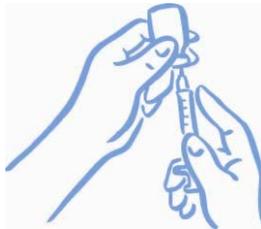


Figure 3: Prepare for extraction

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).



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.