304345-02

PACKAGE LEAFLET:
INFORMATION FOR THE USER

Immukin® 2 x 10^6 IU (0.1 mg) solution for injection

Boehringer Ingelheim

Active substance: recombinant human interferon gamma-1b

Read all of this leaflet carefully before you start using this medicine.
- 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. Do not pass it on to others. It may harm them, even if the symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT IMMUKIN IS AND WHAT IT IS USED FOR

IMMUKIN contains a substance called recombinant human interferon gamma-1b. Interferons are so-called immunomodulators. These are small proteins that can stimulate the body's immune system defences. They protect against micro-organisms (e.g. bacteria, viruses and fungi) that can cause disease.

IMMUKIN is for use by patients with chronic granulomatous disease (CGD). CGD is a defect in the metabolism of neutrophils, a type of white blood cell. These normally kill invading bacteria or fungi. The defect with CGD makes neutrophils less able to prevent infections.

IMMUKIN is used to reduce the number of serious infections that may occur with this disease.

IMMUKIN is also used in patients with severe, progressive marble bone disease (osteopetrosis). This is an inherited defect in bone cells, which leads to excessive, abnormal bone growth. It also affects the bone marrow and the blood cells that are usually formed in it. As a result, patients with osteopetrosis are also at risk of serious infections.

2. BEFORE YOU USE IMMUKIN

Do NOT use IMMUKIN
- if you are allergic (hypersensitive) to interferon gamma or to other related interferons or any of the other ingredients of IMMUKIN (please refer to section 6 for further ingredients). Ask your doctor or pharmacist if you are unsure about whether you are allergic to interferons.

Take special care with IMMUKIN
- if you have heart disease, because higher than usual doses can make your heart condition worse (see section 3 for dosage information)
- if you have seizure disorder and/or compromised central nervous system function
- if your liver does not function as effectively as normal (hepatic insufficiency)
- if your kidneys do not function as effectively as normal (renal insufficiency)
- if your bone marrow does not produce as many blood cells as normal (myelo-suppression)
- if you are allergic to latex, because the stopper of the glass vial contains natural rubber (a derivative of latex) which may cause allergic reactions

Consult your doctor if one of the warnings above applies to you now or if it did in the past.

You should avoid using IMMUKIN at the same time as other types of protein-based medicines. You should also avoid taking IMMUKIN at the same time as you are given a vaccine. If you have any questions about this, ask your doctor.

You should continue to have the tests used in the management of CGD and severe, progressive osteopetrosis. Your blood count, urine, kidney and liver function should be carefully checked, both before and during the treatment.

High interferon gamma-1b levels in the body may possibly harm the fertility of men and women.

Using other medicines
You may also require antibiotics to treat infections that still occur while you are taking IMMUKIN for the treatment of CGD. There is no evidence that IMMUKIN affects the efficacy of antibiotics or corticosteroids, commonly used medications in CGD and severe, malignant osteopetrosis patients. Medicines that affect the liver or the kidneys may affect the excretion of IMMUKIN from the body.

It is possible that IMMUKIN might prolong the activity of other medicines that are broken down and removed from the body by the liver.

If you use IMMUKIN at the same time as medicines or vaccines that have effects upon the heart, blood, bone marrow, nervous system or immune system, the risk of side effects may be increased.

Please tell your doctor or pharmacist if you are taking or have recently taken or regularly take any medicines, including medicines obtained without a prescription.

Fertility, pregnancy and breast feeding
Based on the information available, effects on fertility are not known but cannot be excluded. You should not use IMMUKIN during pregnancy, unless your doctor thinks it is essential. You are recommended not to breast-feed while using IMMUKIN.

Ask your doctor or pharmacist for advice before using any medicine.

Driving and using machines
IMMUKIN can cause fatigue, fits (seizures), confusion, disorientation or distorted or imaginary sensations (hallucinations). These side effects can reduce the ability to respond and can thus have a negative effect upon the ability to drive and use machines. Do not drive or use machines if you realize reduced responsiveness.

Important information about some of the ingredients of IMMUKIN
This medicinal product contains less than 1 mmol sodium (23 mg) per 0.5 ml vial, i.e. it is 'sodium-free'. This may be important for people with high blood pressure and others wishing to maintain a low sodium diet.

3. HOW TO USE IMMUKIN

IMMUKIN is for injection under the skin (subcutaneous use) and can be administered by a doctor or nurse. You or a family member could also administer IMMUKIN. You or your family member should be trained by a doctor or nurse in giving this type of injection.

The recommended dosage of IMMUKIN for the treatment of patients with CGD or severe, malignant osteopetrosis is 50 mcg/m^2 for patients whose body surface area is greater than 0.5 m^2 and 1.5 mcg/kg for patients whose body surface area is equal to or less than 0.5 m^2.

Your doctor will decide how much IMMUKIN you need to take to treat CGD or severe, progressive osteopetrosis.

Always use IMMUKIN as your doctor has told you. Check with your doctor or pharmacist if you are not sure how to use IMMUKIN or if you need any other advice.

You should inject (or should have injected) under your skin the exact amount of IMMUKIN your doctor has told you that you need. You should give the injections three times per week (for example, Monday, Wednesday and Friday), preferably in the evening. The recommended injection sites are the upper arm or the top of the thigh.

- *Always check the amount of IMMUKIN solution before giving the injection.*

- *Do not use IMMUKIN if you can see small particles or discolouration of the solution.*

- *Do not mix IMMUKIN with other medicines.*

- *Do not strongly shake IMMUKIN vials.*

If you use more IMMUKIN than you should
Immediately consult your doctor if you have administered more IMMUKIN than your doctor has told you.

Symptoms after having administered too much IMMUKIN can include the following:
- central nervous system side effects such as difficulty in thinking, difficulty in walking, and dizziness
- if you have heart disease, this may get worse for a short time
- blood disorders can occur during treatment with IMMUKIN
  These include:
  - temporary changes in the number of some blood cells
  - increases in blood levels of certain substances (liver enzymes and triglycerides)
  These changes can be detected by your doctor with a blood test.

These symptoms resolve with reduction in dose or with discontinuing IMMUKIN.

If you forget to use IMMUKIN
Have your injections at the times your doctor has recommended. If you forget to take a dose, do not inject a double dose to make up for it. You can still administer it on the same or following day. Contact your doctor if you think you have gone too long without taking a dose.

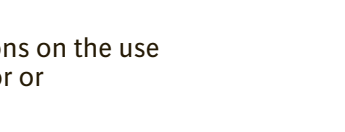
If you stop using IMMUKIN
Please inform your doctor if you stop using IMMUKIN.

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

File information		Mandatory in TD	Mandatory in Printfile
Issue date of TD:	15.11.2012	Yes	Yes
PPM SKU:	P004535	No	Yes
PPM SKU version:	011	No	Yes
Issue date of artwork:	09.04.2015	No	Yes
Print colors:	PAN Black	No	Yes
Mat. No. Pack. Site:	304345-02	No	Yes
Min. font size:	10.2 pt		
Legend case version:	V4.0 01/OCT/2012 (please do not change or remove it)		

Technical information			
a = Batch No.		b = Expiry date	
c = Manufacturing date		d = Price/Sample/Clinic	
Technical colors			
BI-Diecut-Legendcase		Free area	Gluepoints

Additional Requirements of Packaging site	
Template name: TD-PI_160x630	Index: b



MASS A 8,5 mm
MASS B 2,2 mm
MASS C max. 42,5 mm

Example
Technical information
control code

4. POSSIBLE SIDE EFFECTS

Like all medicines, IMMUKIN can cause side effects, although not everybody gets them. The risk of side effects occurring depends on the dose and the dosing schedule you have been given.

The most common side effects are flu-like symptoms such as fever, headache, cold chills, and fatigue.

These may become less severe over time as the treatment is continued. Some of these symptoms can be reduced by administering IMMUKIN just before going to sleep. A medicine such as paracetamol can be used to reduce some of these side effects.

Some people who take IMMUKIN may develop short-term skin problems, such as a temporary skin rash, spotty skin rash, the sudden formation of blisters on the skin, and reddening of the skin at the injection site. However, these are rarely severe enough to stop treatment with IMMUKIN.

The side effects listed below are grouped by how likely they are to happen.

Very common side effects (more than 1 in 10 patients treated) are:
- fever
- headache
- chills
- pain at the injection site
- vomiting
- nausea (feeling sick)
- diarrhoea
- fatigue
- raised levels of liver enzymes
- rash

Common side effects (less than 1 in 10 patients treated) are:
- muscle pain
- joint aching or pain
- back pain
- stomach pain
- depression

Not known (cannot be estimated from the available data):
- shortage of white blood cells (neutropenia)
- shortage of blood platelets (thrombo-cytopenia) which might be associated with bruises and a tendency towards bleeding
- proteins in the urine

Side effects have also been seen in patients with conditions other than CGD or malignant osteopetrosis. These events have not been seen in clinical trials involving CGD or osteopetrosis.

The following side effects have been reported in clinical trials with patients suffering from other diseases/conditions than CGD or osteopetrosis. Often the doses used in these studies were higher than the recommended dose for CGD and osteopetrosis. For this reason it is not possible to say accurately how often they occurred.

Not known (cannot be estimated from the available data):
- low blood levels of sodium which can cause tiredness and confusion, muscle twitching, fits or coma (hyponatraemia)
- high levels of a sugar called glucose (hyperglycaemia)
- fatty acids called triglycerides (hyper-triglyceridaemia) in the blood

The following nervous system disorders have been observed:
- confusion
- disorientation
- effects on ability to walk such as Parkinsonian gait
- trembling
- fits (seizures)
- distorted or imaginary sensations (hallucinations)

The following heart disorders have also been seen to occur:
- additional and irregular heart beats
- disturbance in the heart rate, such as faster or slower heart rate
- heart problems which can cause shortness of breath or ankle swelling (heart failure)
- heart attack

The following blood system disorders have been reported:
- low blood pressure
- fainting
- mild, temporary stroke (transient ischemic attack)
- blood clot or blockage of a lung artery (deep venous thrombosis and pulmonary embolism); symptoms can include shortness of breath

The following respiratory disorders have occurred:
- rapid breathing
- chest tightness (bronchospasm or interstitial lung disease)

- bleeding in the digestive system
- inflammation of the pancreas, which can lead to death
- damage to the liver that affects its function (liver failure)
- damage to the kidneys that affect their function but can be treated effectively (reversible kidney failure)
- pains in the chest
- worsening of a skin condition called dermatomyositis (seen as a skin rash accompanying muscle weakness)
- development of the long-term disease called systemic lupus erythematosus (i.e. the patient's own immune system attacks various parts of the body)
- autoimmune reaction (Autoantibody response)

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 (see details below). By reporting side effects you can help provide more information on the safety of this medicine.

United Kingdom
Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard

Ireland
HPRA Pharmacovigilance
Earlsfort Terrace
IRL – Dublin 2
Tel: +353 1 6764971
Fax: +353 1 6762517
Website: www.hpra.ie
e-mail: medsafety@hpra.ie

Malta
ADR Reporting
The Medicines Authority
Post-Licensing Directorate
203 Level 3, Rue D'Argens
GŻR-1368 Gżira
Website: www.medicinesauthority.gov.mt
e-mail: postlicensing.medicinesauthority@gov.mt

5. HOW TO STORE IMMUKIN

Keep out of the reach and sight of children.

Do not use IMMUKIN after the expiry date which is stated on the carton and vial, after 'Do not use after' or 'EXP'. The expiry date refers to the last day of that month.

Store in a refrigerator (2°C – 8°C). Do not freeze.

IMMUKIN solution for injection vials are for single use only.

IMMUKIN contains no preservatives. Once opened, you should use the contents of a vial immediately. Dispose of any unused contents of the vial.

Do not use IMMUKIN if you notice particles or discolouration in it before use.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What IMMUKIN contains

Each vial (0.5 ml) contains 2 x 10^6 IU (0.1 mg) recombinant human interferon gamma-1b. This is a substance produced using E. coli bacteria modified by gene technology.

The other ingredients are D-mannitol, disodium succinate hexahydrate, polysorbate 20, succinic acid and water for injections.

The stopper of the glass vial contains natural rubber (a derivative of latex).

What IMMUKIN looks like and contents of the pack

IMMUKIN is a clear, colourless solution for injection. IMMUKIN is available in 3 ml vials containing 0.5 ml solution for injection.

Pack sizes: 1, 3, 5, 6 and 12 vial(s) in one folding box.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder
Boehringer Ingelheim Limited
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This medicinal product is authorised in the Member States of the EEA under the following names:

Austria:	Imukin®	Latvia:	-
Belgium:	Immukine®	Liechtenstein:	-
Bulgaria:	-	Lithuania:	-
Cyprus:	Imukin®	Luxembourg:	Immukine®
Czech Republic:	-	Malta:	Immukin®
		Netherlands:	Immukine®
Denmark:	Imukin®	Norway:	Imukin®
Estonia:	-	Poland:	-
Finland:	Imukin®	Portugal:	Imukin®
France:	Imukin®	Romania:	-
Germany:	Imukin®	Slovakia:	-
Greece:	Imukin®	Slovenia:	-
Hungary:	Imukin®	Spain:	Imukin®
Iceland:	-	Sweden:	Imukin®
Ireland:	Immukin®	United Kingdom:	Immukin®
Italy:	Imukin®		

This leaflet was last approved in April 2015.