Package leaflet: Information for the patient

Imlygic 10^6 plaque forming units (PFU)/mL solution for injection
Imlygic 10^8 plaque forming units (PFU)/mL solution for injection
talimogene laherparepvec

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 healthcare professional (doctor or nurse).
- If you get any side effects, talk to your healthcare professional. This includes any possible side effects not listed in this leaflet. See section 4.
- Your doctor will give you a Patient Alert Card. Read it carefully and follow the instructions on it.
- Always show the Patient Alert Card to your doctor or nurse when you see them or if you go to hospital.

What is in this leaflet

1. What Imlygic is and what it is used for

Imlygic is used to treat adult patients with a type of skin cancer called melanoma that has spread in the skin or to the lymph nodes, when surgery is not an option.

The active ingredient of Imlygic is talimogene laherparepvec. This is a weakened form of herpes simplex virus type-1 (HSV-1), which is commonly called the cold sore virus. To get Imlygic from HSV-1, the virus has been changed so that it multiplies more effectively in tumours than in normal cells. This leads to destruction of infected tumour cells. This medicine also works by helping your immune system to recognise and destroy tumours throughout your body.

2. What you need to know before and during Imlygic treatment

You will not be given Imlygic:
- if you are allergic to talimogene laherparepvec or any of the other ingredients of this medicine (listed in section 6).
- if your healthcare professional has told you that you have a severely weakened immune system.

Warnings and precautions

Talk to your healthcare professional before being given this medicine.

Life-threatening herpes infection

Life-threatening herpes infection including spreading to any part of the body far from the injection site (disseminated herpetic infection) may occur. If you have any new or worsening symptoms, tell your healthcare professional immediately. Tell your healthcare professional if you have or have ever had a

weakened immune system, if you have HIV/AIDS, blood or bone marrow cancer, or if you are taking steroids or other medicines that suppress your immune system because you may be at increased risk of life-threatening herpes infection.

Accidental spread of Imlygic to yourself and others

Imlygic can be spread to other parts of your body or to other people through direct contact with your body fluids or injection sites.

You should do the following to avoid spreading Imlygic to other areas of your body or to your close contacts (close contacts include household members, caregivers, sex partners, or someone you share a bed with):

- Avoid direct contact between your injection sites or body fluids (e.g. blood and urine) and close contacts (e.g. use latex condoms when engaging in sexual activity, avoid kissing close contacts if either of you has an open mouth sore) while you are being treated with this medicine and up to 30 days after your last dose.
- Avoid touching or scratching the injection sites.
- Keep injection sites covered with airtight and watertight dressings at all times. Apply the dressing as instructed by your healthcare professional. If the dressing comes loose or falls off, replace it immediately with a clean dressing.
- Place all used dressings and cleaning materials in a sealed plastic bag and throw them away in your household waste.

You should tell your close contacts to:

- Avoid direct contact with your body fluids or injection sites.
- Wear gloves while changing your dressing.

If your close contacts are accidentally exposed to Imlygic, they should clean the affected area on their body with soap and water and/or a disinfectant. If they develop signs or symptoms of herpes infection, you should ask them to contact their healthcare professional. If herpetic lesions (blisters or sores) are suspected, patients or close contacts have the option of follow-up testing by the Marketing Authorisation Holder for further characterisation of the infection. Please discuss with your healthcare professional.

Close contacts who are pregnant or who have a weakened immune system, and newborns

Ensure that your close contacts who are pregnant or who have a weakened immune system do not touch injection sites, used dressings and cleaning materials. Keep used dressings and cleaning materials away from newborns.

Herpes infection

Cold sores or a more serious herpes infection may occur during or after treatment with Imlygic. Signs and symptoms related to treatment with Imlygic may be the same as for herpes infections, and include but are not limited to pain, burning or tingling in a blister around the mouth, genitals, on the fingers or ears, eye pain, light sensitivity, discharge from the eyes, or blurry vision, weakness in arms or legs, extreme drowsiness (feeling sleepy), and mental confusion. If you have these signs or any new symptoms, you should follow standard hygiene practices to prevent viral transmission to others. If herpetic lesions (blisters or sores) are suspected, patients or close contacts have the option of follow-up testing by the Marketing Authorisation Holder for further characterisation of the infection. Please discuss with your healthcare professional.

Infection and delayed healing at injection site

Imlygic may cause infection at the injection site. Signs and symptoms of infection include pain, redness, warmth, swelling, discharge or a sore (ulcer), fever, and chills. The injection site may take

longer to heal than normal. You should tell your healthcare professional if you notice any of these symptoms.

Autoimmune reactions

Imlygic may cause autoimmune reactions (an over-reaction of the body's immune system). Some people taking this medicine have developed inflammation in the kidneys (glomerulonephritis), narrowing or blockage of blood vessels (vasculitis), swelling of the lungs (pneumonitis), worsening skin scaling (psoriasis), and areas of skin without any colour (vitiligo). Inform your healthcare professional if you have a history of autoimmune disease.

Plasmacytoma

Imlygic may cause cancerous white blood cells to gather at or near the injection site (plasmacytoma). Inform your healthcare professional if you have a history of blood cancer including multiple myeloma.

Difficulty breathing

If you have a tumour in your neck, your healthcare professional may warn you that you might experience compression of your airways during treatment.

Patients with no prior herpes infection

If you have never had herpes infection in the past, you may be more likely to get fever, chills, and flu-like illness within the period of the first 6 treatments.

Children and adolescents

Imlygic is not recommended for children and adolescents since the effects of this medicine in people younger than 18 years old are not known.

Other medicines and Imlygic

Tell your healthcare professional if you are taking, have recently taken or might take any other medicines, including medicines, such as acyclovir, to treat or prevent herpes infections. Acyclovir and other anti-viral treatments may decrease the effects of Imlygic.

Pregnancy and breast-feeding

Ask your healthcare professional for advice if you:
- think you may be pregnant; or
- are planning to have a baby.

Your healthcare professional will determine if Imlygic is right for you.

If you are pregnant or breast-feeding, ask your healthcare professional for advice before being given this medicine. Imlygic may harm your unborn baby.

Women who are able to become pregnant should use effective contraception to avoid pregnancy during treatment with Imlygic. Talk to your healthcare professional about suitable methods of contraception.

It is not known whether Imlygic passes into breast milk. It is important to tell your healthcare professional if you are breast-feeding or plan to do so. They will then help you decide whether to stop breast-feeding, or whether to stop taking Imlygic, taking into account the benefit of breast-feeding to the baby and the benefit of Imlygic to you.

Driving and using machines

When you are being treated with Imlygic you may experience symptoms such as dizziness or confusion. This may impair your ability to drive or operate machinery. Use caution when driving or operating machinery until you are certain that this medicine does not adversely affect you.

Imlygic contains sodium and sorbitol

This medicine contains 7.7 mg sodium (main component of cooking/table salt) in each 1 mL vial. This is equivalent to 0.4% of the recommended maximum daily dietary intake of sodium for an adult.

This medicine contains 20 mg sorbitol in each 1 mL vial.

3. How Imlygic is given

This medicine is given in a healthcare facility under the supervision of a healthcare professional. The initial recommended dose is up to 4 mL of Imlygic at a concentration of 10^6 (1 million) PFU/mL. Subsequent doses will be up to 4 mL of Imlygic at a concentration of 10^8 (100 million) PFU/mL.

Your healthcare professional will inject this medicine directly into your tumour(s) with a needle and a syringe. Your second injection will be given 3 weeks after the first injection. After that, you will receive injections every 2 weeks for as long as you have the tumour(s).

Your healthcare professional will decide which tumour(s) to inject and may not inject every tumour. Your existing tumour(s) may increase in size and new tumour(s) could appear while you are being treated with Imlygic.

You can expect to be treated with Imlygic for at least 6 months or longer.

If you miss a dose of Imlygic

It is important for you to keep all your appointments to receive this medicine. If you miss an appointment, ask your healthcare professional when to schedule your next dose.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Keeping wounds clean and dressed can help prevent infections caused by bacteria (cellulitis) at the injection site.

Flu-like illness, fevers and chills have been seen in patients treated with Imlygic. These symptoms generally resolve within the first 72 hours after treatment.

The following side effects have been reported in patients receiving Imlygic:

Very common (may affect more than 1 in 10 people):
- Tissue swelling (peripheral oedema)
- Headache
- Cough
- Vomiting, diarrhoea, constipation, nausea
- Muscle pain (myalgia), painful/swollen joints (arthralgia), limb pain
- Flu-like illness, fever (pyrexia), chills, fatigue, pain
- Pain, redness, bleeding, swelling, inflammation, secretion, discharge, and warmth at the injection site

Common (may affect up to 1 in 10 people):
- Infection caused by bacteria (cellulitis), cold sores (oral herpes)
- Tumour pain, infected tumour
- Tiredness, headaches, dizziness and looking pale (low red blood cell numbers - anaemia)
- Side effects related to the immune system:
  - fever, fatigue, weight loss, muscle and joint pain (narrowing or blockage of blood vessels - vasculitis)
  - shortness of breath, cough, fatigue, loss of appetite, unintentional weight loss (inflammation of the lungs - pneumonitis)
  - increase in patches of skin which are dry, red and covered in silvery scales (worsening scaling of the skin - worsening psoriasis)
  - pink or cola-coloured urine, frothy urine, high blood pressure, fluid retention (inflammation of kidneys - glomerulonephritis)
- Dehydration
- Confusion, anxiety, depression, dizziness, difficulty sleeping (insomnia)
- Pain in ear, throat, abdomen, groin, back and underarm
- Faster heart rate at rest (tachycardia)
- Pain, swelling, heat, and tenderness in a leg or arm due to a blood clot within a vein (deep vein thrombosis), high blood pressure (hypertension), redness in the face (flushing)
- Shortness of breath (dyspnoea), upper respiratory infection
- Abdominal discomfort
- Areas of skin without any colour (vitiligo), rash, inflamed skin (dermatitis)
- Generally feeling unwell
- Weight loss
- Wound complication, secretion, bruising (contusion), pain after procedure

Uncommon (may affect up to 1 in 100 people):
- Incision site infection
- A tumour of cancerous white blood cells that grows at or near the injection site (plasmacytoma)
- Eye infection caused by herpes (keratitis herpetic)
- Compressed airways (obstructive airways disorder)
- Allergic reaction (hypersensitivity)

Reporting of side effects

If you get any side effects, talk to your healthcare professional. 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.

Yellow Card Scheme
Website: https://yellowcard.mhra.gov.uk or search for MHRA Yellow Card in the Google Play or Apple App Store

5. How Imlygic is stored

Imlygic will be stored by the healthcare professionals at your healthcare facility.

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

Store and transport frozen at -90°C to -70°C.
Store in the original carton in order to protect from light.

This medicinal product contains genetically modified cells. Local guidelines should be followed.

6. Contents of the pack and other information

What Imlygic contains

- The active substance is talimogene laherparepvec.
  Each vial contains 1 extractable mL of solution at a nominal concentration of 1×10^6 (1 million) plaque forming units (PFU)/mL or 1×10^8 (100 million) PFU/mL.
- The other ingredients are di-sodium phosphate dihydrate, sodium dihydrogen phosphate dihydrate, sodium chloride, myo-inositol, sorbitol (E420), water for injections (see section 2).

What Imlygic looks like and contents of the pack

Imlygic is a clear to semi-translucent (10^6 PFU/mL) or semi-translucent to opaque (10^8 PFU/mL) liquid. It is supplied as a 1 mL preservative free solution in a single–use vial (cyclic olefin polymer plastic resin) with stopper (chlorobutyl elastomer) and seal (aluminium) with flip-off cap (polypropylene).

The vial cap is colour coded: 10^6 PFU/mL is light green and 10^8 PFU/mL is royal blue.

Marketing Authorisation Holder
Amgen Limited
216 Cambridge Science Park
Milton Road
Cambridge
CB4 0WA
United Kingdom

Manufacturer
Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

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

Amgen Limited
Tel: +44 (0)1223 420305

This leaflet was last revised in February 2023.

The following information is intended for healthcare professionals only:

This medicinal product contains genetically modified organisms. Personal protective equipment (e.g. protective gown or laboratory coat, safety glasses, or face shield and gloves) should be worn while preparing or administering talimogene laherparepvec.

After administration, change gloves prior to applying occlusive dressings to injected lesions. Wipe the exterior of occlusive dressing with an alcohol wipe. It is recommended to keep injection sites covered with airtight and watertight dressings at all times, if possible.

Thawing Imlygic vials

- Before use, thaw frozen Imlygic vials at room temperature (20°C to 25°C) until Imlygic is liquid. The time to achieve complete vial thaw is expected to be 30 to 70 minutes, depending on the ambient temperature. Gently swirl. Do NOT shake.
- Vials should be thawed and stored in the original carton until administration in order to protect from light.

After thawing

- After thawing, administer Imlygic as soon as practically feasible.
- Thawed Imlygic is stable when stored at temperatures of 2°C up to 25°C protected from light in its original vial, in a syringe, or in the original vial followed by a syringe. Do not exceed the storage times specified in table 1 and table 2.
- If storing thawed Imlygic in the original vial followed by a syringe:
  - the same temperature range should be maintained throughout the duration of storage until administration.
  - the storage time in the syringe at ambient temperature up to 25°C cannot exceed 2 hours for 10^6 (1 million) PFU/mL and 4 hours for 10^8 (100 million) PFU/mL (see table 1).
  - the maximum cumulative storage time (storage time in vial plus storage time in syringe) cannot exceed the durations in table 2.
- Imlygic must not be refrozen once it has thawed. Discard any thawed Imlygic in the vial or syringe stored longer than the specified times below.

Table 1. Maximum storage time for thawed Imlygic in syringe

	10^6 (1 million) PFU/mL	**10^8 (100 million) PFU/mL**
2°C to 8°C	8 hours	8 hours
up to 25°C	2 hours	4 hours

Table 2. Maximum cumulative storage time (storage time in vial plus storage time in syringe) for thawed Imlygic

	10^6 (1 million) PFU/mL	**10^8 (100 million) PFU/mL**
2°C to 8°C	24 hours	1 week (7 days)
up to 25°C	12 hours	24 hours

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.