



# IMLYGIC®

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## Clinical Overview and Handling Guide

### INDICATION

IMLYGIC® is a genetically modified oncolytic viral therapy indicated for the local treatment of unresectable cutaneous, subcutaneous, and nodal lesions in patients with melanoma recurrent after initial surgery.

Limitations of use: IMLYGIC® has not been shown to improve overall survival or have an effect on visceral metastases.

### IMPORTANT SAFETY INFORMATION

#### Contraindications

- Do not administer IMLYGIC® to immunocompromised patients, including those with a history of primary or acquired immunodeficient states, leukemia, lymphoma, AIDS or other clinical manifestations of infection with human immunodeficiency viruses, and those on immunosuppressive therapy, due to the risk of life-threatening disseminated herpetic infection.
- Do not administer IMLYGIC® to pregnant patients.

**Please see full Prescribing Information [here](#).**  
**Please see Important Safety Information**  
**throughout this booklet and on page 26.**



**IMLYGIC®**  
(talimogene laherparepvec)  
SUSPENSION FOR INJECTION  
10<sup>6</sup> PFU/mL and 10<sup>8</sup> PFU/mL single-use vials



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PART I:

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## **What Is IMLYGIC®?**

# PRODUCT CHARACTERISTICS

## INDICATION

IMLYGIC® is a genetically modified oncolytic viral therapy indicated for the local treatment of unresectable cutaneous, subcutaneous, and nodal lesions in patients with melanoma recurrent after initial surgery.

Limitations of use: IMLYGIC® has not been shown to improve overall survival or have an effect on visceral metastases.

## Administration

- IMLYGIC® is administered by intralesional injection into cutaneous, subcutaneous, and/or nodal lesions that are visible, palpable, or detectable by ultrasound guidance<sup>1</sup>
- Available in single-use [1 mL] vials, in 2 concentrations:<sup>1</sup>

**Initial dose** — $10^6$  (1 million) PFU/mL (light green cap; NDC 55513-078-01)

**All subsequent doses** — $10^8$  (100 million) PFU/mL (royal blue cap; NDC 55513-079-01)

**Please see full Prescribing Information for important dosing and administration information.**

## Biochemical Composition

- Active Ingredients<sup>1</sup>
  - Each vial contains IMLYGIC®, an attenuated and genetically modified herpes virus (rHSV-1<sup>hGM-CSF</sup>)
- Inactive Ingredients<sup>1</sup>
  - Each vial contains di-sodium hydrogen phosphate dihydrate (15.4 mg), sodium dihydrogen phosphate dihydrate (2.44 mg), sodium chloride (8.5 mg), myo-inositol (40 mg), sorbitol (20 mg), and water for injection

PFU = plaque-forming units.

## IMPORTANT SAFETY INFORMATION

### Warnings and Precautions

- **Accidental exposure to IMLYGIC®** may lead to transmission of IMLYGIC® and herpetic infection, including during preparation and administration. Health care providers, close contacts, pregnant women, and newborns should avoid direct contact with injected lesions, dressings, or body fluids of treated patients. The affected area in exposed individuals should be cleaned thoroughly with soap and water and/or a disinfectant.

**Please see full Prescribing Information [here](#).**  
**Please see Important Safety Information throughout this booklet and on page 26.**

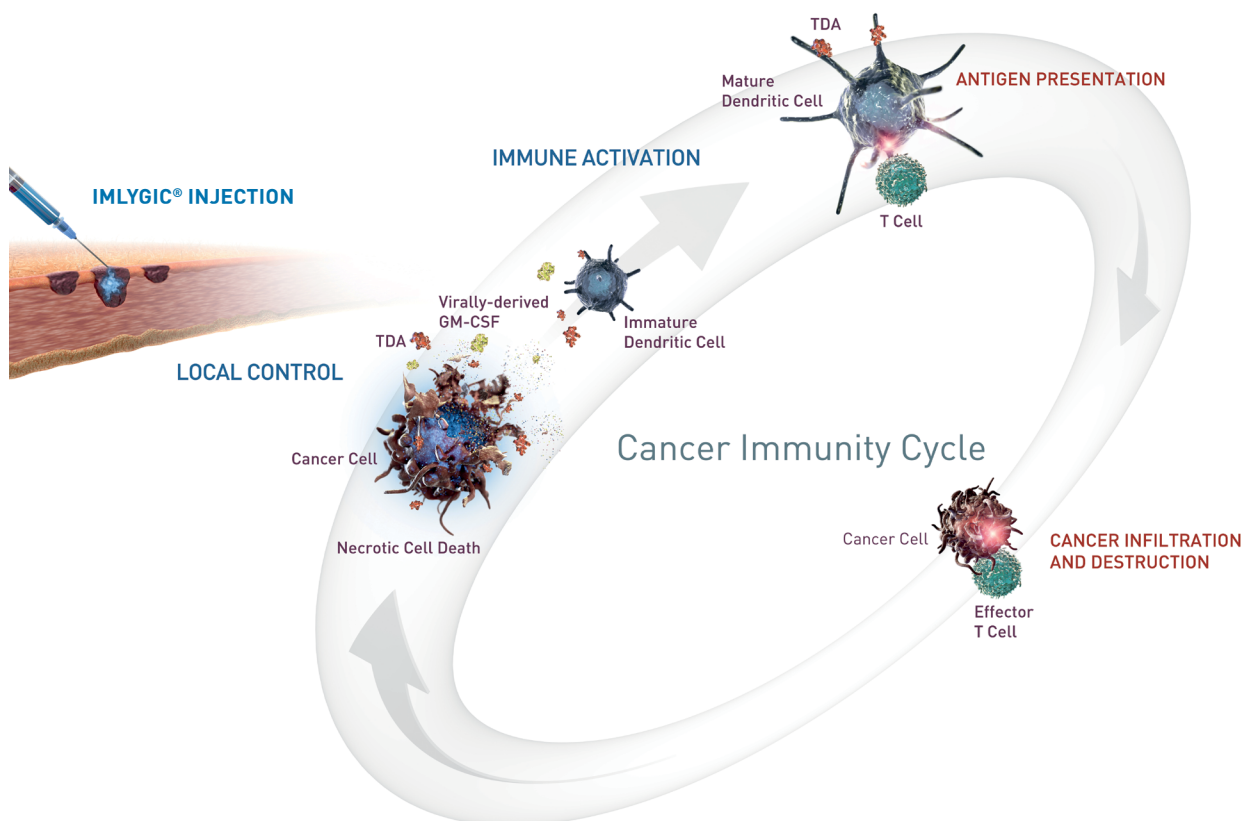


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# MECHANISM OF ACTION

## INJECT THE LESION. TRIGGER AN ANTITUMOR IMMUNE RESPONSE.

IMLYGIC® is the first and only approved oncolytic viral therapy in the U.S. designed to achieve local control and trigger a specific immune response against melanoma<sup>1,3</sup>



The exact mechanism of action is unknown, and is for illustrative purposes only. It is not meant to imply clinical efficacy.<sup>1</sup>

### 1. Local Control

IMLYGIC® is designed to replicate in cancer cells, leading to oncolysis.<sup>1</sup>

### 2. Immune Activation

Oncolysis releases tumor-derived antigens (TDA), virally derived GM-CSF, and replicated IMLYGIC®, which may promote an antitumor immune response.<sup>1</sup>

GM-CSF = granulocyte macrophage colony-stimulating factor; TDA = tumor-derived antigens.

## IMPORTANT SAFETY INFORMATION

### Warnings and Precautions (Cont'd)

- To prevent possible inadvertent transfer of IMLYGIC® to other areas of the body, patients should be advised to avoid touching or scratching injection sites or occlusive dressings.

Please see full Prescribing Information [here](#). Please see Important Safety Information throughout this booklet and on page 26.

# MECHANISM OF ACTION

## MODIFIED VIRUS. MULTIPLE EFFECTS.

Using recombinant DNA technology, HSV-1 has been genetically modified to replicate in cancer cells and may promote immune activation<sup>4</sup>

### 1. CONTROLLED REPLICATION<sup>4</sup>

- Deletion of the infected cell protein (ICP) 34.5 gene promotes specific replication of IMLYGIC® in tumor tissue



IMLYGIC®

### 2. INCREASED ANTIGEN EXPRESSION AND PRESENTATION<sup>4</sup>

- Deletion of ICP 47 prevents down-regulation of antigen presentation molecules
- Inserted GM-CSF may recruit and activate antigen-presenting cells which can process and present TDA to promote an effector T-cell response

The exact mechanism of action is unknown, and is for illustrative purposes only. It is not meant to imply clinical efficacy.<sup>1</sup>

HSV-1 = herpes simplex virus-1.

## IMPORTANT SAFETY INFORMATION

### Warnings and Precautions (Cont'd)

- Caregivers should wear protective gloves when assisting patients in applying or changing occlusive dressings and observe safety precautions for disposal of used dressings, gloves, and cleaning materials. Exposed individuals should clean the affected area thoroughly with soap and water and/or a disinfectant.



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# CLINICAL TRIAL DATA

## IMLYGIC® PIVOTAL PHASE 3 STUDY

### Study Description<sup>1,5</sup>

The safety and efficacy of intralesional IMLYGIC® was compared with subcutaneously administered GM-CSF in a pivotal phase 3, multicenter, open-label, randomized (2:1) trial comparing 436 previously treated and untreated patients [IMLYGIC® (n = 295) GM-CSF (n = 141)] with stages IIIB, IIIC, and IV melanoma that was surgically unresectable.

### Primary Endpoint<sup>1</sup>

**Durable Response Rate (DRR):** defined as the percent of patients with **Complete Response (CR)** or **Partial Response (PR)** maintained continuously for a minimum of 6 months.\*

### Key Secondary Endpoints<sup>1</sup>

Overall Survival (OS), Time to Response.

### Key Definitions

**Complete Response:**<sup>2</sup> disappearance of all evidence of tumor

**Partial Response:**<sup>2</sup> a  $\geq 50\%$  reduction in the sum of the products of the perpendicular diameters of all measurable tumors at the time of assessment, as compared with baseline

- Previous systemic treatment for melanoma was allowed
- Patients with active cerebral metastases, bony metastases, extensive visceral disease, primary ocular or mucosal melanoma, evidence of immunosuppression, or receiving treatment with a systemic anti-herpetic agent were excluded from the study
- IMLYGIC® was injected into cutaneous, subcutaneous or nodal melanoma lesions and was not injected into visceral lesions

\*Tumor responses determined using modified WHO criteria by a blinded, independent Endpoint Assessment Committee (EAC).<sup>1</sup>

## IMPORTANT SAFETY INFORMATION

### Warnings and Precautions (Cont'd)

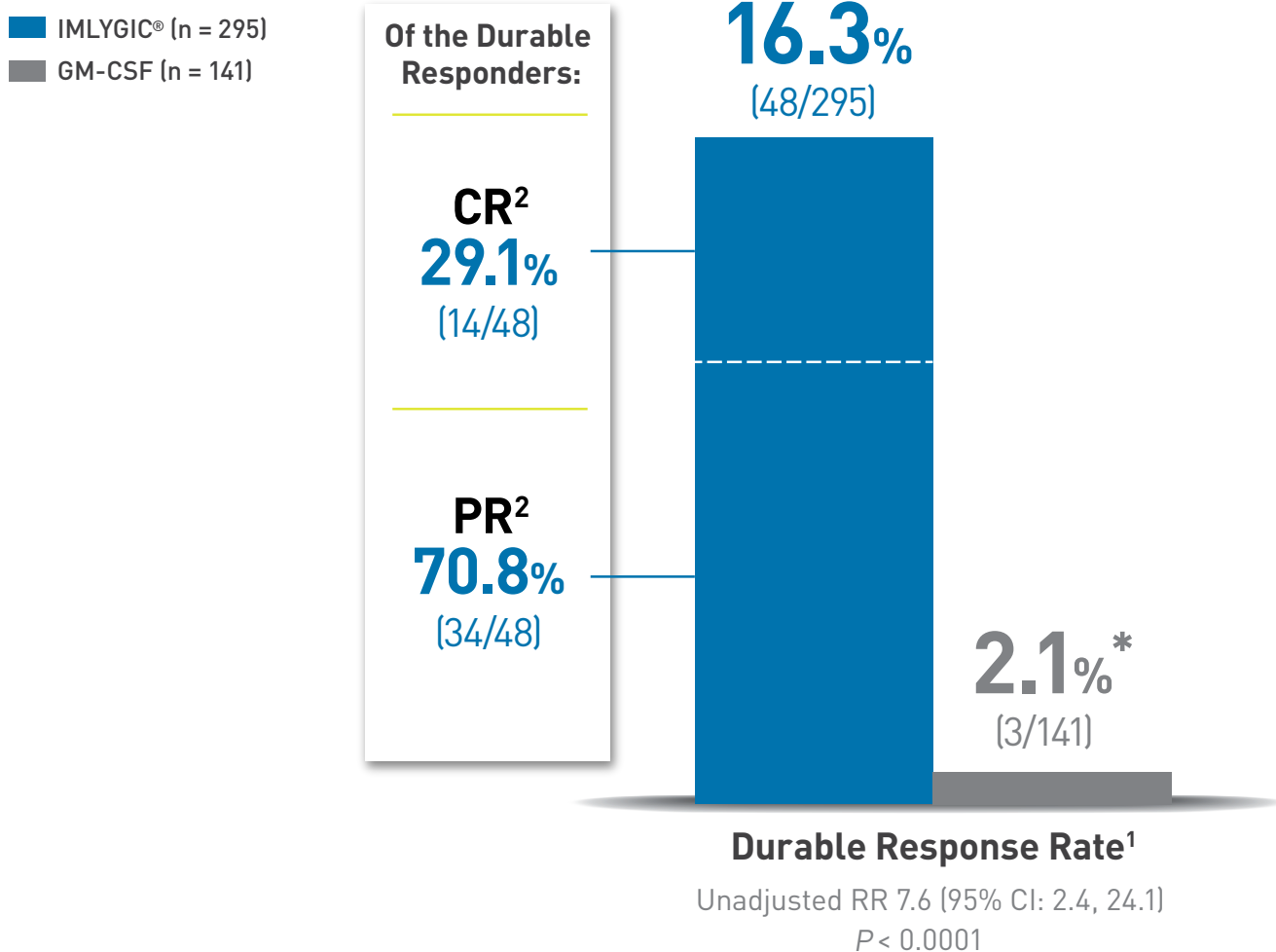
- **Injection Site Complications:** Necrosis or ulceration of tumor tissue may occur during IMLYGIC® treatment. Cellulitis and systemic bacterial infection have been reported in clinical studies. Careful wound care and infection precautions are recommended, particularly if tissue necrosis results in open wounds.

**Please see full Prescribing Information [here](#). Please see Important Safety Information throughout this booklet and on page 26.**



# CLINICAL TRIAL DATA

## DURABLE RESPONSE RATE<sup>1,2</sup>



\*GM-CSF: CR of DRR 0% (0/3), PR of DRR 100% (3/3).<sup>2</sup>

## IMPORTANT SAFETY INFORMATION

### Warnings and Precautions (Cont'd)

- **Immune-Mediated events** including glomerulonephritis, vasculitis, pneumonitis, worsening psoriasis, and vitiligo have been reported in patients treated with IMLYGIC®. Consider the risks and benefits of IMLYGIC® before initiating treatment in patients who have underlying autoimmune disease or before continuing treatment in patients who develop immune-mediated events.



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# CLINICAL TRIAL DATA

## ADVERSE REACTIONS (ARs)

ARs reported with at least a 5% greater incidence in patients treated with IMLYGIC® compared with GM-CSF<sup>1</sup>

Adverse Reactions	IMLYGIC® (n = 292)		GM-CSF (n = 127)	
	Any grade n(%)	Grade 3 n(%)	Any grade n(%)	Grade 3 n(%)
Fatigue	147 (50.3)	6 (2.1)	46 (36.2)	1 (< 1)
Chills	142 (48.6)	-	11 (8.7)	-
Pyrexia	125 (42.8)	-	11 (8.7)	-
Nausea	104 (35.6)	1 (< 1)	25 (19.7)	-
Influenza like illness	89 (30.5)	2 (< 1)	19 (15.0)	-
Injection site pain	81 (27.7)	2 (< 1)	8 (6.3)	-
Vomiting	62 (21.2)	5 (1.7)	12 (9.5)	-
Diarrhea	55 (18.8)	1 (< 1)	14 (11.0)	-
Headache	55 (18.8)	2 (< 1)	12 (9.5)	-
Myalgia	51 (17.5)	1 (< 1)	7 (5.5)	-
Arthralgia	50 (17.1)	2 (< 1)	11 (8.7)	-
Pain in extremity	48 (16.4)	4 (1.4)	12 (9.5)	1 (< 1)
Constipation	34 (11.6)	-	8 (6.3)	1 (< 1)
Dizziness	28 (9.6)	-	4 (3.2)	-
Abdominal pain	26 (8.9)	2 (< 1)	3 (2.4)	-
Oropharyngeal pain	17 (5.8)	-	1 (< 1)	-
Weight decreased	17 (5.8)	1 (< 1)	1 (< 1)	-

Most ARs reported were mild to moderate and generally resolved within 72 hours.

The most common ARs reported (≥ 25%) in IMLYGIC®-treated patients were fatigue, chills, pyrexia, nausea, influenza-like illness, and injection site pain.

In the IMLYGIC® arm the most common grade 3 or higher AR was cellulitis.

**Please see full Prescribing Information [here](#). Please see Important Safety Information throughout this booklet and on page 26.**

# CLINICAL TRIAL DATA

## PRELIMINARY BIODISTRIBUTION AND VIRAL SHEDDING RESULTS

An ongoing prospective, open label, interventional, phase 2 study assessed the biodistribution and shedding of IMLYGIC®. Available data are located below from the initial 20 melanoma subjects who received a dose and schedule similar to the pivotal study.

- The biodistribution and shedding of intralesionally administered IMLYGIC® is being investigated in an ongoing study measuring IMLYGIC® DNA and virus in blood, oral mucosa, urine, injection site and occlusion dressings
- Biodistribution within the body and viral shedding through excretion and secretion were determined by measuring IMLYGIC® viral DNA using a quantitative polymerase chain reaction<sup>1</sup>
- Infectious IMLYGIC® was quantified using viral infectivity assays<sup>1</sup>

### TOTAL AMOUNT OF DETECTABLE LEVELS OF IMLYGIC® AT ANY TIME<sup>1</sup>

#### Ongoing Biodistribution and Viral Shedding

Area Tested	IMLYGIC® DNA N = 20	IMLYGIC® Infectious Virus
Blood	17 (85%)	NA
Urine	4 (20%)*	NA
Site of Injection	NA	3 (15%) <sup>†</sup>
Exterior of Occlusive Dressing	14 (70%) <sup>‡</sup>	0

Preliminary results demonstrated that live virus has not been detected on the outside of the occlusive dressing applied after the injection.

\*The peak levels detected on the day of treatment.

<sup>†</sup>All within the first week after the initial injection.

<sup>‡</sup>Declined over time with no measurable DNA by the third treatment in 13 subjects tested.

## IMPORTANT SAFETY INFORMATION

### Warnings and Precautions (Cont'd)

- Patients or close contacts with suspected signs or symptoms of a herpetic infection should contact their health care provider to evaluate the lesions. Suspected herpetic lesions should be reported to Amgen at 1-855-IMLYGIC (1-855-465-9442). Patients or close contacts have the option of follow-up testing for further characterization of the infection.



# DOSING

## ADMINISTRATION, DOSAGE STRENGTHS, AND DOSING SCHEDULE

### Administration<sup>1</sup>

IMLYGIC® is administered by intralesional injection into cutaneous, subcutaneous, and/or nodal lesions that are visible, palpable, or detectable by ultrasound guidance.

Do not administer IMLYGIC® intravenously.

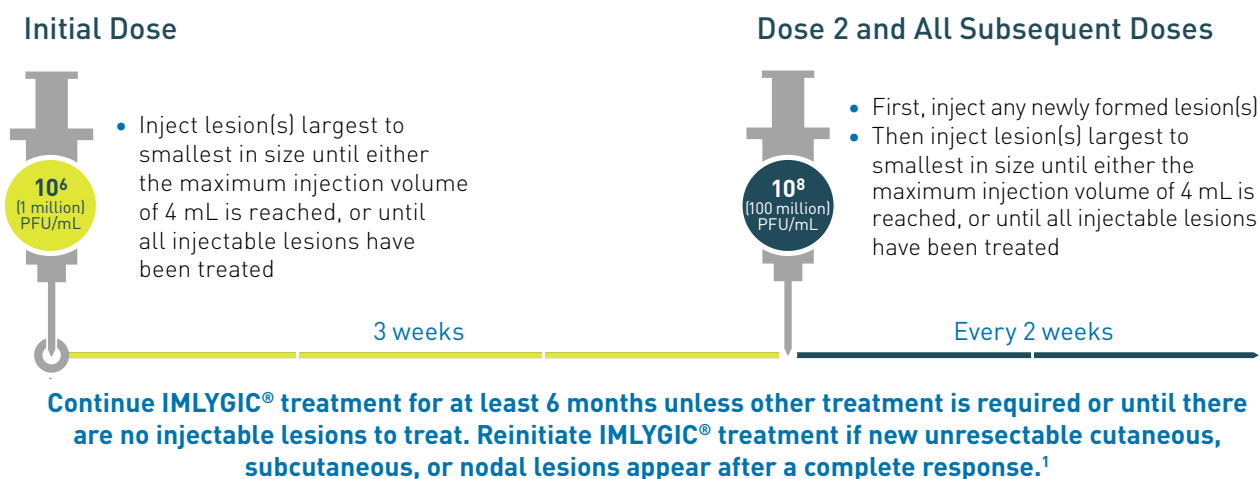
### Dosage Strengths<sup>1</sup>

IMLYGIC® is available in single-use vials of 1 mL each in 2 different concentrations:

**Initial dose** — $10^6$  (1 million) PFU/mL (light green cap)

**All subsequent doses** — $10^8$  (100 million) PFU/mL (royal blue cap)

### RECOMMENDED DOSE AND SCHEDULE<sup>1</sup>



**The total injection volume for each treatment visit should not exceed 4 mL for all injected lesions combined. It may not be possible to inject all lesions at each treatment visit or over the full course of treatment. Previously injected and/or uninjected lesion(s) may be injected at subsequent treatment visits.<sup>1</sup>**

### IMPORTANT SAFETY INFORMATION

- To minimize accidental exposure to IMLYGIC® by health care providers, patients, and their close contacts, it is very important that the instructions for storage and handling, preparation, dosing, and administration of IMLYGIC® in the full Prescribing Information are strictly followed.

**Please see full Prescribing Information [here](#). Please see Important Safety Information throughout this booklet and on page 26.**

# DOSING

## DOSING VOLUME DEPENDS ON LESION SIZE AND DOSING STAGE

### Recommended dosing volume by concentration<sup>1</sup>

- The number of vials and the concentration needed are dependent on the number and size of injectable lesions. Total volume of IMLYGIC® injection for each lesion should be determined according to the table below:

### DETERMINATION OF IMLYGIC® INJECTION VOLUME BASED ON LESION SIZE

Lesion Size (longest dimension)	IMLYGIC® Injection Volume
> 5 cm	up to 4 mL
> 2.5 cm to 5 cm	up to 2 mL
> 1.5 cm to 2.5 cm	up to 1 mL
> 0.5 cm to 1.5 cm	up to 0.5 mL
≤ 0.5 cm	up to 0.1 mL

When lesions are clustered together, inject them as you would for a single lesion according to table above.<sup>1</sup>

### During the course of therapy:<sup>1</sup>

- IMLYGIC® treatment should be continued for at least 6 months unless other treatment is required or until no injectable lesions are remaining
- Reinitiate IMLYGIC® treatment if new unresectable cutaneous, subcutaneous, or nodal lesions appear after a complete response

### Safe Handling:<sup>1</sup>

- Health care providers who are immunocompromised or pregnant should not prepare or administer IMLYGIC® and should not come into direct contact with the IMLYGIC® injection sites, dressings, or body fluids of treated patients
- Avoid accidental exposure to IMLYGIC® especially contact with skin, eyes, and mucous membranes. Refer to the USPI Section 2.2 for more information.



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10<sup>6</sup> PFU/mL and 10<sup>8</sup> PFU/mL single-use vials



PART II:

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## **Handling and Usage**

# PRODUCT HANDLING

**IMLYGIC® is a live, attenuated HSV-1 and should be handled following the instructions below<sup>1</sup>**

- A risk assessment should be conducted. Institution choice of containment and work practices should be based on local regulations and/or institutional guidelines.<sup>6</sup>

**Below are definitions of Biosafety Levels (BSL) and work practice criteria:<sup>6</sup>**

- **BSL-1** represents a basic level of containment that relies on standard microbiological practices for agents not known to consistently cause disease in immunocompetent adult humans and that present minimal potential hazard to personnel and the environment.
- **BSL-2** practices are suitable for work involving agents of moderate potential risk to personnel and the environment. These agents can cause disease in healthy individuals and pose a moderate risk to the environment

## **Proper handling of IMLYGIC®**

Health care providers who are immunocompromised or pregnant should not prepare or administer IMLYGIC® and should not come into direct contact with the IMLYGIC® injection sites, dressings, or body fluids of treated patients.

Avoid accidental exposure to IMLYGIC® and follow the instructions below for preparation, administration, and handling of IMLYGIC®:

- Wear personal protective equipment (protective gown or laboratory coat, safety glasses or face shield, and gloves) while preparing or administering IMLYGIC®
- Avoid accidental exposure to IMLYGIC®, especially contact with skin, eyes, and mucous membranes
  - Cover any exposed wounds before handling
  - In the event of an accidental occupational exposure (eg, through a splash to the eyes or mucous membranes), flush with clean water for at least 15 minutes
  - In the event of exposure to broken skin or needle stick, clean the affected area thoroughly with soap and water and/or disinfectant
- Clean all surfaces that may have come into contact with IMLYGIC® and treat all IMLYGIC® spills with a virucidal agent such as 1% sodium hypochlorite or 70% isopropyl alcohol and blot using absorbent materials
- Dispose of all materials that may have come in contact with IMLYGIC® (eg, vial, syringe, needle, cotton gauze, gloves, masks or dressings) as biohazardous waste
- Advise patients to place used dressings and cleaning materials into a sealed plastic bag, and dispose in household waste

CDC = Centers for Disease Control and Prevention; HSV-1 = herpes simplex virus type 1.

## **IMPORTANT SAFETY INFORMATION**

- Patients or close contacts with suspected signs or symptoms of a herpetic infection should contact their health care provider to evaluate the lesions. Suspected herpetic lesions should be reported to Amgen at 1-855-IMLYGIC (1-855-465-9442). Patients or close contacts have the option of follow-up testing for further characterization of the infection.

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# PRODUCT HANDLING

Proper handling, preparation, administration and disposal of IMLYGIC® is critical.

## HANDLING AND STABILITY INFORMATION

### How Supplied<sup>1</sup>



IMLYGIC® is a sterile, frozen suspension, in a single-use vial, which is supplied in 2 concentrations:

- 10<sup>6</sup> (1 million) PFU/mL (light green cap on vial)
- 10<sup>8</sup> (100 million) PFU/mL (royal blue cap on vial)

### Storage<sup>1</sup>



There are 2 storage options for IMLYGIC®:

- 1) An ultra-low freezer (-90°C to -70°C)
- 2) The storage container that IMLYGIC® is shipped in includes specific handling instructions

Protect IMLYGIC® from light.

Store IMLYGIC® in the carton until use.

### Product Sensitivity<sup>2</sup>



When frozen, IMLYGIC® should not be exposed to room temperatures for more than 60 seconds. When storing IMLYGIC® in a freezer you must quickly transfer it from the storage container.

Please see specific instructions contained within the storage container.

## IMPORTANT SAFETY INFORMATION

- To minimize accidental exposure to IMLYGIC® by health care providers, patients, and their close contacts, it is very important that the instructions for storage and handling, preparation, dosing, and administration of IMLYGIC® in the full Prescribing Information are strictly followed.

**Please see full Prescribing Information [here](#). Please see Important Safety Information throughout this booklet and on page 26.**



# PRODUCT HANDLING

## HANDLING AND STABILITY INFORMATION

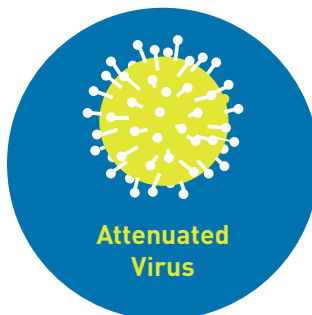
### Thawing<sup>1</sup>



After thawing, administer IMLYGIC® immediately or store in its original vial and carton, as follows:

- Thawed IMLYGIC® is stable when stored at temperatures of 2°C (36°F) up to 25°C (77°F) protected from light in its original vial and carton for the storage times specified in the table below. Do not exceed the storage times specified in the table below.
- IMLYGIC® must not be refrozen once it is thawed. Discard any thawed IMLYGIC® in the vial stored longer than the specified times in the table below.

### Handling<sup>2</sup>



Follow the instructions below for preparation, administration, and handling of IMLYGIC® at your institution:

- Wear personal protective equipment (protective gown or laboratory coat, safety glasses or face shield, and gloves) while preparing or administering IMLYGIC®.
- Avoid accidental exposure to IMLYGIC®, especially contact with skin, eyes, and mucous membranes.
- Clean all surfaces that may have come in contact with IMLYGIC® and treat all IMLYGIC® spills with a virucidal agent such as 1% sodium hypochlorite or 70% isopropyl alcohol and blot using absorbent materials.

### Disposal<sup>2</sup>



Dispose of all materials that have come in contact with IMLYGIC® (eg, vial, syringe, needle, cotton gauze, gloves, masks, or dressings) in accordance to the prescribing information.

Advise patients to place used dressings and cleaning materials into a sealed plastic bag, and dispose in household waste.

### Maximum Storage Time for Thawed IMLYGIC® in Vial

	10 <sup>6</sup> (1 million) PFU/mL	10 <sup>8</sup> (100 million) PFU/mL
2°C to 8°C (36°F to 46°F)	24 hours	1 week (7 days)
up to 25°C (77°F)	12 hours	24 hours



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# PRODUCT HANDLING

## HOW IMLYGIC® IS DELIVERED

### IMLYGIC® is delivered in a time-sensitive storage container

- The storage container will maintain the correct temperature for up to 96 hours after being sealed. The time the container will expire is printed on the exterior of the shipment
- Printed on the outside of the storage container are instructions on how to properly store IMLYGIC®
- **IMPORTANT:** If you are using the container to store IMLYGIC®, the product may only be inventoried once. Once the product container is removed, you will have 60 seconds to either place it back in the storage container or transfer it to a freezer<sup>2</sup>

### An Instruction Card for how to properly inventory and store IMLYGIC® is delivered in each shipment

- Instructions detail each component of the shipment, including how to remove the dry ice container and product container to inventory the product



Please see full Prescribing Information [here](#). Please see Important Safety Information throughout this booklet and on page 26.

# PRODUCT HANDLING

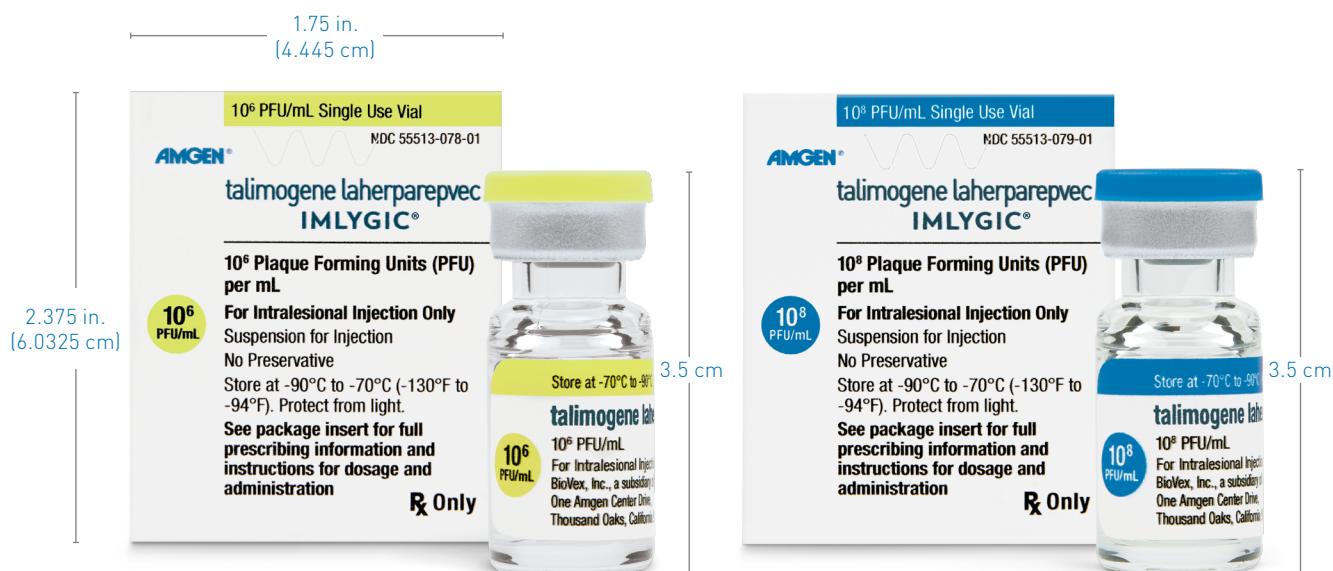
## VIAL AND CARTON LABEL DESCRIPTION

- IMLYGIC® is provided as a sterile, single-use, preservative-free frozen suspension in a cyclic olefin polymer (COP) plastic resin vial with chlorobutyl elastomer stopper, aluminum seal, and polypropylene cap. Each vial contains a retrievable minimal volume of 1 mL<sup>1</sup>
- The vials do not contain latex<sup>1</sup>

The vial caps are color coded to reflect the 2 different dosing concentrations:<sup>1</sup>


10<sup>6</sup> (1 million) PFU/mL is light green  
(NDC 55513-078-01)

10<sup>8</sup> (100 million) PFU/mL is royal blue  
(NDC 55513-079-01)



Product shown is not actual size.

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## PRODUCT HANDLING

### IMLYGIC® IS TIME AND TEMPERATURE SENSITIVE

Read all instructions to make sure you store IMLYGIC® appropriately.

**FROZEN IMLYGIC® VIALS MUST BE STORED AND TRANSPORTED  
at -90°C to -70°C (-130°F to -94°F)<sup>1</sup>**

#### Recommendations:<sup>1</sup>

- Store and transport IMLYGIC® at -90°C to -70°C (-130°F to -94°F)
- Protect IMLYGIC® from light
- Store IMLYGIC® in the carton until use
- Thaw IMLYGIC® immediately prior to administration
- Do not draw IMLYGIC® into a syringe until immediately prior to administration

#### Shelf Life

Approximately 4 years, if stored as directed.

Please see full Prescribing Information [here](#). Please see Important Safety Information throughout this booklet and on page 26.

# DRUG PREPARATION

## HOW TO THAW AND PRESERVE IMLYGIC® PRIOR TO ADMINISTRATION

### Thawing Instructions for IMLYGIC® Vials<sup>1</sup>

1. Determine the total volume required for injection, up to 4 mL.
2. Thaw frozen IMLYGIC® vials at room temperature [20°C to 25°C (68°F to 77°F)] until IMLYGIC® is liquid (approximately 30-70 minutes). Do not expose the vial to higher temperatures. Keep the vial in original carton during thawing.
3. Swirl gently. Do NOT shake.
4. After thawing, administer IMLYGIC® immediately or store in its original vial and carton, as follows:
  - Thawed IMLYGIC® is stable when stored at temperatures of 2°C (36°F) up to 25°C (77°F) protected from light in its original vial and carton for the storage times specified in the table below. Do not exceed the storage times specified in the table below.
  - IMLYGIC® must not be refrozen once it is thawed. Discard any thawed IMLYGIC® in the vial stored longer than the specified times in the table below.
5. Prepare sterile syringes and needles. A detachable needle of 18-26G may be used for IMLYGIC® withdrawal and a detachable needle of 22-26G may be used for injection. Small unit syringes (eg, 0.5 milliliter insulin syringes) are recommended for better injection control.
6. Using aseptic technique, remove the vial cap and withdraw the product from the vial into the syringe(s), noting the total volume. Avoid generating aerosols when loading syringes with product, and use a biologic safety cabinet if available.

### Maximum Storage Time for Thawed IMLYGIC® in Vial

	10 <sup>6</sup> (1 million) PFU/mL	10 <sup>8</sup> (100 million) PFU/mL
2°C to 8°C (36°F to 46°F)	24 hours	1 week (7 days)
up to 25°C (77°F)	12 hours	24 hours

### IMPORTANT SAFETY INFORMATION

- To minimize accidental exposure to IMLYGIC® by health care providers, patients, and their close contacts, it is very important that the instructions for storage and handling, preparation, dosing, and administration of IMLYGIC® in the full Prescribing Information are strictly followed.



# DRUG PREPARATION

## PREPARATION AND HANDLING<sup>1</sup>

Health care providers who are immunocompromised or pregnant should not prepare or administer IMLYGIC® and should not come into direct contact with the IMLYGIC® injection sites, dressings, or body fluids of treated patients.

Avoid accidental exposure to IMLYGIC® and follow below instructions for preparation, administration, and handling of IMLYGIC®:

- Wear personal protective equipment (protective gown or laboratory coat, safety glasses or face shield, and gloves) while preparing or administering IMLYGIC®
- Avoid accidental exposure to IMLYGIC® especially contact with skin, eyes, and mucous membranes
  - Cover any exposed wounds before handling
  - In the event of an accidental occupational exposure (eg, through a splash to the eyes or mucous membranes), flush with clean water for at least 15 minutes
  - In the event of exposure to broken skin or needle stick, clean the affected area thoroughly with soap and water and/or disinfectant
- Clean all surfaces that may have come into contact with IMLYGIC® and treat all IMLYGIC® spills with a virucidal agent such as 1% sodium hypochlorite or 70% isopropyl alcohol and blot using absorbent materials
- Dispose of all materials that may have come in contact with IMLYGIC® (eg, vial, syringe, needle, cotton gauze, gloves, masks, or dressings) as biohazardous waste
- Advise patients to place used dressings and cleaning materials into a sealed plastic bag, and dispose in household waste

## IMPORTANT SAFETY INFORMATION

- Caregivers should wear protective gloves when assisting patients in applying or changing occlusive dressings and observe safety precautions for disposal of used dressings, gloves, and cleaning materials. Exposed individuals should clean the affected area thoroughly with soap and water and/or a disinfectant.
- To prevent possible inadvertent transfer of IMLYGIC® to other areas of the body, patients should be advised to avoid touching or scratching injection sites or occlusive dressings.

**Please see full Prescribing Information [here](#). Please see Important Safety Information throughout this booklet and on page 26.**



PART III:

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## **Resources**

# ORDER SETS

## CONSIDERATIONS FOR DEVELOPING IMLYGIC® ORDER SETS

An objective assessment of potential issues related to IMLYGIC® ordering and documentation was conducted. Below are some considerations that may help as you determine the appropriate plan for your institution.<sup>2</sup>

### ORDER SET CONSIDERATIONS

- Build medication orders using the full generic name (talimogene laherparepvec)<sup>2</sup> followed by the branded name (IMLYGIC®)<sup>2</sup>
- Input the 2 concentrations with standard text, since the use of exponents may be confusing<sup>2</sup>
  - $10^6$  = 1 million PFU/mL
  - $10^8$  = 100 million PFU/mL
- Develop a standard order set (electronic or printed) for the patient's first dose (1 million PFU/mL) and a separate order set for subsequent doses (100 million PFU/mL)<sup>2</sup>
- Create an order verification dose alert/message that indicates a patient can receive a maximum of 4 mL (4 vials) per visit<sup>2</sup>

### PREPARATION CONSIDERATIONS

- When handling the product, all practitioners should be educated on injection safety and the safe use of single-use vials
- If drug is prepared with pharmacy services, consider preparing patient-specific 1 mL-sized pharmacy-labeled syringes. The number of syringes dispensed should be based on the total volume of drug ordered (eg, 4 mL ordered = 4 syringes prepared)<sup>2</sup>
- If the dose is prepared at bedside, practitioners should be educated on injection and the safe use of IMLYGIC®<sup>2</sup>

### CREATING SAFEGUARD RULES

- **Prevent repeating the initial dose:** Patients should not receive the initial dose concentration ( $10^6$  PFU/mL) of IMLYGIC® twice<sup>1</sup>. Create a rule that alerts users when a patient who has already received this concentration is prescribed it again<sup>2</sup>
- **Do not exceed the total dose volume:** Create an IMLYGIC®-specific order entry that warns against exceeding a total of 4 mL per visit<sup>2</sup>
- **Adhere to the dosing schedule:** Create an alert that warns users when a patient has been prescribed an IMLYGIC® treatment less than 14 days since Cycle 1 (initial and second treatment)<sup>2</sup>

**Tip: Work with your Information Technology team to create these rules and order forms in your institution's systems**

Please see full Prescribing Information [here](#). Please see Important Safety Information throughout this booklet and on page 26.



# HANDLING IMLYGIC®

## Key Considerations

- ☐ Are you immunocompromised or pregnant? If so, you should not prepare or administer IMLYGIC®, and you also shouldn't come into direct contact with the IMLYGIC® injection sites, dressings, or body fluids of treated patients.
- ☐ Have you reviewed the IMLYGIC® full Prescribing Information for complete dosing, administration and precautions, storage and handling information?

## Safe Handling Awareness

- ☐ Have you reviewed the precautions for handling IMLYGIC®?
- ☐ Are you aware of the precautions necessary to avoid accidental exposure to IMLYGIC®?
- ☐ Have you reviewed what to do in case of accidental exposure to IMLYGIC®?
- ☐ Have you reviewed what to do in case of an IMLYGIC® spill?
- ☐ Do you know how to dispose of all materials which may have come into contact with IMLYGIC®?

## Thawing, Preparation and Storage Considerations

- ☐ Have you confirmed the correct dose for the IMLYGIC® patient with the physician or nurse?
- ☐ Do you know the appropriate thawing procedure for IMLYGIC®?
- ☐ Is IMLYGIC® being administered immediately after thawing? If not, are you aware of thawed IMLYGIC® storage requirements and time limitations?
- ☐ If thawed IMLYGIC® is being stored, have you recorded the time it was placed in the refrigerator?

## Administration Considerations

- ☐ Have you reviewed the Pre-injection, Injection and Post-injection procedures in the full prescribing information?
- ☐ Do you have the additional necessary materials for Post-injection procedures ready?
- ☐ Do you know how to advise patients to dispose of used dressings and cleaning materials?
- ☐ Do you know how to dispose of all materials which may have come into contact with IMLYGIC®?



**IMLYGIC®**  
(talimogene laherparepvec)  
SUSPENSION FOR INJECTION  
10<sup>6</sup> PFU/mL and 10<sup>8</sup> PFU/mL single-use vials

# IMPORTANT SAFETY INFORMATION

## Contraindications

- Do not administer IMLYGIC® to immunocompromised patients, including those with a history of primary or acquired immunodeficient states, leukemia, lymphoma, AIDS or other clinical manifestations of infection with human immunodeficiency viruses, and those on immunosuppressive therapy, due to the risk of life-threatening disseminated herpetic infection.
- Do not administer IMLYGIC® to pregnant patients.

## Warnings and Precautions

- **Accidental exposure to IMLYGIC®** may lead to transmission of IMLYGIC® and herpetic infection, including during preparation and administration. Health care providers, close contacts, pregnant women, and newborns should avoid direct contact with injected lesions, dressings, or body fluids of treated patients. The affected area in exposed individuals should be cleaned thoroughly with soap and water and/or a disinfectant.
- Caregivers should wear protective gloves when assisting patients in applying or changing occlusive dressings and observe safety precautions for disposal of used dressings, gloves, and cleaning materials. Exposed individuals should clean the affected area thoroughly with soap and water and/or a disinfectant.
- To prevent possible inadvertent transfer of IMLYGIC® to other areas of the body, patients should be advised to avoid touching or scratching injection sites or occlusive dressings.
- **Herpetic infections:** Herpetic infections (including but not limited to cold sores and herpetic keratitis) and serious cases of disseminated herpetic infections have been reported in IMLYGIC®-treated patients, including fatal disseminated herpetic infection in the immunocompromised patient population. Immunocompromised patients may be at increased risk of life-threatening disseminated herpetic infection. Patients who develop suspicious herpes-like lesions should follow standard hygienic practices to prevent viral transmission.
- Patients or close contacts with suspected signs or symptoms of a herpetic infection should contact their health care provider to evaluate the lesions. Suspected herpetic lesions should be reported to Amgen at 1-855-IMLYGIC (1-855-465-9442). Patients or close contacts have the option of follow-up testing for further characterization of the infection.
- IMLYGIC® is sensitive to acyclovir. Acyclovir or other antiviral agents may interfere with the effectiveness of IMLYGIC®. Consider the risks and benefits of IMLYGIC® treatment before administering antiviral agents to manage herpetic infection.
- **Injection Site Complications:** Necrosis or ulceration of tumor tissue may occur during IMLYGIC® treatment. Cellulitis and systemic bacterial infection have been reported in clinical studies. Careful wound care and infection precautions are recommended, particularly if tissue necrosis results in open wounds.
- Impaired healing at the injection site has been reported. IMLYGIC® may increase the risk of impaired healing in patients with underlying risk factors (eg, previous radiation at the injection site or lesions in poorly vascularized areas). If there is persistent infection or delayed healing of the injection site, consider the risks and benefits of continuing treatment.
- **Immune-Mediated events** including glomerulonephritis, vasculitis, pneumonitis, worsening psoriasis, and vitiligo have been reported in patients treated with IMLYGIC®. Consider the risks and benefits of IMLYGIC® before initiating treatment in patients who have underlying autoimmune disease or before continuing treatment in patients who develop immune-mediated events.
- **Plasmacytoma at the Injection Site:** Plasmacytoma in proximity to the injection site has been reported in a patient with smoldering multiple myeloma after IMLYGIC® administration in a clinical study. Consider the risks and benefits of IMLYGIC® in patients with multiple myeloma or in whom plasmacytoma develops during treatment.
- **Obstructive Airway Disorder:** Obstructive airway disorder has been reported following IMLYGIC® treatment. Use caution when injecting lesions close to major airways.
- **Hepatic Hemorrhage from Transcutaneous Intrahepatic Route of Administration:** IMLYGIC® is not indicated for transcutaneous intrahepatic route of administration. In clinical studies, cases of hepatic hemorrhage resulting in hospitalization and death have been reported in patients receiving transcutaneous intrahepatic IMLYGIC® injections.

## Adverse Reactions

- The most commonly reported adverse drug reactions ( $\geq 25\%$ ) in IMLYGIC®-treated patients were fatigue, chills, pyrexia, nausea, influenza-like illness, and injection site pain. Pyrexia, chills, and influenza-like illness can occur at any time during IMLYGIC® treatment, but were more frequent during the first 3 months of treatment.
- The most common Grade 3 or higher adverse reaction was cellulitis.


**Please see full Prescribing Information and Medication Guide for IMLYGIC®.**

## REFERENCES

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**For more information about IMLYGIC®,  
Ordering or Returns, please:**

Call **1-866-IMLYGIC (465-9442)**

Visit: [www.IMLYGIC.com](http://www.IMLYGIC.com)

**For billing and reimbursement assistance, please:**

Contact Amgen SupportPlus at **1-888-4ASSIST**

Visit: [www.AmgenAssistOnline.com](http://www.AmgenAssistOnline.com)

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