IMLYGIC®

Revision Number: 11 **Date Issued: February 20, 2023**

SECTION I - INFECTIOUS AGENT

Name: IMLYGIC®

Synonyms: Talimogene laherparepvec, OncoVEX^{GM-CSF}, AMG 678, TVEC

CAS #: 1187560-31-1

Manufacturer:
Amgen Inc.
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1-805-447-7233 Amgen EHSS Hotline
1-805-447-1000

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NORTH AMERICA 1-800-424-9300
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The OSHA Hazard Communication Standard (29 CFR Section 1910.1200) and UNECE's 2016 Globally Harmonized System of Classification and Labeling of Chemicals do not apply to this material.

Description: IMLYGIC® is an attenuated herpes simplex virus type-1 (HSV-1) derived by functional deletion of 2 genes (ICP34.5 and ICP47) and insertion of coding sequence for human granulocyte macrophage colony-stimulating factor (GM-CSF). These modifications allow IMLYGIC® to efficiently replicate within tumors and to produce the immune stimulatory protein GM-CSF. IMLYGIC® causes lysis of tumors, followed by release of tumor-derived antigens, which together with virally derived GM-CSF may promote an antitumor immune response.

Characteristics: IMLYGIC® is made from a virus that is modified so that replication occurs selectively in tumor cells. The ability of the virus to replicate in normal cells has been attenuated.

Active Ingredient: rHSV-1$^{hGM-CSF}$ oncolytic viral immunotherapy.

SECTION II – HAZARD IDENTIFICATION

Pathogenicity: IMLYGIC® is an attenuated version of HSV-1, modified so that replication occurs selectively in tumor cells. The viral genes ICP34.5 and ICP47 are deleted in IMLYGIC®. HSV-1 deleted for ICP34.5 cannot replicate efficiently in non-tumor tissue in immune competent animals and humans. ICP47 is deleted from IMLYGIC® to improve the presentation of viral and tumor antigens enhancing any anti-tumor immune responses. Additionally, the removal of ICP47 causes the increased expression of another viral protein, US11. Increased US11 expression enhances the replication of ICP34.5-deleted HSV-1 in tumor cells without loss of tumor selectivity.

There is the theoretical possibility that IMLYGIC® could recombine with HSV-1 in cells simultaneously infected with both IMLYGIC® and HSV-1. These variants would be predicted to be no more pathogenic than HSV-1. Additionally, IMLYGIC® and HSV-1 do not integrate into the host cell genome.

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Host Range: Humans

Infectious Dose: IMLYGIC® is provided in single use vials of 1 mL each in two different concentrations, Product 10^6 (1 million) PFU/mL or 10^8 (100 million) PFU/mL containing:

Phosphate Buffer Solution	102mM
Sodium Chloride	145mM
Sorbitol	2% (w/v)
Myo-inositol	4% (w/v)
pH 7.4	

Mode of Transmission: Accidental exposure may occur during the manufacture of drug product, during the handling and administration of drug product by healthcare providers, or due to close contact with treated patients. Accidental exposure to IMLYGIC® may include: accidental spills and/or splashing of mucous membranes**,** accidental needlestick, direct contact of skin with injected lesions, the inside of protective dressings, or physical contact with body fluids of treated patients, during preparation and administration of injections, dressing changes or close physical contact with treated patients.

Incubation Period: The incubation period for HSV-1 is 7-10 days. The incubation period for IMLYGIC® has not been determined, but none of the modifications made to HSV-1 in the construction of IMLYGIC® are expected to change this incubation period.

Communicability: IMLYGIC® virus is attenuated and has limited replicative capacity in normal cells in vivo. HSV-1 is fragile and readily inactivated by desiccation, lipid solvents and mild detergents. HSV-1 is thought to be transmitted via contact with infected secretions, mucous membranes, or skin.

SECTION III - DISSEMINATION

Zoonosis: None

Vectors: None

SECTION IV – STABILITY AND VIABILITY

Drug Susceptibility: IMLYGIC® is sensitive to anti-viral drugs such as acyclovir, valacyclovir, famciclovir, and cidofovir.

Drug Resistance: None

Susceptibility to Disinfectants: IMLYGIC® is susceptible to common disinfectants and cleaning agents such as 2.5% bleach, 70% isopropyl alcohol, 0.8% vesphene, or 0.8% LpH all reduced IMLYGIC® infectivity by more than 6 logs within 1 minute.

Physical Inactivation: Temperature of greater than 56° C maintained for 30 minutes eliminates infectivity, readily inactivated by lipid solvents, exposure to pH of less than 4.

Survival Outside Host: Like HSV-1, IMLYGIC® is not expected to survive for long periods outside the host under normal environmental conditions.

SECTION V – FIRST AID/MEDICAL

First Aid/ Treatment: In the event of accidental exposure 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 site thoroughly with soap and water or a skin disinfectant. See a physician for monitoring for signs of infection. Acyclovir or other anti-viral drugs may be administered prophylactically or if signs and symptoms of herpetic infection are present.

Immunization: None

Prophylaxis: Acyclovir or other anti-viral drugs

SECTION VI – LABORATORY HAZARDS

Primary Hazards: Ingestion; accidental parenteral inoculation; droplet exposure of the mucous membranes or broken skin.

Special Hazards: None

SECTION VII – EXPOSURE CONTROLS/PERSONAL PROTECTION

Containment Requirements: The choice of containment and work practices should be based on local regulations and/or institutional guidelines. In addition, a risk assessment should be conducted that includes, but is not limited to: job activity, scale, concentration, potential aerosolization and staff exposure. Below are recommended Biosafety Levels (BSL) and work practices developed from the CDC/NIH Guidelines (5th Edition, 2009), "Biosafety in Microbiological and Biomedical Laboratories", WHO "Laboratory Biosafety Manual", 3rd Edition and NIH "Guidelines for Research Involving Recombinant DNA Molecules", Department of Health and Human Services, National Institutes of Health (most recent version).

Use of BSL-1 containment and work practices is recommended for research and development activities handling small volumes. Universal precautions are recommended for healthcare facilities preparing and administering the product in single dose vials.

Use of BSL-1 or BSL-2 containment and work practices is recommended for certain research and development activities involving volumes up to 10L.

Use of Large Scale Biosafety Level 2 (BSL2-LS) containment and work practices is recommended for work tasks performed with volumes greater than 10L (e.g., manufacturing).

Protective Clothing: Laboratory coat/gown, gloves and safety glasses or face shield when there is potential for direct skin contact with the virus (e.g. research activities, manufacturing, and healthcare facilities preparing and administering the product).

Other Precautions: Note to healthcare providers, use of a Closed System Transfer Device (CSTD) is not required when preparing IMLYGIC®. If your healthcare facility utilizes CSTDs for IMLYGIC® preparation, the sleeved vial only fits with the BD PhaSeal™ System CSTD.

SECTION VIII – HANDLING AND STORAGE

Spills: Spills should be contained and treated with a virucidal agent and absorbent materials. All materials contaminated with IMLYGIC® must be disposed of in compliance with federal, state, local authorities, competent authority, and institutional guidelines.

Disposal: Decontaminate waste prior to disposal: steam sterilization, chemical disinfection, or incineration. Dispose of waste in compliance with federal, state, local authorities, competent authority and institutional guidelines.

Storage: In sealed containers that are appropriately labeled. Follow package insert for storage conditions.

Transportation:

DOT Not regulated

IATA Proper Shipping Name: Genetically Modified Micro-Organism
UN Number: 3245

SECTION IX – OTHER INFORMATION

Stability of the Agent in the Environment: IMLYGIC® is unstable due to lipid envelope and is susceptible to wide range of detergents, high temperatures and low pH. It is also not expected to have an adverse impact on the environment due to low persistence and viability outside the host organism (humans) and high sensitivity to physical and chemical agents.

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The above information is based on data available to us and is believed to be correct. Since the information may be applied under conditions beyond our control and with which we may be unfamiliar, we do not assume any responsibility for the results of its use and all persons receiving it must make their own determination of the effects, properties and protections, which pertain to their particular conditions.

No representation, warranty, or guarantee, express or implied (including a warranty of fitness or merchantability for a particular purpose), is made with respect to the materials, the accuracy of this information, the results to be obtained from the use thereof, or the hazards connected with the use of the material. Caution should be used in the handling and use of the material because it may be biologically active.