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Imlygic® (Talimogene Laherparepvec) - Important information: Special Considerations to Minimize the Potential Occurrence of Adverse Events in HSV-1 Seronegative Patients Receiving Vials From Affected Lots.

Dear Healthcare Professional,

Amgen in agreement with the Medicines and Healthcare products Regulatory Agency (MHRA) would like to inform you of the following:

Summary

- Important information to qualified physicians experienced in the treatment of cancer, pharmacists, and nurses: ***Injections from Imlygic 10^6 PFU/mL vials from the affected lot numbers should be administered "as soon as practically feasible" and no later than 18 hours after thaw and storage at 2°C to 8°C.***
- Imlygic 10^6 PFU/mL vials from the lots listed in Annex 1 below may have a lower than the expected level of virus infectivity if they were thawed and subsequently stored at 2°C to 8°C for 18 hours or more prior to administration.
- HSV-1 seronegative patients who have received injections from vials from the affected lots and administered later than 18 hours after thaw and storage at 2°C to 8°C may potentially be at risk for an increased incidence of severe and/or serious adverse events, most likely following the second dose of Imlygic (with 10^8 PFU/mL dose concentration).
- Your site has received in the past Imlygic 10^6 PFU/mL vials from the affected lots listed below

Background on the safety concern

Imlygic® (talimogene laherparepvec 10^6 PFU/mL) is oncolytic immunotherapy indicated for the treatment of adults with unresectable melanoma that is regionally or distantly metastatic (Stage IIIB, IIIC and IVM1a) with no bone, brain, lung or other visceral disease.

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

Imlygic® is thawed at room temperature until liquid. The time to achieve a complete vial thaw is expected to be approximately 30 minutes, depending on room temperature. The label indicates that Imlygic® may be thawed and subsequently stored for up to 24 hours at 2°C to 8°C prior to administration. However, the affected lots listed in Annex 1 may have a lower than expected level of virus infectivity if they were thawed and subsequently stored at 2°C to 8°C for 18 hours or more prior to administration.

As a result, ***Imlygic® from the lots listed in the Annex 1 is to be administered "as soon as practically feasible" and no later than 18 hours after thaw and storage at 2°C to 8°C.***

Lots not included in Annex 1 are not affected by this communication.

In phase 1 Clinical Trial, ascending-dose study of Imlygic, subjects who were HSV-1 seronegative at clinical study entry experienced more adverse events than subjects that were HSV-1 seropositive. The adverse events consisted primarily of flu-like symptoms. Symptoms were mitigated using a dosing regimen that included an initial lower dose concentration of 10^6 PFU/mL in all subjects followed by subsequent dose concentration of 10^8 PFU/mL, regardless of HSV-1 serostatus. Therefore, this letter is provided to make sure the proper viral load necessary for HSV-1 seroconversion is delivered at the initial dose to help mitigate the potential risk for an increased incidence of severe and/or serious drug adverse events following the subsequent dose with a dose concentration of 10^8 PFU/mL.

Instructions for Adverse Event reporting

Healthcare providers are instructed to report adverse events, especially in HSV-1 seronegative patients who received previously Imlygic® with an initial dose concentration of 10^6 PFU/mL from a vial with the less active product (less viral infectivity) via the Yellow Card Scheme.

In order to establish a relationship with the initial dose, reference should be made to the possibly reduced viral infectivity of the initial dose as well as its lot number.

Report via the website https://yellowcard.mhra.gov.uk/, the free Yellow Card app available from the Apple App Store or Google Play Store, and some clinical IT systems (EMIS, SystmOne, Vision, MiDatabank) for healthcare professionals. Suspected side effects can also be reported by calling 0800 731 6789 for free.

When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset timing, treatment dates, and product brand name.

Company contact point

Should you have any questions or require additional information regarding the use of Imlygic®, please contact medical information on gbinfoline@amgen.com.

Yours sincerely

Dr Anthony Patrikios

Executive Medical Director, UK & Ireland

MBBCh MRCGP FFPM MBA

Annex 1

List of affected lots:

Lot numbers
1110758
1114340