Indication	Stage IIIb, stage IIIc or stage IVM1a melanoma with cutaneous, subcutaneous or nodal deposit(s) which is/are suitable for direct injection but is/are not surgically resectable and where systemic immunotherapies/targeted therapies are not deemed more suitable . NB: Stage IVM1a disease (ie metastases to the skin, subcutaneous tissues or distant lymph nodes) should have a normal serum LDH.
Treatment Intent	Palliative treatment
Frequency and number of cycles	2nd treatment should be given 3 weeks after initial treatment and thereafter treatments should be at 2 week intervals. Patients may experience increase in size of existing lesion(s) or the appearance of a new lesion prior to achieving a response. As long as there are injectable lesion(s) remaining, talimogene laherparepvec should be continued for at least 6 months unless the physician considers that the patient is not benefitting from treatment or that other treatment is required. Talimogene laherparepvec treatment may be reinitiated if new lesions appear following a complete response and the physician considers that the patient will benefit from treatment.
Monitoring parameters	• Liaise with Pharmacy with regards to administration time and follow local handling and disposal SOPs. • Monitor FBC, U&Es, LFTs at each cycle. If neuts <1.0 or WBC <3.0 or Hb <90g/L d/w consultant. • Monitor coagulation and ensure adequate clotting parameters prior to first treatment and then as clinically indicated. No dose adjustment necessary in renal or hepatic impairment. • Contraindicated in patients who are severely immuno-compromised. • Patients with rare hereditary problems of fructose intolerance should not take this medicine. • Immune-mediated events including glomerulonephritis, vasculitis, pneumonitis, worsening psoriasis, and vitiligo have been reported. • Pyrexia, chills, and influenza like illness can occur any time during treatment, generally resolved within 72 hours. These events were reported more frequently within the period of the first 6 treatments, particularly in patients who were HSV-1 negative at baseline. Paracetamol may be taken for flu-like symptoms. • Cautions: Obstructive airway disorder has been reported following treatment. Caution should be used when injecting lesions close to major airways. Plasmacytoma has been reported in proximity to the injection site; the risks and benefits should be considered in patients with multiple myeloma or in whom plasmacytoma develops during treatment. In clinical studies, herpetic infections have been reported. Symptoms of a local or systemic infection possibly related to talimogene laherparepvec are anticipated to be similar to symptoms caused by wild-type HSV-1 infections. Patients who develop herpetic infections should be advised to follow standard hygienic practices to prevent viral transmission. Talimogene laherparepvec is sensitive to aciclovir. The risks and benefits should be considered before administering aciclovir or other anti-viral agents. These agents may interfere with the effectiveness of talimogene laherparepvec if administered systemically or topically directly to the injection site. • Each 4 mL dose contains approximately 30 mg (1.3 mmol) sodium. This should be taken into consideration by patients on a controlled sodium diet. • Drug interactions: Aciclovir and other anti-viral agents may interfere with the

	effectiveness of talimogene laherparepvec if administered systemically or topically directly to the injection site. Consider the risks and benefits of treatment before administering aciclovir or other anti-viral agents indicated for management of herpetic infection. • The patient should be provided with the IMLYGIC® Patient Alert card with each prescription. • Patients should be given the Patient Safety Brochure at every visit, which explains how to avoid spreading T-VEC. • The IMLYGIC® lesion tracking sheet may be used to monitor response.
Administration guidance	○ The injection site may be treated with a topical anaesthetic agent. Injectable anaesthetic may be injected around the periphery of the lesion but should not be injected directly into the lesion. ○ Clean the lesion and surrounding areas with an alcohol swab and let dry. ○ Inject talimogene laherparepvec intralesionally into cutaneous, subcutaneous, and/or nodal lesions that are visible, palpable or detectable by ultrasound guidance. ○ Using a single insertion point, inject talimogene laherparepvec along multiple tracks as far as the radial reach of the needle allows within the lesion to achieve even and complete dispersion. Multiple insertion points may be used if a lesion is larger than the radial reach of the needle. (See diagrams below). ○ Disperse talimogene laherparepvec evenly and completely within the lesion by pulling the needle back without exiting the lesion. Redirect the needle as many times as necessary while injecting the remainder of the dose. Continue until the full dose is evenly and completely dispersed. ○ When removing the needle, withdraw it from the lesion slowly to avoid leakage or splash back. ○ Repeat these steps for other lesions that need to be injected. Use a new needle anytime the needle is completely removed from a lesion and each time a different lesion is injected. ○ Post-injection apply pressure to the injection site with sterile gauze for at least 30 seconds. Swab the injection site and surrounding area with alcohol, and cover the injected lesion with an absorbent pad and dry occlusive dressing. ~~for one week~~ Wipe the exterior of occlusive dressing with an alcohol wipe. Injection site should be covered with an airtight and watertight dressing for at least 8 days from last treatment or longer if the injection site is weeping or oozing. ○ Patient should carry Patient Alert Card with them at all times.
Reference(s)	SpC accessed online 3/5/18

NB For funding information, refer to the SACT funding spreadsheet

Initial Treatment

Day	Drug	Dose Concentration	Route	Infusion Time	Administration Details
	The injection site may be treated with a topical anaesthetic agent. Injectable anaesthetic may be injected around the periphery of the lesion but should not be injected directly into the lesion.				
	Talimogene laherparepvec	**10^6 (1 million) PFU/mL**	Intralesional injection into cutaneous, subcutaneous, and/or nodal lesions that are visible, palpable or detectable by ultrasound guidance.		The total injection volume for each treatment visit should be up to a maximum of 4 mL. The volume to be injected into each lesion is dependent on the size of the lesion (see below). Inject largest lesion(s) first. Prioritise injection of remaining lesions based on lesion size until maximum injection volume is reached.
TTO	Drug	Dose	Route	Directions	
	Dressing pack	X 1	Topical	To keep injection site covered for at least 8 days. Supplied by the ward / OP.	

2nd treatment - 3 weeks after initial treatment

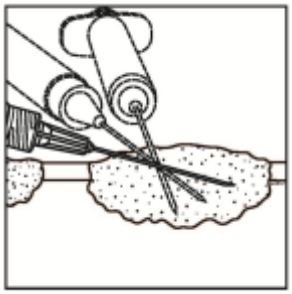
Day	Drug	Dose Concentration	Route	InfusionTime	Administration Details
	The injection site may be treated with a topical anaesthetic agent. Injectable anaesthetic may be injected around the periphery of the lesion but should not be injected directly into the lesion.				
	Talimogene laherparepvec	**10^8 (100 million) PFU/mL**	Intralesional injection into cutaneous, subcutaneous, and/or nodal lesions that are visible, palpable or detectable by ultrasound guidance.		The total injection volume for each treatment visit should be up to a maximum of 4 mL The volume to be injected into each lesion is dependent on the size of the lesion (see below). First inject any new lesions (lesions that may have developed since initial treatment). Prioritise injection of remaining lesions based on lesion size until maximum injection volume is reached.
TTO	Drug	Dose	Route	Directions	
	Dressing pack	X 1	Topical	To keep injection site covered for at least 8 days. Supplied by the ward / OP.	

3rd and subsequent treatments - 2 weeks after previous treatment

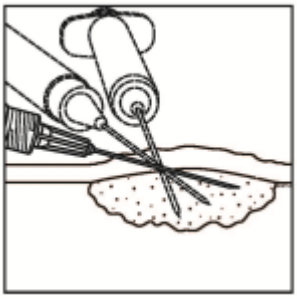
Day	Drug	Dose Concentration	Route	Infusion Time	Administration Details
	The injection site may be treated with a topical anaesthetic agent. Injectable anaesthetic may be injected around the periphery of the lesion but should not be injected directly into the lesion.				
	Talimogene laherparepvec	**10^8 (100 million) PFU/mL**	intralesional injection into cutaneous, subcutaneous, and/or nodal lesions that are visible, palpable or detectable by ultrasound guidance.		The total injection volume for each treatment visit should be up to a maximum of 4 mL. The volume to be injected into each lesion is dependent on the size of the lesion (see below). First inject any new lesions (lesions that may have developed since previous treatment). Prioritise injection of remaining lesions based on lesion size until maximum injection volume is reached.
TTO	Drug	Dose	Route	Directions	
	Dressing pack	X 1	Topical	To keep injection site covered for at least 8 days. Supplied by the ward / OP.	

Lesion size (longest dimension)	**Talimogene laherparepvec 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

Injection administration for cutaneous lesions



Injection administration for subcutaneous lesions



Injection administration for nodal lesions