IMDELLTRA®(tarlatamab)
GUIDE FOR HEALTHCARE PROFESSIONALS
Instructions for Patient Care to minimise the risks of CRS and ICANS

The information in this guide is not intended as a replacement for the Israeli Prescribing Information (PI).
Please read the IMDELLTRA Israeli PI, in conjunction with this guide

PLEASE REVIEW EACH ITEM BELOW

This Healthcare Professional (HCP) Guide contains information for HCPs on the risks of Cytokine Release Syndrome (CRS) and Immune Effector Cell Associated Neurotoxicity Syndrome (ICANS), and instructions on monitoring requirements during and after treatment. It also serves as a reminder for HCPs to discuss the risks of CRS and ICANS with patients, including reviewing the Patient Alert Card (PAC) with them.

Section 1: Information on tarlatamab, CRS and ICANS for HCPs

IMDELLTRA®(tarlatamab) is a bispecific DLL3-directed CD3 T-cell engager that binds to DLL3 expressed on the surface of tumour cells and CD3 expressed on the surface of T cells. The bispecific binding of tarlatamab to T cells and DLL3-positive tumour cells triggers T-cell activation, production of inflammatory cytokines, release of cytotoxic proteins, which results in redirected lysis of tumour cells.

IMDELLTRA® is used for the treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC) with disease progression on or after platinum-based chemotherapy.

CRS is a frequently observed adverse event occurring with the use of T cell activators, such as tarlatamab, and results from the release of cytokines from T cells targeted by the molecule as well as immune effector cells recruited to the area. CRS can be serious and/or life-threatening. CRS may be associated with symptoms including pyrexia, hypotension, fatigue, hypoxia, tachycardia, headache, chills, nausea, and vomiting. Potentially life-threatening complications of CRS may include cardiac dysfunction, acute respiratory distress syndrome, neurologic toxicity, renal and/or hepatic failure, and disseminated intravascular coagulation (DIC). Events of CRS commonly occur after the first two doses but can also occur after the third dose or later. The median time to onset of Grade≥ 2 CRS from most recent dose of IMDELLTRA was 15 hours (range: start of infusion to 15 days).

ICANS is a syndrome that can occur in the days to weeks following administration of certain types of immunotherapies including T-cell activators such as tarlatamab. ICANS can be serious and/or life-threatening.

The median time to onset of ICANs from the first dose was 16 days (range 1 day to 28 months).

following administration of IMDELLTRA®. Adverse events that may be associated with ICANS include headache, encephalopathy, confusion, delirium, seizure, ataxia, neurotoxicity, and tremor. Patients should be closely monitored for signs and symptoms of CRS and ICANS.

Section 2: Preparing for Administration

Administer IMDELLTRA® as a 1-hour intravenous infusion in an appropriate healthcare setting equipped to monitor and manage CRS and ICANS. Ensure patients are well-hydrated prior to administration of IMDELLTRA®. Premedicate with dexamethasone 8 mg IV 1 hour prior to first two doses (Day 1 and Day 8).

Administer 1 liter of normal saline intravenously over 4-5 hours for patients after infusion of IMDELLTRA® (Day 1, Day 8 and Day 15).

Section 3: Monitoring Requirements during and after Treatment

Patients should be closely monitored for signs and symptoms of CRS and ICANS during tarlatamab treatment. Tarlatamab infusion should be immediately interrupted at the first sign of CRS or ICANS and appropriate care should be started.

Monitor patients from the start of the IMDELLTRA infusion for 22 to 24 hours on Cycle 1 Day 1 and Cycle 1 Day 8 in an appropriate healthcare setting.

On Day 1 and Day 8, recommend patients to remain within 1 hour of an appropriate healthcare setting, such as the treatment hospital, for a total of 48 hours starting from each IMDELLTRA® infusion, accompanied by a caregiver.

At the first sign of CRS or ICANS, immediately interrupt IMDELLTRA® infusion, evaluate the patient for hospitalisation and institute supportive care based on severity. Management of these events may require the dose to be either modified or permanently discontinued.

Please refer to the Prescribing Information (PI) for the full safety profile, recommended dosing schedule of tarlatamab, details on administration, recommendations on patient monitoring and the grading, dose modification and management of CRS and ICANS.

Link to PI: IMDELLTRA® **1mg, 10mg** -

https://israeldrugs.health.gov.il/#!/medDetails/178%2021%2037927%2000

Section 4: Prior to Patient Discharge

Prior to discharge, remind the patient/caregiver that **IMDELLTRA®** may cause side effects that may be severe or life-threatening. Advise patients to seek immediate medical attention if they experience CRS and ICANS symptoms.

CRS and ICANS are important risks associated with treatment of **IMDELLTRA®** with possible signs and symptoms as follows:

CRS:

- Pyrexia
- Hypotension
- Fatigue
- Hypoxia
- Tachycardia
- Headache
- Chills
- Nausea
- Vomiting

ICANS:

- Headache
- Encephalopathy
- Confusion
- Delirium
- Seizure
- Ataxia
- Neurotoxicity
- Tremor

On Day 1 and Day 8 of Cycle 1, recommend patients to remain within 1 hour of an appropriate healthcare setting for a total of 48 hours starting from each IMDELLTRA® infusion, accompanied by a caregiver.

Following an IMDELLTRA® infusion, advise patients to refrain from driving and engaging in hazardous occupations or activities, such as operating heavy or potentially dangerous machinery, in the event of any neurologic symptoms until they resolve.

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Complete the **Patient Alert Card** with your contact details before giving it to the patient/caregiver and ask them to also add their contact details to the card. Review the instructions on the card with the patient/caregiver and instruct the patient/caregiver about the importance of early recognition of signs and symptoms of CRS and ICANS and prompt treatment. Tell them to call or see their Healthcare Professional or go to the hospital emergency room RIGHT AWAY if they experience any symptoms of CRS or ICANS at home. Remind the patient/caregiver to KEEP the **Patient Alert Card** with them at all times and to show the card to any healthcare professional who may treat them.

Section 5: For Further Information

For further information on IMDELLTRA and the management of CRS and ICANS with IMDELLTRA® (tarlatamab), please refer to the Israeli PI available at https://israeldrugs.health.gov.il/#!/medDetails/178%2021%2037927%2000

or contact our local distributor Medison Pharma Medical Information by email at medinfoisrael@medisonpharma.com

Section 6: Reporting information

Adverse events can be reported to the Ministry of Health via https://sideeffects.health.gov.il/

Or report to local distributor Medison: PVIsrael@Medisonpharma.com

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(tarlatamab)