swissmedic

Date: 15 July 2026
Swissmedic, Swiss Agency for Therapeutic Products

Swiss Public Assessment Report

IMDYLLTRA

International non-proprietary name:	tarlatamab
Pharmaceutical form:	powder for concentrate and solution stabiliser for solution for infusion
Dosage strength(s):	1 mg, 10 mg
Route(s) of administration:	intravenous use
Marketing authorisation holder:	Amgen Switzerland AG
Marketing authorisation no.:	69132
Decision and decision date:	approved on 8 May 2026

Note:

This assessment report is as adopted by Swissmedic with all information of a commercially confidential nature deleted.

SwissPARs are final documents that provide information on submissions at a particular point in time. They are not updated after publication.

Table of contents

1 Terms, Definitions, Abbreviations

ADA	Anti-drug antibody
ADME	Absorption, distribution, metabolism, elimination
AE	Adverse event
CD3	T-cell receptor-associated complex cluster of differentiation 3
CI	Confidence interval
CRS	Cytokine release syndrome
CYP	Cytochrome P450
DCR	Disease control rate
DLL3	Delta-like ligand 3
DOR	Duration of response
ECOG	Eastern Cooperative Oncology Group
EMA	European Medicines Agency
ERA	Environmental risk assessment
FDA	Food and Drug Administration (USA)
HR	Hazard ratio
ICANS	Immune effector cell-associated neurotoxicity syndrome
IVSS	Intravenous solution stabiliser
LoQ	List of Questions
MAH	Marketing Authorisation Holder
Max	Maximum
Min	Minimum
NCI-ODWG	National Cancer Institute Organ Dysfunction Working Group
ORR	Objective response rate
OS	Overall survival
PD	Pharmacodynamics
PFS	Progression-free survival
PK	Pharmacokinetics
PopPK	Population pharmacokinetics
Q2W	Once every second week
QTcF	Corrected QT Interval using Fridericia's formula
RMP	Risk management plan
SAE	Serious adverse event
SCLC	Small cell lung cancer
scFc	Single-chain crystallisable fragment
scFv	Single-chain variable fragment
SwissPAR	Swiss Public Assessment Report
TEAE	Treatment-emergent adverse event
TPA	Federal Act of 15 December 2000 on Medicinal Products and Medical Devices (SR 812.21)
TPO	Ordinance of 21 September 2018 on Therapeutic Products (SR 812.212.21)

2 Background information on the procedure

2.1 Applicant's request(s) and information regarding procedure

New active substance status
The applicant requested new active substance status for tarlatamab in the above-mentioned medicinal product.

Fast-track authorisation procedure
The applicant requested a fast-track authorisation procedure in accordance with Article 7 TPO.

Orphan drug status
The applicant requested orphan drug status in accordance with Article 4 paragraph 1 letter a^{decies} no. 2 TPA.
Orphan drug status was granted on 19 June 2023.

2.2 Indication and dosage

2.2.1 Requested indication

IMDYLLTRA is indicated for the treatment of adult patients with small cell lung cancer (SCLC) with disease progression on or after platinum-based chemotherapy.

2.2.2 Approved indication

IMDYLLTRA is indicated for the treatment of adult patients with locally advanced or metastatic small cell lung cancer (SCLC) with disease progression on or after platinum-based chemotherapy.

2.2.3 Requested dosage

Summary of the requested standard dosage:
60-minute IV infusion with an initial dose of 1 mg tarlatamab on cycle 1 day 1 followed by 10 mg target doses on cycle 1 days 8 and 15, and every 2 weeks (Q2W) thereafter (i.e. cycle 2 and following cycles day 1/day 15 dosing). Cycles of 28 days.

2.2.4 Approved dosage

(see appendix)

2.3 Regulatory history (milestones)

Application	1 September 2025
Formal control completed	5 September 2025
List of Questions (LoQ)	5 November 2025
Response to LoQ	3 February 2026
Preliminary decision	24 March 2026
Response to preliminary decision	21 April 2026
Final decision	8 May 2026
Decision	approval

3 Medical context

Small cell lung cancer (SCLC), a poorly differentiated neuroendocrine carcinoma, is a distinct histological form of lung cancer. SCLC accounts for 13% of newly diagnosed cases of lung cancer worldwide. SCLC tumours are highly aggressive, rapidly growing, and often present with metastatic disease at time of diagnosis. First-line treatment of metastatic SCLC with platinum-based combination chemotherapy leads to rapid responses; however, most patients relapse within 6 months, with less than 5% surviving at 5 years[1]. Recent addition of immunotherapy to platinum-based chemotherapy improved the survival outcomes of these patients. In these studies, the median overall survival (OS) was 10.3 months for platinum-based chemotherapy alone versus 12.3 to 13.0 months in patients with the added immune checkpoint-inhibitor[2,3]. For patients who exhaust these options, the current available second-line treatments in Switzerland include topotecan and lurbinectedin (at the time of the assessment the latter is authorised under temporary approval and only for patients without metastases to the central nervous system). In Japan, amrubicin is a widely accepted second-line treatment even though it did not demonstrate improved OS over topotecan in clinical trials. The reported median OS for these second-line chemotherapies ranges from approximately 8 to 10 months[4,5]. There is an unmet medical need to improve the survival outcomes of patients who experience disease progression under or after platinum-based chemotherapy.

References:

1. GF Cittolin-Santos et al., The changing landscape of small cell lung cancer, Cancer, 2024 Jul 15;130(14):2453-2461.
2. L Horn et al., First-Line Atezolizumab plus Chemotherapy in Extensive-Stage Small-Cell Lung Cancer, N Engl J Med 2018;379:2220-2229
3. L Paz-Ares et al., Durvalumab plus platinum–etoposide versus platinum–etoposide in first-line treatment of extensive-stage small-cell lung cancer (CASPIAN): a randomised, controlled, open-label, phase 3 trial, Lancet 2019 Nov 23;394(10212):1929-1939.
4. J von Pawel et al., Randomized phase III trial of amrubicin versus topotecan as second-line treatment for patients with small-cell lung cancer, J Clin Oncol 2014;32:4012-4019.
5. J Trigo et al., Lurbinectedin as second-line treatment for patients with small-cell lung cancer: a single-arm, open-label, phase 2 basket trial, Lancet Oncol 2020;21:645-654.

4 Quality aspects

4.1 Drug substance

Tarlatamab is a novel single-chain antibody derivative of the bispecific T-cell engager (BiTE®) class, expressed in a Chinese hamster ovary (CHO) cell line. Tarlatamab consists of two single-chain variable fragment (scFv) binding domains, specific for antigen delta-like ligand 3 (DLL3) and for the T-cell receptor-associated complex cluster of differentiation 3 (CD3). The scFv binding domains are fused to a single-chain fragment crystallisable half-life extension (scFc HLE) moiety. Tarlatamab is aglycosylated through engineering by eliminating the glycosylation site in the Fc domain.

Tarlatamab is produced in a Chinese hamster ovary (CHO) cell system using a well-established Master Cell Bank and Working Cell Bank, each extensively characterised for identity, stability, and absence of adventitious agents. The manufacturing process includes sequential stages of cell expansion, perfusion bioreactor operation, harvest, protein A chromatography, low-pH viral inactivation, cation-exchange chromatography, mixed-mode anion exchange purification, viral filtration, and ultrafiltration/diafiltration.

These steps collectively ensure efficient removal of impurities including host cell proteins, DNA, leached protein A and process reagents. Process validation demonstrated consistent performance across multiple consecutive batches, confirming reproducible cell growth, product expression, viral safety, and control of product-related variants.

Several changes were implemented during development of the manufacturing process for the drug substance, including changes to manufacturing site and production scale. However, comparability studies, including batch release data, extended characterisation data, and stress stability data, demonstrated comparability between the different processes.

The characterisation of the physicochemical and biological properties of the tarlatamab drug substance and its impurities were performed using state-of-the-art methods.

The specifications for release and stability of the drug substance include relevant tests and acceptance criteria, e.g. for identity, purity and impurities, quantity, and potency. Specifications are based on published limits, stability data, clinical experience and batch analysis data.

Batch analysis data for development, clinical, and process validation batches of tarlatamab drug substance were provided. All specific analytical methods are described and are fully validated.

No significant changes were observed during storage of tarlatamab drug substance under the proposed storage conditions.

4.2 Drug product

Drug Product
Tarlatamab drug product is supplied as a sterile lyophilised powder for reconstitution, available in 1 mg/vial and 10 mg/vial presentations. The formulation contains sucrose, L-glutamic acid, polysorbate 80, sodium hydroxide and water for injection, selected to ensure product stability, cake integrity, and consistent reconstitution time. The excipients are commonly used in parenteral products and comply with applicable compendia. The product is filled into Type I glass vials with an elastomeric stopper and aluminium seal, and the container closure system complies with relevant compendial requirements for sterility, extractables, leachables and mechanical performance.

Due to the low concentration of tarlatamab administered to patients, an IV solution stabiliser (IVSS) is included in the tarlatamab intravenous infusion preparation to prevent loss through adsorption of tarlatamab to the surfaces of the infusion bag and tubing. The tarlatamab IV infusion is prepared by first aseptically adding the appropriate amount of the IVSS to an infusion bag containing normal

saline. Following reconstitution of the drug product with sterile water for injection, an appropriate amount of tarlatamab is added aseptically to the infusion bag containing the IVSS and saline.

Several drug product dosage strengths, formulations, presentations, and filling facilities were used during clinical development. However, comparability studies, which included batch release data, extended characterisation data, and stress stability data, demonstrated comparability of the relevant quality attributes between the different processes.

Compatibility studies were conducted to establish the in-use stability of diluted drug product with the intended materials and conditions of use.

Manufacture of the drug product comprises drug substance thawing, preparation of formulation buffer, mixing, bioburden reduction filtration, sterile filtration, aseptic filling, lyophilisation, capping and visual inspection. Process controls include in-process measurements of pH, protein concentration, polysorbate 80 concentration, osmolality, bioburden and filter integrity

The drug product manufacturing process is validated with several consecutive batches. The data demonstrated a consistent production.

The specifications for release and stability of the drug product include relevant tests and acceptance criteria, e.g. for identity, purity and impurities, quantity, potency, appearance, pH, osmolality, visible and subvisible particles, bacterial endotoxins, and sterility. The drug product specifications comply with current compendial or regulatory guidelines.

Batch analysis data for several batches of the drug product, including development batches, clinical batches, and process validation batches, were provided. All batch release data comply with the drug product specifications, which were valid at the time of batch release. All specific analytical methods are validated.

The vials are stored at 2°C to 8°C. The stability data support a shelf life of 48 months.

IV Solution Stabiliser (IVSS)
The IVSS is supplied as a sterile solution in a 10R glass vial containing 7 mL of deliverable solution. The IVSS is a buffered, preservative-free, colourless to slightly yellow, and clear solution. The container closure system for the IVSS is a 10R Type I borosilicate glass vial, with elastomeric stopper, and aluminium seal with flip-off cap. The formulation for IVSS has stayed the same throughout the development of IMDYLLTRA and is the same formulation in the commercial presentation.
IVSS formulation contains citric acid monohydrate, lysine hydrochloride, polysorbate 80, at a final pH of 7.0.
The 7 mL/10R IVSS manufacturing process consists of the following unit operations: formulation, bioburden reduction filtration, filtered IVSS hold, sterile filtration, filling, stoppering, capping, and inspection and storage.
The manufacturing process is validated with several consecutive batches. The data demonstrated a consistent production.

The specifications for release and stability include relevant tests and acceptance criteria. Batch analysis data for several batches were provided and batch release data comply with the specifications, which were valid at the time of batch release.

4.3 Quality conclusions

Satisfactory and consistent quality of the drug substance and drug product has been demonstrated.

5 Nonclinical aspects

For the review of the market authorisation application for IMDYLLTRA, the Division Nonclinical Assessment conducted an abridged evaluation, which was essentially based on the FDA assessment report (“Multi-Disciplinary Review and Evaluation - BLA 761344 IMDELLTRA - Tarlatamab”) provided by the applicant. Impurities, ERA and RMP were subject to a full review.

Overall, the submitted nonclinical documentation is considered appropriate to support the approval of IMDYLLTRA in the proposed indication. The pharmaco-toxicological profile has been sufficiently characterised. All nonclinical data that are relevant for safety are adequately mentioned in the Information for healthcare professionals.

6 Clinical aspects

6.1 Clinical pharmacology

ADME

Absorption
As tarlatamab is administered intravenously, bioavailability is complete and no bioequivalence or bioavailability studies were required.

Distribution
The volume of distribution at steady state is 8.53 L (33%).

Metabolism
No dedicated metabolism studies have been conducted for tarlatamab, which is consistent with its biological nature. As a monoclonal antibody-based molecule, tarlatamab is expected to be degraded into small peptides and amino acids via ubiquitous catabolic proteolytic pathways.

Elimination and Steady State
Tarlatamab exhibited a median terminal elimination half-life of 11.2 days (range: 4.3–26.5 days), with an estimated systemic clearance of 0.65 L/day (CV 44%). PopPK analyses indicated that steady state was reached by approximately Cycle 2 Day 15. Importantly, systemic exposure following the first 10 mg dose (Cycle 1 Day 8) was already comparable to steady-state exposure achieved with repeated dosing of 10 mg every 2 weeks.

No dedicated renal or hepatic impairment studies were conducted; however, patients with varying degrees of renal and hepatic function were included in the popPK analysis. Several covariates were identified, including baseline body weight, hepatic impairment (NCI-ODWG), number of prior anticancer therapies, anti-tarlatamab antibodies, and race.
None of these covariates had a clinically meaningful impact on tarlatamab exposure (generally within ±10–15%). Therefore, no dose adjustment is considered necessary.

Interactions

No clinical drug–drug interaction studies were conducted, which is acceptable given the low intrinsic interaction potential of monoclonal antibodies. Transient cytokine-mediated effects on CYP enzymes cannot be excluded early in treatment or during cytokine release syndrome and are adequately addressed in the Information for healthcare professionals.

Pharmacodynamics

Primary pharmacology
Tarlatamab is a bispecific T-cell engager targeting delta-like ligand 3 (DLL3) on small cell lung cancer cells and CD3 on T cells, thereby redirecting activated T cells toward DLL3-expressing tumour cells. Its antitumour activity is mediated through T-cell activation, cytokine release, and cytotoxic elimination of tumour cells. Treatment induces transient immune activation, characterised by reversible T-cell redistribution, activation marker expression, and short-lived cytokine elevations that attenuate with repeated dosing.

Secondary pharmacology (safety)
Concentration–QTcF analysis showed no clinically meaningful QT prolongation at the recommended 10 mg Q2W dose.

Exposure efficacy/safety relationship
Exposure–response analyses demonstrated significant relationships between tarlatamab exposure and key efficacy endpoints, including overall survival (OS), progression-free survival (PFS), objective

response rate (ORR), disease control rate (DCR), and best tumour size reduction (BTSR), with efficacy increasing with exposure and reaching a plateau at the proposed dose of 10 mg every 2 weeks (Q2W). No exposure–response relationship was observed for duration of response (DOR). While some covariate associations were considered biologically implausible and likely non-causal, higher baseline tumour burden and mild to moderate hepatic impairment were independently associated with poorer OS and PFS outcomes, and higher tumour burden was also associated with a lower DCR.
From a safety perspective, only grade ≥3 neutropenia showed a positive exposure–risk relationship, while no clinically relevant exposure–safety relationships were identified for cytokine release syndrome, neurological events, or other adverse events. Overall, the exposure–efficacy and exposure–safety profiles support 10 mg Q2W as an appropriate and optimal dosing regimen.

Immunogenicity
Treatment-emergent anti-drug antibodies (ADAs) were observed in 7.7% of patients, while neutralising antibodies (NAbs) were rare (3.1%). No clinically meaningful impact of ADA on tarlatamab PK was identified.

6.2 Dose finding and dose recommendation

The requested dose of tarlatamab uses a step-up dosing method: at the first dose (Cycle 1 Day 1 [C1D1]) the administered tarlatamab dose is 1 mg, on Cycle 1 Day 8 (C1D8) and C1D15 a 10 mg dose of tarlatamab is administered. Thereafter, 10 mg of tarlatamab is administered every two weeks (Q2W).

The requested dose was identified based on the results of Phase 1-2 studies. Part 1 of the Study 20200491 was designed to evaluate the safety and efficacy of 10 and 100 mg Q2W doses of tarlatamab. The applicant concluded that compared with the 100 mg group, subjects in the 10 mg group experienced fewer treatment-emergent adverse events (TEAEs) leading to discontinuation of tarlatamab, fewer serious adverse events, and fewer fatal adverse events. Consistent with the dose-response data, exposures with the 10 mg target dose regimen were associated with improved tolerability but comparable efficacy relative to the 100 mg dose. The 10 mg dose was later evaluated in the Phase 3 pivotal study to support the requested authorisation. The proposed tarlatamab dose of 10 mg Q2W is acceptable from a regulatory point of view.

6.3 Efficacy

The applicant submitted results from an open-label, randomised (at 1:1 ratio), Phase 3 study DeLLphi-304, which evaluated tarlatamab over the investigator's choice of single-agent chemotherapy (topotecan, lurbinectedin or amrubicin [in Japan]) in SCLC patients after platinum-based first-line chemotherapy. The study included SCLC patients who had progressed after 1 prior line of platinum-based therapy. Patients were stratified by prior anti-PD-(L)1 exposure, chemotherapy-free interval (≥ 180, < 180 to ≥ 90, or < 90 days), presence of brain metastases, and preferred standard of care (topotecan/amrubicin vs lurbinectedin). The selection of stratification factors in this pivotal study is acceptable, as well as the chosen treatment options in the control arm. The study intended to enrol a total of 490 participants. Patients were treated until disease progression or unacceptable toxicity in both treatment arms.

The primary of endpoint of this study was overall survival (OS). Secondary endpoints (under type 1 error control) were progression-free survival (PFS) as assessed by investigator and the following patient reported outcomes (PROs): change at week 19 in symptom scores with respect to dyspnoea, cough, chest pain, and in scores for physical functioning and global health status. The study had two prespecified analyses: an interim analysis, which was planned to occur at 259 OS events, and the

primary analysis, which was planned to occur at 345 OS events. The applicant assumed that 345 OS events provided 91% power to demonstrate superiority at an alternative hazard ratio (HR) of 0.7 with log-rank test using 2-sided overall type I error of 0.05 in a group sequential design with 1 interim analysis and 1 primary OS analysis. The applicant expected a 3.6-month improvement in OS of the tarlatamab group compared to the chemotherapy group. The overall study design, selection of the primary endpoint, and statistical assumptions are acceptable from a regulatory point of view.

The study randomised 255 patients in the standard of care arm and 254 patients in the tarlatamab arm. In the overall randomised study population, the median age was 65 years, 69% were male, and 47.2% were from Europe. Regarding baseline disease characteristics, 67.2% had an ECOG performance status of 1 and 91.0% had metastatic disease at baseline. Regarding prior treatments, 97.6% had 1 prior line of therapy (2.4% received ≥2 lines of therapy), 70.7% received prior PD-(L)1 therapy, and 62.9% had prior radiotherapy. The studied patient population is representative of the Swiss population of SCLC patients who progressed on or after platinum-based therapy, and both study arms were adequately balanced.

The submitted results included the prespecified interim analysis (data cut-off 29 January 2025). At this analysis point the study demonstrated a clinically meaningful and statistically significant difference in OS with 43.7% (111/254) OS events reported in the tarlatamab arm and 59.6% (152/255) in the chemotherapy group (HR 0.60, 95% confidence intervals [CI]: 0.47, 0.77), 1-sided p-value <0.001,). The median OS in the tarlatamab arm was 13.6 months versus 8.3 months in the comparator arm. Further, the study demonstrated a statistically significant difference in PFS as assessed by investigator. The median PFS was 4.2 months in the tarlatamab arm compared with 3.2 months in the chemotherapy arm. The HR for PFS was 0.72 (95% CI: 0.59, 0.88; p <0.001). See the attached Information for healthcare professionals for further results.

In exploratory subgroup analyses of the pivotal DeLLphi-304 study, in patients with DLL3 expression <25% (staining intensity 2+ or 3+) 34 of 52 patients experienced OS events in the standard therapy arm and 33 of 52 patients in the tarlatamab arm. Median OS was 7.9 months (95% CI: 5.2, 9.2) with standard therapy and 7.8 months (95% CI: 5.6, 11.1) with tarlatamab. The hazard ratio (HR) for OS was 0.95 (95% CI: 0.59, 1.54). In the same subgroup, median PFS was 3.8 months (95% CI: 2.3, 5.6) in the standard therapy arm and 1.6 months (95% CI: 1.3, 2.8) in the tarlatamab arm. The HR for PFS was 1.50 (95% CI: 0.97, 2.30). Nonetheless, the utility of DLL3 expression as a predictive biomarker, as well as the clinical relevance of specific DLL3 expression cut-offs, have not been established or defined.

The requested indication encompasses subsequent lines of treatment after progression on or after platinum-based chemotherapy. Supportive evidence for the inclusion of patients after two lines of treatment is provided in the study DeLLphi-301. This single-arm study included patients who progressed following 1 platinum-based regimen and at least 1 other line of therapy. 99 patients in this study were treated with the 10 mg tarlatamab dose. The following results were reported in these patients: confirmed ORR of 41.4%, median PFS was 4.3 months, and median OS was 14.3 months. See the attached Information for healthcare professionals for further details.

6.4 Safety

In the pivotal study DeLLphi-304, fewer patients experienced grade ≥3 treatment emergent adverse events (TEAEs) in the tarlatamab arm compared with the chemotherapy arm (54.0% versus 79.9%, respectively), as well as lower rates of adverse events (AE) leading to discontinuation of study treatment (2.8% vs 6.1%). Fatal adverse events were reported in 0.4% and 1.6% of patients, respectively.

Tarlatamab has a safety profile that is distinct from chemotherapy. The most frequently reported TEAE of any grade in the tarlatamab arm of the pivotal study was cytokine release syndrome (CRS, 56.3% versus 1.2%, respectively). Grade ≥2 CRS events (i.e. patient requires at least low-flow oxygen) were reported in 13.9% of patients in the tarlatamab arm. According to pooled analyses of patients treated with the 10 mg tarlatamab dose (n=385), the majority of grade ≥2 CRS events occurred during the first two drug administrations (Cycle 1 Day 1 [C1D1]: 13.2%, C1D8: 4.2%, C1D15: 0.8%, C2 and beyond: 0.5%). At C1D1, the median time to onset of first CRS events was 8.8 hours (first quartile [Q1] 5.9, Q3 13.2) and 20.8 hours (Q1 12.2, Q3 25.4) at C1D8. In the pivotal study, 209 of the 255 patients were enrolled under a monitoring protocol requiring 48-hour observation in an appropriate healthcare facility on C1D1 and C1D8. The remaining patients were enrolled later under an amended protocol requiring 6-8 hours of monitoring on C1D1 and C1D8. Nonetheless, the pooled analysis of patients who were monitored under the 6-8 hour protocol (n=104) had comparable baseline characteristics and similar CRS outcomes compared to patients with longer inpatient monitoring. Therefore, the proposed 6-8 hour inpatient monitoring at C1D1 and C1D8 is acceptable. Of note, on C1D1 and C1D8, patients should be advised to remain for 48 hours after the start of each tarlatamab infusion in the vicinity of an appropriate healthcare facility and be accompanied by a caregiver.

Another known safety risk for bispecific T-cell engagers is Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS). In the pooled analysis of patients treated with the 10 mg dose of tarlatamab, 0.4% (2/473) of patients experienced a fatal event of ICANS or an associated neurological event.

See the attached Information for healthcare professionals for other relevant information on the undesirable effects of tarlatamab.

6.5 Final clinical benefit risk assessment

The Phase 3 study DeLLphi-304 demonstrated statistically significant and clinically meaningful OS benefit for tarlatamab over single-agent chemotherapy in SCLC patients who had disease progression on or after platinum-based chemotherapy. Supportive evidence for later lines of treatment come from Phase 2 study DeLLphi-301, which enrolled patients who received prior platinum-based chemotherapy and at least one additional line of treatment.

Regarding safety, the pivotal study demonstrated lower rates of grade ≥3 TEAEs and AEs leading to discontinuation of study treatment in the tarlatamab arm compared with the standard chemotherapy arm. Tarlatamab demonstrated a different safety profile compared to chemotherapy. Mechanism of action-related toxicities such as CRS and ICANS are known for bispecific T-cell engagers. Undesirable effects and management of toxicities are adequately described in the Information for healthcare professionals.

In conclusion, the benefit-risk assessment is positive.

7 Risk management plan summary

The RMP summaries contain information on the medicinal products′ safety profiles and explain the measures that are taken to further investigate and monitor the risks, as well as to prevent or minimise them.
The RMP summaries are published separately on the Swissmedic website. It is the responsibility of the marketing authorisation holder to ensure that the content of the published RMP summaries is accurate and correct. As the RMPs are international documents, their summaries might differ from the content in the Information for healthcare professionals / product information approved and published in Switzerland, e.g. by mentioning risks that occur in populations or indications not included in the Swiss authorisations.

8 Appendix

Approved Information for healthcare professionals

Please be aware that the following version of the Information for healthcare professionals for IMDYLLTRA was approved with the submission described in the SwissPAR. This Information for healthcare professionals may have been updated since the SwissPAR was published.

Please note that the valid and relevant reference document for the effective and safe use of medicinal products in Switzerland is the Information for healthcare professionals currently authorised by Swissmedic (see www.swissmedicinfo.ch).

Note:
The following Information for healthcare professionals has been translated by the MAH. It is the responsibility of the authorisation holder to ensure the translation is correct. The only binding and legally valid text is the Information for healthcare professionals approved in one of the official Swiss languages.

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected new or serious adverse reactions. See the "Undesirable effects" section for advice on the reporting of adverse reactions.

IMDYLLTRA®

Composition

Active ingredient

Tarlatamab, produced in Chinese Hamster Ovary (CHO) cells by recombinant DNA technology.

Excipients

IMDYLLTRA (1 mg and 10 mg)

L-glutamic acid, Sucrose, Polysorbate 80, Sodium hydroxide (for pH adjustment).

IV Solution Stabiliser

Citric acid monohydrate, Lysine hydrochloride, Polysorbate 80, Sodium hydroxide (for pH adjustment), water for injection.

Pharmaceutical form and active substance quantity per unit

Powder for concentrate and solution Stabiliser for solution for infusion.

White to slightly yellow, lyophilized powder.

Single-use vial containing 1 mg tarlatamab lyophilized powder.

After reconstitution of 1 mg powder with 1.3 mL of Water for Injection, the resulting concentration is 0.9 mg/mL tarlatamab.

Single-use vial containing 10 mg tarlatamab lyophilized powder.

After reconstitution of 10 mg powder with 4.4 mL Water for Injection, the resulting concentration is 2.4 mg/mL tarlatamab.

Indications/Uses

IMDYLLTRA is indicated for the treatment of adult patients with locally advanced or metastatic small cell lung cancer (SCLC) with disease progression on or after platinum-based chemotherapy.

Dosage/Administration

The administration of IMDYLLTRA should only be carried out under the guidance of medical personnel experienced in the treatment of malignant diseases, cytokine release syndrome (CRS), and neurological toxicities, including immune effector cell-associated neurotoxicity syndrome (ICANS). It should be administered in an appropriate healthcare facility.

Traceability

To ensure the traceability of biotechnologically produced medicinal products, it is recommended that the trade name and batch number be documented for each treatment.

Posology

The recommended dosage and schedule of IMDYLLTRA is intravenous infusions over 1 hour, with an initial dose of 1 mg Day 1 of Cycle 1 followed by 10 mg on Days 8, 15, and every 2 weeks thereafter as shown in Table 1. Treat patients until disease progression or unacceptable toxicity.

Table 1. Recommended Dosage Schedule of IMDYLLTRA

Dosing Schedule	**Day**	**Dose of IMDYLLTRA**
Step-up Dose and Schedule Cycle 1 (28-day cycle)	Day 1	Step-up dose 1 mg
	Day 8	10 mg
	Day 15	10 mg
Cycle 2 and subsequent infusions (28-day cycles)	Day 1 and 15	10 mg

- See Table 2 for recommended concomitant medications.
- Monitor patients from the start of the infusion for 6 to 8 hours on Day 1 and Day 8 of Cycle 1.
- On subsequent infusions, monitor patients at the discretion of the healthcare provider.
- On Day 1 and Day 8 of Cycle 1, recommend patients to remain within proximity of an appropriate healthcare setting for 48 hours from the start of each IMDYLLTRA infusion, accompanied by a caregiver.
- Inform both the patients and the caregiver on the signs and symptoms of cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) prior to discharge.

Recommended Concomitant Medications for IMDYLLTRA Administration for Day 1 and Day 8 of Cycle 1

Administer recommended concomitant medications for IMDYLLTRA administration as presented in Table 2 to reduce the risk of cytokine release syndrome (see section “Warnings and Precautions”).

Table 2. Concomitant Medications for IMDYLLTRA Administration for Day 1 and Day 8

Treatment Day	Medication	Administration
Day 1 and Day 8	Administer 8 mg of dexamethasone intravenously (or equivalent)	Within 1-hour prior to IMDYLLTRA administration
	Administration of 1 liter of normal saline intravenously over 2 to 4 hours is recommended per standard of care guidelines	Immediately after completion of IMDYLLTRA infusion

Restarting IMDYLLTRA After Dosage Delay

If a dose of IMDYLLTRA is delayed, restart therapy based on the recommendations listed in Table 3 and resume the dosing schedule accordingly (see section “Recommended Dose

Modifications and Adverse Reaction Management"). Administer recommended concomitant medications as indicated in section "Posology".

Table 3. Recommendations for Restarting Therapy with IMDYLLTRA after Dosage Delay

Last Dose Administered	Time Since the Last Dose Administered	Action[a]
1 mg on Day 1	2 weeks or less (≤ 14 days)	Administer IMDYLLTRA 10 mg, then resume with the planned dosage schedule.
	Greater than 2 weeks (> 14 days)	Administer IMDYLLTRA 1 mg. If tolerated, increase to 10 mg 1 week later. Then resume with the planned dosage schedule.
10 mg on Day 8	3 weeks or less (≤ 21 days)	Administer IMDYLLTRA 10 mg, then resume with the planned dosage schedule.
	Greater than 3 weeks (> 21 days)	Administer IMDYLLTRA 1 mg. If tolerated, increase to 10 mg 1 week later. Then resume with the planned dosage schedule.
10 mg on Day 15 and every 2 weeks thereafter	4 weeks or less (≤ 28 days)	Administer IMDYLLTRA 10 mg, then resume with the planned dosage schedule.
	Greater than 4 weeks (> 28 days)	Administer IMDYLLTRA 1 mg. If tolerated, increase to 10 mg 1 week later. Then resume with the planned dosage schedule.

[a] Administer recommended concomitant medications before and after Day 1 and Day 8 of IMDYLLTRA infusions and monitor patients accordingly (see section "Dosage/Administration", Table 1 and Table 2).

Recommended Dose Modifications and Adverse Reaction Management

No dosage reduction for IMDYLLTRA is recommended. See Table 4 for recommended actions for the management of CRS, Table 5 for recommended actions for the management of ICANS, and Table 6 for the management of neutropenia and other adverse reactions.

Cytokine Release Syndrome (CRS)

Diagnose CRS based on clinical presentation (see section "Warnings and Precautions"). Evaluate for and treat other causes of fever, hypoxia, and hypotension. If CRS is suspected, manage according to the recommendations in Table 4. Patients who experience Grade 2 or higher CRS (e.g., hypotension not responsive to fluids, or hypoxia requiring supplemental

oxygen) should be monitored for CRS signs and symptoms including fever, hypotension and hypoxia using pulse oximetry or cardiac telemetry as indicated. For severe or life-threatening CRS, patients should be treated by local guidelines for CRS management.

Table 4. Guidelines for Grading, Dosage Modification and Management of Cytokine Release Syndrome[a]

CRS Grade	Defining Symptoms	IMDYLLTRA Dosage Modification	Management
Grade 1	Symptoms require symptomatic treatment only (e.g., fever > 38°C without hypotension or hypoxia).	Withhold IMDYLLTRA until event resolves, then resume IMDYLLTRA at the next scheduled dose[b].	• Administer symptomatic treatment (e.g., acetaminophen/paracetamol) for fever. • Consider treatment with dexamethasone 4 mg to 10 mg PO or IV (or equivalent)[c]
Grade 2	Symptoms require and respond to moderate intervention. • Fever ≥ 38°C, • Hypotension responsive to fluids not requiring vasopressors, and/or • Hypoxia requiring low flow nasal cannula or blow-by.	Withhold IMDYLLTRA until event resolves, then resume IMDYLLTRA at the next scheduled dose[b].	• Recommend hospitalization with monitoring for fever, hypotension and hypoxia using pulse oximetry or cardiac telemetry. • Administer symptomatic treatment (e.g., paracetamol) for fever. • Administer supplemental oxygen and intravenous fluids when indicated. • Consider dexamethasone[c] (or equivalent) 8 mg PO or IV. When resuming treatment at the next planned dose, monitor patients at the physician's discretion in an appropriate healthcare setting[b].
Grade 3	Severe symptoms defined as	Withhold IMDYLLTRA until the	In addition to Grade 2 treatment: • Recommend intensive

CRS Grade	Defining Symptoms	IMDYLLTRA Dosage Modification	Management
	temperature ≥ 38°C with: • Hemodynamic instability requiring a vasopressor (with or without vasopressin) and/or • Worsening hypoxia or respiratory distress requiring high flow nasal canula (> 6 L/min oxygen) or face mask.	event resolves, then resume IMDYLLTRA at the next scheduled dose[b]. For recurrent Grade 3 events, permanently discontinue IMDYLLTRA.	monitoring, e.g., ICU care. • Administer dexamethasone[c] (or equivalent) 8 mg IV every 8 hours up to 3 doses. • Vasopressor support as needed. • High flow oxygen support as needed. Prior to the next dose, administer concomitant medications as recommended for Day 1 and Day 8 (see Table 2). When resuming treatment at the next planned dose, monitor patients at the physician's discretion in an appropriate healthcare setting[b].
Grade 4	Life-threatening symptoms defined as temperature ≥ 38°C with: • Hemodynamic instability requiring multiple vasopressors (excluding vasopressin) and/or Worsening hypoxia or respiratory distress despite oxygen administration requiring positive	Permanently discontinue IMDYLLTRA.	• ICU care. • Per Grade 3 treatment.

CRS Grade	Defining Symptoms	IMDYLLTRA Dosage Modification	Management
	pressure.		

[a] CRS based on American Society for Transplantation and Cellular Therapy (ASTCT) Consensus Grading (2019).

[b] See section "Dosage/Administration", Table 3 for recommendations on restarting IMDYLLTRA after dose delays.

[c] Taper steroids per standard of care guidelines.

Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS)

Monitor patient for signs and symptoms of neurotoxicity. Rule out other causes of neurologic symptoms. Provide intensive-care for severe or life-threatening neurologic toxicities. If ICANS is suspected, manage according to the recommendations in Table 5.

Table 5. Guidelines for Grading, Dose Modification and Management of Immune Effector Cell-Associated Neurotoxicity Syndrome[a]

ICANS Grade[a]	Defining Symptoms	IMDYLLTRA Dosage Modifications	Management
Grade 1	ICE score 7-9[b] with no depressed level of consciousness.	• Withhold IMDYLLTRA until ICANS resolves, then resume IMDYLLTRA at the next scheduled dose[c].	• Supportive care.
Grade 2	ICE score 3-6[b] and/or mild somnolence awaking to voice.	• Withhold IMDYLLTRA until ICANS resolves, then resume IMDYLLTRA at the next scheduled dose[c].	• Supportive care. • Dexamethasone[d] (or equivalent) 8 mg to 10 mg PO or IV. Repeat every 12 hours or methylprednisolone (or equivalent) 1 mg/kg IV every 12 hours if symptoms worsen. • Monitor neurologic symptoms and consider consultation with

ICANS Grade[a]	Defining Symptoms	IMDYLLTRA Dosage Modifications	Management
			neurologist and other specialists for further evaluation and management. • Monitor patients at the physician's discretion following the next dose of IMDYLLTRA[c].
Grade 3	ICE score 0-2[b] and/or depressed level of consciousness awakening only to tactile stimulus and/or any clinical seizure focal or generalized that resolves rapidly Or Nonconvulsive seizures on EEG that resolve with intervention and/or focal or local edema seen on neuroimaging.	• Withhold IMDYLLTRA until the ICANS resolves, then resume IMDYLLTRA at the next scheduled dose[c]. • If there is no improvement to Grade ≤ 1 within 7 days, permanently discontinue IMDYLLTRA. • For recurrent Grade 3 events, permanently discontinue.	• Recommend intensive monitoring, e.g., ICU care. • Consider mechanical ventilation for airway protection. Dexamethasone[d] (or equivalent) 10 mg IV every 6 hours or methylprednisolone (or equivalent) 1 mg/kg IV every 12 hours. • Consider repeat neuroimaging (CT or MRI) every 2-3 days if patient has persistent Grade ≥ 3 neurotoxicity. • Monitor patients at the physician's discretion following the next dose of IMDYLLTRA[c].
Grade 4	ICE score 0[b] (patient is unarousable and unable to perform ICE) and/or stupor or coma and/or life-threatening	• Permanently discontinue IMDYLLTRA.	• ICU care. • Consider mechanical ventilation for airway protection. • High-dose corticosteroids, such as

ICANS Grade[a]	Defining Symptoms	IMDYLLTRA Dosage Modifications	Management
	prolonged seizure (> 5 minutes) or repetitive clinical or EEG-detectable seizures without return to baseline in between and/or diffuse cerebral edema on neuroimaging, decerebrate or decorticate posturing or papilledema, cranial nerve VI palsy, or Cushing's triad.		methylprednisolone[d] 1000 mg/day in divided doses IV for 3 days. • Consider repeat neuroimaging (CT or MRI) every 2-3 days if patient has persistent Grade ≥ 3 neurotoxicity. • Treat convulsive status epilepticus per institutional guidelines.

[a] ICANS based on American Society for Transplantation and Cellular Therapy (ASTCT) Consensus Grading (2019).

[b] If patient is arousable and able to perform Immune Effector Cell-Associated Encephalopathy (ICE) Assessment, assess: Orientation (oriented to year, month, city, hospital = 4 points); Naming (names 3 objects, e.g., point to clock, pen, button = 3 points); Following commands (e.g., "show me 2 fingers" or "close your eyes and stick out your tongue" = 1 point); Writing (ability to write a standard sentence = 1 point); and Attention (count backwards from 100 by ten = 1 point). If patient is unarousable and unable to perform ICE Assessment (Grade 4 ICANS) = 0 points.

[c] See Table 3 for recommendations on restarting IMDYLLTRA after dose delays (see section "Dosage/Administration").

[d] Taper steroids per standard of care guidelines.

Table 6. Recommended Treatment Interruptions of IMDYLLTRA for the Management of Neutropenia and Other Adverse Reactions[a,b]

Adverse Reactions	Severity[b]	Dosage Modification[a]
Neutropenia (see section "Warnings and Precautions**"**)	Grades 1 and 2	No treatment interruption needed.
	Grade 3	• Interrupt IMDYLLTRA for at least 3 days and until the event improves to Grade ≤ 2, then restart IMDYLLTRA. Consider using granulocyte colony stimulating factor (G-CSF).
	Grade 4	• Interrupt IMDYLLTRA for at least 3 days and until the event improves to Grade ≤ 2, then restart IMDYLLTRA. • If event lasts for > 7 days or Grade 4 event reoccurs, permanently discontinue IMDYLLTRA. Consider using granulocyte colony stimulating factor (G-CSF).
Other Adverse Reactions (see section "Undesirable effects")	Grade 3 or 4	Withhold IMDYLLTRA until recovery to Grade ≤ 1 or baseline. Consider permanently discontinuing if adverse reaction does not resolve within 28 days.

Adverse Reactions	Severity[b]	Dosage Modification[a]
		• Consider permanent discontinuation for Grade 4 events.

[a] For recommendations on restarting IMDYLLTRA after dose delays see Table 3 (section "Dosage/Administration").

[b] Severity based on National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE), Version 5.0.

Method of administration

- IV line for premedication can be used for IMDYLLTRA. IV line flush should be conducted between administering concomitant medication and IMDYLLTRA.
- Administer the entire contents of IMDYLLTRA as an intravenous infusion over 1-hour at a constant flow rate using an infusion pump. The pump should be programmable, lockable, non-elastomeric, and have an alarm (see section "Other information"). Upon completion of the IMDYLLTRA infusion, the IV administration line should be flushed over 3-5 minutes using 0.9% Sodium Chloride for Injection.

Table 7. IMDYLLTRA Administration Information

Infusion Duration for 250 mL IV Preparation	Infusion Rate (mL/hour)
1-hour	250 mL/hour

- IV tubing is primed with 0.9% Sodium Chloride for Injection OR final prepared IMDYLLTRA.
- For the infusion rate per infusion duration, refer to Table 7.

Special dosage instructions

Patients with impaired hepatic function

Based on the population pharmacokinetic results, no dose adjustment is required in patients with mild or moderate hepatic impairment (see section "Pharmacokinetics"). IMDYLLTRA has not been studied in patients with severe hepatic impairment.

Patients with impaired renal function

Based on the population pharmacokinetic results, no dose adjustment is required in patients with mild or moderate renal impairment (see section “Pharmacokinetics”). IMDYLLTRA has not been studied in patients with severe renal impairment.

Pediatric population

The safety and efficacy of IMDYLLTRA in children and adolescents under 18 years of age have not been established.

Elderly patients

Of the 473 patients with SCLC who received 10 mg IMDYLLTRA as monotherapy, 50.7% were age 65 or older and 11% were 75 years or older. In clinical studies, no overall differences in IMDYLLTRA pharmacokinetics, safety or efficacy were observed between geriatric patients (≥ 65 years old) and younger patients. No dose adjustment is required for geriatric patients.

Contraindications

Hypersensitivity to the active substance or to any of the excipients (see section “Composition”).

Warnings and Precautions

Cytokine release syndrome (CRS)

Administration of IMDYLLTRA has been associated with CRS which may be serious or life-threatening. CRS may be associated with symptoms including pyrexia, hypotension, hypoxia, fatigue, tachycardia, headache, chills, nausea, and vomiting. The majority of these events did not lead to IMDYLLTRA discontinuation in clinical trials.

Administer IMDYLLTRA in a healthcare facility equipped to monitor and manage CRS. Ensure patients are euvolemic prior to initiating the infusions. Closely monitor patients for signs and symptoms of CRS during the initiation of IMDYLLTRA treatment. To mitigate the risk of CRS, it is important to initiate IMDYLLTRA at the recommended starting dose in Table 1. CRS should be managed according to the recommendations in Table 4.

Immune Effector Cell-associated Neurotoxicity Syndrome (ICANS)

Administration of IMDYLLTRA has been associated with ICANS which may be serious or life-threatening. ICANS can occur up to several weeks following administration of IMDYLLTRA. 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 ICANS during IMDYLLTRA treatment. ICANS should be managed according to the recommendations in Table 5.

Cytopenia

Administration of IMDYLLTRA has been associated with cytopenias including neutropenia, thrombocytopenia, and anemia. For neutropenia Grade 3 or 4 supportive measure with the use of G-CSF is recommended. Patients should be closely monitored for signs and symptoms of neutropenia during IMDYLLTRA treatment. Neutropenia should be managed according to the recommendations in Table 6.

Monitor complete blood counts prior to administration of all doses of IMDYLLTRA up through Cycle 5 Day 15 and then prior to administration of IMDYLLTRA on Day 1 of each cycle starting with Cycle 6. More frequent evaluation may be necessary as clinically indicated. Withhold or permanently discontinue based on severity.

Infections

Administration of tarlatamab has been associated with serious infections, including life threatening and fatal infections. The most frequent infections include pneumonia, urinary tract infection, COVID 19, upper respiratory tract infection, respiratory tract infection, candida infection, oral candidiasis and nasopharyngitis.

Patients should be monitored for signs and symptoms of infections prior to and during treatment with tarlatamab. Infections should be managed according to the recommendations in Table 6.

Hepatotoxicity

IMDYLLTRA can cause transient liver lab abnormalities.

Monitor liver enzymes and bilirubin prior to treatment and before each dose with IMDYLLTRA, and as clinically indicated. Withhold IMDYLLTRA or permanently discontinue based on severity.

Hypersensitivity

Hypersensitivity reactions have been reported in patients treated with IMDYLLTRA including rare severe events. Clinical signs and symptoms of hypersensitivity may include but are not limited to rash and bronchospasm. Monitor patients for signs and symptoms of hypersensitivity during treatment with IMDYLLTRA and manage as clinically indicated. Withhold or consider permanent discontinuation of IMDYLLTRA based on severity.

Women of childbearing potential

In women of childbearing potential, pregnancy status should be verified before starting treatment with IMDYLLTRA (see section “Pregnancy, lactation”).

Sodium

This medicinal product provides less than 1 mmol (23 mg) sodium over a 24 hour infusion i.e., “essentially sodium-free”.

Interactions

No formal drug interaction studies have been conducted with IMDYLLTRA. Initiation of IMDYLLTRA treatment causes transient release of cytokines that may suppress CYP450 enzymes and may result in increased exposures of concomitant CYP substrates. In patients who are receiving concomitant CYP450 substrates, particularly those with a narrow therapeutic index, monitor for known undesirable effects. Adjust the dose of the concomitant drug as needed.

Pregnancy, lactation

Women of childbearing potential

In women of childbearing potential, pregnancy status should be verified before starting treatment with IMDYLLTRA.

Women of childbearing potential should use a reliable method of contraception during treatment with IMDYLLTRA and for 2 months after the last dose.

Pregnancy

There are no data from the use of IMDYLLTRA in pregnant women. In a study conducted in mice using a murine surrogate molecule, there was no indication of embryo-fetal toxicity (see "Preclinical data" section). However, based on its mechanism of action, tarlatamab may cause fetal harm when administered to pregnant women. Therefore, IMDYLLTRA should not be administered during pregnancy unless clearly necessary.

Breast-feeding

It is unknown whether tarlatamab is secreted in human milk or has effects on breastfed infants. Because many medicinal products, including antibodies, can be secreted in human milk, a risk to the newborns/infants cannot be excluded. Therefore, breastfeeding is not recommended during treatment with IMDYLLTRA and for 2 months after the last dose.

Fertility

There are no clinical studies to evaluate the effect of IMDYLLTRA on fertility.

Effect on ability to drive and use machines

Studies of the effects of IMDYLLTRA on the ability to drive and use machines have not been performed. However, due to the potential for ICANS and other associated neurological events following IMDYLLTRA 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.

Undesirable effects

Summary of the safety profile

The safety of IMDYLLTRA was evaluated in 473 patients with metastatic small cell lung cancer (SCLC) who received 10 mg as monotherapy. The mean/average duration of exposure to IMDYLLTRA was 18 weeks (range: 6 to 38 weeks).

The most common adverse reactions (≥ 15%) are: CRS (56.7%), decreased appetite (36.4%), pyrexia (31.9%), dysgeusia (31.3%), constipation (30.4%), anaemia (30.0%), fatigue (29.8%), nausea (24.9%), asthenia (19.0%), neutropenia (16.9%), hyponatremia (16.7%), headache (16.3%), lymphopenia (15.6%).

Tabulated list of adverse reactions

Adverse reactions reported in IMDYLLTRA clinical studies are displayed in Table 8 below.

Adverse reactions are listed according to the MedDRA system organ classification and by frequency. Frequency categories are defined as very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1 000 to < 1/100), rare (≥ 1/10 000 to < 1/1 000), or very rare (< 1/10 000). Within each frequency grouping, where relevant, adverse reactions are presented in order of decreasing seriousness.

Table 8. Adverse Reactions Reported in IMDYLLTRA 10 mg Pooled Clinical Studies

MedDRA system organ class	**Undesirable effect**	**All grades**	**Grade ≥ 3**
Blood and lymphatic system disorders	Anaemia	Very common (30.0%)	Common
	Neutropenia[a,c]	Very common (16.9%)	Common
	Lymphopenia[b]	Very common (15.6%)	Very common (10.6%)
	Thrombocytopenia	Common	Uncommon
	Leukopenia	Common	Uncommon
Gastrointestinal disorders	Constipation	Very common (30.4%)	Uncommon
	Nausea	Very common (24.9%)	Uncommon
	Vomiting	Very common (14.2%)	Uncommon
General disorders and administration site conditions	Pyrexia	Very common (31.9%)	Uncommon
	Fatigue	Very common (29.8%)	Common
	Asthenia	Very common (19.0%)	Common
	Chills	Common	Very rare*
Immune system disorders	Cytokine release syndrome[c]	Very common (56.7%)	Common
Investigations	Weight decreased	Very common (14.8%)	Common
	Alanine aminotransferase increased	Very common (10.4%)	Common
	Aspartate aminotransferase increased	Common	Common
	White blood cell count	Common	Common

MedDRA system organ class	Undesirable effect	All grades	Grade ≥ 3
	decreased		
Metabolism and nutrition disorders	Decreased appetite	Very common (36.4%)	Common
	Hyponatraemia	Very common (16.7%)	Common
	Hypokalaemia	Very common (10.4%)	Common
	Hypomagnesaemia	Common	Uncommon
Musculoskeletal and connective tissue disorders	Myalgia	Common	Very rare*
Nervous system disorders	Dysgeusia	Very common (31.3%)	Very rare*
	Headache	Very common (16.3%)	Very rare*
	Dizziness	Common	Very rare*
	Immune effector cell-associated neurotoxicity syndrome[c]	Common	Uncommon
	Tremor	Common	Very rare*
	Neurotoxicity	Uncommon	Very rare*
	Seizure	Uncommon	Uncommon
	Ataxia	Uncommon	Uncommon
	Encephalopathy	Uncommon	Uncommon
Psychiatric disorders	Confusional state	Common	Uncommon
	Delirium	Common	Uncommon
Respiratory, thoracic and mediastinal disorders	Dyspnoea	Very common (11.0%)	Common
Skin and subcutaneous tissue disorders	Pruritus	Very common (10.4%)	Uncommon
	Rash	Common	Uncommon

* No Grade ≥ 3 were reported.

[a] Includes neutrophil count decreased

[b] Includes lymphocyte count decreased.

[c] Additional information is provided in “Descriptions of selected adverse reactions”.

Description of selected adverse reactions

Cytokine release syndrome (CRS)

In clinical trials with pooled safety data for 473 patients with SCLC enrolled in DeLLphi-300, DeLLphi-301 and Study DeLLphi-304, receiving the IMDYLLTRA 10 mg dose, CRS occurred in 56.7% of patients, with Grade 1 in 39.3%, Grade 2 in 15.4% of patients, Grade 3 in 1.7% of patients and grade 4 events in 0.2% of patients. Serious events of CRS were reported in 19.7% of patients. After the first dose of IMDYLLTRA, 41.4% of patients experienced CRS, with 34% of patients experiencing any grade CRS after the second dose. The majority of CRS events occurred after the first two doses, with 8.5% of patients experiencing CRS following third dose or later. Following the Day 1 infusion, 13.7% of patients experienced ≥ Grade 2 CRS. Following the Day 8 infusion, 4.4% of patients experienced ≥ Grade 2 CRS. The median time from the most recent dose of IMDYLLTRA to the first onset of CRS was 15.9 hours (range: 9 to 26.5 hours).

In patients treated with IMDYLLTRA at 10 mg enrolled in Study DeLLphi-304 (n = 252), CRS occurred in 56.3% of patients, including Grade 1 in 42.5%, Grade 2 in 12.7% and Grade 3 in 1.2% of patients. No patients had Grade 4 or Grade 5 events. Most patients experienced CRS after the first two doses of IMDYLLTRA with 6.3% experiencing CRS after the third dose or later. Following the Day 1 infusion, 11.5% of patients experienced ≥ Grade 2 CRS. Following the Day 8 infusion, 4.8% of patients experienced ≥ Grade 2 CRS. For those Grade 1 events that progressed to Grade 2 or greater, the median time from Grade 1 event to Grade 2 event is 22.3 hours (range: 6.5 to 40.1 hours).

ICANS

In clinical trials with pooled safety data for 473 patients with SCLC enrolled in Study DeLLphi-300, Study DeLLphi-301 and Study DeLLphi-304 receiving IMDYLLTRA 10 mg dose, ICANS was reported in 4.7% of patients. The median time from the first dose of IMDYLLTRA to the first onset of ICANS was 9.0 days (range: 2 to 13 days). The median time to resolution of ICANS was 4 days (range: 2 to 8 days).

Cytopenia

IMDYLLTRA can cause cytopenias including neutropenia, thrombocytopenia, and anemia.

In the pooled safety population, (see “Undesirable effects”) based on laboratory data, decreased neutrophils occurred in 16% of patients, including 9% Grade 3 or 4. The median

time to onset for Grade 3 or 4 decreased neutrophil count was 41 days (range: 2 to 306 days). Decreased platelets occurred in 30%, including 2.2% Grade 3 or 4. The median time to onset for Grade 3 or 4 decreased platelets was 67 days (range: 3 to 420 days). Decreased hemoglobin occurred in 56% of patients, including 4.7% Grade 3 or 4.

Febrile neutropenia was reported as an adverse event in 1.5% of patients treated with IMDYLLTRA.

Infections

IMDYLLTRA can cause serious infections, including life threatening and fatal infections.

In the pooled safety population, (see “Undesirable effects”), infections including opportunistic infections occurred in 43% of patients who received IMDYLLTRA, including 14% Grade 3 or 4. The most frequent infections were pneumonia (11%), urinary tract infection (9%), COVID 19 (6%), upper respiratory tract infection (4.7%), respiratory tract infection (4%), candida infection (2.1%), oral candidiasis (2.1%) and nasopharyngitis (2.1%).

Monitor patients for signs and symptoms of infection prior to and during treatment with IMDYLLTRA and treat as clinically indicated. Withhold or permanently discontinue IMDYLLTRA based on severity.

Hepatotoxicity

IMDYLLTRA can cause hepatotoxicity.

In the pooled safety population (see “Undesirable effects”), based on laboratory data, elevated ALT occurred in 39% of patients who received IMDYLLTRA, including 2.5% Grade 3 or 4 ALT. Elevated AST occurred in 43% of patients, including 3.2% Grade 3 or 4. Elevated bilirubin occurred in 16% of patients, including 1.3% Grade 3 or 4 (see “Undesirable effects”). Liver enzyme elevation can occur with or without concurrent CRS.

Monitor liver enzymes and bilirubin prior to treatment with IMDYLLTRA, and as clinically indicated. Withhold IMDYLLTRA or permanently discontinue based on severity.

Immunogenicity

The observed incidence of anti-drug antibodies is highly dependent on the sensitivity and specificity of the assay. Differences in assay methods preclude meaningful comparisons of the incidence of anti-drug antibodies in the studies described below with the incidence of

anti-tarlatamab antibodies in other studies, including those of tarlatamab or of other DLL3 T-cell engager products. Across Study DeLLphi-300, Study DeLLphi-301 and Study DeLLphi-304, the incidence of anti-tarlatamab antibody development was 7.7% (34/444) in patients receiving the dose of 10 mg. In Studies DeLLphi-301 and DeLLphi-304 which employed the neutralising assay, 7.5% (27/359) of the patients developed anti-tarlatamab antibody, including 3.1% (11/359) of patients developed anti-tarlatamab neutralising antibodies. Positive anti-tarlatamab antibody binding status had no clinically relevant impact on efficacy, safety and pharmacokinetics.

Reporting suspected adverse reactions after authorisation of the medicinal product is very important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected new or serious adverse reactions online via the EIViS portal (Electronic Vigilance System). You can obtain information about this at www.swissmedic.ch.

Overdose

There is no clinical experience with overdose with IMDYLLTRA. Doses up to 100 mg every two weeks and 200 mg every three weeks have been administered in clinical trials. In the event of an overdose, the patient should be treated symptomatically, and supportive measures instituted as required.

Properties/Effects

ATC code

L01FX33

Mechanism of action

Tarlatamab is a bispecific DLL3-directed CD3 T-cell engager that binds to DLL3 expressed on the surface of tumor cells and CD3 expressed on the surface of T cells. The 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.

Pharmacodynamics

The pharmacodynamic response after a single infusion of tarlatamab was characterised by T-cell redistribution and activation, and transient cytokine elevation. Peripheral T-cell redistribution (i.e., T-cell adhesion to blood vessel endothelium and/or transmigration into tissue) occurred within 24 hours after the initial dose of tarlatamab at 1 mg on Day 1. T-cell counts declined within 6 hours post infusion and returned to baseline levels in majority of the patients prior to the next infusion on Day 8.

Serum cytokines IL-2, IL-6, IL-8, IL-10, IFN-γ and TNF-α were transiently elevated following the initial dose of tarlatamab at 1 mg on Day 1. Cytokine levels peaked within the first 2 days following the start of tarlatamab infusion and generally returned to baseline levels prior to the next infusion on Day 8. In subsequent treatments, cytokine elevation occurred in fewer patients with lesser intensity compared to the initial infusion on Day 1.

Clinical efficacy

Study DeLLphi-304

The efficacy of IMDYLLTRA was demonstrated in patients enrolled in a phase 3 multicenter, randomized, open-label trial (Study DeLLphi-304). Eligible patients were required to have SCLC with disease progression following platinum-based regimen. In regions where Standard of Care (SOC) first-line systemic treatment for extensive -stage disease included platinum-based containing chemotherapy in combination with PD-L1 inhibitor, patients were required to have failed PD-L1 inhibitor as part of their first line systemic treatment or to be ineligible to receive PD-L1 inhibitor therapy. Additionally, patients were required to have an ECOG Performance Status of 0-1, and at least one measurable lesion as defined by Response Evaluation Criteria in Solid Tumors (RECIST v1.1). The trials excluded patients with symptomatic brain metastases or active immunodeficiency.

A total of 509 patients with SCLC previously treated with platinum-based chemotherapy were enrolled and randomized 1:1 to receive either IMDYLLTRA or Standard of Care (SOC) chemotherapy. 254 patients were randomized to IMDYLLTRA at an initial dose of 1 mg on Day 1 followed by 10 mg on Days 8, 15, and every 2 weeks thereafter until disease progression or unacceptable toxicity. SOC chemotherapies included topotecan, lurbinectedin or amrubicin. Randomization was stratified by prior anti-PD-L1 exposure (yes vs no), platinum sensitivity status (chemotherapy-free interval ≥ 180 days, < 180 to ≥ 90 days, or < 90 days), presence of brain metastases (yes vs no) and standard of care (topotecan/amrubicin vs

lurbinectedin). Treatment continued until disease progression or unacceptable toxicity. Tumor assessments were performed every 6 weeks for the first 48 weeks and every 12 weeks thereafter.

The baseline demographics and disease characteristics of the study population were: median age of 65 years (range: 20 to 86); 52.1% age 65 or older; 69% male; 57.2% White and 40.1% Asian; 32% ECOG PS of 0 and 67.2% ECOG PS of 1; 91% patients had metastatic disease at baseline; 44.8% had brain metastases at baseline; 35.2% had liver metastases at baseline. 68.8% patients were former smokers; 20.6% were current smokers, 10.6% were never smokers. All patients received at least one line of prior platinum-based chemotherapy (range: 1 to 3 lines); 70.7% received prior anti-PD-L1 therapy; 223 patients (43.8%) had chemotherapy-free interval < 90 days after end of first line platinum therapy, while 286 patients (56.2%) had chemotherapy-free interval ≥ 90 days.

The primary efficacy outcome measure was Overall Survival (OS). Key secondary efficacy outcomes included Progression-free survival (PFS) based on investigator assessment per Response Evaluation Criteria in Solid Tumors (RECIST v1.1) and select patient reported outcomes. Additional endpoints were overall response rate (ORR) and duration of response (DOR) based on investigator assessment per RECIST 1.1.

Patients received a median of 5 cycles of IMDYLLTRA treatment (range: 1 to 19 cycles), and a median of 4 cycles of SOC treatment (range: 1 to 21 cycles).

The trial demonstrated a statistically significant and clinically meaningful improvement in OS, stratified hazard ratio (HR) = 0.60 (95 %-CI: 0.47; 0.77) with a 40% reduced risk of death for patients randomized to IMDYLLTRA as compared with SOC at the prespecified interim analysis, when 263 events were observed .The trial also demonstrated a statistically significant and clinically meaningful improvement in PFS, HR = 0.72 [95% CI: 0.59, 0.88] resulting in a 28% reduced risk of disease progression or death in patients randomized to IMDYLLTRA compared with patients randomized to SOC. Efficacy results are summarized in Table 9.

Table 9. Efficacy Results for Patients with SCLC in Study DeLLphi- 304

Efficacy Parameter	IMDYLLTRA (N = 254)	Standard of Care (N = 255)
Overall survival (OS)		
Deaths (%)	111 (43.7)	152 (59.6)
Median[a] in months (95% CI)	13.6 (11.1, NE)	8.3 (7.0, 10.2)
Hazard ratio[b] (95% CI)	0.60 (0.47, 0.77)	
p-value (stratified log-rank)	< 0.001	
Progression-free survival (PFS)[c]		
Events (%)	191 (75.2)	205 (80.4)
Median[a] in months (95% CI)	4.2 (3.0, 4.4)	3.2 (2.9, 4.2)
Hazard ratio[b] (95% CI)	0.72 (0.59, 0.88)	
p-value (stratified log-rank)	< 0.001	
Overall Response Rate (ORR)[c]		
ORR, % (95% CI)	35.0 (29.2, 41.3)	20.4 (15.6, 25.9)
Complete Response, n (%)	3 (1.2)	0 (0.0)
Partial Response, n (%)	86 (33.9)	52 (20.4)
Duration of Response (DOR) [c]		
Median[a] in months (95% CI) Min, Max (+ for censored)	6.9 (4.5, 12.4) 1.9, 15.3[+]	5.5 (4.2, 5.7) 1.3[+], 12.5[+]
Responders with duration ≥ 6 months[d], %	46.1	26.9
Responders with duration ≥ 12 months[d], %	13.5	1.9

[a] per Kaplan-Meier estimates.

[b] Hazard ratio based on the stratified Cox proportional hazard model.

[c] PFS, ORR, DOR based on investigator assessment per RECIST 1.1.

[d] Based on observed duration of response.

[+] Denotes ongoing response. At the time of analysis, 47% (42/89) of responders randomized to IMDYLLTRA and 15% (8/52) of responders randomized to SOC had ongoing responses.

109 patients in the tarlatamab arm and 114 patients in the SOC arm had (CFI) < 90 days at baseline. The hazard ratio for OS was 0.6 (95% CI: 0.43, 0.84) with a median OS of 10.9 months (95% CI: 8.7, 12.3) and 6.4 months (95% CI: 5.0, 7.9) in the tarlatamab and SOC arm, respectively.

145 patients in the tarlatamab arm and 141 patients in the SOC arm had (CFI) ≥ 90 days at baseline. The hazard ratio for OS was 0.65 (95% CI: 0.45, 0.93) with a median OS of 17.1

months (95% CI: 13.6, NE) and 10.6 months (95% CI: 8.7, NE) in the tarlatamab and SOC arm, respectively.

Patient-Reported Outcomes

Patient-reported outcomes were collected using EORTC QLQ-C30 and EORTC QLQ-LC13. Compliance rates were comparable between groups and were above 69% throughout 18 weeks from baseline.

Tarlatamab demonstrated statistically significant improvements in dyspnea and cough. Dyspnea, derived from EORTC QLQ-C30 and EORTC QLQ-LC13, showed a mean difference of –9.14 (95% CI: –12.64 to –5.64; $p < 0.001$) at week 18 in favor of tarlatamab for the patients who answered at least one item in the Week 18 questionnaire (N = 118, 46.6% tarlatamab and N = 88, 34.5% standard chemotherapy). A cough improvement was achieved in 16.1% of patients treated with tarlatamab, compared with 9.0% of patients who received standard chemotherapy (odds ratio [OR] 2.04; 95% CI: 1.17–3.55; $p = 0.012$) of achieving improvement compared with standard of care (SOC).

Study DeLLphi-301

The efficacy of IMDYLLTRA was evaluated in patients enrolled in a phase 2, open label multicentre trial, Study DeLLphi-301. Eligible patients were required to have extensive-stage SCLC with disease progression after receiving previous treatment including platinum-based chemotherapy, an ECOG Performance Status of 0-1, and at least one measurable lesion as defined by Response Evaluation Criteria in Solid Tumours (RECIST v1.1). The trials excluded patients with symptomatic brain metastases, evidence of interstitial lung disease or non-infectious pneumonitis and active immunodeficiency.

Study DeLLphi-301 Part 1 was a dose comparison that randomised 176 patients in a 1:1 ratio to receive either 10 mg or 100 mg of tarlatamab (as a 60-minute intravenous (IV) infusion). At the prespecified interim analysis, 30 patients per arm were used to determine the selected dose for part 2. Part 2 was a dose expansion that enrolled 100 patients (part 1 and 2 combined) at the selected dose of 10 mg. A total of 99 patients received tarlatamab 10 mg intravenously every 2 weeks across Part 1 and Part 2 (combined). Treatment continued until disease progression or unacceptable toxicity. Tumour assessments were performed every 6 weeks for the first 48 weeks and every 12 weeks thereafter.

The key efficacy outcome measures were ORR and DOR as assessed by Blinded Independent Central Review (BICR) according to RECIST v1.1.

For patients who received tarlatamab 10 mg, the baseline demographics and disease characteristics of the study population were: median age of 64 years (range: 35 to 82); 48.5% age 65 or older; 71.7% male; 57.6% White and 41.4% Asian; 26.3% ECOG PS of 0 and 73.7% ECOG PS of 1; 98% had metastatic disease; and 22.2% had a history of brain metastases. 100% received prior platinum therapy, 20.2% received prior topotecan therapy, 69.7% received prior anti- PD-L1 therapy;8.1% had never smoked, 73.7% formerly smoked, and 18.2% currently smoked. Time to progression was < 90 days for 27/69 (39.1%) subjects and ≥ 90 days for 42/69 (60.9%) subjects.

ORR and DOR were generally similar to the total population in the subgroups that had < 90 or ≥ 90 days to progression after first line platinum therapy. Efficacy results are summarised in Table 10.

Table 10. Efficacy Results for Patients with SCLC in Study DeLLphi-301 who Received IMDYLLTRA 10 mg

Efficacy Parameter	IMDYLLTRA (N = 99)
Overall Response Rate (ORR)[f]	
ORR, % (95% CI)[a]	41 (32, 52)
Complete Response, n (%)	1 (1)
Partial Response, n (%)	40 (40)
Duration of Response (DOR) [a, f]	
Median[b], months (range)	9.7 (5.9, NE)
Responders with duration ≥ 6 months[c], %	66
Responders with duration ≥ 9 months[d], %	49
Responders with duration ≥ 12 months[e], %	39

[a] Assessed by Blinded Independent Central Review, CI = Confidence Interval

[b] Median based on Kaplan-Meier estimate.

[c] Observed proportion of responders beyond the 6-month landmark.

[d] Observed proportion of responders beyond the 9-month landmark.

[e] Observed proportion of responders beyond the 12-month landmark.

[f] DOR based on DCO of Jan 12, 2024.

Pharmacokinetics

The peak serum concentration (C_{max}), trough serum concentrations (C_{trough}) and area under the serum concentration versus time curve at steady state (AUC_{tau}), of tarlatamab increased dose

proportionally in the evaluated dose range of 1 mg to 100 mg Q2W (10 times the recommended dosage). Approximate steady state in serum tarlatamab exposures were achieved by Day 15.

Distribution

The mean value (CV%) for volume of distribution at steady state based on individual parameters is 8.53 L (33.3%).

Metabolism

The metabolic pathway of tarlatamab has not been characterised. Like other protein therapeutics, tarlatamab is expected to be degraded into small peptides and amino acids via catabolic pathways.

Elimination

The estimated systemic clearance (inter-subject CV%) was 0.728 L/day (34%) and terminal elimination half-life was approximately 10.6 days in subjects with SCLC.

Kinetics in specific patient groups

No clinically significant differences in the pharmacokinetics of tarlatamab were observed based on age (20 to 86 years), body weight (35 to 149 kg), sex, race (68% White and 27% Asian), mild or moderate renal impairment (eGFR 30 to < 90 mL/min), or mild hepatic impairment (total bilirubin ≤ upper limit of normal (ULN) and AST > ULN).

The effects of severe renal impairment (eGFR 15 to < 30 mL/min), end-stage renal disease (eGFR < 15 mL/min), or moderate to severe hepatic impairment (total bilirubin > 1.5 × ULN and any AST) on the pharmacokinetics of tarlatamab are unknown.

Preclinical data

Carcinogenicity and genotoxicity

No carcinogenicity or genotoxicity studies have been conducted with tarlatamab.

Reproductive and developmental toxicology

Based on its mechanism of action, tarlatamab may cause foetal harm when administered to a pregnant woman. In a murine embryo-foetal development study, there were no effects of the murine surrogate molecule of tarlatamab, designated muS757, on any maternal parameter, including mean maternal body weights or body weight gains. In addition, there were no muS757-related macroscopic findings or effects on any ovarian, uterine, or litter parameters at any dose level and administration of muS757 did not produce any foetal external, visceral, or skeletal malformations or variations.

No studies have been conducted to evaluate the effects of tarlatamab on fertility.

Other information

Incompatibilities

No known incompatibilities.

Shelf life

Unopened vials:

IMDYLLTRA vial and stabiliser solution vial may be used only up to the date indicated with <EXP> on the container.

Special storage precautions

Store IMDYLLTRA and Solution Stabiliser vials in the original package refrigerated at 2°C to 8°C and protect from light until time of use. Do not freeze.

Store lyophilized IMDYLLTRA and Solution Stabiliser vials for a maximum of 24 hours at room temperature in the original carton to protect from light.

The information in Table 11 indicates the storage time for the prepared IMDYLLTRA infusion bag.

Table 11. Maximum Storage Time

	Room Temperature 20°C to 25°C	**Refrigerated 2°C to 8°C protect from light**
Prepared IMDYLLTRA Infusion Bag	8 hours[a]	7 days[a]

[a] Storage time includes total time permitted from point of reconstitution of the vial to the end of administration. Once removed from the refrigerator, bring the infusion bag to room temperature and complete administration of the diluted IMDYLLTRA infusion solution within 8 hours (including preparation and infusion time).
If the prepared IMDYLLTRA infusion bag is not administered within the time frames and temperatures indicated, it must be discarded; it should not be refrigerated again.

Instructions for use

Aseptic preparation

IMDYLLTRA does not contain antimicrobial preservatives. Therefore, if the in-use storage time is to exceed 24 hours, the solution for infusion must be prepared using validated aseptic techniques. Reconstitution of IMDYLLTRA is with Water for Injection.

Do not use Solution Stabiliser for reconstitution of IMDYLLTRA. The Solution Stabiliser is used to coat the intravenous bag prior to addition of reconstituted IMDYLLTRA to prevent adsorption of IMDYLLTRA to IV bags and IV tubing.

Table 12. Required Amount of Water for Injection to Reconstitute IMDYLLTRA[a]

IMDYLLTRA vial Strength (mg)	**Amount of Water for Injection, needed to reconstitute IMDYLLTRA (mL)**	**Final Concentration (mg/mL)**
1 mg	1.3 mL	0.9 mg/mL
10 mg	4.4 mL	2.4 mg/mL

[a] Each vial contains overfill to allow for withdrawal of 1.1 mL (1 mg vial) or 4.2 mL (10 mg vial) after reconstitution to ensure delivery at the stated concentration of labelled vial strength.

a. Transfer required amount of Water for Injection (refer to Table 12) into the IMDYLLTRA vial to provide a final IMDYLLTRA concentration of 0.9 mg/mL (1 mg vial) or 2.4 mg/mL (10 mg

vial). Direct Water for Injection along the walls of the IMDYLLTRA vial and not directly on the lyophilizat.

- Do not use IV Solution Stabiliser to reconstitute IMDYLLTRA.

b. Gently swirl contents. Do not shake.

c. Inspect that the solution is clear to slightly opalescent, colourless to slightly yellow. Do not use if solution is cloudy or has particulates.

Preparation of solution for infusion

Table 13. Preparation Guide for 1-hour infusion

IMDYLLTRA Vial Strength (mg)[a]	**IMDYLLTRA Dose (mg)**	**Volume of 0.9% NaCl to withdraw from IV bag (mL)**	**Volume of Solution Stabiliser to add to IV bag (mL)**	**Volume of reconstituted IMDYLLTRA to add to IV bag (mL)**
1	1	14	13	1.1
10	10	17	13	4.2

[a] The final concentrations for the different strength vials are NOT the same following reconstitution.

Withdraw 0.9% Sodium Chloride for Injection

- Withdraw the required volume from a pre-filled 250 mL 0.9% Sodium Chloride bag. Refer to Table 13. Disregard any overfill in the IV bag.

Add Solution Stabiliser

- Transfer 13 mL of IVSS to the IV bag containing 0.9% Sodium Chloride for Injection.
- Gently mix the contents of the bag to avoid foaming. Do not shake**.**

Add reconstituted IMDYLLTRA

- Transfer the required volume of reconstituted IMDYLLTRA into the stabilised IV bag containing 0.9% Sodium Chloride for Injection and Solution Stabiliser. Refer to Table 13.
- Gently mix the contents of the bag to avoid foaming. Do not shake.

Remove the air from the IV bag.

- Remove air from the IV bag using an empty syringe to avoid foaming.

- Prime the IV tubing separately with 0.9% Sodium Chloride for Injection OR final prepared IMDYLLTRA solution for infusion.

Other considerations

Material Compatibility Information

- IV bags composed of ethyl vinyl acetate (EVA), polyolefin, and polyvinyl chloride (PVC) have been shown to be compatible with tarlatamab at the specified administration conditions.
- IV line and catheter materials composed of polyolefin, PVC, and polyurethane have been shown to be compatible with tarlatamab at the specified administration conditions.
- The use of Closed System Transfer Device (CSTD) is not recommended due to potential risk for medication error. Amgen has not performed compatibility testing of vial adaptor CSTDs with IMDYLLTRA.

Authorisation number

69132 (Swissmedic)

Packs

Pack with 1 vial of IMDYLLTRA 1 mg and 2 vials of Stabiliser solution 7 mL [A]

Pack with 1 vial of IMDYLLTRA 10 mg and 2 vials of Stabiliser solution 7 mL [A]

Marketing authorisation holder

Amgen Switzerland AG, Risch

Domicile: 6343 Rotkreuz

Date of revision of the text

March 2026