ספטמבר 2026

Lunsumio® 1 mg/1ml
mosunetuzumab
Concentrate for solution for infusion

רופא/ה יקר/ה, רוקח/ת יקר/ה,

חברת רוש פרמצבטיקה (ישראל) בע"מ מבקשת להודיעכם על עדכון בעלון לרופא של התכשיר לאנסומיו. בהודעה זו מצוינים רק עדכונים מהותיים ועדכונים אשר מהווים החמרה.

ההתוויות הרשומות לתכשיר בישראל:

Lunsumio as monotherapy is indicated for the treatment of adult patients with relapsed or refractory follicular lymphoma (FL) who have received at least two prior systemic therapies.

למידע נוסף יש לעיין בעלון לרופא כפי שאושר ע"י משרד הבריאות.
העלון המעודכן נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות, וניתן לקבלו מודפס על-ידי פנייה לבעל הרישום: רוש פרמצבטיקה (ישראל) בע"מ, ת.ד 6391 , הוד השרון 4524079 טלפון 09-9737777. כתובתנו באינטרנט: www.roche.co.il.

ב ב ר כ ה,

בתאור צפרי חגג
מנהלת תחום רישום

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4.2 Posology and method of administration

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It is important to check the product labels to ensure that the correct formulation (intravenous or subcutaneous fixed dose) is being administered to the patient, as prescribed. Lunsumio intravenous formulation is not intended for subcutaneous administration and should be administered via intravenous infusion only.

[…]

Delayed or missed dose

~~If any dose in cycle 1 is delayed for > 7 days, the previous tolerated dose should be repeated prior to resuming the planned treatment schedule.~~

~~If a dose interruption occurs between Cycles 1 and 2 that results in a treatment-free interval of ≥ 6 weeks, Lunsumio should be administered at 1 mg on Day 1, 2 mg on Day 8, then resume the planned Cycle 2 treatment of 60 mg on Day 15.~~

~~If a dose interruption occurs that results in a treatment-free interval of ≥ 6 weeks between any Cycles in Cycle 3 onwards, Lunsumio should be administered at 1 mg on Day 1, 2 mg on Day 8, then resume the planned treatment schedule of 30 mg on Day 15.~~

Table 3: Recommendations for restarting therapy with Lunsumio intravenous infusion after dose delay

Last dose administered	**Time since the last dose administered**	**Action for next dose(s)**
1 mg Cycle 1 Day 1	1 to 2 weeks	Administer 2 mg (Cycle 1 Day 8), then resume the planned treatment schedule.
	Greater than 2 weeks	Repeat 1 mg (Cycle 1 Day 1), then administer 2 mg (Cycle 1 Day 8) and resume the planned treatment schedule.
2 mg Cycle 1 Day 8	1 to 2 weeks	Administer 60 mg (Cycle 1 Day 15), then resume the planned treatment schedule.
	Greater than 2 weeks to less than 6 weeks	Repeat 2 mg (Cycle 1 Day 8), then administer 60 mg (Cycle 1 Day 15) and resume the planned treatment schedule.
	Greater than or equal to 6 weeks	Repeat 1 mg (Cycle 1 Day 1) and 2 mg (Cycle 1 Day 8), then administer 60 mg (Cycle 1 Day 15) and resume the planned treatment schedule.
60 mg Cycle 1 Day 15	1 week to less than 6 weeks	Administer 60 mg (Cycle 2 Day 1), then resume the planned treatment schedule.
	Greater than or equal to 6 weeks	Repeat 1 mg (Cycle 2 Day 1) and 2 mg (Cycle 2 Day 8), then administer 60 mg (Cycle 2 Day 15), followed by 30 mg (Cycle 3 Day 1) and then resume the planned treatment schedule.
60 mg Cycle 2 Day 1	3 weeks to less than 6 weeks	Administer 30 mg (Cycle 3 Day 1), then resume the planned treatment schedule.
	Greater than or equal to 6 weeks	Repeat 1 mg (Cycle 3 Day 1) and 2 mg (Cycle 3 Day 8), then administer 30 mg (Cycle 3 Day 15)*, followed by 30 mg (Cycle 4 Day 1) and then resume the planned treatment schedule.
30 mg Cycle 3	3 weeks to less than 6 weeks	Administer 30 mg, then resume the planned treatment schedule.

Last dose administered	Time since the last dose administered	Action for next dose(s)
onwards	Greater than or equal to 6 weeks	Repeat 1 mg on Day 1 and 2 mg on Day 8 during the next cycle, then administer 30 mg on Day 15*, followed by 30 mg on Day 1 of subsequent cycles.

*For the Day 1, Day 8, and Day 15 doses in the next cycle, administer premedication as per Table 1 for all patients

Note that all references to Cycle and Day are to the nominal Cycle and Day.

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Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) grading and management

ICANS should be identified based on clinical presentation (see Section 4.4). Rule out other causes of neurologic symptoms. If ICANS is suspected, it should be managed according to the recommendations in Table 5.

Table 5 Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS)

Grade[a]	Actions
Grade 1 ICE[b] 7-9 or depressed level of consciousness but awakens spontaneously	Withhold Lunsumio and monitor neurologic toxicity symptoms until ICANS resolves.[c,d] Provide supportive therapy and consider neurologic consultation and evaluation. Consider a single dose of dexamethasone 10mg, if not taking other corticosteroids. Consider non-sedating, anti-seizure medicinal products (e.g., levetiracetam) for seizure prophylaxis.
Grade 2 ICE[b] 3-6 or depressed level of consciousness but awakens to voice	Withhold Lunsumio and monitor neurologic toxicity symptoms until ICANS resolves.[c,d] Provide supportive therapy and consider neurologic consultation and evaluation. Treat with dexamethasone 10 mg intravenously every 6 hours, if not taking other corticosteroids, until improvement to Grade 1, then taper. Consider non-sedating, anti-seizure medicinal products (e.g., levetiracetam) for seizure prophylaxis.
Grade 3 ICE[b] 0-2 or depressed level of consciousness but awakens to tactile stimulus or any clinical seizure that resolves rapidly or focal/local oedema on neuroimaging	Withhold Lunsumio and monitor neurologic toxicity symptoms until ICANS resolves.[d,e] Provide supportive therapy, which may include intensive care, and consider neurologic consultation and evaluation. Treat with dexamethasone 10 mg intravenously every 6 hours, if not taking other corticosteroids,

	until improvement to Grade 1, then taper. Consider non-sedating anti-seizure medication for seizure prophylaxis until resolution of ICANS. Use anti-seizure medication for seizure management as needed. For recurrent grade 3 ICANS, consider permanently discontinuing Lunsumio.
Grade 4 ICE[b] is 0 or patient is unarousable or requires vigorous or repetitive tactile stimuli, or life-threatening prolonged seizure (>5 min) or repetitive seizures without return to baseline or deep focal motor weakness or diffuse cerebral oedema on neuroimaging	Permanently discontinue Lunsumio. Provide supportive therapy, which may include intensive care, and consider neurologic consultation and evaluation. Treat with dexamethasone 10 mg intravenously every 6 hours, if not taking other corticosteroids, until improvement to Grade 1, then taper. Alternatively, consider administration of methylprednisolone 1 000 mg per day intravenously for 3 days, if symptoms improve, then manage as above. Consider non-sedating anti-seizure medication for seizure prophylaxis until resolution of ICANS. Use anti-seizure medication for seizure management as needed.

[a] American Society for Transplantation and Cellular Therapy (ASTCT) consensus grading criteria.
[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 (name 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] Consider the type of neurologic toxicity before deciding to withhold Lunsumio.
[d] See *Delayed or missed dose* for guidance on restarting Lunsumio after dose delay.
[e] Evaluate benefit/risk before restarting Lunsumio.

4.4 Special warnings and precautions for use

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Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS)

[…]

At the first signs or symptoms of ICANS, manage according to the ICANS guidance provided in Table 5. Treatment with Lunsumio should be withheld or discontinued permanently as recommended.

4.8 Undesirable effects

Summary of safety profile

The adverse reactions (ARs) described in this section were identified from the pivotal clinical trial GO29781 in patients treated at the recommended intravenous dose (n=218)) and the recommended subcutaneous dose (n=139). Patients had follicular lymphoma (41.351.8%), diffuse large B-cell lymphoma (26.9%), transformed follicular lymphoma (40.49.8%) mantle cell lymphoma (11.57.3%), Richter's transformation (6.43.9%), and other histologies (0.53%). The median number of cycles of Lunsumio intravenously received was 8 (range 1 -17), 37% of patients received 8 cycles, and 15% received more than 8 cycles up to 17 cycles.

Patients who received the recommended intravenous dose (n=218) and subcutaneous (n=139) dose are pooled (n=357) for this safety population. In this pooled safety population, the most common adverse reactions (≥ 20%) observed were cytokine release syndrome, neutropenia, pyrexia, hypophosphatemia and headache. rash and upper respiratory tract infection. The most common serious adverse reactions (≥ 2%) observed included cytokine release syndrome (CRS) (2117% by ASTCT grading system), pyrexia (%), 3%), sepsis (3%), upper respiratory tract infection (3%) 5%), and pneumonia (35%). Permanent discontinuation Nine of 218 patients (4.1%) discontinued of Lunsumio due to an adverse reaction occurred in 5.8% (21/357) of patients. In patients who received the recommended intravenous dose (n=218), event. CRS was the only adverse reaction that led to discontinuation in more than one patient (2 patients [0.9%]).

Table 6 Adverse reactions occurring in patients treated with Lunsumio

System organ class / preferred term or adverse reaction	All grades[19]	Grade 3 – 4
Infections and infestations		
Upper respiratory tract infection[1]	Very Common	Common
Urinary tract infection[2]	Common	Common
Pneumonia[3]	Common	Common
Lower respiratory tract infection[4]	Common	Uncommon
Sepsis[5]	Common	Common
Neoplasms benign, malignant and unspecified (including cysts and polyps)		
Tumour flare[6]	Common	UncommonCommon
Blood and lymphatic system disorders		
Neutropenia[1]Neutropenia[7]	Very common	Very common

System organ class / preferred term or adverse reaction	All grades[19]	Grade 3 – 4
Anaemia	Very common	Common
~~Thrombocytopenia~~[8]Thrombocytopenia[8]	Very common	Common
Febrile neutropenia	Common	Common
~~Haemophagocytic lymphohistiocytosis~~[5]	~~Uncommon~~	~~Uncommon~~
Immune system disorders		
Cytokine release syndrome[3,10]	Very common	Common
Haemophagocytic lymphohistiocytosis[9,17]	Uncommon	Uncommon
Metabolism and nutrition disorders		
Hypophosphataemia[11]	Very common	Very common
Hypokalaemia[12]	Very common	Common
Hypomagnesaemia[13]	~~Very~~ common	Very rare
Tumour lysis syndrome	Uncommon	Uncommon
Nervous system disorders		
Headache[14]	Very common	Uncommon
Dizziness[15]	Common	Uncommon
Immune effector cell-associated neurotoxicity syndrome[4,5,16,17]	Common	Very rare
Gastrointestinal disorders		
Diarrhoea	Very common	Uncommon~~Very rare~~
Nausea	Very common	Uncommon
Skin and subcutaneous tissue disorders		
Rash[18]	Very common	~~unc~~Common
Pruritus	Very common	Very rare
Dry skin	Very common	Very rare
Skin exfoliation	Common	Very rare
General disorders and administration site conditions		
Pyrexia	Very common	Common
Chills	Very common	Uncommon

System organ class / preferred term or adverse reaction	All grades[19]	Grade 3 – 4
Investigations		
Alanine aminotransferase, increased	~~Very~~ Common	Common
Aspartate aminotransferase, increased	Common	Common

~~[1]Neutropenia includes neutropenia and neutrophil count decreased~~
~~[2]Thrombocytopenia includes thrombocytopenia and platelet count decreased~~
~~[3]By American Society for Transplant and Cellular Therapy~~
~~[4]Consistent with the medical concept of ICANS according to American Society for Transplant and Cellular Therapy and includes confusional state, ICANS, lethargy, encephalopathy, depressed level of consciousness, and memory impairment~~
~~[5]The frequency calculation is based on additional clinical studies~~

[1] Upper respiratory tract infection includes upper respiratory tract infection, viral upper respiratory tract infection, nasopharyngitis, sinusitis, rhinovirus infection, sinusitis bacterial, viral sinusitis, respiratory tract infection, COVID-19 and respiratory tract infection viral
[2] Urinary tract infection (UTI) includes UTI, Escherichia UTI, pyelonephritis acute
[3] Pneumonia includes pneumonia and COVID-19 pneumonia
[4] Lower respiratory tract infection includes lower respiratory tract infection and bronchitis
[5] Sepsis includes sepsis, septic shock, bacteraemia, Candida sepsis
[6] Tumour flare includes tumour flare, pleural effusion, tumour inflammation and flank pain
[7] Neutropenia includes neutropenia and neutrophil count decreased
[8] Thrombocytopenia includes thrombocytopenia and platelet count decreased
[9] Haemophagocytic lymphohistocytosis (HLH) includes HLH
[10] By American Society for Transplantation and Cellular Therapy
[11] Hypophosphatemia includes hypophosphatemia and blood phosphorus decreased
[12] Hypokalemia includes hypokalemia and blood potassium decreased
[13] Hypomagnesemia includes hypomagnesemia and blood magnesium decrease
[14] Headache includes headache, migraine and head discomfort
[15] Dizziness includes dizziness and vertigo
[16] Consistent with the medical concept of ICANS according to American Society for Transplantation and Cellular Therapy and includes confusional state, ICANS, lethargy, encephalopathy, depressed level of consciousness, and memory impairment
[17] The frequency calculation is based on additional clinical studies
[18] Rash includes rash, rash erythematous, exfoliative rash, rash macular, rash maculo-papular, rash pruritic, rash pustular, erythema, palmar erythema, dermatitis, dermatitis acneiform, dermatitis contact, palmar-planta erythrodysaesthesia and rash morbiliform
[19] Grade 5 AEs only occurred for ADR terms HLH, pneumonia, sepsis and URTI (i.e., COVID-19) in mosunetuzumab subcutaneous injection (1 each) and for ADR terms Pneumonia and Sepsis in mosunetuzumab intravenous infusion (1 each)

Description of selected adverse reactions

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Neutropenia

In patients treated with Lunsumio intravenous infusion or subcutaneous injection, Neutropenia of any grade occurred in 26.1% (93/357) ~~28%~~ of patients, including ~~24~~22.7% Grade 3-4 events. The median time to onset of first neutropenia/neutrophil count decreased events was ~~48~~ 50 days (range: 1-280 days), with median duration of 8 days (range: 1-~~314~~ 487 days). Of the ~~60~~ 93 patients who had neutropenia/neutrophil count decreased events 68%(63/93) received treatment G-CSF to treat the events.

Serious infections

In patients treated with Lunsumio intravenous infusion or subcutaneous injection, Serious infections of any grade occurred in 17% (60/357) of patients. Five (1.~~8~~4%) of patients experienced serious infections concurrently with grade 3-4 neutropenia. The median time to onset of first serious infection was ~~50~~ 92 days (range: 1-~~561~~ 408 days), with median duration of ~~12~~ 15.5 days (range: 2-174 days). Grade 5 events occurred in ~~0.9~~2.5% (9/357) of patients, which included COVID-19 pneumonia, COVID-19, pneumonia, septic shock and sepsis.

Immune Effector Cell-Associated Neurotoxicity Syndrome

Across a broader clinical trial population, Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) occurred in 2.1% (20/949) of patients, 19 patients had Grade 1-2 events and 1 patient had Grade 3 event. The majority of events occurred during the first cycle of treatment. The majority of cases resolved. The median time to onset from initial dose was 17 days (range: 1 to 48 days). The median duration was 3 days (range: 1-20 days). Immune Effector Cell-Associated Encephalopathy (ICE) scoring was not systematically performed across the referenced trial population.

In patients treated with Lunsumio intravenous infusion or subcutaneous injection, tumour~~Tumour~~ flare (including pleural effusion and tumour inflammation) occurred in 43.1% (11/357) of patients, which included 1.~~8~~4% grade 2 and ~~2.3~~1.4% grade 3 events. The median time to onset was 13 days (range ~~5~~2-84 days), and median duration was ~~10~~ 36 days (range ~~1-77~~15-105 days).

Tumour Lysis Syndrome (TLS)

In patients treated with Lunsumio intravenous infusion or subcutaneous injection, TLS occurred in 0.~~9~~6% (2/357) of patients, concurrent with CRS. One patient with follicular lymphoma was in the leukemic phase who experienced Grade 4 TLS. TLS onset was on days 2 and 24, and resolved within ~~4~~3 and 6 days, respectively.