ספטמבר 2026

Columvi® (glofitamab) 1 mg/1 mL
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 קולומבי. בהודעה זו מצוינים רק עדכונים מהותיים ועדכונים אשר מהווים החמרה.

ההתוויות הרשומות לתכשיר בישראל:

- Columvi in combination with gemcitabine and oxaliplatin is indicated for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma not otherwise specified (DLBCL NOS) who are ineligible for autologous stem cell transplant (ASCT).

- Columvi is indicated for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from indolent lymphoma, and high-grade B cell lymphoma after two or more lines of systemic therapy.

למידע נוסף יש לעיין בעלון לרופא כפי שאושר ע"י משרד הבריאות.

העלון המעודכן נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות, וניתן לקבלו מודפסים 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,

אביטל ויסברוט
מחלקת רישום

לילי אדר
רוקחת ממונה

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4.2 Posology and method of administration

Columvi must only be administered under the supervision of a healthcare professional experienced in the diagnosis and treatment of cancer patients and who has access to appropriate medical support to manage severe reactions associated with cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS).

[…]

All patients must be monitored for signs and symptoms of CRS and immune effector cell-associated neurotoxicity syndrome (ICANS) following Columvi administration.

All patients must be counselled on the risk, signs and symptoms of CRS and ICANS and advised to contact the healthcare provider immediately should they experience signs and symptoms of CRS and/or ICANS at any time (see section 4.4).

[…]

Table 3. ASTCT CRS grading and CRS management guidance

Grade[1]	CRS management	For next scheduled Columvi infusion
Grade 1 Fever ≥ 38 °C	If CRS occurs during infusion: • Interrupt infusion and treat symptoms • Restart infusion at slower rate when symptoms resolve • If symptoms recur, discontinue current infusion If CRS occurs post-infusion: • Treat symptoms If CRS lasts more than 48 h after symptomatic management: • Consider corticosteroids[3] • Consider tocilizumab[4] For CRS with concurrent ICANS, refer to Table 5.	• Ensure symptoms are resolved for at least 72 hours prior to next infusion • Consider slower infusion rate[2]
Grade 2 Fever ≥ 38 °C and/or hypotension not requiring vasopressors and/or hypoxia requiring low-flow oxygen by nasal cannula or blow-by	If CRS occurs during infusion: • Discontinue current infusion and treat symptoms • Administer corticosteroids[3] • Consider tocilizumab[4] If CRS occurs post-infusion: • Treat symptoms • Administer corticosteroids[3] • Consider tocilizumab[4] For CRS with concurrent ICANS, refer to Table 5.	• Ensure symptoms are resolved for at least 72 hours prior to next infusion • Consider slower infusion rate[2] • Monitor patients post-infusion[5, 6]
For Grade 2: Tocilizumab use Do not exceed 3 doses of tocilizumab in a period of 6 weeks. If no prior use of tocilizumab or if 1 dose of tocilizumab was used within the last 6 weeks: • Administer first dose of tocilizumab[4] • If no improvement within 8 hours, administer second dose of tocilizumab[4] • After 2 doses of tocilizumab, consider alternative anti-cytokine therapy and/or alternative immunosuppressant therapy If 2 doses of tocilizumab were used within the last 6 weeks: • Administer only one dose of tocilizumab[4] • If no improvement within 8 hours, consider alternative anti-cytokine therapy and/or alternative immunosuppressant therapy		

Grade[1]	CRS management	For next scheduled Columvi infusion
Grade 3 Fever ≥ 38 °C and/or hypotension requiring a vasopressor (with or without vasopressin) and/or hypoxia requiring high-flow oxygen by nasal cannula, face mask, non-rebreather mask, or Venturi mask	If CRS occurs during infusion: • Discontinue current infusion and treat symptoms • Administer corticosteroids[3] • Administer tocilizumab[4] If CRS occurs post-infusion: • Treat symptoms • Administer corticosteroids[3] • Administer tocilizumab[4] For CRS with concurrent ICANS, refer to Table 5.	• Ensure symptoms are resolved for at least 72 hours prior to next infusion • Consider slower infusion rate[2] • Monitor patients post-infusion[5, 6] • If Grade ≥ 3 CRS recurs at subsequent infusion, stop infusion immediately and permanently discontinue Columvi
Grade 4 Fever ≥ 38 °C and/or hypotension requiring multiple vasopressors (excluding vasopressin) and/or hypoxia requiring oxygen by positive pressure (e.g., CPAP, BiPAP, intubation, and mechanical ventilation)	If CRS occurs during infusion or post-infusion: • Permanently discontinue Columvi and treat symptoms • Administer corticosteroids[3] • Administer tocilizumab[4] For CRS with concurrent ICANS, refer to Table 5.	
For Grade 3 and Grade 4: Tocilizumab use Do not exceed 3 doses of tocilizumab in a period of 6 weeks. If no prior use of tocilizumab or if 1 dose of tocilizumab was used within the last 6 weeks: • Administer first dose of tocilizumab[4] • If no improvement within 8 hours or rapid progression of CRS, administer second dose of tocilizumab[4] • After 2 doses of tocilizumab, consider alternative anti-cytokine therapy and/or alternative immunosuppressant therapy If 2 doses of tocilizumab were used within the last 6 weeks: • Administer only one dose of tocilizumab[4] • If no improvement within 8 hours or rapid progression of CRS, consider alternative anti-cytokine therapy and/or alternative immunosuppressant therapy		

[1] ASTCT consensus grading criteria (Lee 2019).

[2] Duration of infusion may be extended up to 8 hours, as appropriate for that cycle (see Table 2).

[3] Corticosteroids (e.g., 10 mg intravenous dexamethasone, 100 mg intravenous prednisolone, 1-2 mg/kg intravenous methylprednisolone per day, or equivalent).

[4] Tocilizumab 8 mg/kg intravenously (not to exceed 800 mg), as administered in Study NP30179.

[5] In Study NP30179, Grade ≥ 2 CRS following Columvi 10 mg dose at Cycle 1 Day 15 occurred in 5.2% of patients, with a median time to onset of 26.2 hours from the start of infusion (range: 6.7 to 144.2 hours).

[6] In Study NP30179, Grade ≥ 2 CRS following Columvi 30 mg dose at Cycle 2 Day 1 occurred in one patient (0.8%), with a time to onset of 15.0 hours from the start of infusion.

~~Neurologic Toxicity, Including ICANS (Immune Effector Cell-Associated Neurotoxicity Syndrome) recommendations for neurologic toxicity, including ICANS, is summarized in Table 5~~
Management of immune effector cell-associated neurotoxicity syndrome (ICANS)
At the first sign of ~~neurologic toxicity, including~~ ICANS, based on the type and severity, consider supportive therapy, neurology evaluation and withholding Columvi ~~based on the type and severity of neurotoxicity~~. (see Table 5).
Rule out other causes of neurologic symptoms. ~~Provide supportive therapy, which may include intensive care~~
If ICANS is suspected, it should be managed according to the recommendations in Table 5.

~~**Recommended Dosage Modification for Neurologic Toxicity (Including ICANS)**~~

Table 5: ICANS grading and management guidance

~~Adverse Reaction~~ Grade[1]	~~Severity~~[1,2] Presenting symptoms[2]	~~Actions~~ ICANS management	
		Concurrent CRS	No concurrent CRS
~~Neurologic Toxicity[1] (including ICANS[2])~~ Grade 1	~~Grade 1~~ ICE3 score 7-9 Or depressed level of consciousness[4]: awakens spontaneously	~~Continue Columvi and monitor neurologic toxicity symptoms. If ICANS, manage per current practice guidelines.~~ • Manage CRS per Table 4. • Monitor neurologic symptoms and consider neurology consultation and evaluation, per physician discretion.	Monitor neurologic symptoms and consider neurology consultation and evaluation, per physician discretion.
		Withhold Columvi until ICANS resolves. Consider non-sedating, anti-seizure medicinal products (e.g., levetiracetam) for seizure prophylaxis.	
Grade 2	~~Grade 2~~ ICE3 score 3-6 Or depressed level of consciousness4: awakens to voice	~~Withhold Columvi until neurologic toxicity symptoms improve to Grade 1 or baseline.[3, 4] Provide supportive therapy, and consider neurologic evaluation . If ICANS, manage per current practice guidelines.~~ • Administer tocilizumab per Table 3 for management of CRS. • If no improvement after starting tocilizumab, administer dexamethasone5 10 mg intravenously every 6 hours if not already taking other corticosteroids. Continue dexamethasone use until resolution to Grade 1 or less, then taper.	• Administer dexamethasone[5] 10 mg intravenously every 6 hours. • Continue dexamethasone use until resolution to Grade 1 or less, then taper.

<table>
<tr><td></td><td></td><td colspan="2">Withhold Columvi until ICANS resolves.

Consider non-sedating, anti-seizure medicinal products (e.g., levetiracetam) for seizure prophylaxis. Consider neurology consultation and other specialists for further evaluation, as needed.</td></tr>
<tr><td rowspan="2">Grade 3</td><td rowspan="2">~~Grade 3~~
ICE[3] score 0-2

Or depressed level of consciousness4: awakens only to tactile stimulus;

Or seizures4, either:
•any clinical seizure, focal or generalised that resolves rapidly, or
•non-convulsive seizures on electroencephalogram (EEG) that resolve with intervention;

Or raised intracranial pressure: focal/local oedema on neuroimaging[4]</td><td>• Administer tocilizumab per Table 3 for management of CRS.
• In addition, administer dexamethasone[5] 10 mg intravenously with the first dose of tocilizumab, and repeat dose every 6 hours, if not already taking other corticosteroids. Continue dexamethasone use until resolution to Grade 1 or less, then taper.

~~Withhold Columvi until neurologic toxicity symptoms improve to Grade 1 or baseline for at least 7 days.[4, 5] For Grade 3 neurologic events lasting more than 7 days, consider permanently discontinuing Columvi. Provide supportive therapy, and consider neurology evaluation. If ICANS, manage per current practice guidelines~~</td><td>• Administer dexamethasone[5] 10 mg intravenously every 6 hours.
• Continue dexamethasone use until resolution to Grade 1 or less, then taper.</td></tr>
<tr><td colspan="2">Withhold Columvi until ICANS resolves.
For Grade 3 ICANS events which do not improve within 7 days, consider permanently discontinuing Columvi.

Consider non-sedating, anti-seizure medicinal products (e.g., levetiracetam) for seizure prophylaxis. Consider neurology consultation and other specialists for further evaluation, as needed.</td></tr>
</table>

Grade 4	~~Grade 4~~ ICE[3] score 0 Or depressed level of consciousness[4], either: • patient is unarousable or requires vigorous or repetitive tactile stimuli to arouse, or • stupor or coma; Or seizures[4], either: • life-threatening prolonged seizure (> 5 minutes), or • repetitive clinical or electrical seizures without return to baseline in between; Or motor findings[4]: • deep focal motor weakness such as hemiparesis or paraparesis; Or raised intracranial pressure/cerebral oedema[4], with signs/symptoms, such as: • diffuse cerebral oedema on neuroimaging, or • decerebrate or decorticate posturing, or • cranial nerve VI palsy, or • papilloedema, or • Cushing's triad	~~Permanently discontinue Columvi. Provide supportive therapy, which may include intensive care, and consider neurology evaluation .~~ ~~If ICANS, manage per current practice guidelines.~~ Administer tocilizumab per Table 3 for management of CRS. •As above, or consider administration of methylprednisolone 1 000 mg per day intravenously with first dose of tocilizumab, and continue methylprednisolone 1 000 mg per day intravenously for 2 or more days.	Administer dexamethasone[5] 10 mg intravenously every 6 hours. •Continue dexamethasone use until resolution to Grade 1 or less, then taper. •Alternatively, consider administration of methylprednisolone 1 000 mg per day intravenously for 3 days; if symptoms improve, then manage as above.
		Permanently discontinue Columvi. Consider non-sedating, anti-seizure medicinal products (e.g., levetiracetam) for seizure prophylaxis. Consider neurology consultation and other specialists for further evaluation, as needed. In case of raised intracranial pressure/cerebral oedema, refer to institutional guidelines for management.	

~~[1] Based on National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE), version .4.03~~
~~[2] Based on ASTCT 2019 grading for ICANS.~~
~~[3] Consider the type of neurologic toxicity before deciding to withhold Columvi.~~
~~[4] See Dosage and Administration (2.2) on restarting Columvi after dose delays.~~
~~[5] Evaluate benefit-risk before restarting Columvi.~~

[1] ASTCT consensus grading criteria for ICANS (Lee 2019).
[2] Management is determined by the most severe event, not attributable to any other cause.
[3] 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) ;
Attention (count backwards from 100 by ten = 1 point) .
If patient is unarousable and unable to perform ICE Assessment (Grade 4 ICANS) = 0 points.
[4] Attributable to no other cause.
[5] All references to dexamethasone administration are dexamethasone or equivalent.