Indication	Monotherapy for the treatment of diffuse large B-cell lymphoma (DLBCL) or high-grade B-cell lymphoma following 2 or more lines of systemic therapy, which included an anti-CD20 regimen, an anthracycline-containing regimen and included polatuzumab vedotin (unless the use of polatuzumab vedotin was contraindicated), in patients who are not candidates for any future CAR T cell therapy. Patients must have not been previously treated with loncastuximab tesirine unless loncastuximab tesirine has been accessed via a company compassionate access scheme. NB: Patients with primary CNS lymphoma, Burkitt lymphoma and plasmablastic lymphoma are NOT eligible for treatment with loncastuximab tesirine.
Treatment Intent	Disease modification.
Frequency and number of cycles	Repeat every 21 days Continue until disease progression or unacceptable toxicity or withdrawal of patient consent. A formal medical review as to whether treatment with loncastuximab tesirine should continue or not will be scheduled to occur at least by the end of the first 6 weeks of treatment. NB If loncastuximab is electively stopped (i.e. not for reasons of toxicity), it cannot be restarted.
Monitoring Parameters pre-treatment	• **Virology screening:** All new patients referred for systemic anti-cancer treatment should be screened for hepatitis B and C and the result reviewed prior to the start of treatment. Patients not previously tested who are starting a new line of treatment, should also be screened for hepatitis B and C. Further virology screening will be performed following individual risk assessment and clinician discretion. • FBC, U&Es and LFTs should be monitored at each cycle or more frequently if clinically indicated. • Proceed with treatment if neuts >/=1 x10^9/L and platelets >/=50 x10^9/L. If parameters not met see table 1. • **Hepatic impairment:** No recommended dose modification in mild hepatic impairment, total bilirubin </= ULN and AST > ULN or total bilirubin >1 to 1.5 × ULN and any AST. No data available in moderate or severe impairment, patients should be closely monitored for adverse reactions. • **Renal impairment:** No recommended dose modification for mild to moderate impairment. No data available in severe or end stage renal disease, with or without haemodialysis, patients should be monitored closely. • **Management of adverse reactions:** • **Effusion and oedema** - Patients should be monitored for new or worsening oedema or effusions. Treatment should be withheld for Grade 2 or greater oedema or effusion until the toxicity resolves. Diagnostic imaging should be considered in patients who develop symptoms of pleural effusion or pericardial effusion, such as new or worsened dyspnoea, chest pain, and/or ascites. Appropriate medical management for oedema or effusions should be initiated. • **Photosensitivity and cutaneous reactions -** Patients should be monitored for new or worsening cutaneous reactions, including photosensitivity reactions. Treatment should be withheld for severe (Grade 3) cutaneous reactions until resolution. Patients should be advised to minimise or avoid exposure to direct natural or artificial sunlight including exposure through glass windows. Patients should be instructed to protect skin by wearing sun-protective clothing and/or the use of sunscreen products. If a skin reaction or rash develops, dermatologic consultation should be considered.

	• **Dose Modification: See table 1**
	  ○ If treatment is delayed by more than 3 weeks due to toxicity, subsequent doses should be reduced by 50%. If toxicity requires dose reduction following the second dose of 0.15 mg/kg (Cycle 2), the patient should receive the dose of 0.075 mg/kg for Cycle 3.
	  ○ If toxicity reoccurs after two dose reductions following an adverse reaction, permanent discontinuation should be considered.
	• **<u>Common drug interactions (for comprehensive list refer to BNF/SPC)</u>:** No drug to drug studies have been performed.
	• **Missed dose:** If a planned dose is missed, it should be administered as soon as possible, and the schedule of administration should be adjusted to maintain a 21-day interval between doses.
	• **Driving:** Fatigue has been reported in patients taking loncastuximab tesirine, patients should be cautious when driving or operating machinery.

References	SPC accessed online 03.01.2024 Blueteq form accessed online 03.01.2024

NB For funding information, refer to CDF and NICE Drugs Funding List

<u>Table 1 Dose modification for haematological and non-haematological adverse reactions</u>

Adverse reactions	**Severity**	**Dose modification**
Haematological adverse reactions		
Neutropenia	Absolute neutrophil count less than 1 x 10^9/L	Withhold until neutrophil count returns to 1 x 10^9/L or higher
Thrombocytopenia	Platelet count less than 50 x10^9/L	Withhold until platelet count returns to 50 x10^9/L or higher
Non-haematological adverse reactions		
Oedema or effusion	Grade 2 or higher	Withhold until the toxicity resolves to Grade 1 or less
Other adverse reactions	Grade 3 or higher	Withhold until the toxicity resolves to Grade 1 or less

Repeat every 21 days cycle 1 and 2 only.

Day	Drug	Dose	Route	Infusion Duration	Administration
1	Dexamethasone	4mg	PO	stat	Use TTO supply If the dexamethasone has not been taken the day before LONCASTUXIMAB TESIRINE, treatment may still be given as long as dexamethasone 4mg PO is administered 2 hours prior to treatment.
	LONCASTUXIMAB TESIRINE	**0.15mg/kg**	IV	30 minutes	In 50ml 5% glucose Give via a dedicated infusion line with a sterile, non-pyrogenic, low-protein binding in-line or add-on filter (0.2 or 0.22 micrometre pore size) and catheter.
TTO	Drug	Dose	Route	Directions	
Day 1	Dexamethasone	4mg	PO	BD for 3 days starting the **day before** loncastuximab tesirine infusion.	

Repeat every 21 days cycle 3 onwards:

Day	Drug	Dose	Route	Infusion Duration	Administration
1	Dexamethasone	4mg	PO	stat	Use TTO supply If the dexamethasone has not been taken the day before LONCASTUXIMAB TESIRINE, treatment may still be given as long as dexamethasone 4mg PO is administered 2 hours prior to treatment.
	LONCASTUXIMAB TESIRINE	**0.075 mg/kg**	IV	30 minutes	In 50ml 5% glucose. Give via a dedicated infusion line with a sterile, non-pyrogenic, low-protein binding in-line or add-on filter (0.2 or 0.22 micrometre pore size) and catheter.
TTO	Drug	Dose	Route	Directions	
Day 1	Dexamethasone	4mg	PO	BD for 3 days starting the **day before** loncastuximab tesirine infusion.	