Indication	Newly diagnosed acute myeloid leukaemia (AML) that is secondary to therapy or myelodysplasia or chronic myelomonocytic leukaemia in line with commissioning criteria.
Treatment Intent	Curative
Frequency and number of cycles	Induction- up to 2 cycles: A second cycle of induction may be administered in patients who do not show disease progression or unacceptable toxicity. The attainment of a normal-appearing bone marrow may require more than one induction course. Evaluation of the bone marrow following recovery from the previous course of induction therapy determines whether a further course of induction is required. Consolidation- up to 2 cycles: First consolidation starts 5-8 weeks after the start of the last induction in patients achieving remission and with neuts >0.5 x 10^9/L and PLT >50 x 10^9/L. Administer the second cycle of consolidation 5 to 8 weeks after the start of the first consolidation cycle in patients who do not show disease progression or unacceptable toxicity. NB: Liposomal cytarabine and daunorubicin is exempt from the NHS England Treatment Break policy.
Monitoring Parameters pre-treatment	• ECG baseline and every cycle. • MUGA or ECHO baseline for patients at high risk of cardiac toxicity. • LFTs, FBC and U&Es before start of treatment and prior to each DOSE of Vyxeos®. Prior to 1st consolidation treatment ensure neuts >0.5 x 10^9/L and PLT >50 x 10^9/L. • **Renal Impairment**: no dose modification in mild to moderate renal impairment (CrCl 30-89ml/min). No data in patients with CrCl <30ml/min. • **Hepatic Impairment**: no dose modification for patients with a bilirubin ≤ 50 µmol/L. No data in patients with bilirubin > 50 µmol/L. • **Cardiotoxicity:** Treatment should be discontinued in patients with signs of cardiomyopathy unless the benefit of initiating or continuing treatment outweighs the risk. • **Severe myelosuppression:** Due to the long plasma half-life of Vyxeos®, time to recovery of ANC and platelets may be prolonged and require additional monitoring. • **Haemorrhage:** Haemorrhagic events have been reported due to prolonged severe thrombocytopenia. Monitor blood counts regularly until recovery, and administer platelet transfusion support as required. • **Hypersensitivity reactions:** For hypersensitivity reactions of any grade/severity, interrupt Vyxeos® infusion immediately and manage symptoms. Reduce the rate of infusion or discontinue treatment as outlined below: Mild symptoms: If a mild reaction occurs, stop treatment and monitor. Administer chlorphenamine 10mg IV and dexamethasone 10mg IV. When symptoms have resolved restart at half the infusion rate. Moderate symptoms: If a moderate reaction occurs, stop treatment and monitor. Administer chlorphenamine 10mg IV and dexamethasone 10mg IV. Do not restart infusion. When the patient is re-treated, give at the same dose and rate with premedication. Severe/life-threatening symptoms: If a severe or life-threatening hypersensitivity reaction occurs, discontinue permanently, administer chlorphenamine 10mg IV

	and dexamethasone 10mg IV (and epinephrine and bronchodilators as needed) and monitor until symptoms resolve. • Blood uric acid levels should be monitored and appropriate therapy initiated in the event that hyperuricemia develops. • **Vyxeos®** has a different posology than daunorubicin injection and cytarabine injection and it **must not be** interchanged with other daunorubicin and/or cytarabine containing products. The medicinal product name and dose should be verified prior to administration to avoid dosing errors. • Each vial contains 100mg copper gluconate – caution in patients with a history of Wilson's disease (or other copper related disorder). • Caution is recommended when driving or operating machines. • Missed Doses of Vyxeos® : If a planned dose of Vyxeos® is missed, administer the dose as soon as possible and adjust the dosing schedule accordingly, maintaining the treatment interval.
References	SPC accessed online 12/11/2018 https://vyxeospro.com/support-materials/

NB For funding information, refer to the SACT funding spreadsheet

Induction 1

Day	Drug	Dose	Route	Infusion Duration	Administration
1,3 & 5	Ondansetron	8mg	PO		BD
1,3 & 5	**Vyxeos®** Liposomal daunorubicin/cytarabine	Daunorubicin 44 mg/m^2 Cytarabine 100 mg/ m^2	IV	90 minutes	500 mL of 0.9% sodium chloride. **Do not use an in-line filter.**
TTO	Drug	Dose	Route		Directions
To be given at induction 1 only	Allopurinol	300mg	PO		OD Review after 4 weeks. Adjust dose in renal impairment
	Aciclovir	400mg	PO		Twice daily
	Chlorhexidine mouthwash	10ml	MW		Four times daily for 4 weeks OR stop after neutrophils > 1.0
	Prescribe anti-fungals				

Induction 2

Day	Drug	Dose	Route	Infusion Duration	Administration
1 & 3	Ondansetron	8mg	PO		BD
1 & 3	**Vyxeos®** Liposomal daunorubicin/cytarabine	Daunorubicin 44 mg/m^2 Cytarabine 100 mg/m^2	IV	90 minutes	500 mL of 0.9% sodium chloride. **Do not use an in-line filter.**
TTO	Drug	Dose	Route		Directions
	Aciclovir	400mg	PO		Twice daily
	Chlorhexidine mouthwash	10ml	MW		Four times daily for 4 weeks OR stop after neutrophils > 1.0
	Prescribe anti-fungals				

Consolidation for a maximum of 2 cycles.

Day	Drug	Dose	Route	Infusion Duration	Administration
1 & 3	Ondansetron	8mg	PO		BD
1 & 3	**Vyxeos®** Liposomal daunorubicin/cytarabine	Daunorubicin 29 mg/m^2 Cytarabine 65mg/ m^2	IV	90 minutes	500 mL of 0.9% sodium chloride. **Do not use an in-line filter**.
TTO	Drug	Dose	Route		Directions
	Aciclovir	400mg	PO		Twice daily
	Chlorhexidine mouthwash	10ml	MW		Four times daily for 4 weeks OR stop after neutrophils > 1.0
	Prescribe anti-fungals				