Indication	For the treatment of relapsed or refractory chronic lymphocytic leukaemia after a BTK inhibitor, where retreatment with a covalent BTK inhibitor (including after fixed-duration regimens) is not clinically appropriate.
Treatment Intent	Disease modification
Frequency and number of cycles	Repeat every 28 days continuously Continue until disease progression, unacceptable toxicity or patient's choice.

Monitoring Parameters	• **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.
	• **ECG** prior to cycle 1and as clinically indicated throughout treatment.
	• **FBC, U&Es** and **LFTs** at baseline and then at each cycle or more frequently if clinically indicated.
	• **Hepatic impairment:** no dose adjustment in mild, moderate or severe impairment.
	• **Renal impairment:** no dose adjustment in mild, moderate or severe impairment. No data in patients on dialysis, clinician's decision to use in these patients.
	• **Management of adverse reactions and dose adjustments:** Treatment should be interrupted until recovery to Grade 1 (neuts >/=1.5 and PLTS >/=75) or baseline for,
	  ○ neutropenia: neuts <1 with fever and/or infection
	  ○ neutropenia: neuts <0.5 lasting >/= 7 days
	  ○ thrombocytopenia: PLTS <50 with bleeding or PLTS <25
	  ○ Grade 3 or 4 non-haematologic toxicity
	• Asymptomatic lymphocytosis is not regarded as an adverse reaction and no dose interruption is required.
	• **Haemorrhages,** including major haemorrhagic events, with and without thrombocytopenia have been reported; the risk may be increased with concomitant use of anticoagulants and antiplatelets. Patients should be monitored for signs and symptoms of bleeding throughout treatment.
	• **Tumour lysis syndrome (TLS)** has been reported in some patients. Patients should be assessed for possible risk of TLS and closely monitored as clinically indicated.
	• **Atrial fibrillation/ flutter (AF):** patients should be monitored for signs and symptoms of AF, perform ECGs as clinically indicated and if indicated dose interruption may be required.
	• **Sun Exposure:** Patients should be monitored for the appearance of skin cancers and advised to use protection from sun exposure (e.g. broad-spectrum sunscreen (SPF >/=30) and to wear protective clothing to include sunglasses/sunhat).
	• **Common drug interactions (for comprehensive list refer to BNF/SPC):**
	• Avoid concomitant use with strong CYP3A inducers (e.g. rifampicin, carbamazepine, phenytoin).
	• Use with caution with CYP2C8 substrates (e.g. repaglinide, dasabuvir, selexipag, rosiglitazone, pioglitazone, and montelukast).
	• If co-administration with narrow therapeutic index substrates of BCRP (e.g. high dose methotrexate, mitoxantrone), P-gp (e.g. dabigatran etexilate and digoxin), CYP2C19 (e.g. phenobarbital and mephenytoin) and CYP3A (e.g. alfentanil, midazolam, tacrolimus) cannot be avoided, close clinical monitoring should be considered.
	• **Missed dose:** If a dose is missed by more than 12 hours the dose should be omitted and the patient should take the next dose at the usual scheduled time. If vomiting occurs an additional dose should not be taken.
	• **Pregnancy and contraception:** Women of childbearing potential should use an effective method of contraception during treatment and for 5 weeks after the last dose**.** Men are advised to use an

	effective method of contraception and not father a child during treatment and for 3 months after the last dose. • **Driving and machinery:** Fatigue, dizziness, and asthenia have been reported during treatment, patients should be advised not to drive or use machines if they experience these symptoms or any other adverse reactions that may affect their ability to drive and use machines. • Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take pirtobrutinib. • For oral self-administration: refer to local Trust policy on oral anti-cancer medicines and supply Patient Information Leaflet and Macmillan information sheet.
References	SPC accessed online 27.04.2026 CDF list V1.394 accessed online 27.04.2026

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

Repeat every 28 days

TTO	Drug	Dose	Route	Directions
Day 1	**PIRTOBRUTINIB**	**200mg**	PO	OD at approximately the same time each day. Swallow whole with a glass of water. Do not split, crush or chew the tablets. Available as 50mg and 100mg tablets
	Loperamide	2mg-4mg	PO	Take 4mg (2 capsules) initially, then 2mg (1 capsule) after each loose stool when required. Maximum 16mg (8 capsules) a day. Dispense 30 capsules on cycle 1 then only if required.
	Metoclopramide	10mg	PO	Take 10mg up to TDS when required. Do not take for more than 5 days continuously.
	Aciclovir	400mg	PO	BD continuously (plus 3 more months after completion of last pirtobrutinib treatment dose).
	Co-trimoxazole	480mg	PO	TWICE daily on Mondays, Wednesdays and Fridays (plus 3 more months after completion of last pirtobrutinib treatment dose).
	Allopurinol	300mg	PO	OD, starting 24hrs before first cycle and reviewed after 4 weeks. Prescribe continuing supply if required from cycle 2 onwards.
	Consider antifungal prophylaxis			