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| **Indication** | Monotherapy for the treatment of patients with:<br>• previously untreated chronic lymphatic leukaemia (CLL) or small lymphocytic lymphoma (SLL) which has a 17p deletion and/or TP53 mutation<br>• previously untreated chronic lymphatic leukaemia or small lymphocytic lymphoma (SLL)which **does not** have a 17p deletion or a TP53 mutation and in whom chemotherapy with FCR or BR is unsuitable.<br>• Patients with chronic lymphatic leukaemia (CLL) or small lymphocytic lymphoma (SLL) who have had at least one previous line of treatment.<br><br>NB the patient has not received any previous Bruton's kinase inhibitor for CLL/SLL unless first line acalabrutinib was previously commenced via the AstraZeneca early access scheme or first line ibrutinib or zanubrutinib has had to be stopped as a consequence of dose-limiting toxicity and in the clear absence of disease progression<br>or<br>the patient received 1st line ibrutinib plus venetoclax and was in response to treatment on completion and this regimen is the first BTK inhibitor to be prescribed since relapse. |
| **Treatment Intent** | Disease modification. |
| **Frequency and number of cycles** | Repeat every 28 days.<br><br>Continue until disease progression or unacceptable toxicity or patient choice to stop treatment<br><br>A formal medical review as to whether treatment with acalabrutinib should continue or not will be scheduled to occur at least by the end of the first 8 weeks of treatment |
| **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.<br>• Monitor FBC, U&Es and LFTs at each cycle.<br>• ECG baseline in patients with cardiac history.<br>• **Hepatic impairment:** Avoid administration of acalabrutinib in patients with severe hepatic impairment (Child-Pugh C or total bilirubin >3xULN and any AST). Dose modifications are not required for patients with mild or moderate hepatic impairment (Child-Pugh A, Child-Pugh B, or total bilirubin between 1.5-3x ULN and any AST), however patients with moderate impairment should be monitored closely for signs of toxicity.<br>• **Renal impairment:** No dose adjustment in mild to moderate renal impairment (CrCl>/=30ml/min). No data in patients with severe renal impairment (CrCl<30ml/min). Treatment should only be administered in patients with severe renal impairment only if the benefit outweighs the risk and these patients should be monitored closely for signs of toxicity.<br>• **Management of adverse reactions and dose adjustments:**<br>o For Grade 3 or greater non- haematological toxicities, Grade 3 thrombocytopenia (PLT 25-49) with bleeding, Grade 4 thrombocytopenia (<25) or Grade 4 neutropenia (<0.5) lasting longer than 7 days (supporting neutrophil growth factors could be considered) the recommended dose adjustments are: |

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| | ▪ First and Second occurrence - Interrupt acalabrutinib. Once toxicity has resolved to Grade 1 (neuts >/=1, platelets >/= 75) or baseline level, acalabrutinib may be resumed at 100 mg approximately every 12 hours.<br>▪ Third occurrence - Interrupt acalabrutinib. Once toxicity has resolved to Grade 1 (neuts >/=1, platelets >/= 75) or baseline level, acalabrutinib may be resumed at a reduced frequency of 100 mg once daily.<br>▪ Fourth occurrence - Discontinue acalabrutinib.<br>o **Haemorrhage:** Use with caution with antithrombotic agents and consider additional monitoring for signs of bleeding when concomitant use is medically necessary. Consider withholding acalabrutinib for 3-7 days pre and post-surgery depending on the type of surgery and the risk of bleeding.<br>o **Progressive multifocal leukoencephalopathy (PML):** PML has been reported in patients receiving acalabrutinib. Patients should be monitored for new or worsening neurological, cognitive or behavioural changes. All treatment should be held if PML is suspected and permanently discontinued if PML is confirmed.<br>o **Sun exposure:** Monitor patients for skin cancers and advise protection.<br>o **Monitor for symptoms of arrhythmia** (e.g. palpitations, dizziness, syncope, dyspnoea) and manage as appropriate. The risk of arrhythmia may be increased in patients with cardiac risk factors, hypertension, previous arrhythmias, and acute infection.<br>• **<u>Common drug interactions/cautions (for comprehensive list refer to BNF/SPC)</u>:**<br>o Avoid concomitant use of strong CYP3A inhibitors (e.g. ketoconazole, ritonavir, clarithromycin, itraconazole, voriconazole, posaconazole), if the short-term use of a strong CYP3A inhibitor cannot be avoided, interrupt treatment with acalabrutinib. If a moderate CYP3A inhibitor is required monitor closely for adverse reactions.<br>o Avoid concomitant use with strong CYP3A inducers (e.g. phenytoin, rifampicin, and carbamazepine).<br>o Avoid grapefruit, grapefruit juice and Seville oranges.<br>o Concomitant use of preparations containing St John's Wort should be avoided.<br>o Warfarin or other vitamin K antagonists should not be administered concomitantly.<br>• **Missed dose:** If the dose has been missed by less than 3 hours the patient should take their usual dose. If more than 3 hours have passed, the patient should be instructed to miss that dose and take next dose of acalabrutinib at the usual time. Do not take extra to make up for the missed dose.<br>• For oral self-administration: refer to local Trust policy on oral anti-cancer medicines and supply Patient Information Leaflet.<br>• **Driving:** Acalabrutinib may cause fatigue and dizziness; patients should be advised to avoid driving or operating machinery if affected. |
| **References** | Calquence 100 mg film-coated tablets SPC accessed online 01.11.2023 CDF V1.278 accessed on line 01.11.2023 KMCC protocol HAEM-CLL-036 V3 |

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

**Repeat every 28 days.**

| TTO | Drug | Dose | Route | Directions |
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| Day 1 | **ACALABRUTINIB** | **100mg** | PO | BD<br>Should be swallowed whole with a glass of water. Do not crush, chew, dissolve or split the tablets. |
| | Allopurinol | 300mg | PO | OD.<br>**Cycle 1** only. |
| | Metoclopramide | 10mg | PO | Take 10mg up to 3 times a day as required. Do not take for more than 5 days continuously. |
| | Loperamide | 2mg-4mg | PO | Take two capsules (4mg) after first loose stool, then one capsule (2mg) after each loose stool when required. (Maximum 16mg per day).<br>Dispense on Cycle 1 then only if required. |
| | Co-trimoxazole | 480mg | PO | BD on Mondays, Wednesdays and Fridays. |
| | Aciclovir | 400mg | PO | BD |
| | Consider the use of prophylactic anti-fungals. Caution drug interaction with some anti-fungals. | | | |