Chemotherapy Protocol

Chronic Lymphocytic Leukaemia

Ibrutinib

Regimen

- CLL – Ibrutinib

Indication

- NICE TA 429 recommends ibrutinib alone within its marketing authorisation as an option for treating chronic lymphocytic leukaemia in adults who have had at least one prior therapy or who have a 17p deletion or TP53 mutation, and in whom chemo-immunotherapy is unsuitable and only when the company provides ibrutinib with the discount agreed in the patient access scheme.

- Performance status 0, 1, 2

Toxicity

Drug	Adverse Effect
Ibrutinib	Diarrhoea, musculoskeletal pain, upper respiratory tract infection, bruising, rash, nausea, pyrexia, neutropenia, thrombocytopenia, constipation, atrial fibrillation, ventricular tachycardia, hypertension, onycholclasis

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

Monitoring

- FBC, U&Es and LFTs prior to starting treatment and then every twenty-eight days for the first twelve weeks of treatment. Thereafter if counts are stable monitoring may take place every twelve weeks.

- Hepatitis B status prior to starting treatment as re-activation is a known adverse effect of treatment

Dose Modifications

The dose modifications listed are for haematological, liver and renal function and drug specific toxicities only. Dose adjustments may be necessary for other toxicities as well. Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances.

Haematological

Dose modifications for haematological toxicity in the table below are for general guidance only. Always refer to the responsible consultant as any dose reductions or delays will be dependent on clinical circumstances and treatment intent.

Consider blood transfusion or the use of erythropoietin according to NICE TA323 if the patient is symptomatic of anaemia or where the haemoglobin is less than 8g/dL.

Dose delay if neutrophils are less than $1x10^9$/L with infection or fever or the neutrophils are less than $0.5x10^9$/L or the platelets are less than $30x10^9$/L. Restart treatment once the toxicity has resolved to grade 1 using the dosing table below.

Toxicity Occurrence	Dose modification after recovery
First	restart at 420 mg once a day
Second	restart at 280 mg once a day
Third	restart at 140 mg once a day
Fourth	discontinue

Hepatic Impairment

Ibrutinib is metabolized in the liver. When using ibrutinib in patients with mild or moderate hepatic impairment, monitor patients for signs of toxicity and follow dose modification guidance as needed.

Liver Function	Ibrutinib Dose Modifications
Child Pugh A (mild hepatic impairment)	280mg once a day
Child Pugh B (moderate hepatic impairment)	140mg once a day
Child Pugh C (severe hepatic impairment)	Not recommended

Renal Impairment

No dose adjustments are required for patients with a creatinine clearance of more than 30ml/minute. There are no data in patients with a creatinine clearance of less than 30ml/min or patients on dialysis. In this latter instance prescribed ibrutinib only if the benefit outweighs the risk, monitor patients carefully for signs of toxicity.

Regimen

28 day cycle until disease progression or intolerance (12 cycles will be set in Aria)

Drug	Dose	Days	Administration
Ibrutinib	420mg	1- 28 (inclusive)	Oral

Dose Information

- Ibrutinib is available as 140mg, 280mg and 420mg tablets.
- The dose will be rounded to the nearest 140mg (up if halfway).

Administration Information

- Ibrutinib tablets should be swallowed whole with water at approximately the same time each day.

Additional Therapy

- Anti-infective prophylaxis with
    - co-trimoxazole 960mg once day on Monday, Wednesday and Friday oral

Additional Information

- The National Patient Safety Alert on oral chemotherapy (NPSA/2008/RRR001) must be followed in relation to ibrutinib.
- It must be made clear to all staff, including those in the community, that ibrutinib is should only be prescribed under the supervision of a consultant haematologist or oncologist.
- There are many drug interactions associated with ibrutinib. Caution is advised when concurrently prescribing agents that affect coagulation or platelet function or that influence the hepatic enzyme system CYP3A4.
- Ibrutinib should be withheld at least 3 to 7 days pre- and post-surgery, depending upon the type of surgery and the risk of bleeding.
- Grapefruit and grapefruit juice, and Seville oranges, should be avoided while on ibrutinib

Coding

- Procurement – X
- Delivery – X

References

1. Byrd JC, Furman RR, Coutre SE et al. Three year follow up of treatment naïve and previously treated patients with CLL receiving single agent ibrutinib. Blood 2015; 125 (16): 2497-2506.

REGIMEN SUMMARY

Ibrutinib

Cycle 1 onwards

Day 1-28 inclusive

1. Ibrutinib 420mg once a day oral
   Administration Information
   Oral Chemotherapy

   Ibrutinib tablets should be swallowed whole with water at approximately the same time each day.

   Avoid grapefruit and grapefruit juice, and Seville oranges while on ibrutinib. Always check for drug interactions.

2. Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday oral
   Administration Instructions
   Co-trimoxazole 960mg once a day on Mondays, Wednesdays and Fridays. Please supply 28 days.
   This may be dispensed as 480mg twice a day on Mondays, Wednesdays and Fridays according to local practice.

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.3	October 2019	Ibrutinib capsules changed to tablets	Nanda Basker Pharmacist	Dr Deborah Wright Pharmacist
1.2	February 2018	Co-trimoxazole added	Dr Deborah Wright Pharmacist	Rebecca Wills Pharmacist
1.1	September 2017	Ventricular tachycardia added to adverse effects Hepatitis B status added to monitoring	Dr Deborah Wright Pharmacist	Rebecca Wills Pharmacist
1	February 2017	None	Dr Deborah Wright Pharmacist	Dr Helen Dignam Consultant Haematologist

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust
NHS Isle of Wight
Portsmouth Hospitals NHS Trust
Salisbury NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors that occur as a result of following these guidelines.