

## Chemotherapy Protocol

### Mantle Cell Lymphoma

#### Ibrutinib

##### Regimen

- MCL – Ibrutinib (560mg)

##### Indication

- Mantle Cell Lymphoma with cyclin D1 overexpression or translocation breakpoints at t(11;14)
- Failure to achieve at least a partial response (PR) with, or documented disease progression disease after, the most recent treatment regimen
- At least one but no more than five previous lines of treatment
- WHO 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, onycholysis

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 (80g/L).

Dose delay if neutrophils are less than  $1 \times 10^9/L$  with infection or fever or the neutrophils are less than  $0.5 \times 10^9/L$  or the platelets are less than  $30 \times 10^9/L$ . Restart treatment once the toxicity has resolved to grade 1 using the dosing table below.

Toxicity Occurrence	Dose Modification after Recovery
First	Re-start at 560 mg once a day
Second	Re-start at 420 mg once a day
Third	Re-start at 280 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.

### Other Toxicity

Dose delay for any new onset or worsening grade non-haematological toxicity as described in the table below. Restart treatment once the toxicity has resolved to NCI-CTC grade 1 or below using the table below.

NCI-CTC Grade	Ibrutinib Dose Adjustment
0, 1, 2	No change
3 or more	Withhold, restart once the toxicity has resolved to grade 1 using the dosing table shown above

## [Regimen](#)

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

Drug	Dose	Days	Administration
Ibrutinib	560mg	1- 28 (inclusive)	Oral

## [Dose Information](#)

- Ibrutinib is available as 140mg, 280mg, 420mg and 560mg 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 – X71.5
- Delivery – X73.1

## [References](#)

1. Wang ML, Rule S, Martin P et al. Targeting BTK with Ibrutinib in Relapsed or Refractory Mantle-Cell Lymphoma. NEJM 2013; 369: 507-16.

## REGIMEN SUMMARY

Ibrutinib (560mg)

### Cycle 1 onwards

#### Day 1-28 inclusive

1. Ibrutinib 560mg 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. This may be dispensed as 480mg twice a day on Mondays, Wednesdays and Fridays according to local practice. Please dispense 28 days.

## 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 as supportive therapy. Grapefruit interaction moved to additional information section. Some re-formatting in tables	Dr Deborah Wright Pharmacist	Dr Rob Lown Consultant Haematologist
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.