

## Chemotherapy Protocol

### LYMPHOMA

#### CYCLOPHOSPHAMIDE-CYTARABINE-DOXORUBICIN-PREDNISOLONE-RITUXIMAB-VINCRIStINE (Nordic 3000)

#### Inpatient-Outpatient Regimen

**There are multiple versions of this protocol in use. The choice of protocol depends on the age of the patient. Please ensure you have the correct version.**

#### Regimen

- Lymphoma – Nordic (3000)-Cyclophosphamide-Cytarabine-Doxorubicin-Prednisolone-Rituximab-Vincristine

#### Indication

- CD20 positive Mantle Cell Lymphoma
- Performance status 0 or 1, consider using in those aged 59 years and below

#### Toxicity

Drug	Adverse Effect
Cyclophosphamide	Dysuria, haemorrhagic cystitis (rare), taste disturbances
Cytarabine	CNS toxicity, conjunctivitis, flu-like syndrome, pulmonary toxicity
Doxorubicin	Cardiomyopathy, alopecia, urinary discolouration (red),
Prednisolone	Weight gain, gastro-intestinal disturbances, hyperglycaemia, CNS disturbances, cushingoid changes, glucose intolerance
Rituxumab	Severe cytokine release syndrome, increased incidence of infective complications, progressive multifocal leukoencephalopathy
Vincristine	Peripheral neuropathy, constipation, jaw pain

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

## [Monitoring](#)

### [Drugs](#)

- FBC, LFTs and U&Es prior to day one of treatment
- Ensure adequate cardiac function before starting therapy. Baseline LVEF should be measured in patients with a history of cardiac problems, cardiac risk factors or in the elderly. Discontinue doxorubicin if cardiac failure develops
- Check hepatitis B status before starting treatment with rituximab
- CMV serology status
- LDH, beta 2 microglobulin, DAT and immunoglobulin levels

## [Dose Modifications](#)

The dose modifications listed are for haematological, liver and renal function and limited drug specific toxicities. Dose adjustments may be necessary for other toxicities as well.

In principle all dose reductions due to adverse drug reactions should not be re-escalated in subsequent cycles without consultant approval. It is also a general rule for chemotherapy that if a third dose reduction is necessary treatment should be stopped.

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](#)

There are no dose modifications for haematological toxicity. Treatment should be delayed until minimum criteria detailed below are reached.

Criteria	Eligible Level
Neutrophil	equal to or more than $1 \times 10^9/L$
Platelets	equal to or more than $75 \times 10^9/L$

Consider blood transfusion if the patient is symptomatic of anaemia or has a haemoglobin of less than 8g/dL (80g/L).

## Hepatic Impairment

Please note that the approach may be different where abnormal liver function tests are due to disease involvement.

Drug	Bilirubin (μmol/L)		AST/ALT (units)	Dose (%of original dose)
Cyclophosphamide	more than 30*	or	2-3xULN	Clinical decision. Evidence that exposure to active metabolites may not be increased, suggesting dose reduction may not be necessary
Cytarabine	more than 40*			50%
Doxorubicin	less than 30*	and	2-3xULN	75%
	30-50*	and/or	More than 3xULN	50%
	51-85		N/A	25%
	more than 85		N/A	omit
Rituximab	N/A		N/A	No dose adjustment needed
Vincristine	30-51*	or	60-180	50%
	more than 51	and	normal	50%
	more than 51	and	more than 180	omit

\* Limits reflect local practice and may vary from published sources

## Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Cyclophosphamide*	more than 20	100%
	10-20	75%
	less than 10	50%
Cytarabine	N/A	No dose adjustment needed
Doxorubicin	less than 10	Consider dose reduction in severe renal failure
Rituximab	N/A	No dose adjustment needed
Vincristine	N/A	No dose adjustment needed

\*Consider mesna in patients with pre-existing bladder disorders. Give an oral dose of 40% of the cyclophosphamide dose (rounded upwards to the nearest 400mg) at 0, 2 and 6 hours after the administration of the cyclophosphamide.

## Other

Dose reductions or interruptions in therapy are not necessary for those toxicities that are considered unlikely to be serious or life threatening. For example, alopecia, altered taste or nail changes.

Where appropriate, if dose reductions made at cycle one are well tolerated, dose increases can be considered on subsequent cycles according to tolerability.

## Cytarabine

Cytarabine may cause conjunctivitis. The prophylactic use of corticosteroid eye drops may reduce the incidence of this ocular toxicity

## Doxorubicin

Discontinue doxorubicin if cardiac failure develops

## Rituximab

Infusion related adverse reactions have been observed in 10% of patients treated with rituximab.

Rituximab administration is associated with the onset of cytokine release syndrome. This condition is characterised by severe dyspnoea, often accompanied by bronchospasm and hypoxia, in addition to fever, chills, rigors, urticaria, and angioedema. It may be associated with some features of tumour lysis syndrome such as hyperuricaemia, hyperkalaemia, hypocalcaemia, acute renal failure, elevated lactate dehydrogenase (LDH) and can lead to

acute respiratory failure and death. This effect on the lungs may be accompanied by events such as pulmonary interstitial infiltration or oedema, visible on a chest x-ray.

Cytokine release syndrome frequently occurs within one or two hours of initiating the first infusion.

Hypersensitivity reactions, including anaphylaxis, have been reported following the intravenous administration of proteins. In contrast to cytokine release syndrome, true hypersensitivity reactions typically occur within minutes of starting the infusion. Medicinal products for the treatment of allergic reactions should be available for immediate use in the event of hypersensitivity developing during the administration of rituximab.

Use of rituximab may be associated with an increased risk of progressive multifocal leukoencephalopathy (PML). Patients must be monitored at regular intervals for any new or worsening neurological, cognitive or psychiatric symptoms that may be suggestive of PML. If PML is suspected, further dosing must be suspended until PML has been excluded. If PML is confirmed the rituximab must be permanently discontinued.

The presence of a viral upper respiratory tract infection prior to treatment may increase the risk of rituximab associated hepatotoxicity. Patients should be assessed for any cold or flu like symptoms prior to treatment.

### [Vincristine](#)

Reduce the vincristine dose to 1mg if a NCI-CTC grade 2 motor or grade 3 sensory neurological toxicity occurs. For higher toxicity grades or if toxicity increases despite dose reduction stop the vincristine.

### [Regimen](#)

#### **21 day cycle for 6 cycles**

#### **Cycle 1, 3, 5 (Maxi-CHOP plus rituximab) – this will be set as an outpatient regimen in Aria**

Consider omitting the rituximab on cycle one if the white cell count is  $25 \times 10^9/L$  or greater. Seek consultant advice.

Drug	Dose	Days	Administration
Cyclophosphamide	1200mg/m <sup>2</sup>	1	Intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes or as an intravenous bolus over 10 minutes
Doxorubicin	75mg/m <sup>2</sup>	1	Intravenous bolus over 10 minutes
Rituximab	375mg/m <sup>2</sup>	1	Intravenous infusion in 500ml sodium chloride 0.9%
Vincristine	2mg	1	Intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes
Prednisolone	100mg	1, 2, 3, 4, 5	Oral

**Cycle 2 and 4 (High dose cytarabine plus rituximab) – this will be set as an inpatient regimen in Aria**

Drug	Dose	Days	Administration
Cytarabine	3000mg/m <sup>2</sup> every 12 hours	1 and 2 (4 doses)	Intravenous infusion in 1000ml sodium chloride 0.9% over 180 minutes
Rituximab	375mg/m <sup>2</sup>	1	Intravenous infusion in 1000ml sodium chloride 0.9%

**Cycle 6 (High dose cytarabine plus rituximab day 1 and 9) – this will be set as an inpatient regimen in Aria for day 1 and 2 and as an outpatient on day 9**

Drug	Dose	Days	Administration
Cytarabine	3000mg/m <sup>2</sup> every 12 hours	1 and 2 (4 doses)	Intravenous infusion in 1000ml sodium chloride 0.9% over 180 minutes
Rituximab	375mg/m <sup>2</sup>	1 and 9	Intravenous infusion in 500ml sodium chloride 0.9%

### Dose Information

- Cyclophosphamide will be dose banded according to the national dose bands (20mg/ml)
- Cytarabine will be dose banded according to the national dose bands (100mg/ml)
- Doxorubicin will be dose banded according to the national dose bands (2mg/ml)
- The maximum lifetime cumulative dose of doxorubicin is 450mg/m<sup>2</sup>. However, prior radiotherapy to the mediastinal / pericardial area should receive a lifetime cumulative doxorubicin dose of no more than 400mg/m<sup>2</sup>
- Rituximab dose will be rounded to the nearest 100mg (up if half way)
- Vincristine will be dose banded according to the national dose bands (1mg/ml) when dose reductions are necessary
- The maximum dose of vincristine is 2mg

### Administration Information

#### Extravasation

- Cyclophosphamide – neutral
- Cytarabine - neutral
- Doxorubicin – vesicant
- Rituximab - neutral

- Vincristine - vesicant

### Other

- Prednisolone should be taken in the morning with or after food. Administration of prednisolone begins on the morning of chemotherapy.
- The rate of administration of rituximab varies. Please refer to the rituximab administration guidelines.

### Additional Therapy

- Rituximab pre-medication

30 minutes prior to rituximab

- chlorphenamine 10mg intravenous bolus
- hydrocortisone 100mg intravenous bolus (cycles 2, 4 and 6 only)
- paracetamol 1000mg oral

On the morning of treatment (cycles 3 and 5 only)

- prednisolone 100mg oral to be self administered by the patient on the morning of treatment and for four days after rituximab treatment (this is part of the chemotherapy schedule as well as rituximab pre-medication)

- Rituximab infusion reactions

- hydrocortisone 100mg intravenous bolus when required for rituximab infusion related reactions
- salbutamol 2.5mg nebule when required for rituximab related bronchospasm
- consider pethidine 25-50mg intravenous bolus for rituximab related rigors that fail to respond to corticosteroids.

- Antiemetics

15-30 minutes prior to chemotherapy

- dexamethasone 4mg twice a day for 3 days oral (cycles 2, 4 and 6 only)
- metoclopramide 10mg three times a day when required oral
- ondansetron 8mg twice a day for 3 days oral

- Allopurinol 300mg once a day for 7 days cycle 1 only

- Corticosteroid eye drops such as prednisolone 0.5% or dexamethasone 0.1% 1 drop into both eyes four times a day for 4 days with cytarabine administration

- Anti-infective prophylaxis as follows:

- aciclovir 400mg twice a day oral
- co-trimoxazole 960mg once a day on Monday, Wednesday and Friday only oral (cycles 1-5)

- pentamidine 300mg nebuliser once a month from cycle 6 only continued for 6 months after the completion of treatment or in accordance with CD4 count.
- Growth factors following each cycle continued until the neutrophil count is above  $1 \times 10^9/L$ , for example;
  - filgrastim or bioequivalent 30 million units once a day from day 8 subcutaneous
  - lenograstim or bioequivalent 33.6million units once a day from day 8 subcutaneous
- Mouthcare for the prophylaxis or treatment of mucositis
  - nystatin mouthwash 1ml four times a day
  - sodium chloride 0.9% mouthwash 10ml four times a day
- Gastric protection with a proton pump inhibitor or a  $H_2$  antagonist may be considered in patients considered at high risk of GI ulceration or bleed.
- In female patients consider norethisterone 5mg three times a day oral to delay menstruation

#### Additional Information

- The National Patient Safety Agency report NPSA/2008/RRR04 must be followed in relation to intravenous administration of vinca alkaloids.

#### Coding

- Procurement – X71.5 (Maxi-CHOP & Rituximab-Cytarabine)
- Delivery – X72.2 (Maxi-CHOP)

#### References

1. Geisler C, Kolstad A, Laurell A et al. Long term progression-free survival of mantle cell lymphoma after intensive front line immunochemotherapy with in vivo purged stem cell rescue: a nonrandomised phase 2 multicentre study by the Nordic Lymphoma Group. Blood 2008; 112: 2687-2693.



## REGIMEN SUMMARY

Nordic (3000)-Cyclophosphamide-Cytarabine-Doxorubicin-Prednisolone-Rituximab-Vincristine

Cycles 1, 3 and 5 will be given in the outpatient setting and contain all the supportive medicines. Other than those listed below, supportive medication for this regimen will not appear in Aria as prescribed agents for cycles 2, 4 and 6. The administration instructions for each warning describes the agents which must be prescribed on the in-patient chart or general electronic prescribing system

### Cycle 1 Day 1 (Maxi-CHOP plus rituximab – outpatient schedule)

1. Prednisolone 100mg oral
2. Chlorphenamine 10mg intravenous bolus
3. Paracetamol 1000mg oral
4. Rituximab 375mg/m<sup>2</sup> intravenous infusion in 500ml sodium chloride 0.9% as per the rituximab administration guidelines  
Administration Instructions  
The rate of administration varies. Please refer to the rituximab administration guidelines.
5. Ondansetron 8mg oral or intravenous
6. Doxorubicin 75mg/m<sup>2</sup> intravenous bolus over 10 minutes
7. Vincristine 2mg intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes
8. Cyclophosphamide 1200mg/m<sup>2</sup> intravenous bolus over 10 minutes  
Administration Instructions  
This may be administered as an intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes
9. Hydrocortisone 100mg intravenous bolus once only when required for the relief of rituximab infusion related reactions
10. Salbutamol 2.5mg nebule once only when required for the relief of rituximab related bronchospasm

### Take home medicines

11. Prednisolone 100mg once a day for 4 days starting on day two of the cycle
12. Metoclopramide 10mg three times a day when required for the relief of nausea  
Administration Instructions  
Please supply 28 tablets or nearest equivalent pack size
13. Ondansetron 8mg twice a day for 3 days starting on the evening of day one of the cycle oral
14. Aciclovir 400mg twice a day for 21 days oral
15. Co-trimoxazole 960mg once a day on Mondays, Wednesdays and Fridays only for 21 days oral

## 16. Growth Factors

Growth factor as per local formulary choice:

- filgrastim or bioequivalent 30 million units once a day for 7 days starting on day 8 of the cycle subcutaneous
- lenograstim or bioequivalent 33.6 million units once a day for 7 days starting on day 8 of the cycle subcutaneous

## 17. Allopurinol 300mg once a day oral for 7 days oral

## Cycle 2 Day 1 (high dose cytarabine + rituximab – inpatient schedule)

## 18. Warning – Check supportive medication prescribed

Administration Instructions

1. Dexamethasone 4mg twice a day on days 1 to 3 oral or intravenous
2. Metoclopramide 10mg three times a day when required oral or intravenous
3. Ondansetron 8mg twice a day on days 1 to 3 oral or intravenous
4. Aciclovir 400mg twice a day oral
5. Co-trimoxazole 960mg once a day on Mondays, Wednesdays and Fridays only oral
6. Growth factors following each cycle continued until the neutrophil count is above  $1 \times 10^9/L$ , for example;
  - filgrastim or bioequivalent 30 million units once a day from day 8 subcutaneous
  - lenograstim or bioequivalent 33.6million units once a day from day 8 subcutaneous
7. Prednisolone 0.5% or dexamethasone 0.1% eye drops one drop into both eyes four times a day on days 1, 2, 3, 4
8. Prednisolone 100mg oral (take home supply) to be taken on the morning of the next cycle of treatment
9. Consider gastric protection
10. Consider mouthwashes
11. Consider norethisterone 5mg three times a day in menstruating women
12. Consider pethidine 25-50mg intravenous bolus for rituximab related rigors that fail to respond to corticosteroids.

## 19. Chlorphenamine 10mg intravenous bolus

## 20. Hydrocortisone 100mg intravenous bolus

## 21. Paracetamol 1000mg oral

## 22. Rituximab 375mg/m<sup>2</sup> intravenous infusion in 500ml sodium chloride 0.9% as per the rituximab administration guidelines

Administration Instructions

The rate of administration varies. Please refer to the rituximab administration guidelines.

## 23. Hydrocortisone 100mg intravenous bolus once only when required for the relief of rituximab infusion related reactions

## 24. Salbutamol 2.5mg nebule once only when required for the relief of rituximab related bronchospasm

## 25. Warning – Cytarabine is TWICE a day (12 hours apart)

Administration Instructions

Cytarabine doses are to be given at 12 hour intervals

## 26. Cytarabine 3000mg/m<sup>2</sup> intravenous infusion in 1000ml sodium chloride 0.9% over 180 minutes twice a day

Administration Instructions

Cytarabine doses are to be given at 12 hour intervals

## Cycle 2 Day 2

### 27. Warning – Check supportive medication prescribed

#### Administration Instructions

1. Dexamethasone 4mg twice a day on days 1, 2 and 3 oral or intravenous
2. Metoclopramide 10mg three times a day when required oral or intravenous
3. Ondansetron 8mg twice a day on days 1, 2 and 3 oral or intravenous
4. Aciclovir 400mg twice a day oral
5. Co-trimoxazole 960mg once a day on Mondays, Wednesdays and Fridays only oral
6. Growth factors following each cycle continued until the neutrophil count is above  $1 \times 10^9/L$ , for example;
  - filgrastim or bioequivalent 30 million units once a day from day 8 subcutaneous
  - lenograstim or bioequivalent 33.6million units once a day from day 8 subcutaneous
7. Prednisolone 0.5% or dexamethasone 0.1% eye drops one drop into both eyes four times a day on days 1, 2, 3 and 4
8. Prednisolone 100mg oral (take home supply) to be taken on the morning of the next cycle of treatment
9. Consider gastric protection
10. Consider mouthwashes
11. Consider norethisterone 5mg three times a day in menstruating women
12. Consider pethidine 25-50mg intravenous bolus for rituximab related rigors that fail to respond to corticosteroids.

### 28. Warning – Cytarabine is TWICE a day (12 hours apart)

#### Administration Instructions

Cytarabine doses are to be given at 12 hour intervals

### 29. Cytarabine $3000\text{mg}/\text{m}^2$ intravenous infusion in 1000ml sodium chloride 0.9% over 180 minutes twice a day

#### Administration Instructions

Cytarabine doses are to be given at 12 hour intervals

## Cycle 3 Day 1 (Maxi-CHOP plus rituximab)

### 30. Warning – Check patient has taken prednisolone dose

#### Administration instructions

Please check the patient has taken prednisolone 100mg oral on the morning of rituximab administration. On occasions where individuals attend for treatment and have forgotten to take the prednisolone dose please administer prednisolone 100mg oral 30 minutes prior to rituximab administration.

### 31. Chlorphenamine 10mg intravenous bolus

### 32. Paracetamol 1000mg oral

### 33. Rituximab $375\text{mg}/\text{m}^2$ intravenous infusion in 500ml sodium chloride 0.9% as per the rituximab administration guidelines

#### Administration Instructions

The rate of administration varies. Please refer to the rituximab administration guidelines.

### 34. Ondansetron 8mg oral or intravenous injection

### 35. Doxorubicin $75\text{mg}/\text{m}^2$ intravenous bolus over 10 minutes

### 36. Vincristine 2mg intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes

### 37. Cyclophosphamide $1200\text{mg}/\text{m}^2$ intravenous bolus over 10 minutes

#### Administration Instructions

This may be administered as an intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes

### 38. Hydrocortisone 100mg intravenous bolus once only when required for the relief of rituximab infusion related reactions

### 39. Salbutamol 2.5mg nebule once only when required for the relief of rituximab related bronchospasm

## Take home medicines

40. Prednisolone 100mg once a day for 4 days starting on day two of the cycle
41. Metoclopramide 10mg three times a day when required for the relief of nausea oral
42. Ondansetron 8mg twice a day for 3 days starting on the evening of day one of the cycle
43. Aciclovir 400mg twice a day for 21 days oral
44. Co-trimoxazole 960mg once a day on Mondays, Wednesdays and Fridays only for 21 days oral
45. Growth Factors
  - Growth factor as per local formulary choice:
    - filgrastim or bioequivalent 30 million units once a day for 7 days starting on day 8 of the cycle subcutaneous
    - lenograstim or bioequivalent 33.6 million units once a day for 7 days starting on day 8 of the cycle subcutaneous

## Cycle 4 Day 1 (high dose cytarabine plus rituximab)

### 46. Warning – Check supportive medication prescribed

#### Administration Instructions

1. Dexamethasone 4mg twice a day on days 1, 2 and 3 oral or intravenous
2. Metoclopramide 10mg three times a day when required oral or intravenous
3. Ondansetron 8mg twice a day on days 1, 2 and 3 oral or intravenous
4. Aciclovir 400mg twice a day oral
5. Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday only oral
6. Growth factors following each cycle continued until the neutrophil count is above  $1 \times 10^9/L$ , for example;
  - filgrastim or bioequivalent 30 million units once a day from day 8 subcutaneous
  - lenograstim or bioequivalent 33.6million units once a day from day 8 subcutaneous
7. Prednisolone 0.5% or dexamethasone 0.1% eye drops one drop into each eye four times a day, days 1, 2, 3 and 4
8. Prednisolone 100mg oral (take home supply) to be taken on the morning of the next cycle of treatment
9. Consider gastric protection
10. Consider mouthwashes
11. Consider norethisterone 5mg three times a day in menstruating women
12. Consider pethidine 25-50mg intravenous bolus for rituximab related rigors that fail to respond to corticosteroids.

### 47. Chlorphenamine 10mg intravenous bolus

### 48. Hydrocortisone 100mg intravenous bolus

### 49. Paracetamol 1000mg oral

### 50. Rituximab $375\text{mg}/\text{m}^2$ intravenous infusion in 500ml sodium chloride 0.9% as per the rituximab administration guidelines

#### Administration Instructions

The rate of administration varies. Please refer to the rituximab administration guidelines.

### 51. Hydrocortisone 100mg intravenous bolus once only when required for the relief of rituximab infusion related reactions

### 52. Salbutamol 2.5mg nebule once only when required for the relief of rituximab related bronchospasm

### 53. Warning – Cytarabine is TWICE a day (12 hours apart)

#### Administration Instructions

Cytarabine doses are to be given at 12 hour intervals

### 54. Cytarabine $3000\text{mg}/\text{m}^2$ intravenous infusion in 1000ml sodium chloride 0.9% over 180 minutes twice a day

Administration Instructions  
Cytarabine doses are to be given at 12 hour intervals

## Cycle 4 Day 2

### 55. Warning – Check supportive medication prescribed

Administration Instructions

1. Dexamethasone 4mg twice a day on days 1, 2 and 3 oral or intravenous
2. Metoclopramide 10mg three times a day when required oral or intravenous
3. Ondansetron 8mg twice a day on days 1, 2 and 3 oral or intravenous
4. Aciclovir 400mg twice a day oral
5. Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday only oral
6. Growth factors following each cycle continued until the neutrophil count is above  $1 \times 10^9/L$ , for example;
  - filgrastim or bioequivalent 30 million units once a day from day 8 subcutaneous
  - lenograstim or bioequivalent 33.6million units once a day from day 8 subcutaneous
7. Prednisolone 0.5% or dexamethasone 0.1% eye drops one drop into both eyes four times a day on days 1, 2, 3 and 4
8. Prednisolone 100mg oral (take home supply) to be taken on the morning of the next cycle of treatment
9. Consider gastric protection
10. Consider mouthwashes
11. Consider norethisterone 5mg three times a day in menstruating women
12. Consider pethidine 25-50mg intravenous bolus for rituximab related rigors that fail to respond to corticosteroids.

### 56. Warning – Cytarabine is TWICE a day (12 hours apart)

Administration Instructions

Cytarabine doses are to be given at 12 hour intervals

### 57. Cytarabine $3000\text{mg}/\text{m}^2$ intravenous infusion in 1000ml sodium chloride 0.9% over 180 minutes twice a day

Administration Instructions

Cytarabine doses are to be given at 12 hour intervals

## Cycle 5 Day 1

### 58. Warning – Check patient has taken prednisolone dose

Administration instructions

Please check the patient has taken prednisolone 100mg oral on the morning of rituximab administration. On occasions where individuals attend for treatment and have forgotten to take the prednisolone dose please administer prednisolone 100mg oral 30 minutes prior to rituximab administration.

### 59. Chlorphenamine 10mg intravenous bolus

### 60. Paracetamol 1000mg oral

### 61. Rituximab $375\text{mg}/\text{m}^2$ intravenous infusion in 500ml sodium chloride 0.9% as per the rituximab administration guidelines

Administration Guidelines

The rate of administration varies. Please refer to the rituximab administration guidelines.

### 62. Ondansetron 8mg oral or intravenous injection

### 63. Doxorubicin $75\text{mg}/\text{m}^2$ intravenous bolus over 10 minutes

### 64. Vincristine 2mg intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes

### 65. Cyclophosphamide $1200\text{mg}/\text{m}^2$ intravenous bolus over 10 minutes

Administration Instructions

This may be administered as an intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes

### 66. Hydrocortisone 100mg intravenous bolus once only when required for the relief of rituximab infusion related reactions

67. Salbutamol 2.5mg nebule once only when required for the relief of rituximab related bronchospasm

### Take home medicines

68. Prednisolone 100mg once a day for 4 days starting on day two of treatment

69. Metoclopramide 10mg three times a day when required

70. Ondansetron 8mg twice a day for 3 days starting on the evening of day one of treatment

71. Aciclovir 400mg twice a day for 21 days oral

72. Co-trimoxazole 960mg once a day on Mondays, Wednesdays and Fridays only for 21 days oral

### 73. Growth Factors

Growth factor as per local formulary choice:

- filgrastim or bioequivalent 30 million units once a day for 7 days starting on day 8 of the cycle subcutaneous
- lenograstim or bioequivalent 33.6 million units once a day for 7 days starting on day 8 of the cycle subcutaneous

### Cycle 6 Day 1 (high dose cytarabine plus rituximab day 1 and 9)

#### 74. Warning – Check supportive medication prescribed

Administration Instructions

1. Dexamethasone 4mg twice a day, days 1, 2 and 3 oral
2. Metoclopramide 10mg three times a day when required oral or intravenous
3. Ondansetron 8mg twice a day on days 1, 2 and 3 oral or intravenous
4. Aciclovir 400mg twice a day oral
5. Pentamidine 300mg nebuliser once a month
6. Growth factors following each cycle continued until the neutrophil count is above  $1 \times 10^9/L$ , for example;
  - filgrastim or bioequivalent 30 million units once a day from day 8 subcutaneous
  - lenograstim or bioequivalent 33.6million units once a day from day 8 subcutaneous
7. Prednisolone 0.5% or dexamethasone 0.1% eye drops one drop into both eyes four times a day on days 1, 2, 3 and 4
8. Consider gastric protection
9. Consider mouthwashes
10. Consider norethisterone 5mg three times a day in menstruating women
11. Consider pethidine 25-50mg intravenous bolus for rituximab related rigors that fail to respond to corticosteroids.

75. Chlorphenamine 10mg intravenous bolus

76. Hydrocortisone 100mg intravenous bolus

77. Paracetamol 1000mg oral

78. Rituximab 375mg/m<sup>2</sup> intravenous infusion in 500ml sodium chloride 0.9% as per the rituximab administration guidelines

Administration Guidelines

The rate of administration varies. Please refer to the rituximab administration guidelines.

79. Hydrocortisone 100mg intravenous bolus once only when required for the relief of rituximab infusion related reactions

80. Salbutamol 2.5mg nebule once only when required for the relief of rituximab related bronchospasm

**81. Warning – Cytarabine is TWICE a day (12 hours apart)**

Administration Instructions

Cytarabine doses are to be given at 12 hour intervals

**82. Cytarabine 3000mg/m<sup>2</sup> intravenous infusion in 1000ml sodium chloride 0.9% over 180 minutes twice a day**

Administration Instructions

Cytarabine doses are to be given at 12 hour intervals

**Cycle 6 Day 2**

**83. Warning – Check supportive medication prescribed**

Administration Instructions

1. Dexamethasone 4mg twice a day on days 1, 2 and 3 oral or intravenous
2. Metoclopramide 10mg three times a day when required oral or intravenous
3. Ondansetron 8mg twice a day on days 1, 2 and 3 oral or intravenous
4. Aciclovir 400mg twice a day oral
5. Pentamidine 300mg nebuliser once a month
6. Growth factors following each cycle continued until the neutrophil count is above  $1 \times 10^9/L$ , for example;
  - filgrastim or bioequivalent 30 million units once a day from day 8 subcutaneous
  - lenograstim or bioequivalent 33.6million units once a day from day 8 subcutaneous
7. Prednisolone 0.5% or dexamethasone 0.1% eye drops one drop into both eyes four times a day on days 1, 2, 3 and 4
8. Consider gastric protection
9. Consider mouthwashes
10. Consider norethisterone 5mg three times a day in menstruating women
11. Consider pethidine 25-50mg intravenous bolus for rituximab related rigors that fail to respond to corticosteroids.

**84. Warning – Cytarabine is TWICE a day (12 hours apart)**

Administration Instructions

Cytarabine doses are to be given at 12 hour intervals

**85. Cytarabine 3000mg/m<sup>2</sup> intravenous infusion in 1000ml sodium chloride 0.9% over 180 minutes twice a day**

Administration Instructions

Cytarabine doses are to be given at 12 hour intervals

**Cycle 6 Day 9**

**86. Chlorphenamine 10mg intravenous bolus**

**87. Hydrocortisone 100mg intravenous bolus**

**88. Paracetamol 1000mg oral**

**89. Rituximab 375mg/m<sup>2</sup> intravenous infusion in 500ml sodium chloride 0.9% as per the rituximab administration guidelines**

Administration Guidelines

The rate of administration varies. Please refer to the rituximab administration guidelines.

**90. Hydrocortisone 100mg intravenous bolus once only when required for the relief of rituximab infusion related reactions**

**91. Salbutamol 2.5mg nebule once only when required for the relief of rituximab related bronchospasm**

## DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.1	November 2018	Growth Factors added to supportive medication throughout. OPCS codes updated	Rebecca Wills Pharmacist  Dr Deborah Wright Pharmacist	Prof. Peter Johnson Consultant Haematologist
1	January 2018	None	Rebecca Wills Pharmacist  Dr Deborah Wright Pharmacist	Dr Rob Lown 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 Hospital 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 which occur as a result of following these guidelines.