Chemotherapy Protocol

LYMPHOMA

CYTARABINE-ETOPOSIDE-IFOSFAMIDE-RITUXIMAB

(RIVAC)

66 years and above

Inpatient Regimen

There are multiple versions of this protocol in use. The choice of protocol depends on the age of the patient and whether there is CNS disease present at diagnosis. Please ensure you have the correct version and prescribe the correct number of cycles.

Regimen

Lymphoma – InP-RIVAC(66)-Cytarabine-Etoposide-Ifosfamide-Rituximab

Indication

- Non Hodgkin’s Lymphoma (Burkitts lymphoma or diffuse large B cell lymphoma) that is CD20 positive alternating with RCODOX-M in patient 66 years and above and / or with a poor performance status
- Radical or curative intent

Toxicity

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adverse Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytarabine</td>
<td>CNS toxicity, conjunctivitis, flu-like syndrome, pulmonary toxicity, gastro-intestinal toxicity</td>
</tr>
<tr>
<td>Etoposide</td>
<td>Hypotension on rapid infusion, hyperbilirubinaemia</td>
</tr>
<tr>
<td>Ifosfamide</td>
<td>Haemorrhagic cystitis, encephalopathy, nephrotoxicity</td>
</tr>
<tr>
<td>Rituximab</td>
<td>Severe cytokine release syndrome, increased incidence of infective complications, progressive multifocal leukoencephalopathy</td>
</tr>
</tbody>
</table>

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

Monitoring

Drugs

- FBC, LFTs (including albumin) and U&Es prior to day one of treatment
- EDTA or calculated creatinine clearance prior to each cycle
- Urine dip test for proteinuria and haematuria every four hours the day of and the day after ifosfamide administration. The patient should be instructed to report any signs
or symptoms of cystitis.

- Fluid balance monitoring every four hours the day of and the day after ifosfamide administration. Urine output should be maintained above 100ml/hour
- Hepatitis B screen prior to rituximab

**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.

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 the minimum criteria, described in the table below, are reached.

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Eligible Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutrophil</td>
<td>equal to or more than 1x10⁹/L</td>
</tr>
<tr>
<td>Platelets</td>
<td>equal to or more than 75x10⁹/L</td>
</tr>
</tbody>
</table>

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

**Hepatic Impairment**

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

<table>
<thead>
<tr>
<th>Drug</th>
<th>Bilirubin µmol/L</th>
<th>AST/ALT units</th>
<th>Dose (% of original dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytarabine</td>
<td>more than 34</td>
<td></td>
<td>50% Escalate doses on subsequent cycles in the absence of toxicity</td>
</tr>
<tr>
<td>Etoposide</td>
<td>30-51 or 60-180</td>
<td>or 60-180</td>
<td>Consider dose reducing to 50%</td>
</tr>
<tr>
<td></td>
<td>more than 51</td>
<td>or more than 180</td>
<td>Clinical decision</td>
</tr>
<tr>
<td>Ifosfamide</td>
<td>more than 20 or ALP more than 2.5xULN</td>
<td></td>
<td>Not recommended</td>
</tr>
<tr>
<td>Rituximab</td>
<td>N/A</td>
<td>N/A</td>
<td>No dose adjustments required</td>
</tr>
</tbody>
</table>
### Renal Impairment

<table>
<thead>
<tr>
<th>Drug</th>
<th>Creatinine Clearance (ml/min)</th>
<th>Dose (% of original dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytarabine</td>
<td>more than 60</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>46-60</td>
<td>60%</td>
</tr>
<tr>
<td></td>
<td>31-45</td>
<td>50%</td>
</tr>
<tr>
<td></td>
<td>less than 30</td>
<td>omit</td>
</tr>
<tr>
<td>Etoposide</td>
<td>more than 50</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>15-50</td>
<td>75%</td>
</tr>
<tr>
<td></td>
<td>less than 15</td>
<td>50%</td>
</tr>
<tr>
<td>Ifosfamide</td>
<td>more than 60</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>40-59</td>
<td>70%</td>
</tr>
<tr>
<td></td>
<td>less than 40</td>
<td>Clinical decision</td>
</tr>
<tr>
<td>Rituximab</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

#### 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.

**Cytarabine**

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

**Etoposide**

Where significant reductions in albumin levels occur consider reducing the dose of etoposide.

**Ifosfamide**

In the case of a NCI-CTC grade 1 neurological toxicity, the dose of ifosfamide may be reduced for the next cycle. If a NCI-CTC grade 2 neurological toxicity appears or neurological toxicity worsens despite dose reduction, the ifosfamide should be stopped.

Risk factors for CNS toxicity include a low albumin, renal impairment, prior administration of cisplatin, poor performance status, CNS tumour, bulky pelvic disease, concomitant psychotropic drugs and younger age. Methylene blue 50mg four times a day intravenous infusion in 100ml sodium chloride 0.9% can be used to prevent or treat ifosfamide induced encephalopathy.

**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 maybe 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.

**Regimen**

2 cycles in high risk disease alternating with 2 cycles of R-CODOX-M.

The order of administration is R-CODOX-M, R-IVAC, R-CODOX-M, R-IVAC. Two doses of rituximab should be given on days 21 and 42 after the end of the last R-IVAC to make 8 doses of rituximab in total.

1 cycle will be set in Aria

The next cycle begins on the day that the unsupported neutrophil count is more than $1\times10^9/L$ and the unsupported platelet count is more than $75\times10^9/L$. 
<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Days</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytarabine</td>
<td>1000mg/m²</td>
<td>1 and 2 (4 doses)</td>
<td>Intravenous infusion in 1000ml sodium chloride 0.9% over 180 minutes</td>
</tr>
<tr>
<td>Etoposide</td>
<td>60mg/m²</td>
<td>1,2,3,4,5</td>
<td>Intravenous infusion in 500ml sodium chloride 0.9% over 60 minutes</td>
</tr>
<tr>
<td>Mesna</td>
<td>200mg/m²</td>
<td>1,2,3,4,5</td>
<td>Intravenous infusion in sodium chloride 0.9% 100ml over 15 minutes</td>
</tr>
<tr>
<td>Ifosfamide</td>
<td>1000mg/m²</td>
<td>1,2,3,4,5</td>
<td>Intravenous infusion in sodium chloride 0.9% 1000ml over 60 minutes (the ifosfamide and mesna are mixed in the same bag)</td>
</tr>
<tr>
<td>Mesna</td>
<td>1000mg/m²</td>
<td>1,2,3,4,5</td>
<td>Intravenous infusion in sodium chloride 0.9% 1000ml over 12 hours</td>
</tr>
<tr>
<td>Mesna</td>
<td>600mg/m²</td>
<td>1,2,3,4,5</td>
<td>Intravenous infusion in sodium chloride 0.9% 1000ml over 12 hours</td>
</tr>
<tr>
<td>Rituximab</td>
<td>375mg/m²</td>
<td>1</td>
<td>Intravenous infusion in 500ml sodium chloride 0.9% as per local guidelines</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug (intrathecal)</th>
<th>Dose</th>
<th>Days</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methotrexate</td>
<td>12.5mg</td>
<td>5</td>
<td>Intrathecal</td>
</tr>
</tbody>
</table>

An intensified intrathecal treatment is required for patients with CNS disease at diagnosis. This is given for the first cycle of R- CODOX-M and the first cycle of R-IVAC.

For R-IVAC this is as follows:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Days</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytarabine</td>
<td>70mg</td>
<td>7, 9</td>
<td>Intrathecal</td>
</tr>
</tbody>
</table>

Intrathecal doses that fall on a weekend should be deferred until the next working day

**Dose Information**

- Cytarabine will be dose banded according to the nationally agreed bands (100mg/ml)
- Etoposide will be dose banded according to the nationally agreed bands (20mg/ml)
- Ifosfamide will be dose banded according to the nationally agreed bands (80mg/ml)
- Mesna will be dose banded according to the nationally agreed bands (100mg/ml)
- Rituximab dose will be rounded to the nearest 100mg (up if halfway)
Administration Information

Extravasation

- Cytarabine - neutral
- Etoposide – irritant
- Ifosfamide – neutral
- Mesna - neutral
- Rituximab - neutral

Other

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

Additional Therapy

This is an inpatient regimen please ensure all supportive and take home medication are prescribed on the inpatient chart or general electronic prescribing system.

- Rituximab premedication
  
  30 minutes prior to rituximab
  - chlorphenamine 10mg intravenous bolus
  - hydrocortisone 100mg intravenous bolus (may be omitted if the patient is already taking corticosteroids)
  - paracetamol 1000mg oral

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

- Antiemetics

  Starting 15-30 minutes prior to chemotherapy
  - dexamethasone 4mg twice a day for 7 days oral or intravenous bolus
  - metoclopramide 10mg three times a day for 7 days then when required oral or intravenous bolus
  - ondansetron 8mg twice a day for 7 days oral or intravenous bolus

- Growth factors continued until the neutrophil count is above 1x10^9/L. For example:
- filgrastim or bioequivalent 30 million units once a day from day 7 subcutaneous
- lenograstim or bioequivalent 33.6 million units once a day from day 7 subcutaneous
- pegfilgrastim or bioequivalent 6mg once only on day 7 subcutaneous

- Folinic acid 15mg four times a day for one day starting 24 hours after the administration of the intrathecal methotrexate dose
- Corticosteroid eye drops such as prednisolone 0.5% or dexamethasone 0.1% one drop into both eyes four times a day for 4 days
- Mouthcare for the prophylaxis or treatment of mucositis in accordance with CSCCN guidelines
- 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
- Anti-infective prophylaxis as follows:
  - aciclovir 400mg twice a day oral
  - pentamidine 300mg nebul once a month
  - fluconazole 50mg once a day oral

Additional Information

- HSC 2008/001: Updated national guidance on the safe administration of intrathecal chemotherapy must be followed.

Coding

- Procurement – X71.5
- Delivery – Not Required

References
REGIMEN SUMMARY

InP-RIVAC (65)-Cytarabine-Etoposide-Ipofamide-Rituximab

Other than those listed below, supportive medication for this regimen will not appear in Aria as prescribed agents. The administration instructions for each warning describes the agents which must be prescribed on the in-patient chart or general electronic prescribing system.

Day 1

1. Warning – Check supportive medication prescribed
   Administration instructions
   1. Dexamethasone 4mg twice a day, days 1 to 7 oral or intravenous
   2. Metoclopramide 10mg three times a day, days 1 to 7 days then as required oral or intravenous
   3. Ondansetron 8mg twice a day, days 1 to 7 oral or intravenous
   4. Prednisolone 0.5% or dexamethasone 0.1% eye drops once drop into both eyes four times a day, days 1 to 4
   5. Growth factor continued until the neutrophil count is above 1x10^9/L
      - filgrastim or bioequivalent 30 million units once a day from day 7 subcutaneous
      - lenograstim or bioequivalent 33.6 million units once a day from day 7 subcutaneous
      - pegfilgrastim or bioequivalent 6mg once only on day 7 subcutaneous
   6. Folinic acid 15mg four times a day for one day starting 24 hours after the administration of intrathecal methotrexate (normally day 6)
   7. Aciclovir 400mg oral twice a day
   8. Pentamidine 300mg nebul once a month
   9. Fluconazole 50mg once a day
   10. Consider gastric protection
   11. Consider mouthwashes
   12. Consider norethisterone for menstruating women
   13. Consider pethidine 25-50mg intravenous bolus for rituximab related rigors unresponsive to corticosteroids
   2. Chlorphenamine 10mg intravenous injection
   3. Hydrocortisone 100mg intravenous injection
      Administration Instructions
      1. Do not administer if corticosteroids have been given as part of the antiemetic or chemotherapy regimen
   4. Paracetamol 1000mg oral
   5. Rituximab 375mg/m^2 intravenous infusion in 500ml sodium chloride 0.9% (administer according to local guidelines)
   6. Hydrocortisone 100mg intravenous bolus once only when required for the relief of rituximab infusion related reactions
   7. Salbutamol 2.5mg nebul when required for rituximab related bronchospasm
   8. Warning – Cytarabine is TWICE a day
      Administration Instructions
      The cytarabine is to be given twice a day at twelve hourly intervals.
   9. Cytarabine 1000mg/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
   10. Etoposide 60mg/m^2 intravenous infusion in 500ml sodium chloride 0.9% over 60 minutes
   11. Mesna 200mg/m^2 intravenous infusion in 100ml sodium chloride 0.9% over 15 minutes
12. Warning – Ifosfamide and Mesna Combination Bag  
Administration Instructions  
The ifosfamide is mixed in the same infusion bag as the mesna.

13. Ifosfamide 1000mg/m^2 and mesna 1000mg/m^2 intravenous infusion in 1000ml sodium chloride 0.9% over 60 minutes  
Administration Instructions  
The ifosfamide and mesna are mixed in the same infusion bag of 1000ml sodium chloride 0.9%.

14. Mesna 600mg/m^2 intravenous infusion in 1000ml sodium chloride 0.9% over 12 hours  
Administration instructions  
Starting immediately after the ifosfamide/mesna

Day 2

15. Warning – Check supportive medication prescribed  
Administration instructions  
1. Dexamethasone 4mg twice a day, days 1 to 7 oral or intravenous  
2. Metoclopramide 10mg three times a day, days 1 to 7 days then as required oral or intravenous  
3. Ondansetron 0.5% or dexamethasone 0.1% eye drops one drop into both eyes four times a day, days 1 to 4  
5. Growth factor continued until the neutrophil count is above 1x10^9/L  
   - filgrastim or bioequivalent 30 million units once a day from day 7 subcutaneous  
   - lenograstim or bioequivalent 33.6million units once a day from day 7 subcutaneous  
   - pegfilgrastim or bioequivalent 8mg once only on day 7 subcutaneous  
6. Folinic acid 15mg four times a day starting 24 hours after the administration of intrathecal methotrexate (normally day 6)  
7. Aciclovir 400mg oral twice a day  
8. Pentamidine 300mg nebul once a month  
9. Fluconazole 50mg once a day  
10. Consider gastric protection  
11. Consider mouthwashes  
12. Consider norethisterone for menstruating women  
13. Consider pethidine 25-50mg intravenous bolus for rituximab related rigors unresponsive to corticosteroids

16. Warning – Cytarabine is TWICE a day  
Administration Instructions  
The cytarabine is to be given twice a day at twelve hourly intervals.

17. Cytarabine 1000mg/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

18. Etoposide 60mg/m^2 intravenous infusion in 500ml sodium chloride 0.9% over 60 minutes

19. Mesna 200mg/m^2 intravenous infusion in 100ml sodium chloride 0.9% over 15 minutes

20. Warning – Ifosfamide and Mesna Combination Bag  
Administration Instructions  
The ifosfamide is mixed in the same infusion bag as the mesna.

21. Ifosfamide 1000mg/m^2 and mesna 1000mg/m^2 intravenous infusion in 1000ml sodium chloride 0.9% over 60 minutes  
Administration Instructions  
The ifosfamide and mesna are mixed in the same infusion bag of 1000ml sodium chloride 0.9%.

22. Mesna 600mg/m^2 intravenous infusion in 1000ml sodium chloride 0.9% over 12 hours  
Administration instructions  
Starting immediately after the ifosfamide/mesna
Day 3, 4

23. Warning – Check supportive medication prescribed
Administration instructions
1. Dexamethasone 4mg twice a day, days 1 to 7 oral or intravenous
2. Metoclopramide 10mg three times a day, days 1 to 7 then as required oral or intravenous
3. Ondanestron 8mg twice a day, days 1 to 7 oral or intravenous
4. Prednisolone 0.5% or dexamethasone 0.1% eye drops one drop into both eyes four times a day, days 1 to 4
5. Growth factor continued until the neutrophil count is above 1x10^9/L
   - filgrastim or bioequivalent 30 million units once a day from day 7 subcutaneous
   - lenograstim or bioequivalent 33.6 million units once a day from day 7 subcutaneous
   - pegfilgrastim or bioequivalent 6mg once only on day 7 subcutaneous
6. Folinic acid 15mg four times a day for one day starting 24 hours after the administration of intrathecal methotrexate (normally day 6)
7. Aciclovir 400mg oral twice a day
8. Pentamidine 300mg nebulé once a month
9. Fluconazole 50mg once a day
10. Consider gastric protection
11. Consider mouthwashes
12. Consider norethisterone for menstruating women
13. Consider pethidine 25-50mg intravenous bolus for rituximab related rigors unresponsive to corticosteroids

24. Etoposide 60mg/m^2 intravenous infusion in 500ml sodium chloride 0.9% over 60 minutes

25. Mesna 200mg/m^2 intravenous infusion in 100ml sodium chloride 0.9% over 15 minutes

26. Warning – Ifosfamide and Mesna Combination Bag
Administration Instructions
The ifosfamide is mixed in the same infusion bag as the mesna.

27. Ifosfamide 1000mg/m^2 and mesna 1000mg/m^2 intravenous infusion in 1000ml sodium chloride 0.9% over 60 minutes
Administration Instructions
The ifosfamide and mesna are mixed in the same infusion bag of 1000ml sodium chloride 0.9%

28. Mesna 600mg/m^2 intravenous infusion in 1000ml sodium chloride 0.9% over 12 hours
Administration instructions
1. Starting immediately after the ifosfamide/mesna

Day 5

29. Warning – Check supportive medication prescribed
Administration instructions
1. Dexamethasone 4mg twice a day, days 1 to 7 oral or intravenous
2. Metoclopramide 10mg three times a day, days 1 to 7 then as required oral or intravenous
3. Ondanestron 8mg twice a day, days 1 to 7 oral or intravenous
4. Prednisolone 0.5% or dexamethasone 0.1% eye drops one drop into both eyes four times a day, days 1 to 4
5. Growth factor continued until the neutrophil count is above 1x10^9/L
   - filgrastim or bioequivalent 30 million units once a day from day 7 subcutaneous
   - lenograstim or bioequivalent 33.6 million units once a day from day 7 subcutaneous
   - pegfilgrastim or bioequivalent 6mg once only on day 7 subcutaneous
6. Folinic acid 15mg four times a day for one day starting 24 hours after the administration of intrathecal methotrexate (normally day 6)
7. Aciclovir 400mg oral twice a day
8. Pentamidine 300mg nebulé once a month
9. Fluconazole 50mg once a day
10. Consider gastric protection
11. Consider mouthwashes
12. Consider norethisterone for menstruating women
13. Consider pethidine 25-50mg intravenous bolus for rituximab related rigors unresponsive to corticosteroids

30. Etoposide 60mg/m^2 intravenous infusion in 500ml sodium chloride 0.9% over 60 minutes

31. Mesna 200mg/m^2 intravenous infusion in 100ml sodium chloride 0.9% over 15 minutes
32. Warning – Ifosfamide and Mesna Combination Bag
   Administration Instructions
   The ifosfamide is mixed in the same infusion bag as the mesna.

33. Ifosfamide 1000mg/m\(^2\) and mesna 1000mg/m\(^2\) intravenous infusion in 1000ml sodium chloride 0.9% over 60 minutes
   Administration Instructions
   The ifosfamide and mesna are mixed in the same infusion bag of 1000ml sodium chloride 0.9%

34. Mesna 600mg/m\(^2\) intravenous infusion in 1000ml sodium chloride 0.9% over 12 hours
   Administration instruction
   Starting immediately after the ifosfamide/mesna. This infusion may be replaced with oral mesna at a dose of 360mg/m\(^2\), rounded upwards to the nearest 400mg capsule, at 0, 2 and 6 hours post ifosfamide infusion.

35. Warning – Intrathecal
   Administration Instructions
   Methotrexate 12.5mg intrathecal is due on day 5 of the cycle. This must be prescribed on an intrathecal chart to comply with national guidance. Ensure Folinic acid 15mg four times a day for one day starting 24 hours after the administration of intrathecal methotrexate. This warning is a reminder, not a prescription.

**Day 7 and 9**

36. Warning – CNS disease - Intrathecal cycle 1 only
   Administration Instructions
   For patients presenting with CNS disease please prescribe cytarabine 70mg intrathecal at cycle 1 only. Intrathecal chemotherapy must be prescribed on an intrathecal chart to comply with national guidance. This warning is a reminder, not a prescription.
## DOCUMENT CONTROL

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<th>Date</th>
<th>Amendment</th>
<th>Written By</th>
<th>Approved By</th>
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<td>1</td>
<td>August 2012</td>
<td>None</td>
<td>Rebecca Wills (Pharmacist)</td>
<td>Dr Alison Milne (Consultant Haematologist)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Dr Deborah Wright (Pharmacist)</td>
<td>Dr Andrew Davies (Consultant Medical Oncologist)</td>
</tr>
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