Chemotherapy Protocol

Acute lymphoblastic leukaemia (ALL)

Blinatumomab (3, 4 day)

Regimen

- ALL – Blinatumomab (3, 4 day schedule)

Indication

- Treatment of Philadelphia-chromosome-negative relapsed or refractory B-precursor acute lymphoblastic leukaemia.

Toxicity

Drug	Adverse Effect
Blinatumomab	Cytokine release syndrome, tumour lysis syndrome, neurological toxicity, elevated liver enzymes.

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 on day 1 of the cycle
- Hepatitis B, C and HIV serology prior to cycle one

Dose Modifications

- Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances.
- Consideration to discontinue blinatumomab temporarily or permanently as appropriate should be made in the case of the following severe (NCI-CTC grade 3) or life-threatening (NCI-CTC grade 4) toxicities. For example, cytokine release syndrome, tumour lysis syndrome, neurological toxicity, elevated liver enzymes and any other clinically relevant toxicities.
- If the treatment is interrupted for more than four hours it is recommended that the patient is examined by a heathcare professional. If the interruption of treatment after an adverse event is 7 days or less, continue the same cycle to a total of 28 days of infusion inclusive of days before and after the interruption in that cycle. If an interruption due to an adverse event is longer than 7 days, start a new cycle. If the toxicity takes more than 14 days to resolve, discontinue blinatumomab permanently, except if described differently in the table below:

Toxicity	Action
Cytokine release syndrome, tumour lysis syndrome	**Grade 3** Interrupt blinatumomab until resolved, then restart at 9micrograms/day. Escalate to 28micrograms/day after 7 days if the toxicity does not recur.
	Grade 4 Discontinue blinatumomab permanently.
Neurological toxicity	**Convulsion** Discontinue blinatumomab permanently if more than one convulsion occurs.
	Grade 3 • Interrupt blinatumomab until no more than grade 1 (mild) and for at least 3 days, then restart blinatumomab at 9micrograms/day. Escalate to 28micrograms/day after 7 days if the toxicity does not recur. • On re-initiation, pre-medicate with a 24mg dose of dexamethasone. Then reduce dexamethasone step-wise over 4 days. • If the toxicity occurred at 9micrograms/day, or if the toxicity takes more than 7 days to resolve, discontinue blinotumumab permanently.
	Grade 4 Discontinue blinatumomab permanently.
Elevated liver enzymes	**Grade 3** If clinically relevant, interrupt blinatumomab until no more than grade 1 (mild), then restart blinatumomab at 9micrograms/day. Escalate to 28micrograms/day after 7 days if the toxicity does not recur.
	Grade 4 Consider discontinuing blinatumomab permanently.
Other clinically relevant (as determined by treating physician) adverse reactions	**Grade 3** Interrupt blinatumomab until no more than grade 1 (mild), then restart blinatumomab at 9micrograms/day. Escalate to 28micrograms/day after 7 days if the toxicity does not recur.
	Grade 4 Consider discontinuing blinatumomab permanently.
*Based on the NCI Common Terminology Criteria for Adverse Events (CTCAE) version 4.0. Grade 3 is severe, and grade 4 is life-threatening.	

Haematological

No dose modifications for haematological toxicity are necessary for blinatumomab. If treatment with blinatumomab is not tolerated it should be stopped.

Hepatic Impairment

Based on pharmacokinetic analyses, dose adjustment is not necessary in patients with mild to moderate hepatic dysfunction. The safety and efficacy of blinatumomab have not been studied in patients with severe hepatic impairment. See table above.

Renal Impairment

Based on pharmacokinetic analyses, dose adjustment is not necessary in patients with mild to moderate renal dysfunction. The safety and efficacy of blinotumumab have not been studied in patients with severe renal impairment.

Patients with evidence of impaired renal function should be carefully monitored as they are prone to additional myelosuppression.

Elderly

No dose adjustment is necessary in elderly patients (greater than or equal to 65 years of age). There is limited experience with blinatumomab in patients greater than or equal to 75 years of age.

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 (see table above).

Cytokine Release Syndrome (CRS) and Infusion Related Reactions

Premedication with dexamethasone is intended to prevent CRS events associated with blinatumomab treatment.

Serious adverse events that may be signs and symptoms of CRS included pyrexia, asthenia, headache, hypotension, total bilirubin increased, and nausea. The median time to onset of a CRS event was 2 days. Patients should be closely monitored for signs or symptoms of these events.

Disseminated intravascular coagulation and capillary leak syndrome (e.g. hypotension, hypoalbuminaemia, oedema and haemoconcentration) have been commonly associated with CRS. Patients experiencing capillary leak syndrome should be managed promptly.

Infusion Related Reactions

Infusion reactions may be clinically indistinguishable from manifestations of CRS and include symptoms such as rash, wheezing, flushing, breathlessness, hypotension, facial swelling. The infusion reactions were generally rapid, occurring within 48 hours after initiating infusion. However some patients reported delayed onset of infusion reactions or in later cycles. Patients should be observed closely for infusion reactions, especially during the initiation of the first and second treatment cycles and treated appropriately. Anti-pyretic use (e.g. paracetamol) is recommended to help reduce pyrexia during the first 48 hours of each cycle.

Neurological

In the pivotal study 52% of patients experienced one or more neurologic adverse reactions (including psychiatric disorders). NCI-CTC grade 3 or higher neurologic events following initiation of blinatumomab administration included encephalopathy, seizures, speech disorders, disturbances in consciousness, confusion, disorientation, and coordination and balance disorders. The median time from initiation of blinatumomab to onset of a neurologic event was 9 days. The majority of events resolved after treatment interruption.

It is recommended that a neurological examination be performed in patients prior to starting therapy and that patients be clinically monitored for signs and symptoms of neurologic events (e.g. writing test). Management of these signs and symptoms to resolution may require either temporary interruption or permanent discontinuation of treatment. Elderly patients experience a higher rate of neurological events. Counsel patients on the potential neurologic effects and advise patients not to drive, use heavy machinery, or engage in hazardous activities while on treatment and to promptly report any neurological symptoms.

Tumour lysis syndrome

Tumour lysis syndrome (TLS), which may be life-threatening or fatal (grade equal to or greater than 4) has been observed in patients receiving blinatumomab.

Appropriate prophylactic measures including aggressive hydration and anti-hyperuricaemic therapy (such as allopurinol or rasburicase) should be used for the prevention and treatment of TLS during treatment, especially in patients with higher leukocytosis or a high tumour burden. Patients should be closely monitored for signs or symptoms of TLS, including renal function and fluid balance in the first 48 hours after the first infusion. In clinical studies, patients with moderate renal impairment showed an increased incidence of TLS compared with patients with mild renal impairment or normal renal function, Management of these events may require either temporary interruption or discontinuation of blinatumomab.

Regimen

42 day cycle for up to 5 cycles

Patients will receive an initial 2 cycles of treatment. Patients who have achieved complete remission after 2 cycles may receive up to 3 additional cycles, based on an individual benefits-risks assessment.

Consider the administration of pre-phase corticosteroid treatment prior to cycle one if the peripheral blast count is greater than 15% or bone marrow blasts are greater than 50%. This is not included on ARIA

Cycle 1

Drug	Dose	Days	Administration
Blinatumomab	9 micrograms/day	1 to 7 (7 days)	Continuous intravenous infusion in 240ml sodium chloride 0.9% at a rate of 2.5ml/hour via a pump (please see administration instructions below for days the pump is changed).
	28 micrograms/day	8 to 28 (21 days)	

Cycle 2, 3, 4, 5

Drug	Dose	Days	Administration
Blinatumomab	28 micrograms/day	1 to 28 (28 days)	Continuous intravenous infusion in 240ml sodium chloride 0.9% at a rate of 2.5ml/hour via a pump (please see administration instructions below for days the pump is changed).

Dose Information

- Blinatumomab is a set dose and does not require dose banding
- Dosing errors have been observed with blinatumomab treatment. It is very important that the instructions for administration are strictly followed to minimise this risk.
- The administration period must not exceed 28 days in total in any given cycle

Administration Information

- Central venous access is required. Infuse through a dedicated lumen.
- Blinatumomab should be administered as a continuous intravenous infusion delivered at a constant flow rate using a pump system.

  All infusions will contain sufficient volume and drug for a **96 hour** infusion, although they will be administered over **alternate 72 and 96 hours**. The bag will contain;

  - 9microgram/day – 41.25microgram in 275ml
  - 28microgram/day – 133.75microgram in 275ml

- ARIA has been set up to administer the **first**, **third, fifth and seventh** infusions of the same cycle over 72 hours. This means that treatment must start on a Monday, Tuesday or Friday. The infusion will contain sufficient drug and volume for 96 hours and must be programmed to stop after 72 hours. The bag must then be discarded. The **second, fourth, sixth and eighth infusion of each cycle** will be administered over 96 hours. Ensure the pump is set to stop at the correct times.
- Do not flush infusion lines into the patient, as it will cause an inadvertent bolus of blinatumomab to be administered. The line must be replaced with every change of the infusion bag.

- Administer blinatumomab through a Polyolefin, PVC non-DEHP, or EVA intravenous infusion line with a low protein-binding 0.2µm in-line filter.

- The administration period must not exceed more that 28 days in any given cycle

- The days of administration may need to be adjusted on ARIA depending on the time of the start of the day one infusion.

Additional Therapy

- Consider the administration of pre-phase corticosteroid treatment prior to cycle one if the peripheral blast count is greater than 15% or bone marrow blasts are greater than 50%. This is not included on ARIA

- Dexamethasone 20mg or equivalent intravenous 60 minutes prior to day 1 blinatumomab on every cycle

- Paracetamol 1000mg four times a day for the first 48 hours of the day 1 blinatumomab on every cycle oral

- Allopurinol 300mg daily for 7 days (cycle 1 only) oral

- Anti-infective prophylaxis with

  - aciclovir 400mg twice a day oral
  - co-trimoxazole 960mg once a day on Mondays, Wednesdays and Fridays oral
  - fluconazole 50mg once a day oral

- For the treatment of infusion related reactions

  - chlorpheniramine 10mg intravenous when required
  - hydrocortisone 100mg intravenous when required
  - pethidine 12.5-25mg when required for rigors following instruction from a medical practitioner
  - salbutamol 2.5mg nebulised when required
  - pethidine 12.5-25mg intravenous when required for rigors

- 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.

Additional Information

- Patients should be encouraged to drink at least three litres of fluid per 24 hours

- Cycle one and two are started in the hospital setting. It is recommended the patient remain an in-patient for the first 9 days of cycle one and at least two days of cycle two. Take home (supportive) medicines have been included in this protocol. If an in-patient stay is necessary these must be prescribed on the in-patient chart

Coding

- Procurement – X71.3
- Delivery – X72.2

References
1. National Institute for Health and Clinical Excellance (2017). Blinatumomab for previously treated Philadelphia-chromosome-negative acute lymphoblastic leukaemia. Technology appraisal guidance [TA450] Published date: 28 June 2017
2. Kantarilan H, Stein A, Gokbuget N et al. Blinatumomab versus Chemotherapy for Advanced Acute Lymphoblastic Leukemia. N Eng J Med 2017; 376 (9):836-847.

REGIMEN SUMMARY

Blinatumomab (3, 4 day schedule)

Cycle 1 Day 1

1. Warning – Check Supportive Medicines Prescribed (if I/P)
   Administration Instructions
   If an in-patient ensure the following medicines are prescribed;
   1. Paracetamol 1000mg four times a day for the first 48 hours then as required oral (see below)
   2. Aciclovir 400mg twice a day
   3. Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday only oral
   4. Fluconazole 50mg once a day oral
   5. Allopurinol 300mg once a day for 7 days oral
   6. Chlorphenamine 10mg intravenous when required for infusion related reactions
   7. Hydrocortisone 100mg intravenous when required for infusion related reactions
   8. Salbutamol 2.5mg nebulised when required for infusion related reactions
   9. Pethidine 12.5-25mg intravenous when required for rigors (following medical instruction)

2. Dexamethasone 20mg or equivalent intravenous
   Administration Instructions
   Administer 20mg or equivalent dose intravenously 60 minutes before the start of the blinatumomab infusion

3. Paracetamol 1000mg oral
   Administration Instructions
   Administer 60 minutes before the start of the blinatumomab infusion. Check if the patient has already taken paracetamol (maximum dose is 4000mg/24 hours)

4. Blinatumomab 9micrograms/day by continuous intravenous infusion in 240ml sodium chloride 0.9% at a rate of 2.5ml/hour for **72 hours** via a pump
   Administration Instructions
   Central venous access is required. Infuse through a dedicated lumen.

   Blinatumomab should be administered as a continuous intravenous infusion delivered at a constant flow rate using a pump.

   All infusions will contain sufficient volume and drug for a **96 hour** infusion, although they will be administered over **alternate 72 and 96 hours**. The bag will contain;

   - 9microgram/day – 41.25microgram in 275ml
   - 28microgram/day – 133.75microgram in 275ml

   ARIA has been set up to administer the **first**, **third, fifth and seventh** infusions of the same cycle **over 72 hours**. This means that treatment must start on a Monday, Tuesday or Friday. The pump will contain sufficient drug and volume for **96 hours** and must be programmed to stop after **72 hours**. The bag must then be discarded. The **second, fourth, sixth and eighth infusion of each cycle** will be administered over **96 hours**. Ensure the pump is set to stop at the correct times.

   Do not flush the remaining volume left in the infusion line into the patient, as it will cause an inadvertent bolus of blinatumomab to be administered. The line must be replaced with every change of pump.

   Administer blinatumomab through a Polyolefin, PVC non-DEHP, or EVA intravenous infusion line with a low protein-binding 0.2µm in-line filter.

   The administration period must not exceed more that 28 days in any given cycle. The day of administration may need to be adjusted on ARIA depending on the time of the start of the day one infusion

5. Chlorpheniramine 10mg intravenous when required for the relief of infusion related reactions

6. Hydrocortisone 100mg intravenous when required for the relief of infusion related reactions

7. Pethidine 25mg when required for the relief of rigors
   Administration Instructions
   For the relief of rigors following a verbal confirmation from a doctor that the dose is to be given.

8. Salbutamol 2.5mg nebulised when required for the relief of infusion related reactions

Cycle 1 Day 4

9. Blinatumomab 9micrograms/day by continuous intravenous infusion in 240ml sodium chloride 0.9% at a rate of 2.5ml/hour for **96 hours** via a pump
   Administration Instructions
   Central venous access is required. Infuse through a dedicated lumen.

   Blinatumomab should be administered as a continuous intravenous infusion delivered at a constant flow rate using a pump.

   All infusions will contain sufficient volume and drug for a **96 hour** infusion, although they will be administered over **alternate 72 and 96 hours**. The bag will contain;

   - 9microgram/day – 41.25microgram in 275ml
   - 28microgram/day – 133.75microgram in 275ml

   ARIA has been set up to administer the **first**, **third, fifth and seventh** infusions of the same cycle **over 72 hours**. This means that treatment must start on a Monday, Tuesday or Friday. The pump will contain sufficient drug and volume for **96 hours** and must be programmed to stop after **72 hours**. The bag must then be discarded. The **second, fourth, sixth and eighth infusion of each cycle** will be administered over **96 hours**. Ensure the pump is set to stop at the correct times.

   Do not flush the remaining volume in the infusion line into the patient, as it will cause an inadvertent bolus of blinatumomab to be administered. The line must be replaced with every change of pump.

   Administer blinatumomab through a Polyolefin, PVC non-DEHP, or EVA intravenous infusion line with a low protein-binding 0.2µm in-line filter.

   The administration period must not exceed more that 28 days in any given cycle. The day of administration may need to be adjusted on ARIA depending on the time of the start of the day one infusion

10. Chlorpheniramine 10mg intravenous when required for the relief of infusion related reactions

11. Hydrocortisone 100mg intravenous when required for the relief of infusion related reactions

12. Pethidine 25mg when required for the relief of rigors
    Administration Instructions
    For the relief of rigors following a verbal confirmation from a doctor that the dose is to be given.

13. Salbutamol 2.5mg nebulised when required for the relief of infusion related reactions

Cycle 1 Days 8, 15, 22

14. Blinatumomab 28micrograms/day by continuous intravenous infusion in 240ml sodium chloride 0.9% at a rate of 2.5ml/hour for **72 hours** via a pump
    Administration Instructions
    Administration Instructions
    Central venous access is required. Infuse through a dedicated lumen.

    Blinatumomab should be administered as a continuous intravenous infusion delivered at a constant flow rate using a pump.

    All infusions will contain sufficient volume and drug for a **96 hour** infusion, although they will be administered over **alternate 72 and 96 hours**. The bag will contain;

    - 9microgram/day – 41.25microgram in 275ml
    - 28microgram/day – 133.75microgram in 275ml

ARIA has been set up to administer the **first**, **third, fifth and seventh** infusions of the same cycle **over 72 hours**. This means that treatment must start on a Monday, Tuesday or Friday. The pump will contain sufficient drug and volume for **96 hours** and must be programmed to stop after **72 hours**. The bag must then be discarded. The **second, fourth, sixth and eighth infusion of each cycle** will be administered over **96 hours**. Ensure the pump is set to stop at the correct times.

Do not flush the remaining volume left in the infusion line into the patient, as it will cause an inadvertent bolus of blinatumomab to be administered. The line must be replaced with every change of pump.

Administer blinatumomab through a Polyolefin, PVC non-DEHP, or EVA intravenous infusion line with a low protein-binding 0.2µm in-line filter.

The administration period must not exceed more that 28 days in any given cycle. The day of administration may need to be adjusted on ARIA depending on the time of the start of the day one infusion

15. Chlorpheniramine 10mg intravenous when required for the relief of infusion related reactions

16. Hydrocortisone 100mg intravenous when required for the relief of infusion related reactions

17. Pethidine 25mg when required for the relief of rigors
    Administration Instructions
    For the relief of rigors following a verbal confirmation from a doctor that the dose is to be given.

18. Salbutamol 2.5mg nebulised when required for the relief of infusion related reactions

Cycle 1 Days 11, 18, 25

19. Blinatumomab 28micrograms/day by continuous intravenous infusion in 240ml sodium chloride 0.9% at a rate of 2.5ml/hour for **96 hours** via a pump
    Administration Instructions
    Central venous access is required. Infuse through a dedicated lumen.

    Blinatumomab should be administered as a continuous intravenous infusion delivered at a constant flow rate using a pump.

    All infusions will contain sufficient volume and drug for a **96 hour** infusion, although they will be administered over **alternate 72 and 96 hours**. The bag will contain;

    - 9microgram/day – 41.25microgram in 275ml
    - 28microgram/day – 133.75microgram in 275ml

    ARIA has been set up to administer the **first**, **third, fifth and seventh** infusions of the same cycle **over 72 hours**. This means that treatment must start on a Monday, Tuesday or Friday. The pump will contain sufficient drug and volume for **96 hours** and must be programmed to stop after **72 hours**. The bag must then be discarded. The **second, fourth, sixth and eighth infusion of each cycle** will be administered over **96 hours**. Ensure the pump is set to stop at the correct times.

    Do not flush the remaining volume left in the infusion line into the patient, as it will cause an inadvertent bolus of blinatumomab to be administered. The line must be replaced with every change of pump.

    Administer blinatumomab through a Polyolefin, PVC non-DEHP, or EVA intravenous infusion line with a low protein-binding 0.2µm in-line filter.

    The administration period must not exceed more that 28 days in any given cycle. The day of administration may need to be adjusted on ARIA depending on the time of the start of the day one infusion

20. Chlorpheniramine 10mg intravenous when required for the relief of infusion related reactions

21. Hydrocortisone 100mg intravenous when required for the relief of infusion related reactions

22. Pethidine 25mg when required for the relief of rigors
    Administration Instructions
    For the relief of rigors following a verbal confirmation from a doctor that the dose is to be given.

23. Salbutamol 2.5mg nebulised when required for the relief of infusion related reactions

Take Home Medicines (day 1 only)

24. Paracetamol 1000mg four times a day for days 1 and 2 of the cycle then 1000mg four times a day as required

25. Allopurinol 300mg once a day for 7 days oral

26. Aciclovir 400mg twice a day for 42 days oral

27. Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday only for 42 days

28. Fluconaole 50mg once a day for 42 days oral

Cycle 2, 3, 4, 5 Day 1

29. Warning – Check Supportive Medicines Prescribed (if I/P)
    Administration Instructions
    If an in-patient ensure the following medicines are prescribed;
    10. Paracetamol 1000mg four times a day for the first 48 hours then as required oral (see below)
    11. Aciclovir 400mg twice a day
    12. Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday only oral
    13. Fluconazole 50mg once a day oral
    14. Allopurinol 300mg once a day for 7 days oral
    15. Chlorphenamine 10mg intravenous when required for infusion related reactions
    16. Hydrocortisone 100mg intravenous when required for infusion related reactions
    17. Salbutamol 2.5mg nebulised when required for infusion related reactions
    18. Pethidine 25mg intravenous when required for rigors (following medical instruction)

30. Dexamethasone 20mg or equivalent intravenous
    Administration Instructions
    Administer 60 minutes before the start of the blinatumomab infusion

31. Paracetamol 1000mg oral
    Administration Instructions
    Administer 60 minutes before the start of the blinatumomab infusion. Check if the patient has already taken paracetamol (maximum dose is 4000mg/24 hours)

32. Blinatumomab 28micrograms/day by continuous intravenous infusion in 240ml sodium chloride 0.9% at a rate of 2.5ml/hour for **72 hours** via a pump
    Administration Instructions
    Administration Instructions
    Central venous access is required. Infuse through a dedicated lumen.

    Blinatumomab should be administered as a continuous intravenous infusion delivered at a constant flow rate using a pump.

    All infusions will contain sufficient volume and drug for a **96 hour** infusion, although they will be administered over **alternate 72 and 96 hours**. The bag will contain;

    - 9microgram/day – 41.25microgram in 275ml
    - 28microgram/day – 133.75microgram in 275ml

    ARIA has been set up to administer the **first**, **third, fifth and seventh** infusions of the same cycle **over 72 hours**. This means that treatment must start on a Monday, Tuesday or Friday. The pump will contain sufficient drug and volume for **96 hours** and must be programmed to stop after **72 hours**. The bag must then be discarded. The **second, fourth, sixth and eighth infusion of each cycle** will be administered over **96 hours**. Ensure the pump is set to stop at the correct times.

Do not flush the remaining volume left in the infusion line into the patient, as it will cause an inadvertent bolus of blinatumomab to be administered. The line must be replaced with every change of pump.

Administer blinatumomab through a Polyolefin, PVC non-DEHP, or EVA intravenous infusion line with a low protein-binding 0.2µm in-line filter.

The administration period must not exceed more that 28 days in any given cycle. The day of administration may need to be adjusted on ARIA depending on the time of the start of the day one infusion

33. Chlorpheniramine 10mg intravenous when required for the relief of infusion related reactions

34. Hydrocortisone 100mg intravenous when required for the relief of infusion related reactions

35. Pethidine 25mg when required for the relief of rigors
    Administration Instructions
    For the relief of rigors following a verbal confirmation from a doctor that the dose is to be given.

36. Salbutamol 2.5mg nebulised when required for the relief of infusion related reactions

Days 8, 15, 22

37. Blinatumomab 28micrograms/day by continuous intravenous infusion in 240ml sodium chloride 0.9% at a rate of 2.5ml/hour for **72 hours** via a pump
    Administration Instructions
    Central venous access is required. Infuse through a dedicated lumen.

    Blinatumomab should be administered as a continuous intravenous infusion delivered at a constant flow rate using a pump.

    All infusions will contain sufficient volume and drug for a **96 hour** infusion, although they will be administered over **alternate 72 and 96 hours**. The bag will contain;

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    Do not flush the remaining volume left in the infusion line into the patient, as it will cause an inadvertent bolus of blinatumomab to be administered. The line must be replaced with every change of pump.

    Administer blinatumomab through a Polyolefin, PVC non-DEHP, or EVA intravenous infusion line with a low protein-binding 0.2µm in-line filter.

    The administration period must not exceed more that 28 days in any given cycle. The day of administration may need to be adjusted on ARIA depending on the time of the start of the day one infusion

38. Chlorpheniramine 10mg intravenous when required for the relief of infusion related reactions

39. Hydrocortisone 100mg intravenous when required for the relief of infusion related reactions

40. Pethidine 25mg when required for the relief of rigors
    Administration Instructions.
    For the relief of rigors following a verbal confirmation from a doctor that the dose is to be given.

41. Salbutamol 2.5mg nebulised when required for the relief of infusion related reactions

Cycle 2, 3, 4, 5 Days 4, 11, 18, 25

42. Blinatumomab 28micrograms/day by continuous intravenous infusion in 240ml sodium chloride 0.9% at a rate of 2.5ml/hour for **96 hours** via a pump
    Administration Instructions
    Central venous access is required. Infuse through a dedicated lumen.

    Blinatumomab should be administered as a continuous intravenous infusion delivered at a constant flow rate using a pump.

    All infusions will contain sufficient volume and drug for a **96 hour** infusion, although they will be administered over **alternate 72 and 96 hours**. The bag will contain;

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    ARIA has been set up to administer the **first**, **third, fifth and seventh** infusions of the same cycle **over 72 hours**. This means that treatment must start on a Monday, Tuesday or Friday. The pump will contain sufficient drug and volume for **96 hours** and must be programmed to stop after **72 hours**. The bag must then be discarded. The **second, fourth, sixth and eighth infusion of each cycle** will be administered over **96 hours**. Ensure the pump is set to stop at the correct times.

    Do not flush the remaining volume in the infusion line into the patient, as it will cause an inadvertent bolus of blinatumomab to be administered. The line must be replaced with every change of pump.

    Administer blinatumomab through a Polyolefin, PVC non-DEHP, or EVA intravenous infusion line with a low protein-binding 0.2µm in-line filter.

    The administration period must not exceed more that 28 days in any given cycle. The day of administration may need to be adjusted on ARIA depending on the time of the start of the day one infusion

43. Chlorpheniramine 10mg intravenous when required for the relief of infusion related reactions

44. Hydrocortisone 100mg intravenous when required for the relief of infusion related reactions

45. Pethidine 25mg when required for the relief of rigors
    Administration Instructions
    For the relief of rigors following a verbal confirmation from a doctor that the dose is to be given.

46. Salbutamol 2.5mg nebulised when required for the relief of infusion related reactions

Take Home Medicines (day 1 only)

47. Paracetamol 1000mg four times a day for days 1 and 2 of the cycle then 1000mg four times a day as required

48. Aciclovir 400mg twice a day for 42 days oral

49. Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday only for 42 days

50. Fluconaole 50mg once a day for 42 days oral

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	July 2017	None	Stuart Martin Pharmacist Dr Deborah Wright Pharmacist	Dr Christopher Dalley 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.