Chemotherapy Protocol

LYMPHOMA

GLOFITAMAB-GEMCITABINE-OXALIPLATIN

Regimen

- Lymphoma-Glofitamab-Gemcitabine-Oxaliplatin

Indication

- Treatment of relapsed or refractory diffuse large B-cell lymphoma (DLBCL), after ONE line of treatment only in adult patients who are NOT eligible for an autologous stem cell transplant
- Blueteq form must be completed for funding -NICE ID6202

Toxicity

Drug	Adverse Effect
Obinutuzumab	Infusion related reactions, progressive multifocal leukoencephalopathy (PML), cardiac toxicity, thrombocytopenia, neutropenia, tumour lysis syndrome
Glofitamab	Cytokine release syndrome (CRS), serious infection, tumour flare, tumour lysis syndrome (TLS), cytopenia
Gemcitabine	Peripheral oedema, diarrhoea, constipation, rash, respiratory problems, influenza-like symptoms, radiosensitising
Oxaliplatin	Peripheral neuropathy (cumulative), acute laryngopharyngeal dysasthesia (increase duration of infusion)

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

Symptoms of CRS can occur weeks after infusion and therefore the patient must be issued with an alert card to **always carry with them**.

See Trust Protocol for management and grading of CRS following bispecific antibody treatment.

Monitoring

Regimen

- FBC, LFTs, U&Es, bone profile, CRP and LDH prior to day one of treatment
- Documented viral screen – Baseline hepatitis B core antibody and hepatitis B surface antigen, hepatitis C antibody, EBV, CMV, VZV, HIV. Patients with positive hepatitis B serology should consult a liver disease expert before the start of treatment and should be monitored and managed following local medical standards to prevent hepatitis re-activation.

Cytokine Release Syndrome (CRS)

- See Trust Protocol on the management of bi-specific antibody treatment for the management of CRS/ICANS, including monitoring and grading requirements.
- The prescriber must inform the patient of the risk of CRS and signs and symptoms of CRS (see below).
- Patients must be instructed to seek immediate medical attention if they experience signs and symptoms of CRS.
- Patients should be provided with an alert card and instructed to **always carry the card**. This card states their treatment regimen and emergency contact details in case of reaction or CRS.

Symptoms of CRS
Pyrexia; tiredness; cardiac failure; tachycardia, cardiac arrythmias; dyspnoea; hypoxia; capillary leak syndrome; chills; renal impairment; headache; malaise; transaminitis; nausea; diarrhoea; hypotension.

Patient monitoring of CRS

- All patients **must be hospitalised for the first glofitamab dose (Cycle 1 Day 8), or treated on an established ambulatory bispecific pathway,** to monitor for signs and symptoms of CRS. Patients must be monitored throughout the whole infusion time and for 12 hours after completion of the first glofitamab infusion (cycle 1 day 8).
- Temperature, blood pressure and oxygen saturation should be monitored 4-hourly after Glofitamab administration on Day 8 and then twice daily or as directed in accordance with local procedures.
- This must be documented, and CRS graded on the CRS Assessment Form in the patient's notes, as per local policy.
- At least 1 dose of tocilizumab for use in the event of CRS must be available on the ward, or pre-specified location, prior to glofitamab infusion, during dosing of Cycles 1

and 2. Access to an additional dose of tocilizumab within 8 hours of use of the previous tocilizumab dose must be ensured.

- Patients who experienced Grade ≥ 2 CRS or received tocilizumab with their most recent infusion should be hospitalised for their next scheduled infusion.

ICANS

- Serious cases of immune effector cell-associated neurotoxicity syndrome (ICANS) (Grade 3 and higher) were reported in clinical trials and with post-marketing experience. Clinical signs and symptoms of ICANS may include but are not limited to confusion, depressed level of consciousness, disorientation, seizure, aphasia, and dysgraphia.
- Patients and carers should be made aware of this risk and counselled to seek immediate medical attention should signs or symptoms occur at any time.
- At the first signs or symptoms of ICANS, manage according to the Trust Protocol on the management of bi-specific antibody treatment for the management of CRS/ICANS.

Tumour Lysis Syndrome

- Tumour lysis syndrome (TLS) has been reported with glofitamab. Patients should be assessed for risk of tumour lysis prior to treatment. Ensure patients are well hydrated.
- In patients who are considered to be at risk of TLS (e.g. patients with a high tumour burden and/or a high circulating lymphocyte count (greater than $25x10^9$/L) and/or renal impairment (CrCl less than 70 ml/min) should receive prophylaxis.
- Prophylaxis should consist of adequate hydration and administration of allopurinol or a suitable alternative such as rasburicase prior to the infusion. All patients considered at risk should be carefully monitored during the initial days of treatment with a special focus on renal function, potassium, and uric acid values. Any additional guidelines according to standard practice should be followed.

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.

No dose reductions of glofitamab are recommended. Adverse events should be managed with dose interruption, treatment discontinuation and reduction of the infusion rate.

Haematological toxicities

Neutrophils ($x10^9$/L)		**Platelets ($x10^9$/L)**	
<1.0	OR	<100	Delay until count recovery.

Patient may require blood product support and/or growth factors. Always refer to the responsible consultant as any dose delays will be dependent on clinical circumstances and treatment intent.

Hepatic Impairment

Drug	**Bilirubin µmol/L**		**AST/ALT units/L**	**Dose (% of original dose)**
Obinutuzumab	N/A		N/A	No information available
Glofitamab	>30	OR	>49	No information available, clinical decision
Oxaliplatin				Limited information available but there is probably little need to adjust the dose.
Gemcitabine	Greater than 27		n/a	Initiate dose at 800mg/m^2

Renal Impairment

Drug	**Creatinine Clearance (ml/min)**	**Dose (% of original dose)**
Obinutuzumab	<30ml/min	No information available, clinical decision
Glofitamab	<30ml/min	No information available, clinical decision
Oxaliplatin		For moderate renal impairment treat at normal dose and monitor renal function. Dose adjust according to toxicity. If the CrCl is less than 30ml/min then dose reduce.
Gemcitabine	<30ml/min	Consider dose reduction

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.

For all other non-haematological NCI-CTC grade 3 and above toxicities delay treatment until the adverse effect has resolved to NCI-CTC grade 1 or below. The dose should then be reduced to 75% of the original dose or discontinued as appropriate.

Gemcitabine may be reduced to 750mg/m^2 to maintain dose intensity

Oxaliplatin

If the neurosensory toxicity is NCI-CTC grade 1–2 and lasts less than 7 days administer full dose oxaliplatin. If the toxicity is NCI-CTC grade 2 and persists for more than 7 days reduce the oxaliplatin dose to 75mg/m2 . Oxaliplatin should be discontinued for neurosensory toxicities NCI-CTC grade 3 or above.

If NCI-CTC grade 3-4 diarrhoea or stomatitis recurs despite appropriate reduction in the dose the oxaliplatin dose should be reduced to 75mg/m2 . There are rare case reports of acute interstitial lung disease or lung fibrosis in association with oxaliplatin. Where an unexplained respiratory symptom occurs stop treatment until pulmonary investigations have been conducted to exclude an interstitial cause.

Regimen

The regimen starts with Obinutuzumab pre-treatment on Cycle 1 Day 1.
Glofitamab dosing begins on cycle 1 day 8 with a step-up dosing schedule to decrease the risk of CRS, leading to the recommended dose of 30 mg.
Each cycle is 21 days. Treatment duration is for a maximum of 12 cycles.

Aria regimen is built as an in-patient regimen on Cycle 1 Day 8 and all other treatment days are built as an out-patient regimen. If the patient is admitted as an in-patient on any other days, the supportive medicines must be prescribed on the in-patient prescribing system.

Cycle 1

Drug	Days	Dose	Administration
Obinutuzumab	1	1000mg	Intravenous infusion in 250ml sodium chloride 0.9%. Start the administration at 50mg/hour. The rate of the infusion can be escalated in increments of 50 mg/hour every 30 minutes to a maximum rate of 400mg/hour.
Gemcitabine	2	1000mg/m^2	Intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes
Oxaliplatin	2	100mg/m^2	Intravenous infusion in 500ml glucose 5% in 120 minutes
Glofitamab[1]	8	2.5 mg	Intravenous infusion in 25ml sodium chloride 0.9% over 4 hours
Glofitamab[1]	15	10 mg	Intravenous infusion in 50ml sodium chloride 0.9% over 4 hours

Cycle 2

Drug	Days	Dose	Administration
Glofitamab[1]	1	30 mg	Intravenous infusion in 100ml sodium chloride 0.9% over 4 hours
Gemcitabine	1	1000mg/m^2	Intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes
Oxaliplatin	1	100mg/m^2	Intravenous infusion in 500ml glucose 5% in 120 minutes

Cycle 3-8

Drug	Days	Dose	Administration
Glofitamab[1]	1	30 mg	Intravenous infusion in 100ml sodium chloride 0.9% over 2 hours
Gemcitabine	1	1000mg/m^2	Intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes
Oxaliplatin	1	100mg/m^2	Intravenous infusion in 500ml glucose 5% in 120 minutes

Cycle 9-12

Drug	Days	Dose	Administration
Glofitamab	1	30 mg	Intravenous infusion in 100ml sodium chloride 0.9% over 2 hours[2]

[1] For patients who experience CRS with their previous dose of glofitamab, the duration of infusion may be extended up to 8 hours.

Dose Information

Delayed or missed doses

During step-up dosing (weekly dosing):

- Following pre-treatment with Obinutuzumab:
  - If the glofitamab 2.5 mg dose is delayed by more than 1 week (i.e. treatment interval of more than 2 weeks following obinutuzumab), then repeat pre-treatment with Obinutuzumab.

- Following 2.5mg or 10mg dose of glofitamab:
  - If there is a treatment-free interval of 2 weeks to 6 weeks: repeat the last tolerated glofitamab dose and resume the planned step-up dosing.
  - If there is a treatment-free interval of more than 6 weeks: repeat pre-treatment with obinutuzumab and glofitamab step-up dosing.

After Cycle 2 (30 mg dose):

- If there is a glofitamab treatment-free interval of more than 6 weeks between cycles: repeat pre-treatment with obinutuzumab and glofitamab step-up dosing and then resume the planned treatment cycle (30 mg dose).

Gemcitabine will be dose banded in accordance with the national dose bands (38mg/ml).

Oxaliplatin will be dose banded in accordance with the national dose bands (5mg/ml).

Administration Information

Hydration

Obinutuzumab and glofitamab should be administered to **well-hydrated patients.**

- 2-3L/day of oral fluids should start 1-2 days prior to cycle 1 day 1.

- **High risk TLS** patients may need additional IV fluids to maintain a urine output of 100mL/m^2/hour (~3L/m^2/day); consider loop diuretic if diuresis is not adequate; avoid additional potassium in hydration fluids.

Pre-medications

Obinutuzumab

Pre-medications 60 minutes prior to obinutuzumab:

- Methylprednisolone sodium succinate 80mg intravenous
- Chlorphenamine 10mg intravenous
- Paracetamol 1000mg oral

Glofitamab

Pre-medication to reduce the risk of CRS should be administered as outlined below.

Pre-medication (60 minutes prior to glofitamab)	**Cycle 1 (day 8, day 15)**	**Cycle 2 & Cycle 3**	**Cycle 4 to 13**	
	All Patients	**All patients**	**Patients with no CRS experience with previous dose**	**Patients who experienced CRS with the previous dose**
Dexamethasone 20mg intravenous (60 minutes before)	√	√		√
Chlorphenamine 10mg intravenous (30 minutes before)	√	√		√
Cetirizine 10mg oral (30 minutes before)			√	
Paracetamol 1000mg oral (30 minutes before)	√	√	√	√

Supportive Treatments

Tocilizumab must be prescribed as when required in advance of glofitamab infusion, in the event of CRS.Tocilizumab (8 mg/kg, maximum dose 800 mg) intravenously 8-hourly if required. ***See CRS management* in *Trust Bi-specific Antibody Protocol.***

- Do not exceed 3 doses of tocilizumab in a period of 6 weeks
- One dose of tocilizumab must be available on the ward or pre-specified location prior to infusion of glofitamab.
- Follow local procedures for administration.
- If no prior use of tocilizumab or if 1 dose of tocilizumab was used within the last 6 weeks:
    - Administer first dose of tocilizumab
    - If no improvement within 8 hours, administer second dose of tocilizumab
    - After 2 doses of tocilizumab, consider alternative anti-cytokine therapy and/or alternative immunosuppressant therapy
- If 2 doses of tocilizumab were used within the last 6 weeks:
    - Administer only one dose of tocilizumab
    - If no improvement within 8 hours consider alternative anti-cytokine therapy and/or alternative immunosuppressant therapy

Corticosteroids may be indicated (*See CRS management* in *Trust Bi-Specific Antibody Protocol)* can be either:

- 10 mg intravenous dexamethasone, 100 mg intravenous prednisolone, 1-2 mg/kg intravenous methylprednisolone per day, or equivalent

Tumour lysis syndrome (TLS) prophylaxis should be prescribed according to the individual patient TLS risk and at consultant discretion:

- In high-risk patients, consider 3 mg rasburicase intravenous once prior to obinutuzumab +/- first dose glofitamab followed by allopurinol 300 mg once daily oral starting 24 hours after rasburicase.
- For low to moderate risk patients, start allopurinol 300 mg once daily oral.

Infusion related reactions on an as required basis:

- Salbutamol 2.5mg nebulised when required for infusion related bronchospasm
- Consider pethidine 25-50mg intravenous for infusion related rigors that fail to respond to steroids.
- chlorphenamine 10mg intravenous for infusion reactions
- lorazepam 1mg oral for rigors
- methylprednisolone sodium succinate 80mg intravenous for infusion reactions
- paracetamol 1000mg oral for pyrexia

Anti-infective prophylaxis

- Aciclovir 400mg oral twice a day
- Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday oral

Gastric protection with a proton pump inhibitor or a H_2 antagonist according to local formulary choice;

- esomeprazole 20mg once a day oral
- omeprazole 20mg once a day oral
- lansoprazole 15mg once a day oral
- pantoprazole 20mg once a day oral
- rabeprazole 20mg once a day oral
- cimetidine 400mg twice a day oral
- famotidine 20mg once a day oral
- nizatidine 150mg twice a day oral

Growth factors (G-CSF) to support during neutropenia. During cycle 1 it should only be started after resolution of any grade CRS following day 8 glofitamab.

- Cycle 1: Filgrastim or bioequivalent 30 million units subcutaneous once a day for 7 days starting on day 9 of the cycle or after resolution of CRS.
- Cycle 2 onwards: Pegfilgrastim 6mg subcutaneous or Filgrastim (or bioequivalent) 30 million units subcutaneous once a day for 7 days starting on day 9 of the cycle

Extravasation

- Obinutuzumab – neutral
- Glofitamab – neutral
- Oxaliplatin – exfoliant
- Gemcitabine – neutral

References

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4. Roche Products Limited (2023). Gazyvaro 1000mg concentrate for solution for infusion. Summary of Product Characteristics. Online at https://www.medicines.org.uk/emc/product/3279/smpc
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REGIMEN SUMMARY

Glofitamab-Gemcitabine-Oxaliplatin

Cycle 1

Day ONE

1. Warning – Ensure TLS assessment completed.
   - High-risk patients - rasburicase 3mg intravenous once prior to obinutuzumab followed by allopurinol 300 mg once daily oral for 21 days. Rasburicase to be prescribed on ARIA internal if required.
   - Low to moderate risk patients - allopurinol 300 mg once daily oral for 21 days.

2. Warning – check hydration status
   Ensure adequate hydration is given 12-24 hours prior to starting treatment

3. Sodium chloride 0.9% 500ml intravenous infusion over 60 minutes

4. Chlorphenamine 10mg intravenous
   Administration Instructions
   Administer 60 minutes prior to obinutuzumab

5. Methylprednisolone sodium succinate 80mg intravenous
   Administration Instructions
   Administer 60 minutes prior to obinutuzumab

6. Paracetamol 1000mg oral
   Administration Instructions
   Please check if the patient takes regular paracetamol for pain control and take dose into account. Maximum dose is 4g per 24 hours. There should be 4 hours between doses.
   Administer 60 minutes prior to obinutuzumab

7. Obinutuzumab 1000mg intravenous infusion in 250ml sodium chloride 0.9%
   Administration Instructions
   Start the administration at 50mg/hour.The rate of the infusion can be escalated in increments of 50 mg/hour every 30 minutes to a maximum rate of 400mg/hour.

8. Chlorphenamine 10mg when required for infusion related reactions
   Administration Instructions
   For the relief of infusion related reactions

9. Lorazepam 1mg oral when required for rigors
   Administration Instructions
   For the relief of rigors

10. Methylprednisolone sodium succinate 80mg intravenous bolus when required for the relief of infusion related reactions
    Administration Instructions
    For the relief of infusion related reactions

11. Paracetamol 1000mg oral when required for pyrexia
    Administration Instructions
    For the relief of pyrexia. Please check if the patient takes regular paracetamol for pain control and take dose into account

12. Salbutamol 2.5mg nebulised when required for the relief of infusion related bronchospasm

13. Pethidine 25mg intravenous bolus in 10ml sodium chloride 0.9% over 5 minutes for the relief of rigors
    Administration Instructions
    For the relief of rigors following a verbal confirmation to administer from a doctor

Take home medicines (Day 1)

14. Co-trimoxazole 960mg tablet once a day on Monday, Wednesday and Friday oral
    Administration Instructions
    This may be administered as 480mg twice a day according to local practice

15. Aciclovir 400mg tablet twice a day oral for 21 days.
    Administration Instructions
    Please supply 21 days or the nearest original pack size.

16. Gastric Protection
    Administration Instructions: The choice of gastric protection is dependent on local formulary choice and may include;
    - esomeprazole 20mg once a day oral
    - omeprazole 20mg once a day oral
    - lansoprazole 15mg once a day oral
    - pantoprazole 20mg once a day oral
    - rabeprazole 20mg once a day ora
    - cimetidine 400mg twice a day oral
    - famotidine 20mg once a day oral
    - nizatidine 150mg twice a day oral

    Please supply 21 days or the nearest original pack size.

17. Allopurinol 300mg tablet once a day oral for 21 days.
    Administration Instructions
    To be supplied in accordance with patient TLS assessment.
    Please supply 21 days or the nearest original pack size.

18. Dexamethasone 4mg tablet twice a day for 3 days. Oral
    Administration Instructions:
    Take with or after food starting on the day after chemotherapy (Day 3 on cycle 1, day 2 on subsequent cycles)

19. Metoclopramide 10mg tablet three times a day when required, oral
    Administration instructions
    When required for the relief of nausea. Please supply 5 days or an original pack if appropriate.

20. Ondansetron 8mg tablet twice a day for 3 days. Oral
    Administration Instructions:
    Starting in the evening of the day of treatment (Day 2 on cycle 1, day 1 on subsequent cycles)

21. Growth factor according to local formulary choice.

Once daily for 7 days, starting on day 9 or after resolution of any grade CRS following day 8 Glofitamab. For example:
- filgrastim or bioequivalent 30 million units once a day subcutaneously
- lenograstim or bioequivalent 33.6 million units once a day subcutaneously

Cycle 1 Day TWO

22. Dexamethasone 8mg Oral
    Administration instructions:
    Administer 30 minutes prior to Oxaliplatin. This may be given as dexamethasone 8mg IV stat if required.

23. Ondansetron 8mg Oral
    Administration instructions
    Administer 15-30 minutes prior to chemotherapy. This may be given as ondansetron 8mg IV stat if required.

24. Gemcitabine 1000mg/m^2 intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes

25. Oxaliplatin 100mg/m^2 intravenous infusion in 500ml glucose 5% over 120 minutes
    Administration instructions:
    The rate of administration may be increased to 360 minutes if the patient suffers from an acute larynogopharyngeal dysphagia.

Cycle 1 Day EIGHT

26. Warning – Ensure TLS assessment completed.
    TLS prophylaxis allopurinol supplied as pick-up internal on day 1.
    Rasburicase if required will need prescribing on Aria internal prescription

27. Warning -Check supportive medication prescribed (if inpatient)
    Administration instructions
    1. Chlorphenamine 10mg when required for infusion related reactions.
    2. Lorazepam 1mg oral when required for rigors.
    3. Methylprednisolone sodium succinate 80mg intravenous bolus when required for the relief of infusion related reactions.
    4. Paracetamol 1000mg oral when required for pyrexia.
    5. Salbutamol 2.5mg nebulised when required for the relief of infusion related bronchospasm.
    6. Pethidine 25mg intravenous bolus in 10ml sodium chloride 0.9% over 5 minutes for the relief of rigors. -Following verbal confirmation to administer from a doctor.
    7. Tocilizumab 8mg/kg (maximum 800mg) intravenous 8-hourly if required in the event of CRS. Maximum 3 doses. See Trust protocol for CRS Management post glofitamab. One dose of tocilizumab must be available on the ward or pre-specified location prior to infusion of glofitamab. Follow local procedures for administration.
    8. TLS prophylaxis -as per TLS assessment.
    9. Co-trimoxazole 960mg once a day oral on Monday, Wednesday, Friday.
    10. Aciclovir 400mg twice a day oral.

28. Warning - Ensure patient has been issued with a CRS treatment alert card.

29. Warning - check hydration status
    Administration instructions
    Ensure adequate hydration is given 12-24 hours prior to starting treatment

30. Sodium chloride 0.9% 500ml intravenous infusion over 60 minutes

31. Dexamethasone 20mg intravenous
    Administration Instructions
    Administer 60 minutes prior to glofitamab.

32. Chlorphenamine 10mg intravenous
    Administration Instructions

Administer 30 minutes prior to glofitamab

33. Paracetamol 1000mg oral
    Administration Instructions
    Please check if the patient takes regular paracetamol for pain control and take dose into account. Maximum dose is 4g per 24 hours. There should be 4 hours between doses.
    Administer 30 minutes prior to glofitamab

34. Glofitamab 2.5mg intravenous infusion in 25ml sodium chloride 0.9% syringe over 240 minutes
    Administration Instructions
    Please refer to the protocol for information regarding infusion rates and infusion related reactions. These may be decreased according to CRS response as per the protocol.

35. Chlorphenamine 10mg when required for infusion related reactions
    Administration Instructions
    For the relief of infusion related reactions

36. Lorazepam 1mg oral when required for rigors
    Administration Instructions
    For the relief of rigors

37. Methylprednisolone sodium succinate 80mg intravenous bolus when required for the relief of infusion related reactions
    Administration Instructions
    For the relief of infusion related reactions

38. Paracetamol 1000mg oral when required for pyrexia
    Administration Instructions
    For the relief of pyrexia. Please check if the patient takes regular paracetamol for pain control and take dose into account

39. Salbutamol 2.5mg nebulised when required for the relief of infusion related bronchospasm
    Administration Instructions
    When required for the relief of infusion related bronchospasm

40. Pethidine 25mg intravenous bolus in 10ml sodium chloride 0.9% over 5 minutes for the relief of rigors
    Administration Instructions
    For the relief of rigors following a verbal confirmation to administer from a doctor

41. Tocilizumab 8mg/kg (maximum 800mg) intravenous 8-hourly if required in the event of CRS. Maximum 3 doses.
    Administration Instructions
    See Trust protocol for CRS Management post glofitamab.
    One dose of tocilizumab must be available on the ward or pre-specified location prior to infusion of glofitamab. Follow local procedures for administration

Cycle 1 Day FIFTEEN

42. Warning – Ensure TLS assessment completed.
    TLS prophylaxis allopurinol supplied as pick-up internal on day 1.
    Rasburicase if required will need prescribing on Aria internal prescription.

43. Warning - Ensure patient has been issued with a CRS treatment alert card.

44. Warning – Check hydration status
    Administration instructions
    Ensure adequate hydration is given 12-24 hours prior to starting treatment

45. Sodium chloride 0.9% 500ml intravenous infusion over 60 minutes

46. Dexamethasone 20mg intravenous
    Administration Instructions
    Administer 60 minutes prior to glofitamab.

47. Chlorphenamine 10mg intravenous
    Administration Instructions
    Administer 30 minutes prior to glofitamab

48. Paracetamol 1000mg oral
    Administration Instructions
    Please check if the patient takes regular paracetamol for pain control and take dose into account. Administer 30 minutes prior to glofitamab

49. Glofitamab 10mg intravenous infusion in 50ml sodium chloride 0.9% over 240 minutes
    Administration Instructions
    Please refer to the protocol for information regarding infusion rates and infusion related reactions. These may be decreased according to CRS response as per the protocol.

50. Chlorphenamine 10mg when required for infusion related reactions
    Administration Instructions
    For the relief of infusion related reactions

51. Lorazepam 1mg oral when required for rigors
    Administration Instructions
    For the relief of rigors

52. Methylprednisolone sodium succinate 80mg intravenous bolus when required for the relief of infusion related reactions
    Administration Instructions
    For the relief of infusion related reactions

53. Paracetamol 1000mg oral when required for pyrexia
    Administration Instructions
    For the relief of pyrexia. Please check if the patient takes regular paracetamol for pain control and take dose into account

54. Salbutamol 2.5mg nebulised when required for the relief of infusion related bronchospasm
    Administration Instructions
    When required for the relief of infusion related bronchospasm

55. Pethidine 25mg intravenous bolus in 10ml sodium chloride 0.9% over 5 minutes for the relief of rigors
    Administration Instructions

For the relief of rigors following a verbal confirmation to administer from a doctor

56. Tocilizumab 8mg/kg (maximum 800mg) intravenous 8-hourly if required in the event of CRS. Maximum 3 doses.
    Administration Instructions
    See Trust protocol for CRS Management post glofitamab.
    One dose of tocilizumab must be available on the ward or pre-specified location prior to infusion of glofitamab. Follow local procedures for administration

Cycle 2 Day ONE

57. Warning – Ensure TLS assessment completed.
    -TLS prophylaxis allopurinol supplied as pick-up internal.
    - Rasburicase if required will need prescribing on Aria internal prescription.

58. Warning - Ensure patient has been issued with a CRS treatment alert card.

59. Warning -Consider tocilizumab 8mg/kg (maximum 800mg) in the event of CRS symptoms.
    Administration Instructions
    See Trust protocol for CRS Management post glofitamab.

60. Warning – Check hydration status
    Administration instructions
    Ensure adequate hydration is given 12-24 hours prior to starting treatment

61. Sodium chloride 0.9% 500ml intravenous infusion over 60 minutes

62. Dexamethasone 20mg intravenous
    Administration Instructions
    Administer 60 minutes prior to glofitamab.

63. Chlorphenamine 10mg intravenous
    Administration Instructions
    Administer 30 minutes prior to glofitamab

64. Paracetamol 1000mg oral
    Administration Instructions
    Please check if the patient takes regular paracetamol for pain control and take dose into account. Administer 30 minutes prior to glofitamab

65. Ondansetron 8mg Oral
    Administration instructions
    Administer 15-30 minutes prior to chemotherapy. This may be given as ondansetron 8mg IV stat if required.

66. Glofitamab 30mg intravenous infusion in 100ml sodium chloride 0.9% over 240 minutes
    Administration Instructions
    Please refer to the protocol for information regarding infusion rates and infusion related reactions. These may be decreased according to CRS response as per the protocol.

67. Gemcitabine 1000mg/m^2 intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes

68. Oxaliplatin 100mg/m^2 intravenous infusion in 500ml glucose 5% over 120 minutes
    Administration instructions:
    The rate of administration may be increased to 360 minutes if the patient suffers from an acute larynogopharyngeal dysphagia.

69. Chlorphenamine 10mg when required for infusion related reactions
    Administration Instructions
    For the relief of infusion related reactions

70. Lorazepam 1mg oral when required for rigors
    Administration Instructions
    For the relief of rigors

71. Methylprednisolone sodium succinate 80mg intravenous bolus when required for the relief of infusion related reactions
    Administration Instructions
    For the relief of infusion related reactions

72. Paracetamol 1000mg oral when required for pyrexia
    Administration Instructions
    For the relief of pyrexia. Please check if the patient takes regular paracetamol for pain control and take dose into account. Maximum dose is 4g per 24 hours. There should be 4 hours between doses.

73. Salbutamol 2.5mg nebulised when required for the relief of infusion related bronchospasm.
    Administration Instructions
    When required for the relief of infusion related bronchospasm

74. Pethidine 25mg intravenous bolus in 10ml sodium chloride 0.9% over 5 minutes for the relief of rigors
    Administration Instructions
    For the relief of rigors following a verbal confirmation to administer from a doctor

Take home medicines (Day 1)

75. Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday oral
    Administration Instructions
    This may be administered as 480mg twice a day according to local practice

76. Aciclovir 400mg twice a day oral for 21 days
    Administration Instructions
    Please supply 21 days or the nearest original pack size.

77. Gastric Protection
    Administration Instructions: The choice of gastric protection is dependent on local formulary choice and may include;
    - esomeprazole 20mg once a day oral
    - omeprazole 20mg once a day oral
    - lansoprazole 15mg once a day oral
    - pantoprazole 20mg once a day oral
    - rabeprazole 20mg once a day oral
    - cimetidine 400mg twice a day oral
    - famotidine 20mg once a day oral
    - nizatidine 150mg twice a day oral

    Please supply 21 days or the nearest original pack size.

78. Allopurinol 300mg once daily for 21 days.
    Administration Instructions

This should be in accordance with patient TLS assessment.
Please supply 21 days or the nearest original pack size.

79. Dexamethasone 4mg tablet twice a day for 3 days. Oral
    Administration Instructions:
    Take with or after food starting on the day after chemotherapy (Day 3 on cycle 1, day 2 on subsequent cycles)

80. Metoclopramide 10mg tablet three times a day when required, oral
    Administration instructions
    When required for the relief of nausea. Please supply 5 days or an original pack if appropriate.

81. Ondansetron 8mg tablet twice a day for 3 days. Oral
    Administration Instructions:
    Starting the evening of the day of treatment (Day 2 on cycle 1, day 1 on subsequent cycles)

82. Growth factor according to local formulary choice. For example:
    - Filgrastim or bioequivalent 300microgram once a day subcutaneous for seven days starting on day 9 of the cycle
    - Lenograstim or bioequivalent 263microgram once a day subcutaneous for seven days starting on day 9 of the cycle
    - Pegfilgrastim or bioequivalent 6mg once a day subcutaneous on day 2

Cycle 3 Day ONE

83. Warning - Ensure patient has been issued with a CRS treatment alert card.

84. Warning -Consider tocilizumab 8mg/kg (maximum 800mg) in the event of CRS symptoms.
    Administration Instructions
    See protocol for CRS Management post glofitamab.

85. Warning – Check hydration status
    Administration instructions
    Ensure adequate hydration is given 12-24 hours prior to starting treatment

86. Sodium chloride 0.9% 500ml intravenous infusion over 60 minutes

87. Dexamethasone 20 mg intravenous
    Administration Instructions
    Administer 60 minutes prior to glofitamab.

88. Chlorphenamine 10mg intravenous
    Administration Instructions
    Administer 30 minutes prior to glofitamab

89. Paracetamol 1000mg oral
    Administration Instructions
    Please check if the patient takes regular paracetamol for pain control and take dose into account. Administer 30 minutes prior to glofitamab

90. Ondansetron 8mg Oral
    Administration instructions
    Administer 15-30 minutes prior to chemotherapy. This may be given as ondansetron 8mg IV stat if required.

91. Glofitamab 30mg intravenous infusion in 100ml sodium chloride 0.9% over 120 minutes
    Administration Instructions

Please refer to the protocol for information regarding infusion rates and infusion related reactions. These may be decreased according to CRS response as per the protocol.

92. Gemcitabine 1000mg/m^2 intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes

93. Oxaliplatin 100mg/m^2 intravenous infusion in 500ml glucose 5% over 120 minutes
    Administration instructions:
    The rate of administration may be increased to 360 minutes if the patient suffers from an acute larynogopharyngeal dysphagia.

94. Chlorphenamine 10mg when required for infusion related reactions
    Administration Instructions
    For the relief of infusion related reactions

95. Lorazepam 1mg oral when required for rigors
    Administration Instructions
    For the relief of rigors

96. Methylprednisolone sodium succinate 80mg intravenous bolus when required for the relief of infusion related reactions
    Administration Instructions
    For the relief of infusion related reactions

97. Paracetamol 1000mg oral when required for pyrexia
    Administration Instructions
    For the relief of pyrexia. Please check if the patient takes regular paracetamol for pain control and take dose into account

98. Salbutamol 2.5mg nebule once only when required for the relief of infusion related bronchospasm
    Administration Instructions
    When required for the relief of infusion related bronchospasm

99. Pethidine 25mg intravenous bolus in 10ml sodium chloride 0.9% over 5 minutes for the relief of rigors
    Administration Instructions
    For the relief of rigors following a verbal confirmation to administer from a doctor

Take home medicines (Day 1)

100. Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday oral
    Administration Instructions
    This may be administered as 480mg twice a day according to local practice

101. Aciclovir 400mg twice a day oral for 21 days
    Administration Instructions
    Please supply 21 days or the nearest original pack size.

102. Gastric Protection
    Administration Instructions: The choice of gastric protection is dependent on local formulary choice and may include;
    - esomeprazole 20mg once a day oral
    - omeprazole 20mg once a day oral
    - lansoprazole 15mg once a day oral
    - pantoprazole 20mg once a day oral
    - rabeprazole 20mg once a day oral

- cimetidine 400mg twice a day oral
- famotidine 20mg once a day oral
- nizatidine 150mg twice a day oral

Please supply 21 days or the nearest original pack size.

103. Dexamethasone 4mg tablet twice a day for 3 days. Oral

Administration Instructions:
Take with or after food starting on the day after chemotherapy (Day 3 on cycle 1, day 2 on subsequent cycles)

104. Metoclopramide 10mg tablet three times a day when required, oral

Administration instructions
When required for the relief of nausea. Please supply 5 days or an original pack if appropriate.

105. Ondansetron 8mg tablet twice a day for 3 days. Oral

Administration Instructions:
Starting the evening of the day of treatment (Day 2 on cycle 1, day 1 on subsequent cycles)

106. Growth factor according to local formulary choice. For example:

- Filgrastim or bioequivalent 300microgram once a day subcutaneous for seven days starting on day 9 of the cycle
- Lenograstim or bioequivalent 263microgram once a day subcutaneous for seven days starting on day 9 of the cycle
- Pegfilgrastim or bioequivalent 6mg once a day subcutaneous on day two

Cycle 4 to Cycle 8 Day ONE

107. Warning - Ensure patient has been issued with a CRS treatment alert card.

108. Warning -Consider tocilizumab 8mg/kg (maximum 800mg) in the event of CRS symptoms.

Administration Instructions
See protocol for CRS Management post glofitamab.

109. Warning – Consider Dexamethasone 20mg infusion

To be administered 60 minutes prior to glofitamab if patient experienced CRS with the previous dose

110. Warning – Check hydration status

Administration instructions
Ensure adequate hydration is given 12-24 hours prior to starting treatment

111. Sodium chloride 0.9% 500ml intravenous infusion over 60 minutes

112. Dexamethasone 8mg Oral

Administration instructions:
Administer 30 minutes prior to Oxaliplatin. This may be given as dexamethasone 8mg IV stat if required.

113. Cetirizine 10mg oral

Administration Instructions
Administer 30 minutes prior to glofitamab if patient did not experience any reaction with previous dose, otherwise consider administering Chlorphenamine 10mg intravenous

114. Paracetamol 1000mg oral

Administration Instructions
Please check if the patient takes regular paracetamol for pain control and take dose into account. Administer 30 minutes prior to glofitamab

115. Ondansetron 8mg Oral

Administration instructions
Administer 15-30 minutes prior to chemotherapy. This may be given as ondansetron 8mg IV stat if required.

116. Glofitamab 30mg intravenous infusion in 100ml sodium chloride 0.9% over 120 minutes
Administration Instructions
Please refer to the protocol for information regarding infusion rates and infusion related reactions. These may be decreased according to CRS response as per the protocol.

117. Gemcitabine 1000mg/m^2 intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes

118. Oxaliplatin 100mg/m^2 intravenous infusion in 500ml glucose 5% over 120 minutes
Administration instructions:
The rate of administration may be increased to 360 minutes if the patient suffers from an acute larynogopharyngeal dysphagia.

119. Chlorphenamine 10mg when required for infusion related reactions
Administration Instructions
For the relief of infusion related reactions

120. Lorazepam 1mg oral when required for rigors
Administration Instructions
For the relief of rigors

121. Methylprednisolone sodium succinate 80mg intravenous bolus when required for the relief of infusion related reactions
Administration Instructions
For the relief of infusion related reactions

122. Paracetamol 1000mg oral when required for pyrexia
Administration Instructions
For the relief of pyrexia. Please check if the patient takes regular paracetamol for pain control and take dose into account

123. Salbutamol 2.5mg nebule once only when required for the relief of infusion related bronchospasm
Administration Instructions
When required for the relief of infusion related bronchospasm

124. Pethidine 25mg intravenous bolus in 10ml sodium chloride 0.9% over 5 minutes for the relief of rigors
Administration Instructions
For the relief of rigors following a verbal confirmation to administer from a doctor

Take home medicines (Day 1)

125. Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday oral
Administration Instructions
This may be administered as 480mg twice a day according to local practice

126. Aciclovir 400mg twice a day oral for 21 days
Administration Instructions
Please supply 21 days or the nearest original pack size.

127. Gastric Protection

Administration Instructions: The choice of gastric protection is dependent on local formulary choice and may include;

- esomeprazole 20mg once a day oral
- omeprazole 20mg once a day oral
- lansoprazole 15mg once a day oral
- pantoprazole 20mg once a day oral
- rabeprazole 20mg once a day oral
- cimetidine 400mg twice a day oral
- famotidine 20mg once a day oral
- nizatidine 150mg twice a day oral

Please supply 21 days or the nearest original pack size.

128. Dexamethasone 4mg tablet twice a day for 3 days. Oral

Administration Instructions:
Take with or after food starting on the day after chemotherapy (Day 3 on cycle 1, day 2 on subsequent cycles)

129. Metoclopramide 10mg tablet three times a day when required, oral

Administration instructions
When required for the relief of nausea. Please supply 5 days or an original pack if appropriate.

130. Ondansetron 8mg tablet twice a day for 3 days. Oral

Administration Instructions:
Starting the evening of the day of treatment (Day 2 on cycle 1, day 1 on subsequent cycles)

131. Growth factor according to local formulary choice. For example:

- Filgrastim or bioequivalent 300microgram once a day subcutaneous for seven days starting on day 9 of the cycle
- Lenograstim or bioequivalent 263microgram once a day subcutaneous for seven days starting on day 9 of the cycle
- Pegfilgrastim or bioequivalent 6mg once a day subcutaneous on day two

Cycle 9 to Cycle 12 Day ONE

132. Warning – Ensure patient has been issued with a CRS treatment alert card.

133. Warning – Check hydration status

Administration instructions
Ensure adequate hydration is given 12-24 hours prior to starting treatment

134. Sodium chloride 0.9% 500ml intravenous infusion over 60 minutes

135. Warning - Consider dexamethasone 20mg intravenous

Administration Instructions
To be administered 60 minutes prior to glofitamab if patient experienced CRS with the previous dose.

136. Cetirizine 10mg oral

Administration Instructions
Administer 30 minutes prior to glofitamab if patient did not experience any reaction with previous dose, otherwise consider administering Chlorphenamine 10mg intravenous

137. Paracetamol 1000mg oral

Administration Instructions
Please check if the patient takes regular paracetamol for pain control and take dose into account. Administer 30 minutes prior to glofitamab

138. Glofitamab 30mg intravenous infusion in 100ml sodium chloride 0.9% over 120 minutes

Administration Instructions

Please refer to the protocol for information regarding infusion rates and infusion related reactions. These may be decreased according to CRS response as per the protocol.

139. Chlorphenamine 10mg when required for infusion related reactions
Administration Instructions
For the relief of infusion related reactions

140. Lorazepam 1mg oral when required for rigors
Administration Instructions
For the relief of rigors

141. Methylprednisolone sodium succinate 80mg intravenous bolus when required for the relief of infusion related reactions
Administration Instructions
For the relief of infusion related reactions

142. Paracetamol 1000mg oral when required for pyrexia
Administration Instructions
For the relief of pyrexia. Please check if the patient takes regular paracetamol for pain control and take dose into account

143. Salbutamol 2.5mg nebulised when required for the relief of infusion related bronchospasm
Administration Instructions
When required for the relief of infusion related bronchospasm

144. Pethidine 25mg intravenous bolus in 10ml sodium chloride 0.9% over 5 minutes for the relief of rigors
Administration Instructions
For the relief of rigors following a verbal confirmation to administer from a doctor

Take home medicines (Day 1)

145. Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday oral
Administration Instructions
This may be administered as 480mg twice a day according to local practice

146. Aciclovir 400mg twice a day oral for 21 days
Administration Instructions
Please supply 21 days or the nearest original pack size.

147. Gastric Protection
Administration Instructions: The choice of gastric protection is dependent on local formulary choice and may include;
- esomeprazole 20mg once a day oral
- omeprazole 20mg once a day oral
- lansoprazole 15mg once a day oral
- pantoprazole 20mg once a day oral
- rabeprazole 20mg once a day oral
- cimetidine 400mg twice a day oral
- famotidine 20mg once a day oral
- nizatidine 150mg twice a day oral

Please supply 21 days or the nearest original pack size.

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.0	April 2026	New document	Alexandre Guedes Pharmacist	Dr Robert Lown Consultant

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 which occur because of following these guidelines.