Chemotherapy Protocol

ELRANATAMAB

This protocol may require funding

Regimen

- Elranatamab

Indication

- Monotherapy for the treatment of adult patients with relapsed and refractory multiple myeloma, who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy

Toxicity

Drug	Adverse Effect
Elranatamab	Cytokine release syndrome (CRS), Immune effector cell-associated neurotoxicity syndrome (ICANS), Neutropenia, Thrombocytopenia,hypogammaglobulinaemia, Diarrhoea, Fatigue

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

Monitoring

Regimen

- FBC, LFTs, U&Es, bone profile, CRP and LDH prior to day one of treatment
- Documented viral screen – CMV, HSV, EBV, VZV, HIV, hepatitis B, hepatitis C (EBV and CMV PCRs)
- 2 -4 weekly CMV and EBV monitoring
- Urine protein/creatinine ratio (every 3-4 weeks)
- Calcium and magnesium levels at regular intervals throughout treatment
- Immunoglobulins, paraprotein monthly
- Perform a venous thromboembolism (VTE) risk assessment prior to starting treatment. Prescribe thromboprophylaxis for patients with additional risk factors
- Check hepatitis B status before starting. 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

CRS:

Symptoms: pyrexia, tiredness, cardiac failure, tachycardia, cardiac arrythmias, dyspnoea, hypoxia, capillary leak syndrome, chills, renal impairment, headache, malaise, transaminitis, nausea, diarrhoea, hypotension.

- Temperature, blood pressure and oxygen saturation monitored 4-hourly after Elranatamab administration on Day 0 and then twice daily as directed in accordance with local procedures.
- This must be documented, and CRS graded on the WBMT CRS Assessment Form in the patient's notes.

See Trust CRS guidelines for monitoring requirement and grading.

The prescriber must inform the patient of the risk of CRS and signs and symptoms of CRS. Patients must be instructed to seek immediate medical attention if they experience signs and symptoms of CRS. Patients should be provided with the patient card and instructed to carry the card at all times. This card describes symptoms of CRS which, if experienced, should prompt the patient to seek immediate medical attention.

Patient monitoring

- All patients should have arrangements made for the patient to be monitored for signs and symptoms of toxicities including CRS and ICANS for **48 hours after administration of the 2 step up doses in week 1 of elranatamab treatment** and the patient has been instructed to remain within close proximity of a healthcare facility for these 48 hour periods following treatment on both week 1 day 1 and week 1 day 4. For many centres this may mean admitting patients for 7-10 days to adequately monitor them.
- At least 1 dose of tocilizumab for use in the event of CRS must be available on the ward, prior to elranatamab injection, 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 injection should be hospitalised for their next scheduled injection.

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

Dose modifications for haematological toxicity in the table below are for general guidance only. Always refer to the responsible consultant as any dose reductions or delays will be dependent on clinical circumstances and treatment intent. Low counts can be a consequence of bone marrow infiltration as well as drug toxicity.

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

To initiate a new cycle of Elranatamab, ANC ≥ 1.0 x 10^9 /L, Haemoglobin ≥ 80g/l and Platelets ≥ 50 x 109 /L

Elranatamab

Adverse Reaction	Level	Recommendation
Thrombocytopenia	Platelet count less than 25 x 10^9 /L OR Platelet count between 25 x 10^9 /L and 50 x 10^9 /L with bleeding	Withhold treatment until platelet count is 25 x 10^9 /L or higher and no evidence of bleeding
Neutropenia	Absolute neutrophil count less than 0.5 x 10^9 /L Febrile neutropenia	Withhold treatment until absolute neutrophil count is 0.5 × 10^9 /L or higher Withhold treatment until absolute neutrophil count is 1 × 10^9 /L or higher and fever resolves
Anaemia	Haemoglobin less than 8 g/dL	Withhold treatment until haemoglobin is 8 g/dL or higher

Hepatic Impairment

No dose adjustment is required in patients with mild hepatic impairment

There is insufficient data in patients with moderate hepatic impairment and no data in patients with severe hepatic impairment to support a dose recommendation.

Renal Impairment

No dose adjustment is required in patients with mild or moderate renal impairment (eGFR ≥30 mL/min).

There is insufficient data in patients with severe renal impairment to support a dose recommendation

CRS and ICANS management

Please refer to the Wessex guidelines on monitoring and management of bispecific antibodies therapy related CRS and neurological toxicity.

Other

- Consider delaying treatment if the patient is symptomatic for CMV or there is clear indication of a rising titre

Restarting dosages

Last administered dose	Duration of delay from the last administered dose	Action
Step-up dose 1 (12 mg)	2 weeks or less (≤ 14 days)	Restart at step-up dose 2 (32 mg).[a] If tolerated, increase to 76 mg 4 days later.
	Greater than 2 weeks (> 14 days)	Restart step-up dosing schedule at step-up dose 1 (12 mg).[a]
Step-up dose 2 (32 mg)	2 weeks or less (≤ 14 days)	Restart at 76 mg.[a]
	Greater than 2 weeks to less than or equal to 4 weeks (15 days and ≤ 28 days)	Restart at step-up dose 2 (32 mg).[a] If tolerated, increase to 76 mg 1 week later.
	Greater than 4 weeks (> 28 days)	Restart step-up dosing schedule at step-up dose 1 (12 mg).[a]
Any full treatment dose (76 mg)	6 weeks or less (≤ 42 days)	Restart at 76 mg.
	Greater than 6 weeks to less or equal to 12 weeks (43 days to ≤ 84 days)	Restart at step-up dose 2 (32 mg).[a] If tolerated, increase to 76 mg 1 week later.
	Greater than 12 weeks (> 84 days)	Restart step-up dosing schedule at step-up dose 1 (12 mg).[a]

Regimen

28 day cycle – 16 cycles

Cycle 1

Drug	Dose	Days	Administration
Elranatamab	12mg	1	Subcutaneous
Elranatamab	32mg	4	Subcutaneous
Elranatamab	76mg	8, 15, 22	Subcutaneous

Cycle 2-6

Drug	Dose	Days	Administration
Elranatamab	76mg	1, 8, 15, 22	Subcutaneous

Cycle 7 onwards

Drug	Dose	Days	Administration
Elranatamab	76mg	1, 15	Subcutaneous

- Pre-treatment medicinal products should be administered prior to the first three doses of ELREXFIO.
- A minimum of 2 days should be maintained between step-up dose 1 (12 mg) and step-up dose 2 (32 mg).
- A minimum of 3 days should be maintained between step-up dose 2 (32 mg) and the first full treatment (76 mg) dose.
- A minimum of 6 days should be maintained between doses.

Dose Information

- As per dosing regimen

Administration Information

- Premeds on step up dose 1, step up dose 2 and the first full treatment dose are mandatory. Administer 1 hour pre Elranatamab injection.
- The required dose should be injected into the subcutaneous tissue of the abdomen (preferred injection site). Alternatively it may be administered into the subcutaneous tissue of the thigh.

- Elranatamab should not be injected into areas where the skin is red, bruised, tender, hard, or areas where there are scars.
- Elranatamab should be administered according to the step-up dosing schedule in Table 1 to reduce the incidence and severity of CRS and ICANS. Due to the risk of CRS and ICANS, patients should be monitored for signs and symptoms for 48 hours after administration of each of the 2 step-up doses and instructed to remain within proximity of a healthcare facility

Extravasation

- Not known

Additional Therapy

- Elranatamab Pre Medication
  - Chlorphenamine 10mg intravenous
  - Dexamethasone 20mg oral
  - Paracetamol 1000mg oral

- Elranatamab injection reactions

  - hydrocortisone 100mg intravenous when required for Elranatamab injection related reactions
  - salbutamol 2.5mg nebule when required for Elranatamab related bronchospasm
  - consider pethidine 25-50mg intravenous for Elranatamab related rigors that fail to respond to steroids.

- Tocilizumab must be prescribed as when required in advance of Elranatamab injection, in the event of CRS.Tocilizumab (8 mg/kg, maximum dose 800 mg) intravenously 8-hourly if required. *See CRS management*
  - Do not exceed 3 doses of tocilizumab in a period of 6 weeks
  - One dose of tocilizumab must be available on the ward prior to injection of Elranatamab. 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 and Trust CRS guidelines)* can be either:
    - 10 mg intravenous dexamethasone, 100 mg intravenous prednisolone, 1-2 mg/kg intravenous methylprednisolone per day, or equivalent

- Thromboprophylaxis in patients with additional risk factors for VTE

References

1. 1. eMC UK Summary of Product Characteristics for Elranatamab, Pfizer, Feb 2024

REGIMEN SUMMARY

Elranatamab (28 day cycle)

Cycle 1 Day 1

1. Warning – check Tocilizumab available on ward
   Administration Instructions:
   One dose of Tocilizumab should be available on the ward before starting treatment

2. Chlorphenamine 10mg intravenous
   Administration Instructions
   To be administered 60 minutes prior to Elranatamab injection

3. Dexamethasone 20mg Oral
   Administration Instructions
   To be taken 60 minutes prior to Elranatamab injection
   Can be given as 20mg IV Bolus if patient has not taken oral dexamethasone

4. Paracetamol 1000mg oral
   Administration Instructions
   To be taken 60 minutes prior to Elranatamab injection

5. Elranatamab 12mg Subcutaneous injection

6. Hydrocortisone 100mg intravenous once only when required for the relief of elranatamab injection related reactions

7. Salbutamol 2.5mg nebule once only when required for the relief of elranatamab related bronchospasm

Cycle 1 Day 4

8. Warning – check Tocilizumab available on ward
   Administration Instructions:
   One dose of Tocilizumab should be available on the ward before starting treatment

9. Chlorphenamine 10mg intravenous
   Administration Instructions
   To be administered 60 minutes prior to Elranatamab injection

10. Dexamethasone 20mg Oral
    Administration Instructions
    To be taken 60 minutes prior to Elranatamab injection
    Can be given as 20mg IV Bolus if patient has not taken oral dexamethasone

11. Paracetamol 1000mg oral
    Administration Instructions
    To be taken 60 minutes prior to Elranatamab injection

12. Elranatamab 32mg Subcutaneous injection

13. Hydrocortisone 100mg intravenous once only when required for the relief of elranatamab injection related reactions

14. Salbutamol 2.5mg nebule once only when required for the relief of elranatamab related bronchospasm

Cycle 1 Day 8

15. Warning – check Tocilizumab available on ward
    Administration Instructions:
    One dose of Tocilizumab should be available on the ward before starting treatment

16. Chlorphenamine 10mg intravenous
    Administration Instructions
    To be administered 60 minutes prior to Elranatamab injection

17. Dexamethasone 20mg Oral
    Administration Instructions
    To be taken 60 minutes prior to Elranatamab injection
    Can be given as 20mg IV Bolus if patient has not taken oral dexamethasone

18. Paracetamol 1000mg oral
    Administration Instructions
    To be taken 60 minutes prior to Elranatamab injection

19. Elranatamab 76mg Subcutaneous injection

20. Hydrocortisone 100mg intravenous once only when required for the relief of elranatamab injection related reactions

21. Salbutamol 2.5mg nebule once only when required for the relief of elranatamab related bronchospasm

Cycle 1 Day 15, 22

22. Warning – check Tocilizumab available on ward
    Administration Instructions:
    One dose of Tocilizumab should be available on the ward before starting treatment

23. Elranatamab 76mg Subcutaneous injection

24. Hydrocortisone 100mg intravenous once only when required for the relief of elranatamab injection related reactions

25. Salbutamol 2.5mg nebule once only when required for the relief of elranatamab related bronchospasm

Take Home Medicines

Cycle 1 (day 1 only)

26. Allopurinol 300mg once a day for 7 days, oral
    Administration Instructions
    Take in the morning with food and plenty of water. This should be supplied for the first cycle..

27. Aciclovir 400mg twice a day for 28 days oral
    Administration Instructions
    Please supply 28 days or an original pack if appropriate.

28. Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday only for 28 days oral
    Administration Instructions
    Co-trimoxazole 960mg once a day on Mondays, Wednesdays and Fridays. Please supply 28 days. This may be dispensed as 480mg twice a day on Mondays, Wednesdays and Fridays according to local practice..

29. Fluconazole 50mg once a day for 28 days

30. 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
    - ranitidine 150mg twice a day oral

    Please supply 28 days or the nearest original pack size.

31. Thromboprophylaxis according to local formulary choice;
    Administration Instructions
    The choice of thromboprophylaxis is dependent on local formularly choice and may include;
    - dalteparin 5000units once a day subcutaneous injection
    - enoxaparin 40mg once a day subcutaneous injection
    - heparin 5000units twice a day subcutaneous injection
    - apixaban 2.5mg TWICE a day ORAL or equivalent NOAC

    Please supply 28 days or nearest original pack size. Aspirin may be considered after cycle six of treatment.

Cycle 2

Day 1, 8, 15, 22

32. Warning – check Tocilizumab available on ward
    Administration Instructions:
    One dose of Tocilizumab should be available on the ward before starting treatment

33. Elranatamab 76mg Subcutaneous injection

34. Hydrocortisone 100mg intravenous once only when required for the relief of elranatamab injection related reactions

35. Salbutamol 2.5mg nebule once only when required for the relief of elranatamab related bronchospasm

Take home medicines (day 1 only)

36. Aciclovir 400mg twice a day for 28 days oral
    Administration Instructions
    Please supply 28 days or an original pack if appropriate.

37. Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday only for 28 days oral
    Administration Instructions
    Co-trimoxazole 960mg once a day on Mondays, Wednesdays and Fridays. Please supply 28 days. This may be dispensed as 480mg twice a day on Mondays, Wednesdays and Fridays according to local practice..

38. Fluconazole 50mg once a day for 28 days

39. 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
- ranitidine 150mg twice a day oral

Please supply 28 days or the nearest original pack size.

40. Thromboprophylaxis according to local formulary choice;
    Administration Instructions
    The choice of thromboprophylaxis is dependent on local formularly choice and may include;
    - dalteparin 5000units once a day subcutaneous injection
    - enoxaparin 40mg once a day subcutaneous injection
    - heparin 5000units twice a day subcutaneous injection
    - apixaban 2.5mg TWICE a day ORAL or equivalent NOAC

    Please supply 28 days or nearest original pack size. Aspirin may be considered after cycle six of treatment.

Cycle 3-6

Day 1, 8, 15, 22

41. Elranatamab 76mg Subcutaneous injection

42. Hydrocortisone 100mg intravenous once only when required for the relief of elranatamab injection related reactions

43. Salbutamol 2.5mg nebule once only when required for the relief of elranatamab related bronchospasm

Take home medicines (day 1 only)

44. Aciclovir 400mg twice a day for 28 days oral
    Administration Instructions
    Please supply 28 days or an original pack if appropriate.

45. Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday only for 28 days oral
    Administration Instructions
    Co-trimoxazole 960mg once a day on Mondays, Wednesdays and Fridays. Please supply 28 days. This may be dispensed as 480mg twice a day on Mondays, Wednesdays and Fridays according to local practice..

46. Fluconazole 50mg once a day for 28 days

47. 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
    - ranitidine 150mg twice a day oral

    Please supply 28 days or the nearest original pack size.

48. Thromboprophylaxis according to local formulary choice;
    Administration Instructions
    The choice of thromboprophylaxis is dependent on local formularly choice and may include;
    - dalteparin 5000units once a day subcutaneous injection
    - enoxaparin 40mg once a day subcutaneous injection
    - heparin 5000units twice a day subcutaneous injection

- apixaban 2.5mg TWICE a day ORAL or equivalent NOAC
Please supply 28 days or nearest original pack size. Aspirin may be considered after cycle six of treatment.

Cycle 7 onwards
Day 1, 15

49. Elranatamab 76mg Subcutaneous injection

50. Hydrocortisone 100mg intravenous once only when required for the relief of elranatamab injection related reactions

51. Salbutamol 2.5mg nebule once only when required for the relief of elranatamab related bronchospasm

Take home medicines (day 1 only)

52. Aciclovir 400mg twice a day for 28 days oral
Administration Instructions
Please supply 28 days or an original pack if appropriate.

53. Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday only for 28 days oral
Administration Instructions
Co-trimoxazole 960mg once a day on Mondays, Wednesdays and Fridays. Please supply 28 days. This may be dispensed as 480mg twice a day on Mondays, Wednesdays and Fridays according to local practice..

54. Fluconazole 50mg once a day for 28 days

55. 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
- ranitidine 150mg twice a day oral

Please supply 28 days or the nearest original pack size.

56. Thromboprophylaxis according to local formulary choice;
Administration Instructions
The choice of thromboprophylaxis is dependent on local formularly choice and may include;
- dalteparin 5000units once a day subcutaneous injection
- enoxaparin 40mg once a day subcutaneous injection
- heparin 5000units twice a day subcutaneous injection
- apixaban 2.5mg TWICE a day ORAL or equivalent NOAC
Please supply 28 days or nearest original pack size. Aspirin may be considered after cycle six of treatment.

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
2	May 2025	None	Nanda Basker Haematology Pharmacist	Dr Matthew Jenner Haematology 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 Hospitals 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.