

Chemotherapy Protocol

Myeloma

DVd SC (weekly cycles 1-8) Bortezomib-Daratumumab-Dexamethasone

Regimen

- Myeloma – DVd SC (weekly cycles 1-8) bortezomib-daratumumab-dexamethasone

Indication

- Daratumumab in combination with bortezomib and dexamethasone is recommended for use within the Cancer Drugs Fund as an option for treating relapsed multiple myeloma in people who have had 1 previous treatment.
- This weekly bortezomib regimen is for patients who experience neuropathy or those with pre-existing neuropathy. Note both the twice weekly and weekly bortezomib regimens include 32 doses of bortezomib; therefore bortezomib continues to the end of cycle 10 in the weekly regimen. Ensure the correct regimen selected.

Toxicity

Drug	Adverse Effect
Bortezomib	GI disturbances, peripheral neuropathy, hypotension, dizziness, blurred vision, headache, musculoskeletal pain, pyrexia
Daratumumab	Infusion related reactions, hypotension, headache, rash, urticaria, pruritus, nausea, vomiting, respiratory tract infections (including pneumonia), neutropenia, thrombocytopenia, anaemia, lymphopenia, peripheral neuropathy, diarrhoea, muscle spasms, fatigue, pyrexia and peripheral oedema, blood transfusion related events
Dexamethasone	Weight gain, gastrointestinal disturbances, hyperglycaemia, CNS disturbances, Cushingoid changes, glucose intolerance.

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

Monitoring

Bloods

- FBC, U&Es, Ca²⁺ and LFTs prior to day one of each cycle of treatment.
- Paraprotein and / or light chains prior to each cycle.
- All patients should be tested for hepatitis B virus (HBV) before initiating treatment with daratumumab. Those patients who test positive for HBV infection should be discussed with a consultant specialising in HBV prior to initiating treatment with daratumumab to plan monitoring requirements whilst on treatment. Patients may also be tested for hepatitis C, CMV and HIV at the same time if clinically appropriate.

- Send a blood sample to transfusion and inform patient and transfusion laboratory that patient is due to commence daratumumab. Patient will require red cell phenotyping as cross match fails due to binding of daratumumab to red cells.
- Regular monitoring of blood glucose is considered good practice due to dexamethasone use.

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

No dose reductions of daratumumab are recommended. Dose delay may be required to allow recovery of blood cell counts in the event of haematological toxicity. Always refer to the responsible consultant, as any dose 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 or the use of erythropoietin according to NICE TA323 if patient symptomatic of anaemia or where the haemoglobin is less than 8g/dL (80g/L).

Consider growth factor support as an alternative to the options below, particularly where there is evidence of bone marrow suppression.

To initiate a new cycle of daratumumab, the neutrophil count should be $1 \times 10^9/L$ or greater and the platelet count should be $50 \times 10^9/L$ or greater, unless the low counts are due to bone marrow infiltration with myeloma. In this situation the daratumumab may be administered at the discretion of the treating consultant haematologist with the appropriate blood product and growth factor support.

Neutrophils ($\times 10^9/L$)	Dose Modifications (Daratumumab and Bortezomib)
Less than $0.5 \times 10^9/L$ or febrile neutropenia (fever greater than or equal to $38.5^\circ C$ and neutrophils less than 1)	Interrupt daratumumab treatment and monitor FBC weekly. Once neutrophils recover to $1 \times 10^9/L$, resume daratumumab Bortezomib - Consider treatment delay or dose reduction or growth factor support. Seek consultant advice.
Platelets ($\times 10^9/L$)	Dose Modifications
Daratumumab Less than $50 \times 10^9/L$	Interrupt daratumumab treatment and monitor FBC weekly. Once platelets recover to $50 \times 10^9/L$ or greater resume daratumumab
Bortezomib Less than $25 \times 10^9/L$	Consider treatment delay or dose reduction or platelet transfusion. Seek consultant advice.

Hepatic Impairment

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

Drug	Bilirubin $\mu\text{mol/L}$		AST/ALT units/L	Dose (% of original dose)
Bortezomib	1.5xULN or below		N/A	100%
	greater than 1.5xULN		N/A	Initiate treatment at 0.7mg/m^2 . The dose may be escalated to 1mg/m^2 or reduced to 0.5mg/m^2 in subsequent cycles based on patient tolerability.
Daratumumab	No formal studies of daratumumab in patients with hepatic impairment have been conducted. Based on population pharmacokinetic analysis no dosage adjustments are necessary for patients with hepatic impairment			

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Bortezomib	greater than 20	100%
	20 and below	Clinical decision
Daratumumab	No adjustments necessary	

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

Bortezomib

For patients experiencing NCI-CTC grade 1 neuropathy without loss of function or pain continue with full dose bortezomib.

For NCI-CTC grade 1 with pain or grade 2 neuropathy reduce the dose of bortezomib to 1mg/m^2 .

For NCI-CTC grade 2 with pain or grade 3 neuropathy discontinue treatment until symptoms have resolved to NCI-CTC grade 1 or less then reinitiate bortezomib at a dose of 0.7mg/m^2
For NCI-CTC grade 4 neuropathy and/or severe autonomic neuropathy discontinue bortezomib.

For any other NCI-CTC grade 3 non haematological toxicity bortezomib should be discontinued until symptoms have resolved to NCI-CTC grade 1 or below. On the first occurrence treatment may be reinitiated at a dose of 1mg/m^2 . Following second occurrence to dose should be further reduced to 0.7mg/m^2 once symptoms have resolved.

If the toxicity is not resolved or if it recurs at the lowest dose, discontinuation of bortezomib must be considered unless the benefit of treatment clearly outweighs the risk.

Dexamethasone

For patients who are elderly or unable to tolerate the standard dose of dexamethasone the dose given the day after bortezomib alone (days 8 and 15 from cycle 4 onwards) may be reduced. Please note the doses before and the day after each daratumumab are to reduce the risk of infusion related reactions and as a steroid component of the triple combination.

Infusion related reactions (IRR)

Daratumumab solution for subcutaneous injection can cause severe and/or serious IRRs, including anaphylactic reactions. In clinical studies, approximately 11% (52/490) of patients experienced an IRR. Most IRRs occurred following the first injection and were Grade 1-2. IRRs occurring with subsequent injections were seen in less than 1% of patients.

The median time to onset of IRRs following daratumumab injection was 3.7 hours (range 0.15-83 hours). The majority of IRRs occurred on the day of treatment. Delayed IRRs have occurred in less than 1% of patients.

Signs and symptoms of IRRs may include respiratory symptoms, such as nasal congestion, cough, throat irritation, allergic rhinitis, wheezing as well as pyrexia, chest pain, pruritus, chills, vomiting, nausea, and hypotension. Severe reactions have occurred, including bronchospasm, hypoxia, dyspnoea, hypertension and tachycardia.

Patients should be pre-medicated with antihistamines, antipyretics, and corticosteroids as well as monitored and counselled regarding IRRs, especially during and following the first and second injections. If an anaphylactic reaction or life-threatening (Grade 4) reactions occur, appropriate emergency care should be initiated immediately. Daratumumab therapy should be discontinued immediately and permanently.

To reduce the risk of delayed IRRs, oral corticosteroids should be administered to all patients following Daratumumab injection. Patients with a history of chronic obstructive pulmonary disease may require additional post-injection medicinal products to manage respiratory complications. The use of post-injection medicinal products (e.g. short- and long-acting bronchodilators and inhaled corticosteroids) should be considered for patients with chronic obstructive pulmonary disease.

Interference with Serological Testing

Daratumumab binds to CD38 in red blood cells and results in a positive indirect antiglobulin test (Coombs test). Daratumumab mediated positive indirect antiglobulin test may persist for up to six months after the last daratumumab infusion. Daratumumab bound red blood cells masks detection of antibodies to minor antigens in the patients serum. The determination of a patients ABO and Rh blood type are not impacted.

Blood transfusion must be informed that a patient is receiving daratumumab. Patients must be typed and screened prior to daratumumab. All patients must be given an identification card that should be carried for six months after stopping therapy and agree to inform all healthcare professionals who treat them that they have received daratumumab.

Daratumumab is a human IgG kappa monoclonal antibody detectable on both the serum electrophoresis and immunofixation assays used for the clinical monitoring of endogenous

M-protein. This interference can impact the determination of complete response and of disease progression in all patients with IgG kappa myeloma.

Reactivation of Hepatitis B Virus

Hepatitis B virus reactivation has been reported in patients treated with daratumumab. All patients must be screened for hepatitis B before initiation of treatment. This includes all patients with unknown serology who are on treatment already.

Monitoring is required for patients with positive serology for clinical and laboratory signs of hepatitis B reactivation during treatment and for at least six months after completion of daratumumab. Those with positive serology must seek medical help immediately if they experience symptoms of hepatitis B. Daratumumab must be stopped if hepatitis B reactivation occurs during treatment.

Regimen

21 day cycle

If prescribing the DVd regimen the bortezomib is given cycle 1 to 8 only, then continue daratumumab until disease progression. Note that cycle length changes from 21 days to 28 days from cycle 9 onwards hence the need for a separate protocol.

Cycles 1 to 3

Drug	Dose	Days	Administration
Bortezomib	1.3mg/m ²	1,8,15	Subcutaneous
Daratumumab	1800mg	1,8,15	Subcutaneous
Dexamethasone	20mg once a day	1, 8, 15	20mg Oral Reduce dose to 10mg orally (or iv dose equivalent) in over 75yrs
Dexamethasone	20mg once a day	2, 9, 16	Oral Reduce dose to 10mg in over 75yrs

Cycles 4 to 8

Drug	Dose	Days	Administration
Bortezomib	1.3mg/m ²	1,8,15	Subcutaneous
Daratumumab	1800mg	1	Subcutaneous
Dexamethasone	20mg once a day	1	Orally Can be given as 20mg intravenous equivalent. Reduce dose to 10mg in over 75yrs
Dexamethasone	20mg once a day	2, 8, 9, 15, 16	Oral Reduce dose to 10mg in over 75yrs

Cycles 9 onwards – see separate protocol

[Dose Information](#)

- Bortezomib dose will be dose banded in accordance with the national dose bands (2.5).
- Dexamethasone is available as 2mg and 500microgram tablets and 3.3mg in 1ml injection (equivalent to 4mg orally)

[Administration Information](#)

- If the patient experiences no major IRRs after the first three injections, post-injection corticosteroids (excluding any background regimen corticosteroids) may be discontinued.
- Additionally, for patients with a history of chronic obstructive pulmonary disease, the use of post-injection medicinal products including short and long acting bronchodilators, and inhaled corticosteroids should be considered. Following the first four injections, if the patient experiences no major IRRs, these inhaled post-injection medicinal products may be discontinued at the discretion of the physician.
- For first dose a cannula should be inserted to allow emergency treatment of anaphylaxis
- First dose daratumumab that the patient should be observed with hourly observations for 4 hours following subcutaneous administration. If no infusion-related reactions following the first dose then neither cannulation nor additional post injection observations are needed with subsequent doses. If IRR with first dose then continue to observe for 4 hours following subsequent doses until IRRs subside.
- Inject 15 mL daratumumab solution for subcutaneous injection into the subcutaneous tissue of the abdomen approximately 7.5 cm to the right or left of the umbilicus over

approximately 3-5 minutes. Do not inject daratumumab solution for subcutaneous injection at other sites of the body as no data are available.

- Injection sites should be rotated for successive injections
- Daratumumab solution for subcutaneous injection should never be injected into areas where the skin is red, bruised, tender, hard or areas where there are scars.
- Pause or slow down delivery rate if the patient experiences pain. In the event pain is not alleviated by slowing down the injection, a second injection site may be chosen on the opposite side of the abdomen to deliver the remainder of the dose.
- During treatment with daratumumab solution for subcutaneous injection, do not administer other medicinal products for subcutaneous use at the same site as Daratumumab.

Additional therapy

- Consider allopurinol 300mg once a day for seven days for the first cycle only oral
- No anti-emetics are required
- Premedication required 1 to 3 hours before every daratumumab infusion:
 - dexamethasone – see regimen for dose details
 - chlorphenamine 4mg oral
 - paracetamol 1000mg oral
 - montelukast 10mg oral for the first two cycles only
- Consider anti-infective prophylaxis including:
 - aciclovir 400mg twice a day oral
 - co-trimoxazole 960mg once a day oral on Monday, Wednesday and Friday only
 - fluconazole 100mg once a day oral if recurrent oral candidiasis
- Bisphosphonates in accordance with local policies.
- Mouthwashes according to local or national policy on the treatment of mucositis.
- Gastric protection with a proton pump inhibitor or an H₂ antagonist may be considered in patients considered at high risk of GI ulceration or bleed.
- As required for the treatment of infusion related reactions for patients at high risk of respiratory complications:
 - salbutamol 2.5mg nebulised
 - hydrocortisone sodium succinate 100mg intravenous
 - chlorphenamine 10mg intravenous
 - paracetamol 1000mg oral
 - oxygen as required

Additional Information

- All instances of infusion related reaction must be recorded on ARIA.
- Daratumumab interferes with indirect antiglobulin tests as it binds to CD38 on red blood corpuscles (RBCs) and interferes with compatibility testing, including antibody screening and cross matching. Daratumumab interference mitigation methods include treating reagent RBCs with dithiothreitol (DTT) to disrupt daratumumab binding or other locally validated methods. Since the Kell blood group system is also sensitive to DTT treatment, Kell-negative units should be supplied after ruling out or identifying alloantibodies using DTT-treated RBCs. Alternatively, phenotyping or genotyping may also be considered.
- Daratumumab may be detected on serum protein electrophoresis (SPE) and immunofixation (IFE) assays used for monitoring disease monoclonal immunoglobulins (M protein). This can lead to false positive SPE and IFE assay results for patients with IgG kappa myeloma protein impacting initial assessment of complete responses by International Myeloma Working Group (IMWG) criteria. In patients with persistent very good partial response, consider other methods to evaluate the depth of response.

References

1. Janssen-Cilag Limited (18 Dec 2018). Darzalex 20mg/ml Summary of Product Characteristics. Electronic Medicines Compendium. Online at <https://www.medicines.org.uk/emc/product/7250> , accessed 01 July 2019.
2. National Institute for Health and Care Excellence (2019). Daratumumab with bortezomib and dexamethasone for previously treated multiple myeloma. [TA573]. London: National Institute for Health and Care Excellence.
3. Thames Valley Strategic Cancer Network Myeloma Group MM47 DaraVelDex Protocol version 2.0 April 2019.
4. 90 minute daratumumab infusion is safe in multiple myeloma. Leukemia. Hallie Barr et al. Accessed 27/11/18 <https://doi.org/10.1038/s41375-018-0120-2>.

REGIMEN SUMMARY

Myeloma – DVd SC (Weekly cycles 1-8) Bortezomib-Daratumumab-Dexamethasone

Cycle 1 Day 1

1. Warning – Inform blood transfusion

Administration Instructions

Daratumumab interferes with indirect antiglobulin tests as it binds to CD38 on red blood corpuscles (RBCs) and interferes with compatibility testing, including antibody screening and cross matching. Daratumumab interference mitigation methods include treating reagent RBCs with dithiothreitol (DTT) to disrupt daratumumab binding or other locally validated methods. Since the Kell blood group system is also sensitive to DTT treatment, Kell-negative units should be supplied after ruling out or identifying alloantibodies using DTT-treated RBCs. Alternatively, phenotyping or genotyping may also be considered.

Daratumumab may be detected on serum protein electrophoresis (SPE) and immunofixation (IFE) assays used for monitoring disease monoclonal immunoglobulins (M protein). This can lead to false positive SPE and IFE assay results for patients with IgG kappa myeloma protein impacting initial assessment of complete responses by International Myeloma Working Group (IMWG) criteria. In patients with persistent very good partial response, consider other methods to evaluate the depth of response

Please inform blood transfusion when a patient is prescribed daratumumab

2. Antihistamine oral

Administration Instructions

Oral antihistamine according to local formulary choices. To be taken 1 -3 hours prior to daratumumab infusion

For example;

Chlorphenamine 4mg Oral

Loratadine 10mg Oral

Cetirizine 10mg Oral

Fexofenadine 120mg Oral

Acrivastine 8mg Oral

3. Dexamethasone 20mg oral

Administration Instructions

Can be administered as 20mg intravenous. Reduce dose to 10mg intravenous equivalent or 10mg orally in patients over 75 years old..

4. Paracetamol 1000mg oral

Administration Instructions

Please check if the patient has taken paracetamol. The maximum dose is 4000mg/24 hours

5. Montelukast 10mg oral

6. Daratumumab 1800mg subcutaneous injection over 3 – 5 minutes

Administration Instructions

Inject the daratumumab solution for subcutaneous injection into the subcutaneous tissue of the abdomen approximately 7.5 cm to the right or left of the navel over approximately 3-5 minutes. Do not inject daratumumab solution for subcutaneous injection at other sites of the body as no data are available.

Injection sites should be rotated for successive injections

Daratumumab solution for subcutaneous injection should never be injected into areas where the skin is red, bruised, tender, hard or areas where there are scars.

Pause or slow down delivery rate if the patient experiences pain. In the event pain is not alleviated by slowing down the injection, a second injection site may be chosen on the opposite side of the abdomen to deliver the remainder of the dose.

During treatment with daratumumab solution for subcutaneous injection, do not administer other medicinal products for subcutaneous use at the same site as daratumumab.

7. Bortezomib 1.3mg/m² subcutaneous injection

8. Chlorphenamine 10mg intravenous when required for the relief of infusion related reactions
9. Hydrocortisone 100mg intravenous when required for the relief of infusion related reactions
10. Paracetamol 1000mg oral when required for the relief of infusion related reactions
Administration Instructions
Please check if the patient has taken paracetamol. The maximum dose is 4000mg/24 hours
11. Salbutamol 2.5mg nebulised when required for the relief of infusion related reactions

Cycle 1 Days 8, 15

12. Warning – Check if Antihistamine Taken
Administration Instructions
Ensure the patient has taken the antihistamine premedication. If not please administer one of the following according to local formulary choice; To be taken 1 -3 hours prior to daratumumab infusion
Chlorphenamine 4mg Oral
Loratadine 10mg Oral
Cetirizine 10mg Oral
Fexofenadine 120mg Oral
Acrivastine 8mg Oral
13. Warning – Check if the Dexamethasone Taken
Administration Instructions
Ensure the patient has taken the dexamethasone premedication. If not please administer dexamethasone 20mg oral or intravenous if the patient is unable to tolerate the oral dose.
14. Warning – Check if the Paracetamol Taken
Administration Instructions
Please check if the patient has taken paracetamol. If not please administer paracetamol 1000mg. The maximum dose is 4000mg/24 hours
15. Montelukast 10mg oral
16. Daratumumab 1800mg subcutaneous injection over 3 – 5 minutes
Administration Instructions
Inject the daratumumab solution for subcutaneous injection into the subcutaneous tissue of the abdomen approximately 7.5 cm to the right or left of the navel over approximately 3-5 minutes. Do not inject daratumumab solution for subcutaneous injection at other sites of the body as no data are available.

Injection sites should be rotated for successive injections

Daratumumab solution for subcutaneous injection should never be injected into areas where the skin is red, bruised, tender, hard or areas where there are scars.

Pause or slow down delivery rate if the patient experiences pain. In the event pain is not alleviated by slowing down the injection, a second injection site may be chosen on the opposite side of the abdomen to deliver the remainder of the dose.

During treatment with daratumumab solution for subcutaneous injection, do not administer other medicinal products for subcutaneous use at the same site as daratumumab.
17. Bortezomib 1.3mg/m² subcutaneous injection
18. Chlorphenamine 10mg intravenous when required for the relief of infusion related reactions
19. Hydrocortisone 100mg intravenous when required for the relief of infusion related reactions

20. Paracetamol 1000mg oral when required for the relief of infusion related reactions

Administration Instructions

Please check if the patient has taken paracetamol. The maximum dose is 4000mg/24 hours

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

Cycles 1 Take home medicines (day 1 only)

22. Dexamethasone 20mg on days 2, 8, 9 and 15 and 16 oral

Administration Information

Reduce dose to 10mg in patients over 75 years old

Take in the morning with or after food. Please dispense all days on day 1 of the cycle. This may be dispensed in one bottle, or individual bottles according to local practice.

23. Dexamethasone 20mg on day 1 of cycle 2

Take in the morning prior to daratumumab injection

Note to pharmacy; dispense for day 1 of cycle 2

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

Administration information

Take in the morning with food and plenty of water. This should be supplied for the first cycle only.

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

Administration Instructions

Please supply 21 days or an original pack if appropriate.

26. Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday only for 21 days oral

Administration Instructions

Co-trimoxazole 960mg once a day on Mondays, Wednesdays and Fridays. Please supply 21 days.

This may be dispensed as 480mg twice a day on Mondays, Wednesdays and Fridays according to local practice.

27. 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 21 days or the nearest original pack size.

28. Antihistamine on the days of daratumumab administration

Administration Instructions

Take on the day of daratumumab administration. To be taken 1 -3 hours prior to daratumumab infusion Please supply 1 x OP. This is to cover all cycles. To be supplied as per local formulary choice

Chlorphenamine 4mg Oral

Loratadine 10mg Oral

Cetirizine 10mg Oral

Fexofenadine 120mg Oral

Acrivastine 8mg Oral

29. Paracetamol 1000mg oral on the days of daratumumab administration

Administration Instructions

Take 1000mg prior to daratumumab administration. To be taken 1 -3 hours prior to daratumumab infusion Please supply 1 x 100 x 500mg. This is to cover all cycles

Cycles 2 days 1, 8, 15

30. Warning – Check if Antihistamine Taken

Administration Instructions

Ensure the patient has taken the antihistamine premedication. If not please administer one of the following according to local formulary choice;

Chlorphenamine 4mg Oral

Loratadine 10mg Oral

Cetirizine 10mg Oral

Fexofenadine 120mg Oral

Acrivastine 8mg Oral

31. Warning – Check if the Dexamethasone Taken

Administration Instructions

Ensure the patient has taken the dexamethasone premedication. If not please administer dexamethasone 20mg oral or intravenous if the patient is unable to tolerate the oral dose.

32. Warning – Check if the Paracetamol Taken

Administration Instructions

Please check if the patient has taken paracetamol. If not please administer paracetamol 1000mg. The maximum dose is 4000mg/24 hours

33. Montelukast 10mg oral

34. Daratumumab 1800mg subcutaneous injection over 3 – 5 minutes

Administration Instructions

Inject the daratumumab solution for subcutaneous injection into the subcutaneous tissue of the abdomen approximately 7.5 cm to the right or left of the navel over approximately 3-5 minutes. Do not inject daratumumab solution for subcutaneous injection at other sites of the body as no data are available.

35. Injection sites should be rotated for successive injections

Daratumumab solution for subcutaneous injection should never be injected into areas where the skin is red, bruised, tender, hard or areas where there are scars.

Pause or slow down delivery rate if the patient experiences pain. In the event pain is not alleviated by slowing down the injection, a second injection site may be chosen on the opposite side of the abdomen to deliver the remainder of the dose.

During treatment with daratumumab solution for subcutaneous injection, do not administer other medicinal products for subcutaneous use at the same site as daratumumab.

36. Bortezomib 1.3mg/m² subcutaneous injection

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

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

39. Paracetamol 1000mg oral when required for the relief of infusion related reactions

Administration Instructions

Please check if the patient has taken paracetamol. The maximum dose is 4000mg/24 hours

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

Cycle 2 and 3 Take home medicines (day 1 only)

41. Dexamethasone 20mg on days 2, 8, 9, 15 and 16 oral

Administration Information

Reduce dose to 10mg in patients over 75 years old

Take in the morning with or after food. Please dispense all days on day 1 of the cycle. This may be dispensed in one bottle, or individual bottles according to local practice.

42. Dexamethasone 20mg on day 1 of the next cycle

Administration Information

Take in the morning of daratumumab injection

Note to pharmacy – please dispense 1 doses of dexamethasone 20mg to be taken on day 1 of the following cycle prior to daratumumab

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

Administration Instructions

Please supply 21 days or an original pack if appropriate.

44. Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday only for 21 days oral

Administration Instructions

Co-trimoxazole 960mg once a day on Mondays, Wednesdays and Fridays. Please supply 21 days.

This may be dispensed as 480mg twice a day on Mondays, Wednesdays and Fridays according to local practice.

45. 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 21 days or the nearest original pack size.

Cycle 3 Day 1, 8 and 15

46. Warning – Check if Antihistamine Taken

Administration Instructions

Ensure the patient has taken the antihistamine premedication. If not please administer one of the following according to local formulary choice;

Chlorphenamine 4mg Oral
Loratadine 10mg Oral
Cetirizine 10mg Oral
Fexofenadine 120mg Oral
Acrivastine 8mg Oral

47. Warning – Check if the Dexamethasone Taken

Administration Instructions

Ensure the patient has taken the dexamethasone premedication. If not please administer dexamethasone 20mg oral or intravenous if the patient is unable to tolerate the oral dose.

48. Warning – Check if the Paracetamol Taken

Administration Instructions

Please check if the patient has taken paracetamol. If not please administer paracetamol 1000mg. The maximum dose is 4000mg/24 hours

49. Daratumumab 1800mg subcutaneous injection over 3 – 5 minutes

Administration Instructions

Inject the daratumumab solution for subcutaneous injection into the subcutaneous tissue of the abdomen approximately 7.5 cm to the right or left of the navel over approximately 3-5 minutes. Do not inject daratumumab solution for subcutaneous injection at other sites of the body as no data are available.

Injection sites should be rotated for successive injections

Daratumumab solution for subcutaneous injection should never be injected into areas where the skin is red, bruised, tender, hard or areas where there are scars.

Pause or slow down delivery rate if the patient experiences pain. In the event pain is not alleviated by slowing down the injection, a second injection site may be chosen on the opposite side of the abdomen to deliver the remainder of the dose.

During treatment with daratumumab solution for subcutaneous injection, do not administer other medicinal products for subcutaneous use at the same site as daratumumab.

50. Bortezomib 1.3mg/m² subcutaneous injection
51. Chlorphenamine 10mg intravenous when required for the relief of infusion related reactions
52. Hydrocortisone 100mg intravenous when required for the relief of infusion related reactions
53. Paracetamol 1000mg oral when required for the relief of infusion related reactions
Administration Instructions
Please check if the patient has taken paracetamol. The maximum dose is 4000mg/24 hours
54. Salbutamol 2.5mg nebulised when required for the relief of infusion related reactions

Cycle 3 Take home medicines (day 1 only)

55. Dexamethasone 20mg on days 2, 8, 9, 15 and 16 oral
Administration Information
Reduce dose to 10mg in patients over 75 years old
Take in the morning with or after food. Please dispense all days on day 1 of the cycle. This may be dispensed in one bottle, or individual bottles according to local practice.
56. Dexamethasone 20mg on day 1 of the next cycle
Administration Information
Take in the morning of daratumumab injection
Note to pharmacy – please dispense 1 doses of dexamethasone 20mg to be taken on day 1 of the following cycle prior to daratumumab
57. Aciclovir 400mg twice a day for 21 days oral
Administration Instructions
Please supply 21 days or an original pack if appropriate.
58. Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday only for 21 days oral
Administration Instructions
Co-trimoxazole 960mg once a day on Mondays, Wednesdays and Fridays. Please supply 21 days.
This may be dispensed as 480mg twice a day on Mondays, Wednesdays and Fridays according to local practice.
59. 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 21 days or the nearest original pack size.

Cycles 4 to 8 day 1

60. Warning – Check if Antihistamine Taken

Administration Instructions

Ensure the patient has taken the antihistamine premedication. If not please administer one of the following according to local formulary choice;

Chlorphenamine 4mg Oral
Loratadine 10mg Oral
Cetirizine 10mg Oral
Fexofenadine 120mg Oral
Acrivastine 8mg Oral

61. Warning – Check if the Dexamethasone Taken

Administration Instructions

Ensure the patient has taken the dexamethasone premedication. If not please administer dexamethasone 20mg oral or intravenous if the patient is unable to tolerate the oral dose

62. Warning – Check if the Paracetamol Taken

Administration Instructions

Please check if the patient has taken paracetamol. If not please administer paracetamol 1000mg. The maximum dose is 4000mg/24 hours

63. Daratumumab 1800mg subcutaneous injection over 3 – 5 minutes

Administration Instructions

Inject the daratumumab solution for subcutaneous injection into the subcutaneous tissue of the abdomen approximately 7.5 cm to the right or left of the navel over approximately 3-5 minutes. Do not inject daratumumab solution for subcutaneous injection at other sites of the body as no data are available.

Injection sites should be rotated for successive injections

Daratumumab solution for subcutaneous injection should never be injected into areas where the skin is red, bruised, tender, hard or areas where there are scars.

Pause or slow down delivery rate if the patient experiences pain. In the event pain is not alleviated by slowing down the injection, a second injection site may be chosen on the opposite side of the abdomen to deliver the remainder of the dose.

During treatment with daratumumab solution for subcutaneous injection, do not administer other medicinal products for subcutaneous use at the same site as daratumumab.

64. Bortezomib 1.3mg/m² subcutaneous injection

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

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

67. Paracetamol 1000mg oral when required for the relief of infusion related reactions

Administration Instructions

Please check if the patient has taken paracetamol. The maximum dose is 4000mg/24 hours

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

Cycles 4 to 8 days 8 and 15

69. Bortezomib 1.3mg/m² subcutaneous injection

Cycles 4 to 8 Take home medicines (day 1 only)

70. Dexamethasone 20mg on days 2, 8, 9, 15 and 16 oral

Administration Information

Reduce dose to 10mg in patients over 75 years old

Take in the morning with or after food. Please dispense all days on day 1 of the cycle. This may be dispensed in one bottle, or individual bottles according to local practice.

71. Dexamethasone 20mg on day 1 of the next cycle

Administration Information

Take in the morning of daratumumab injection

Note to pharmacy – please dispense 1 doses of dexamethasone 20mg to be taken on day 1 of the following cycle prior to daratumumab

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

Administration Instructions

Please supply 21 days or an original pack if appropriate.

73. Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday only for 21 days oral

Administration Instructions

Co-trimoxazole 960mg once a day on Mondays, Wednesdays and Fridays. Please supply 21 days.

This may be dispensed as 480mg twice a day on Mondays, Wednesdays and Fridays according to local practice.

74. 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 21 days or the nearest original pack size.

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	Oct 2020	None	Nanda Basker Pharmacist	Dr Mathew Jenner 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. These protocols should be used in conjunction with other references such as the Summary of Product Characteristics and relevant published papers.