

Chemotherapy Protocol

Myeloma

Isatuximab-Dexamethasone (40)-Pomalidomide

Regimen

- Myeloma – Isatuximab-Dexamethasone (40)-Pomalidomide

Indication

- Isatuximab is indicated where;
 - the patient has a diagnosis of multiple myeloma
 - the patient has received 3 and only 3 prior lines of treatment and that the numbering of a line of treatment is in accordance with the International Myeloma Workshop Consensus recommendations for the uniform reporting of clinical trials (<http://doi.org/10.1182/blood-2010-10-299487>). A line of therapy is defined as one or more cycles of a planned treatment program. This may consist of one or more planned cycles of single-agent therapy or combination therapy, as well as a sequence of treatments administered in a planned manner (eg induction chemotherapy/chemotherapies if followed by stem cell transplantation is considered to be 1 line of therapy). A new line of therapy starts when a planned course of therapy is modified to include other treatment agents (alone or in combination) as a result of disease progression, relapse or toxicity. A new line of therapy also starts when a planned period of observation off therapy is interrupted by a need for additional treatment for the disease.

Note: the use of isatuximab in combination with pomalidomide and dexamethasone in patients who have had 3 and only 3 prior lines of therapy has been chosen by Sanofi for this EAMS scheme. The use of isatuximab in combination with pomalidomide and dexamethasone in the 1-prior, 2-prior, 4-prior and >4-prior patient groups is not permitted within this EAMS scheme.

- the patient has received prior treatment with at least 2 consecutive cycles of lenalidomide given alone or in combination and has failed treatment with lenalidomide on account of disease progression, refractory disease or intolerance
- the patient has received prior treatment with at least 2 consecutive cycles of a proteasome inhibitor (eg bortezomib or carfilzomib or ixazomib) given alone or in combination and has failed treatment with a proteasome inhibitor on account of disease progression, refractory disease or intolerance
- the patient has responded to at least one previous line of treatment ie the patient does not have primary refractory myeloma
- the patient was refractory to the last line of therapy ie there was progression on or within 60 days of the end of the last line of active anti-myeloma systemic therapy.
- the patient either has had no previous therapy with any anti-CD38 antibody (eg daratumumab) or if there has been previous treatment with an anti-CD38

antibody then the patient did not progress whilst still receiving the anti-CD38 therapy or did not progress within 60 days of the last infusion of anti-CD38 treatment.

- isatuximab is only to be used in combination with pomalidomide and dexamethasone and not with any other active systemic agents for myeloma
 - isatuximab is only to be used in combination with pomalidomide and dexamethasone and not with any other active systemic agents for myeloma
 - the patient has an ECOG performance status of 0 or 1 or 2
 - a formal medical review as to whether treatment with isatuximab should continue or not will be scheduled to occur at least by the end of the first 8 weeks of treatment
- This protocol with a dose of dexamethasone of 40mg is recommended for those aged 75 years and below. Reduce dose to 20mg (or IV dose equivalent) in patients over 75 years.

Toxicity

Drug	Adverse Effect
Isatuximab	<p>Infusion related reactions: dyspnoea, hypertension and bronchospasm. Diarrhoea, nausea, vomiting, upper respiratory tract infections, pneumonia, neutropenia, weight decrease.</p> <p>Isatuximab 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. Isatuximab interference mitigation methods include treating reagent RBCs with dithiothreitol (DTT) to disrupt isatuximab 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 allo-antibodies using DTT-treated RBCs. Alternatively, phenotyping or genotyping may also be considered.</p> <p>Isatuximab 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</p> <p>Please inform blood transfusion when a patient is prescribed isatuximab – before first administration in cycle 1.</p>
Pomalidomide	<p>Teratogenicity, cardiac failure, atrial fibrillation, thromboembolic events, interstitial lung disease, pneumonia, neutropenia, thrombocytopenia, leucopenia, anaemia, decreased appetite, dyspnoea, cough, gastrointestinal disturbance, bone pain, muscle spasm, fatigue, pyrexia, peripheral oedema, renal failure, peripheral neuropathy, skin reactions.</p>
Dexamethasone	<p>Weight gain, gastrointestinal disturbances, hyperglycaemia, CNS disturbances, cushingoid changes, glucose intolerance.</p>

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

Monitoring

Drugs

- FBC at baseline and day 15 in cycle 1 (the full cycle of pomalidomide may be dispensed on day 1). Thereafter monitor prior to each cycle.
- U&Es, Ca²⁺ and LFTs prior to day one of each cycle of treatment.
- Paraprotein and/or light chains prior to each cycle.

- For all women of childbearing potential a negative pregnancy test must be obtained within the 3 days prior to starting pomalidomide. The test must be repeated every 4 weeks (every 2 weeks in women with irregular menstrual cycles) with the final test 4 weeks after the last dose of pomalidomide.
- All patients should be tested for HIV, hepatitis A, B and C before initiating treatment. Active infection is an exclusion criteria in the EAMS scheme for isatuximab. Those patients who test positive for hepatitis B virus (HBV) without active infection should be discussed with a consultant specialist in HBV prior to initiating treatment with pomalidomide. Pomalidomide in combination with dexamethasone should be used cautiously in patients previously infected with HBV, including patients who are anti-HBc positive but HBsAg negative. These patients should be closely monitored for signs and symptoms of active HBV infection throughout therapy.
- Perform a venous thromboembolism (VTE) risk assessment prior to starting treatment. Prescribe thromboprophylaxis.
- Regular monitoring of blood glucose is considered good practice due to use of steroids.

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 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 pomalidomide, the neutrophil count should be $1 \times 10^9/L$ or greater and the platelet count must be $50 \times 10^9/L$ or greater. It is acceptable to use growth factors in order to achieve this apart from prior to first cycle.

Neutrophils (x10 ⁹ /L)	Dose Modifications
Less than 1.0x10 ⁹ /L	Exclusion criteria from EAMS is neutrophil count less than 1.0x10 ⁹ /L at baseline. NOTE growth factors cannot be used to reach this level prior to cycle 1. Delay isatuximab treatment until neutrophil count improves to at least 1.0x10 ⁹ /L. The use of growth factors is permitted within local guidelines.
Less than 0.5x10 ⁹ /L or febrile neutropenia (fever greater than or equal to 38.5°C and neutrophils less than 1) For each subsequent drop to less than 0.5x10 ⁹ /L	See below of isatuximab and interrupt pomalidomide treatment and monitor FBC weekly. Once neutrophils recover to 1x10 ⁹ /L, resume pomalidomide at a dose of 3mg once a day. Interrupt pomalidomide treatment and monitor FBC weekly, once neutrophils recover to 1x10 ⁹ /L or greater then resume pomalidomide at 1mg less than previous dose.
Platelets (x10 ⁹ /L)	Dose Modifications
Less than 75x10 ⁹ /L	Exclusion criteria for isatuximab from EAMS is platelets less than 75x 10 ⁹ /L if less than 50% of bone marrow (BM) nucleated cells are plasma cells and 30x10 ⁹ /L if more than 50% of BM nucleated cells are plasma cells at baseline.
Less than 25x10 ⁹ /L For each subsequent drop to less than 25x10 ⁹ /L	Interrupt pomalidomide treatment and monitor FBC weekly. Once platelets recover to 50x10 ⁹ /L or greater resume pomalidomide at a dose of 3mg once a day. Interrupt pomalidomide and monitor FBC weekly and once platelets recover to 50x10 ⁹ /L, resume pomalidomide at 1mg less than previous dose.

Hepatic Impairment

Patients with serum total bilirubin greater than 2mg/dL were excluded from clinical studies. Hepatic impairment has a modest effect on the pharmacokinetics of pomalidomide. No adjustment of the starting dose of pomalidomide is required for patients with hepatic impairment as defined by the Child-Pugh criteria. However, patients with hepatic impairment should be carefully monitored for adverse reactions and dose reduction or interruption of pomalidomide should be used as needed. However, as markedly elevated levels of alanine aminotransferase and bilirubin have been observed in patients treated with pomalidomide together with cases of hepatitis that resulted in treatment discontinuation, regular monitoring of liver function is recommended for the first 6 months of treatment with pomalidomide and as clinically indicated thereafter.

Drug	Bilirubin μmol/L	AST/ALT units/L	Dose (% of original dose)
Isatuximab	Less than 2 times ULN	Less than 3 times ULN	These are maximum levels permitted at baseline for inclusion in isatuximab in EAMS. No ongoing dose adjustments described. No dose adjustment is recommended in patients with mild hepatic impairment. Data in patients with moderate and severe hepatic impairment are limited, but there is no evidence to suggest that dose adjustment is required in these patients.

Renal Impairment

No dose adjustment of pomalidomide is required for patients with renal impairment. Where patients are receiving haemodialysis, the pomalidomide dose should be taken following haemodialysis.

No dose adjustment for isatuximab is recommended for patients with mild to moderate renal impairment.

Pomalidomide

Cardiac Failure

Cardiac failure is a known common adverse reaction associated with pomalidomide treatment (ie occurs in between 1/10 and 1/100 patients who take pomalidomide). In most cases, this side effect occurs in patients with cardiac disease or cardiac risk factors and within six months of starting pomalidomide. Pomalidomide can cause atrial fibrillation, which may precipitate cardiac failure. Monitor for signs and symptoms of cardiac impairment.

Interstitial Lung Disease

Interstitial lung disease (ILD), including cases of pneumonitis, have been observed with pomalidomide. Careful assessment of patients with an acute onset or unexplained worsening of pulmonary symptoms should be performed to exclude ILD. Pomalidomide should be interrupted during investigation of these symptoms and if ILD is confirmed, appropriate treatment should be initiated. Pomalidomide should only be resumed after a thorough evaluation of the benefits and the risks.

Pregnancy

As pomalidomide is structurally related to thalidomide a teratogenic effect is expected, therefore, it must not be taken during pregnancy. All women of child bearing potential (even if they have amenorrhoea) must use one effective method of pregnancy prevention at least 4 weeks before therapy, during therapy and even in the case of dose interruptions, and for at least a further 4 weeks after stopping therapy. Additionally a negative pregnancy test is required prior to commencing each cycle of therapy. Men are required to undertake to use a barrier method of contraception. The conditions of the Celgene Pregnancy Prevention Programme must be fulfilled for all patients unless there is reliable evidence that the patient does not have childbearing potential.

Skin

Pomalidomide interruption or discontinuation should be considered for WHO grade 2-3 skin rash. Pomalidomide must be discontinued for angioedema, WHO grade 4 rash, exfoliative or bullous rash, or if Stevens-Johnson syndrome (SJS), Toxic Epidermal Necrolysis (TEN) or Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) is suspected, and should not be resumed following discontinuation from these reactions.

Venous Thromboembolism (VTE)

Patients receiving pomalidomide in combination with dexamethasone have developed venous thromboembolic events (predominantly deep vein thrombosis and pulmonary

embolism) and arterial thrombotic events (myocardial infarction and cerebrovascular accident). Appropriate VTE prophylaxis is recommended. All patients should receive aspirin unless contra-indicated. Patients deemed to be at high risk of VTE should receive a low molecular weight heparin.

The duration of thromboprophylaxis remains unclear but guided by risk factors such as active disease (e.g. for the first 4 to 6 months of treatment until disease control achieved) and de-escalated or discontinued unless there are ongoing significant risk factors. If patients are treated with a low molecular weight heparin consider switching patients to aspirin after six cycles of therapy or after maximum response is achieved.

A high index of suspicion for venous thromboembolism should always be maintained. If a venous thrombosis or embolism NCI-CTC grade 3 or above occurs then stop treatment and start full anticoagulation. Pomalidomide may be restarted at the clinician's discretion, once the patient is fully anti-coagulated.

Modifiable risk factors for thromboembolic events should be managed wherever possible to reduce the risk of VTE (e.g. smoking cessation; control of hypertension and hyperlipidaemia). Medicines that may increase the risk of thromboembolism, such as oestrogens and erythropoietic agents, should be used with caution during pomalidomide treatment.

For all other NCI-CTCAE grade 3 or 4 adverse reactions, judged to be related to pomalidomide, stop treatment. Restart treatment when the adverse reaction has resolved to NCI-CTC grade 2 or below at 1 mg less than the previous dose, or at the consultants discretion.

[Dexamethasone](#)

Dose Level	Dose
3 (starting)	40mg
2	20mg
1	10mg

If recovery from toxicities is prolonged beyond 14 days, then the dose of dexamethasone will be decreased by one dose level.

Toxicity	Grade (NCI-CTC)	Dose modification
Dyspepsia	1 - 2	Maintain dose and treat with histamine (H ₂) antagonist or proton pump inhibitor. Decrease by one dose level if symptoms persist.
	3 or above	Interrupt dose until symptoms are controlled. Add H ₂ blocker or proton pump inhibitor and decrease one dose level when dose restarted.
Oedema	3 or above	Use diuretics as needed and decrease dose by one dose level.
Confusion or mood alteration	2 or above	Interrupt dose until symptoms resolve. When dose restarted decrease dose by one dose level.
Muscle weakness	2 or above	Interrupt dose until the muscle weakness is grade 1 or below. Restart with dose decreased by one level.
Hyperglycaemia	3 or above	Decrease dose by one dose level. Treat with insulin or oral hypoglycaemic agents as needed
Acute pancreatitis		Discontinue patient from dexamethasone treatment regimen.
Other	3 or above	Stop dexamethasone dosing until adverse event resolves to grade 2 or below. Resume with dose reduced by one level.

[Regimen](#)

28 day cycle until disease progression or intolerance (12 cycles will be set in Aria)

Cycle 1

Drug	Dose	Days	Administration
Isatuximab	10mg/kg	1,8,15 and 22	Intravenous infusion in 250ml sodium chloride 0.9% at a variable rate
Pomalidomide	4mg once a day	1-21 (inclusive)	Oral
Dexamethasone	40mg	1, 8 15 and 22	Oral Reduce dose to 20mg (or iv dose equivalent) in over 75yrs

Cycle 2 onwards

Drug	Dose	Days	Administration
Isatuximab	10mg/kg	1 and 15	Intravenous infusion in 250ml sodium chloride 0.9% at a variable rate
Pomalidomide	4mg once a day	1-21 (inclusive)	Oral
Dexamethasone	40mg	1, 8 15 and 22	Oral Reduce dose to 20mg (or iv dose equivalent) in over 75yrs

[Dose Information](#)

- The dose of dexamethasone should be reduced to 20mg in those over 75 years of age.
- Dexamethasone is available as 500microgram, 2mg and 4mg tablets and as a 2mg/5ml oral liquid.
- Isatuximab will be dose banded in accordance with national dose banding
- Pomalidomide is available as 1mg, 2mg, 3mg and 4mg hard capsules.

[Administration Information](#)

- Dexamethasone should be taken in the morning with or immediately after food.
- Pomalidomide should be taken at the same time each day. The capsules should be swallowed whole, preferably with water, with or without food and not be opened, broken or chewed.
- Pomalidomide can cause drowsiness it may be advisable to take it at night.
- If a dose of pomalidomide is forgotten on one day, the normal prescribed dose should be taken the next day. Patients should not adjust the dose to make up for missing a dose on previous days.
- It is recommended to press only on one end of the pomalidomide capsule to remove it from the blister thereby reducing the risk of capsule deformation or breakage.
- All prescriptions for pomalidomide must be accompanied by a prescription authorisation form (PAF).
- The rate of isatuximab administration varies and depends on infusion related reactions. In order to determine the rate of the second and ongoing infusions all reactions and the first reaction free infusion must be recorded in the ARIA journal.
- Administer the diluted solution by intravenous infusion using an infusion set fitted with a flow regulator and with an in-line, sterile, non-pyrogenic, low protein-binding

polyethersulfone (PES) filter (pore size 0.22 or 0.2 micrometre). Polyurethane (PU), polybutadiene (PBD), PVC or PE administration sets must be used.

	Final volume	Initial rate (first hour)	Rate increment ^a	Maximum rate
First infusion	250ml	25mL/hour	If absence of infusion reaction for 60 minutes increase by 25mL/hour every 30 minutes	150mL/hour
Second infusion	250mL	50mL/hour	50mL and hour for 30 minutes then increase by 100mL/hour	200mL/hour
Subsequent infusions^a	250ml	200mL/hour		200mL/hour

^a Consider the incremental escalation of the infusion rate only in the absence of infusion reactions with the previous infusion

Administration adjustments should be made if patients experience infusion reactions. In patients who experience Grade 2 (moderate) infusion reactions, a temporary interruption in the infusion should be considered and additional symptomatic medicinal products can be administered. After improvement to grade ≤ 1 (mild), isatuximab infusion may be resumed at half of the initial infusion rate under close monitoring and supportive care, as needed. If symptoms do not recur after 30 minutes, the infusion rate may be increased to the initial rate, and then increased incrementally, as shown in the table above.

If symptoms do not resolve rapidly or do not improve to Grade ≤ 1 after interruption of isatuximab infusion, recur after initial improvement with appropriate medicinal products, or require hospitalization or are life-threatening (Grade ≥ 3), treatment with isatuximab should be permanently discontinued and additional supportive therapy should be administered, as needed.

Check vital signs before the start of the infusion, every 15 minutes during the first 60 minutes of the infusion and at the end of the infusion for all isatuximab infusions.

Additional therapy

- Thromboprophylaxis, the choice depending on risk factors and duration of therapy. Low molecular weight heparin is preferred above aspirin unless there are other clinical reasons to guide thromboprophylaxis.
- Allopurinol 300mg once a day for seven days for the first cycle only oral
- Premedication required 15 – 60 minutes before every isatuximab infusion:
 - dexamethasone – see regimen for dose details
 - chlorphenamine 10mg intravenous
 - omeprazole 20mg oral
 - paracetamol 1000mg oral

- Consider anti-infective prophylaxis including;
 - aciclovir 400mg twice a day oral
 - co-trimoxazole 960mg once a day oral on Monday, Wednesday and Friday only
- Bisphosphonates and calcium/vitamin D 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 a 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;
 - sodium chloride 0.9% 500ml intravenous
 - salbutamol 2.5mg nebulised
 - hydrocortisone sodium succinate 100mg intravenous
 - chlorphenamine 10mg intravenous
 - paracetamol 1000mg oral
 - oxygen as required

Additional Information

- The National Patient Safety Alert on oral chemotherapy (NPSA/2008/RRR001) must be followed in relation to pomalidomide.
- It must be made clear to all staff, including those in the community, that pomalidomide should only be prescribed under the supervision of a consultant haematologist.
- Patients should be assessed for suitability for oral chemotherapy prior to starting treatment.
- For all patients taking pomalidomide; the patient, prescriber and supplying pharmacy must comply with the Celgene pregnancy prevention programme (PPP).
- If strong inhibitors of CYP1A2 (e.g. ciprofloxacin and fluvoxamine) are co-administered with pomalidomide, reduce the dose of pomalidomide by 50%.
- All instances of infusion related reaction must be recorded on ARIA. Isatuximab will continue to be administered at the cycle one rate until a reaction free infusion is noted.
- Isatuximab 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. Isatuximab interference mitigation methods include treating reagent RBCs with dithiothreitol (DTT) to disrupt isatuximab 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.

- Isatuximab 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.

Coding

- Procurement – X71.5
- Delivery – X72.1

References

1. Celgene Limited (2016). Imnovid 4mg Summary of Product Characteristics. Electronic Medicines Compendium. Online at <http://www.medicines.org.uk/emc/medicine/29475>, accessed 25 January 2017.
2. National Institute for Health and Care Excellence (2017). Pomalidomide for multiple myeloma previously treated with lenalidomide and bortezomib. [TA427]. London: National Institute for Health and Care Excellence.
3. Celgene Limited (2013). Imnovid (Pomalidomide) Healthcare Professionals Information Pack UK Version 1.0.
4. Dimopoulos MA, Palumbo A, Corrodini P et al. Safety and efficacy of pomalidomide plus low-dose dexamethasone in STRATUS (MM-010): a phase 3b study in refractory multiple myeloma. Blood (2016); 128 (4): 497-503.

REGIMEN SUMMARY

Isatuximab-Dexamethasone (40)-Pomalidomide

Cycle 1 Day 1

1. Warning – Check blood transfusion status

Administration Instructions

Patients treated with isatuximab carry a lifelong risk of transfusion associated graft versus host disease.

Where blood products are required these patients must receive ONLY IRRADIATED BLOOD PRODUCTS for life.

Ensure transfusion departments are notified and the patient has been issued with an alert card to carry at all times.

1. Chlorphenamine 10mg intravenous

Administration Instructions

Administer 15 – 60 minutes prior to Isatuximab

2. Warning – Dexamethasone Dose in Elderly

Administration Instructions

In those aged over 75 years reduce the dose of dexamethasone to 20mg once a day orally or equivalent intravenous dose

3. Dexamethasone 40mg oral

Administration Instructions

Administer 15 – 60 minutes prior to Isatuximab

Administer 40mg once a day orally. For those unable to tolerate the oral route this can be administered at an

equivalent intravenous dose. Reduce dose to 20mg orally or intravenous equivalent if the patient is over 75 years old.

4. Paracetamol 1000mg oral

Administration Instructions

Administer 15 – 60 minutes prior to Isatuximab

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

5. Omeprazole 20mg Oral

Administration Instructions

Administer 15 – 60 minutes prior to Isatuximab

6. Isatuximab 10mg/kg in 250ml sodium chloride 0.9% intravenous infusion

Administration Instructions

The rate of isatuximab administration varies and is dependant the occurrence and severity of infusion related reactions. Please refer to the protocol for details of the rate of administration and management of such reactions

Administer the diluted solution by intravenous infusion using an infusion set fitted with a flow regulator and with an in-line, sterile, non-pyrogenic, low protein-binding polyethersulfone (PES) filter (pore size 0.22 or 0.2 micrometre).

Polyurethane (PU), polybutadiene (PBD), PVC or PE administration sets must be used.

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

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

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

Administration Instructions

Please check if the patient takes regular paracetamol for pain control and take dose into account

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

11. Sodium chloride 0.9% 500ml intravenous infusion when required for the relief of infusion related reactions

Cycle 1 Days 8, 15 and 22

12. Chlorphenamine 10mg intravenous

Administration Instructions

Administer 15 – 60 minutes prior to Isatuximab

13. Dexamethasone 40mg oral

Administration Instructions

Administer 15 – 60 minutes prior to Isatuximab

Administer 40mg once a day orally. For those unable to tolerate the oral route this can be administered at an equivalent intravenous dose. Reduce dose to 20mg orally or intravenous equivalent if the patient is over 75 years old.

14. Paracetamol 1000mg oral

Administration Instructions

Administer 15 – 60 minutes prior to Isatuximab

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

15. Omeprazole 20mg Oral

Administration Instructions

Administer 15 – 60 minutes prior to Isatuximab

16. Isatuximab 10mg/kg in 250ml sodium chloride 0.9% intravenous infusion

Administration Instructions

The rate of isatuximab administration varies and is dependant the occurrence and severity of infusion related reactions. Please refer to the protocol for details of the rate of administration and management of such reactions. Administer the diluted solution by intravenous infusion using an infusion set fitted with a flow regulator and with an in-line, sterile, non-pyrogenic, low protein-binding polyethersulfone (PES) filter (pore size 0.22 or 0.2 micrometre). Polyurethane (PU), polybutadiene (PBD), PVC or PE administration sets must be used.

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

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

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

Administration Instructions

Please check if the patient takes regular paracetamol for pain control and take dose into account

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

21. Sodium chloride 0.9% 500ml intravenous infusion when required for the relief of infusion related reactions

Take home medicines (day 1 only)

22. Warning – Pregnancy Prevention Programme

Administration Instructions

Pomalidomide is associated with a pregnancy prevention programme. Please ensure this is completed for all patients.

23. Pomalidomide 4mg once a day on days 1-21 oral

Administration Information

Oral SACT

Pregnancy prevention programme

Take at the same time each day. Swallow the capsules whole, preferably with water, with or without food.

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 28 days oral

Administration Instructions

Please supply 28 days or an original pack if appropriate.

26. 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.

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 28 days or the nearest original pack size.

28. Thromboprophylaxis according to risk factors

Administration Instructions

The choice of thromboprophylaxis is dependent on local formulary 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 Days 1 and 15

29. Chlorphenamine 10mg intravenous

Administration Instructions

Administer 15 – 60 minutes prior to Isatuximab

30. Dexamethasone 40mg oral

Administration Instructions

Administer 15 – 60 minutes prior to Isatuximab

Administer 40mg once a day orally. For those unable to tolerate the oral route this can be administered at an equivalent intravenous dose. Reduce dose to 20mg orally or intravenous equivalent if the patient is over 75 years old.

31. Paracetamol 1000mg oral

Administration Instructions

Administer 15 – 60 minutes prior to Isatuximab

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

32. Omeprazole 20mg Oral

Administration Instructions

Administer 15 – 60 minutes prior to Isatuximab

33. Isatuximab 10mg/kg in 250ml sodium chloride 0.9% intravenous infusion

Administration Instructions

The rate of isatuximab administration varies and is dependant the occurrence and severity of infusion related reactions. Please refer to the protocol for details of the rate of administration and management of such reactions

Administer the diluted solution by intravenous infusion using an infusion set fitted with a flow regulator and with an in-line, sterile, non-pyrogenic, low protein-binding polyethersulfone (PES) filter (pore size 0.22 or 0.2 micrometre).

Polyurethane (PU), polybutadiene (PBD), PVC or PE administration sets must be used.

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

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

36. 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

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

38. Sodium chloride 0.9% 500ml intravenous infusion when required for the relief of infusion related reactions

Take home medicines (day 1 only)

39. Dexamethasone 40mg on days 8 and 22, oral

Administration Information

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.

40. Warning – Pregnancy Prevention Programme

Administration Instructions

Pomalidomide is associated with a pregnancy prevention programme. Please ensure this is completed for all patients.

41. Pomalidomide 4mg once a day on days 1-21 oral

Administration Information

Oral SACT

Pregnancy prevention programme

Take at the same time each day. Swallow the capsules whole, preferably with water, with or without food.

42. Aciclovir 400mg twice a day for 28 days oral

Administration Instructions

Please supply 28 days or an original pack if appropriate.

43. 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.

44. 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.

45. Thromboprophylaxis according to risk factors

Administration Instructions

The choice of thromboprophylaxis is dependent on local formulary 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
1	June 2020	None	Nanda Basker Pharmacist	Dr M Jenner Consultant Haematologist
2	February 2024	Pre-medication timings and national dose banding for Isatuximab	Nanda Basker Pharmacist	

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.