

# Isatuximab, Bortezomib, Lenalidomide, Dexamethasone (Isa-VRd) (4 Weekly Induction) (Myeloma)

Please note this protocol has been produced in a new format that is currently being piloted. Any feedback on this new format should be sent to [SSGMeetings@uhbw.nhs.uk](mailto:SSGMeetings@uhbw.nhs.uk)

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## Indication

For untreated multiple myeloma when a stem cell transplant is unsuitable (NICE TA1098).

For patient commenced induction therapy with the combination of daratumumab plus bortezomib, thalidomide and dexamethasone with the intention of proceeding to a stem cell transplant but despite responding to such treatment the patient is now ineligible for transplantation.

## Response Rates

IMROZ phase 3 study\*

- ≥CR rates: Isa-VRd 74.7% vs VRd 64.1%
- MRD-negative status with complete response: Isa-VRd 55.5% vs VRd 40.9%
- PFS at 60 months: Isa-VRd 63.2% vs VRd 45.2%. HR: 0.6

\*please see [additional information](#) section for further details

## Treatment related mortality

Deaths per year on treatment: Isa-VRd 0.03 vs VRd 0.02

## Regimen details

### Cycle 1

Day	Drug	Dose	Route
1, 8, 15, 22	Isatuximab	10mg/kg	IV infusion
1, 8, 15, 22	Bortezomib	1.3mg/m <sup>2</sup>	SC
1-21	Lenalidomide	25mg	PO
1, 2, 8, 9, 15, 16, 22, 23	Dexamethasone	20mg	IV/PO

### Cycle 2-8

Day	Drug	Dose	Route
1, 15	Isatuximab	10mg/kg	IV infusion
1, 8, 15, 22	Bortezomib	1.3mg/m <sup>2</sup>	SC
1-21	Lenalidomide	25mg	PO
1, 8, 15, 22	Dexamethasone	20mg	PO

### Cycle 9-19

Day	Drug	Dose	Route
1, 15	Isatuximab	10mg/kg	IV infusion
1-21	Lenalidomide	25mg	PO
1, 15	Dexamethasone*	20mg	PO

\*consider omitting if VGPR or greater achieved

### Cycle 20 onwards

Day	Drug	Dose	Route
1	Isatuximab	10mg/kg	IV infusion
1-21	Lenalidomide	25mg	PO
1	Dexamethasone*	20mg	PO

\*consider omitting if VGPR or greater achieved

## Cycle frequency

28 days

## Number of cycles

Until disease progression or unacceptable toxicity.

## Pre-medication

15-60 minutes prior to isatuximab infusion:

- Paracetamol 500mg-1g PO.
- Chlorphenamine 10 mg IV for cycle 1 infusions. If no infusion related reactions, may be switched to 4mg PO in subsequent cycles.
- Consider montelukast 10mg PO administered >30 mins prior to first dose and subsequent doses in cycle 1.
- Dexamethasone IV/PO (must be given IV with the first 4 isatuximab doses, PO on the other days in cycle 1).

Patients who do not experience an infusion reaction during their first 2 cycles of isatuximab can have requirement for premedication with subsequent cycles reconsidered.

## Post infusion medication

For patients with a history of obstructive pulmonary disorder, the use of post-infusion medications including short and long acting bronchodilators, and inhaled corticosteroids should be considered. Following the first four infusions,

if the patient experiences no major infusion related reactions, these inhaled post-infusion medications may be discontinued at the discretion of the physician.

### Supportive medication

Cycle 1: Days 1-7: Allopurinol 300 mg OD (100mg OD if CrCl <20mL/min)

Cycles 1-3: Levofloxacin 500mg OD (reduced dose if CrCl <50ml/min)

All cycles: Antiviral prophylaxis as per local policy.

All cycles: Antifungal prophylaxis as per local policy.

All cycles: Proton pump inhibitor or H2 antagonist on steroid days and on day of isatuximab treatment or continuously (as per local policy).

All cycles: Thromboprophylaxis as per local policy. Unless contraindicated, VTE thromboprophylaxis is required. Apixaban 2.5mg BD is recommended. For those unsuitable for apixaban, low molecular weight heparin can be considered.

All cycles: Pneumocystis jirovecii pneumonia (PJP) prophylaxis as per local policy

Bisphosphonates as per SWAG '[Bone Protection Myeloma](#)' protocol

### Emetogenicity

This regimen has low emetogenic potential.

### Administration

#### Isatuximab

Isatuximab is an anti-CD38 IgG1 monoclonal antibody supplied as a 20mg/mL concentrate for solution for infusion and should be given after premedication. Isatuximab should be administered in sodium chloride 0.9% 250mL via an infusion set equipped with a 0.2µm in-line filter at the appropriate infusion rate (as per tables below). Incremental escalation of the infusion rate should be considered in the absence of infusion reactions during cycle 1.

The 'Rapid Infusion Protocol' is unlicensed but there is good evidence to support the safety of this approach.

#### Rapid Infusion Protocol

	Volume of sodium chloride 0.9%	Initial infusion rate (first hour)	*Absence of infusion reaction	Rate increment	Maximum rate
First infusion	250mL	25mL/hour	For 60 minutes	25mL/hour every 30 minutes	150mL/hour
Second infusion	250mL	250mL/hour	-	-	250mL/hour
Subsequent infusions	250mL	500mL/hour	-	-	500mL/hour

\*Infusion reactions – see '[side effects and toxicity management](#)' section.

Where site does not have the necessary equipment/experience to implement the 'Rapid Infusion Protocol', isatuximab should be administered at the rates as per the 'Standard Infusion Protocol' table below:

#### Standard Infusion Protocol

	Volume of sodium chloride 0.9%	Initial infusion rate (first hour)	*Absence of infusion reaction	Rate increment	Maximum rate
First infusion	250mL	25mL/hour	For 60 minutes	25mL/hour every 30 minutes	150mL/hour
Second infusion	250mL	50mL/hour	For 30 minutes	50 mL/hour for 30 minutes then increase by 100 mL/hr	200mL/hour

Subsequent infusions	250mL	200mL/hour	-	-	200mL/hour
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\*Infusion reactions – see '[side effects and toxicity management](#)' section.

**Note:** If the patient is suitable to transition from the 'Standard Infusion Protocol' to the 'Rapid Infusion Protocol' and has not experienced any infusion reactions, premedication must still be administered during the titration phase. If the isatuximab infusion is tolerated at 500mg/hr on two occasions, then the need for premedication may be reviewed at the discretion of the physician.

### Bortezomib

Administration by subcutaneous bolus injection into the thigh or abdomen. Rotate sites, avoid injecting into the same site in the same cycle. The interval between each dose should be at least 72 hours.

### Lenalidomide

Lenalidomide should be swallowed whole with water, either with or without food, at the same time each day and should not be broken, opened or chewed. If a dose is missed it may be taken within 12 hours. However, if more than 12 hours has passed since the dose was due, the patient should miss the dose and resume the usual dose the next day. Lenalidomide must be prescribed and dispensed in accordance with the pregnancy prevention programme.

### Dexamethasone

Tablets should be taken in the morning, with or immediately after food.

### Extravasation

Isatuximab – neutral (Group 1)

Bortezomib – neutral (Group 1)

### Mandatory investigations – pre first cycle

Investigation	Validity period
FBC*	14 days
Renal profile (U&Es including creatinine)	14 days
Liver profile (ALT/AST, ALP, bilirubin)	14 days
Virology (Hep B/C, HIV)	3 months
Extended red cell phenotype	Baseline
Pregnancy test (if woman of childbearing potential)	Within 3 days

\* If cytopenic (neutrophils  $<1.0 \times 10^9/L$  or platelets  $<50 \times 10^9/L$ ) prior to initiating treatment repeat FBC on day 15 of cycle 1. If this is within acceptable limits no additional FBC monitoring is required aside from D1 of future cycles.

### Additional investigations advised pre-first cycle

- HBA1C
- Uric acid
- TLS risk
- Plasma viscosity
- Serum protein electrophoresis
- $\beta 2$  microglobulin
- Bone profile (calcium, phosphate, magnesium)
- CRP
- LDH
- Serum free light chains (SFLC)/Paraprotein (PP)/Immunoglobulins (Igs)
- Urine protein/creatinine ratio
- Bone marrow examination for cytogenetic analysis FISH
- Pulmonary function

- Blood pressure
- Baseline echocardiogram/ECG
- Imaging as per local guidelines
- Evaluate for presence of neuropathy prior to starting bortezomib

### Investigations – pre subsequent cycles

Investigation	Validity period
FBC	7 days
Renal profile (U&Es including creatinine)	7 days
Liver profile (ALT/AST, ALP, bilirubin)	7 days
Pregnancy test (if woman of childbearing potential)	Within 3 days

### Additional investigations advised pre subsequent cycles

- SFLC, PP, Igs – results are not required prior to administration of cycle
- Bone profile (Calcium, phosphate, magnesium)
- HBA1C and glucose as required
- Blood pressure
- Echocardiogram/ECG as required
- Clinical assessment of neuropathy with bortezomib

### Standard limits for administration to go ahead

If blood results not within range, authorisation to administer must be given by prescriber/ consultant

Investigation	Limit
Neutrophils	$\geq 1.0 \times 10^9/L$
Platelets	$\geq 50 \times 10^9/L$
Creatinine clearance (CrCl)	$\geq 50\text{mL/min}$
Bilirubin	$< 1.5 \times \text{ULN}$
ALT	$< 1.5 \times \text{ULN}$

\*Consider the use of G-CSF to maintain dose intensity.

### Dose modifications

#### Bortezomib

Drug	Bortezomib
Full dose	$1.3\text{mg/m}^2$
Dose level -1	$1.0\text{mg/m}^2$
Dose level -2	$0.7\text{mg/m}^2$
Dose level -3	Discontinue bortezomib

#### Lenalidomide

Dose level	Dose
Starting dose	25mg
Dose level -1	20mg
Dose level -2	15mg
Dose level -3	10mg
Dose level -4	5mg
Dose level -5	5mg alternate days

## Haematological toxicity

To commence a new cycle, platelets should be  $\geq 50 \times 10^9/L$  and neutrophils  $\geq 1.0 \times 10^9/L$ . If cytopenia considered to be disease related, treatment may be given at consultant discretion.

**Isatuximab:** no specific modifications or dose reductions are advised. Dose delays maybe considered to allow recovery of blood counts.

**Bortezomib:** Interrupt dosing for Grade 4 toxicity (neutrophils  $< 0.5 \times 10^9/L$  or platelets  $< 25 \times 10^9/L$ ). Bortezomib may be reintroduced at the next dose reduction level once toxicity has resolved (neutrophils  $> 1.0 \times 10^9/L$  and platelets  $> 50 \times 10^9/L$ ).

### Lenalidomide:

Toxicity	Action
Neutrophils $< 1.0 \times 10^9/L$	Interrupt lenalidomide treatment, start GCSF and monitor FBC weekly. If first occurrence, restart at same dose once neutrophils $\geq 1.0 \times 10^9/L$ If recurrent neutropenia, restart at one dose level reduction once neutrophils $\geq 1.0 \times 10^9/L$ .
Platelets $< 30 \times 10^9/L$	Interrupt lenalidomide treatment and monitor FBC weekly. Once platelet count recovered to $\geq 50 \times 10^9/L$ , restart at one dose level reduction.

## Renal impairment

**Isatuximab:** No dose adjustment is recommended

**Bortezomib:** No dose modification is required for renal impairment. For dialysis patients, bortezomib should be given after dialysis

### Lenalidomide:

Creatinine clearance	Lenalidomide dose
$> 50\text{mL/min}$	25mg OD
30-50mL/min	10mg OD
$< 30\text{mL/min}$ (not requiring dialysis)	15mg alternate days
$< 30\text{mL/min}$ (requiring dialysis)	5mg OD (on dialysis days, administer after dialysis)

## Hepatic impairment

**Isatuximab:** No dose adjustment is required in mild hepatic impairment. Patients with moderate or severe hepatic impairment data is limited but there is no evidence for dose adjustment.

**Bortezomib:** If bilirubin  $> 1.5 \times \text{ULN}$  consider starting dose of  $0.7\text{mg/m}^2$  for cycle 1. For subsequent cycles consider increasing dose to  $1\text{mg/m}^2$  or reducing to  $0.5\text{mg/m}^2$  according to tolerability.

**Lenalidomide:** Lenalidomide has not been studied in patients with impaired hepatic function and there are no recommendations in terms of dosing.

For management of LFT derangement during treatment:

Bilirubin		AST/ALT	Lenalidomide dose
$\geq 3 \times \text{ULN}$ (for $\geq 5$ days)	or	AST/ALT $\geq 5 \times \text{ULN}$ (for $\geq 5$ days)	Hold until $\leq 1.5 \times \text{ULN}$ . Then resume at next lower dose level
$\geq 10 \times \text{ULN}$ (any duration)	or	AST/ALT $\geq 20 \times \text{ULN}$ (any duration)	Hold until $\leq 1.5 \times \text{ULN}$ . Then resume at next lower dose level

## Other toxicities

### Isatuximab

To decrease the risk and severity of infusion reactions, patients should be pre-medicated (see above). Vital signs should be frequently monitored during the entire infusion and if required interrupt the infusion and provide appropriate medical and supportive measures.

Infusion related reactions	Action/Dose adjustment
Grade 2 (moderate infusion reactions)	Temporary interruption in the infusion should be considered and additional symptomatic medicinal products can be administered until $\leq$ grade 1 (mild). Once $\leq$ grade 1, resume 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 per infusion table above (see <a href="#">administration section</a> ). If infusion reactions do not resolve or recur after initial improvement with appropriate medicinal products, require hospitalisation or are life-threatening, permanently discontinue treatment and institute appropriate management.
Grade $\geq 3$	Permanently discontinue treatment

### Bortezomib:

Neuropathy grade	Action and bortezomib dose
Grade 1 with no pain	100%
Grade 1 with pain or grade 2 but not interfering with daily living	Reduce to $1.0\text{mg}/\text{m}^2$
Grade 2 with pain or grade 3	Withhold until symptoms resolved. Restart at $0.7\text{mg}/\text{m}^2$
Grade 4	Discontinue

Any other  $\geq$  grade 3 non-haematological toxicity withhold bortezomib until recovered to  $\leq$  grade 1. Recommence with dose reduction of one level.

### Lenalidomide:

Toxicity	Definition	Dose adjustment
Neuropathy	Grade 2 with pain or any grade 3	Hold until $\leq$ grade 2; Resume at reduced dose level.
	Grade 4	Discontinue
Nausea, vomiting, diarrhoea, constipation, dehydration	$\geq$ grade 3	If symptoms persist despite maximal supportive therapy, interrupt lenalidomide until $\leq$ grade 1 then resume at current dose. For each subsequent event, reduce dose level.
Congestive heart failure	Any symptoms, whether or not drug related.	Interrupt treatment until resolution; After resolution continue treatment at reduced dose level.
Fatigue	$\geq$ grade 3	Interrupt lenalidomide until $\leq$ grade 1 then resume at current dose. For each subsequent event, reduce dose level.
Rash	Grade 2 or 3	Other causes for rash (e.g. co-trimoxazole) should be ruled out. Treatment of the rash can include topical steroids and emollients, in addition to antihistamines. Interrupt lenalidomide treatment if indicated. If rash resolves resume at next lower dose level.
	Grade 4 or angioedema, anaphylactic reaction, exfoliative or bullous rash,	Discontinue lenalidomide

	or Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) or Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) is suspected	
Other non-haematological toxicity	≥ grade 3	Interrupt lenalidomide. Assess at least weekly. If toxicity resolves to ≤ grade 1 prior to day 21, resume at reduced dose level and continue the cycle until day 21.

## Side Effects

### IMROZ study:

Toxicity		Any grade (%)	Grade 3 or 4 (%)
Haematological	Neutropenia	87.5	54.4
	Thrombocytopenia	95.4	30
	Anaemia	98.9	17.5
	Lymphopenia	95.4	60.1
	Leukopenia	97.3	31.6
Non-haematological	Pneumonia	30	20.2
	Bronchitis	22.1	2.7
	Upper respiratory tract infection	34.2	0.8
	Diarrhoea	54.8	7.6
	Peripheral sensory neuropathy	54.4	7.2
	Cataract	38	15.6
	Constipation	35.7	2.3
	Fatigue	34.6	8
	Peripheral oedema	32.7	0
	Infusion related reactions	23.6	0.4
	Covid-19	29.7	8.7
	Insomnia	22.4	3.8
	Back pain	22.1	3.4
	Asthenia	21.7	2.7
	Invasive second primary cancer - Solid tumour	8.4	5.3
	Invasive second primary cancer – Haematological cancer	1.1	0.4

### Specific drug related side effects:

#### Isatuximab

Common (>10%)	Uncommon (1-10%)	Rare (<1%)
Atrial fibrillation	Anaphylactic reaction	Not specified
Bronchitis	Secondary malignancy	
Cataract		
Diarrhoea		
Fatigue		
Infusion reaction		
Neutropenia, anaemia		



Respiratory infections		
Solid tumour and skin cancer		
Thrombocytopenia		

- **Isatuximab Infusion reactions**

In IMROZ, infusion reactions started on the infusion day in all patients, mostly during the first isatuximab infusion, and resolved the same day in 97.3% of patients. All infusion reactions resolved. The most common symptoms of an infusion reaction included dyspnoea and chills. The most common severe sign and symptom was hypertension.

### **Bortezomib**

Common (>10%)	Uncommon (1-10%)	Rare (<1%)
Thrombocytopenia, neutropenia, anaemia	Infections	Posterior Reversible Encephalopathy Syndrome
Peripheral sensory neuropathy	Motor neuropathy	Pneumonitis, acute respiratory distress syndrome
Orthostatic hypotension	Rash	Stevens-Johnson syndrome, toxic epidermal necrolysis
Fatigue, asthenia		Hepatitis, hepatic failure
Nausea, vomiting		Heart failure
Diarrhoea, constipation		

- **Peripheral neuropathy**

Patients should be advised to report pain, hypersensitivity, prickling, burning sensation, numbness and paraesthesia. If these occur see above dose reductions for bortezomib and consider use of amitriptyline or gabapentin. Caution in patients with existing peripheral neuropathy.

- **Dizziness/Orthostatic hypotension**

Patients should be advised that bortezomib may cause orthostatic hypotension and they should sit upright for a few minutes prior to standing up from a recumbent position. Caution is advised when treating patients with a history of syncope receiving medications known to be associated with hypotension or in those who are dehydrated. Management of orthostatic hypotension may include adjustment of antihypertensives, rehydration or administration of mineralocorticosteroids and/or sympathomimetics.

### **Lenalidomide:**

Common (>10%)	Uncommon (1-10%)	Rare (<1%)
Infection	Dry mouth	PML
Bruising or bleeding	Peripheral neuropathy	TLS
Constipation or diarrhoea	VTE	Impotence
Skin rash (see below)	Poor appetite	
Taste changes	Hypothyroidism	
Dizziness/hypotension	Tinnitus	
Bile salt malabsorption (see below)	Loss of appetite/weight loss	
*Teratogenicity	Secondary primary malignancies	

\*the pregnancy prevention programme should mitigate this risk

- **Rash**

Other causes for rash (e.g. co-trimoxazole) should be ruled out. Treatment of the rash can include topical steroids and emollients, in addition to antihistamines.

- **Bile salt malabsorption**

Bile salt malabsorption (BSM) is a relatively common side effect of lenalidomide therapy and can occur at any time during therapy. It tends to present with symptoms of diarrhoea, urgency and on occasions, incontinence. It is treated with the addition of bile salt sequestrants (e.g. cholestyramine 4g od, colesevelam 1.25-3.75g/day in 2-3 divided doses) with the dose being titrated according to symptoms. Screening for vitamin B12 deficiency is also advised as this can be a recognised complication of BSM.

- **Thrombosis**

If a patient experiences a thromboembolic event treatment with anticoagulation therapy should be initiated and the lenalidomide continued.

- **Pregnancy Prevention**

The conditions of the Lenalidomide Pregnancy Prevention Programme must be fulfilled for all male and female patients. All women of childbearing potential must use one effective method of pregnancy prevention at least 4 weeks before therapy, during therapy and for at least 4 weeks after stopping therapy. Men are required to use a barrier method of contraception during treatment.

#### **Dexamethasone**

<b>Common (&gt;10%)</b>	<b>Uncommon (1-10%)</b>	<b>Rare (&lt;1%)</b>
*High blood sugars	Blurred vision	Headache
Insomnia	Cataracts	Heart failure
Mood disturbance (depression, anxiety, euphoria)	Osteopenia	
Fluid retention	Acne	
GORD	Abnormal fat deposits	
Increased appetite		

\*pre-treatment HBA1C levels should be checked with monitoring for treatment emergent hyperglycaemia when HBA1C levels are >42mmol/mol. Patients with known diabetes/borderline diabetes should be referred to their diabetic nurse for close monitoring upon commencing dexamethasone

#### **Additional Information**

##### **Isatuximab:**

##### **Interference with Blood Transfusion Serological Testing**

Isatuximab binds to CD38 on red blood cells (RBCs) and may result in a false positive Indirect Antiglobulin Test (Coombs test) which may persist for at least 6 months after the last isatuximab infusion. Isatuximab bound to RBCs masks detection of antibodies to minor antigens in the patient's serum with no impact on ABO and Rh blood type.

- The blood transfusion laboratory must be notified that a patient has received isatuximab
- Patients must have a Blood Group and Antibody screen prior to starting isatuximab.
- Patients require pre-treatment red cell phenotyping/genotyping.
- Ensure patients carry a Patient Alert Card during treatment and for 6 months following discontinuation.
- Counsel patients to inform healthcare professionals that they received isatuximab, particularly before a transfusion.

##### **Interference with determination of complete response**

Isatuximab is a human IgG kappa monoclonal antibody detectable on both serum protein electrophoresis (SPE) and immunofixation (IFE) assays used for the clinical monitoring of endogenous M-protein. This interference can impact the accuracy of the determination of complete response and disease progression in patients with IgG kappa myeloma protein.

##### **Clarification:**

The IMROZ treatment protocol is as follows:

Isatuximab: Cycle 1: weekly for weeks 1-5 inclusive

Cycles 2-17: fortnightly

Cycles 18+: four weekly

Cycles 1-4: 42 day cycle

Bortezomib on days 1, 4, 8, 11, 22, 25, 29, 32

Lenalidomide on days 1-14 and 22-35 inclusive

Dexamethasone on days 1, 2, 4, 5, 8, 9, 11, 12, 15, 22, 23, 25, 26, 29, 30, 32, 33

Cycles 5-17: 28 day cycle

Lenalidomide on days 1-21 inclusive

Dexamethasone on days 1, 8, 15, 22

**This protocol is an adaptation of IMROZ and BENEFIT intended to minimise treatment related toxicities.**

### Drug regimen:

This regimen contains a total of:

- Cycle 1-19: 40 doses of isatuximab
- Cycle 1-8: 32 doses of bortezomib
- Cycle 1-6: 126 doses (6 x 21 days per cycle) of lenalidomide

**Significant drug interactions** – for full details consult product literature/ reference texts

### Isatuximab

No interaction studies have been performed.

### Bortezomib:

**Antihypertensives:** risk of additive hypotensive effect. Close monitoring of blood pressure is required.

**Oral antidiabetic agents:** hyper- and hypoglycaemia has been reported. Close monitoring of blood glucose levels is required.

**Ciclosporin:** increased risk of severe neuropathy - avoid concomitant use.

**High dose vitamin C:** reduced efficacy of bortezomib - avoid concomitant use.

**Cytochrome P34A inhibitors:** (e.g. itraconazole, voriconazole, posaconazole, clarithromycin, ritonavir) may increase bortezomib levels - avoid concomitant use.

**Cytochrome P34A inducers:** (e.g. rifampicin, carbamazepine, phenytoin, phenobarbital, St John's Wort) may reduce bortezomib levels - avoid concomitant use.

### Lenalidomide

**Erythropoietic agents:** increased risk of thrombosis – use with caution in patients with high risk to VTE

**Hormone treatments (including combined contraceptive pill, HRT):** increased risk of thrombosis – use with caution in patients with high risk to VTE

**Digoxin:** may increase plasma digoxin levels – monitor levels

**Statins:** increased risk of rhabdomyolysis when statins are administered with lenalidomide

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Version	Issue date	Review date	Revision	Written/Checked/Authorised
1	17/12/2025	December 2027	New protocol	Written: Dr S Moore (Consultant Haematologist, UHBW NHS Trust) and Dr A Whiteway (Consultant Haematologist, North Bristol NHS Trust) Checked: Anna Wong (Lead Pharmacist for Haematology SACT Protocols, SWAG Cancer Alliance) Authorised: Dr J Braybrooke (Consultant Oncologist, UHBW NHS Trust and SWAG Cancer Alliance)