Talquetamab (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

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Indication

Treatment of relapsed and refractory multiple myeloma after 3 or more lines of treatment (including an immunomodulatory drug, a proteasome inhibitor and an anti-CD38 antibody) and the myeloma has progressed on the last treatment. (NICE TA1114).

Response Rates

Phase I/II MonumenTAL-1 study

- ORR: 69.5%-74.1%
- Median PFS: 7.5-11.2 months
- 36 months OS: 49.3-60.8%

Treatment related mortality

1.4%-2.1%

Regimen details

Biweekly (every 2 weeks) dosing schedule – step up dosing week 1

Day	Drug	Dose	Route
1	Talquetamab	0.01mg/kg	SC injection
3	Talquetamab	0.06mg/kg	SC injection
5	Talquetamab	0.4mg/kg	SC injection
7	Talquetamab	0.8mg/kg	SC injection

A minimum of 2 days should be maintained between step-up doses. For dose delays, see 'administration' section.

Patients should be monitored for cytokine release syndrome (CRS) and immune-effector cell associated neurotoxicity syndrome (ICANS) for 48 hours after step-up doses on days 1, 3, 5 and 7. Patients should remain within the proximity of a healthcare facility or be treated as an inpatient during this period.

Biweekly (every 2 weeks) dosing schedule – ongoing treatment

Starts **two weeks** after week 1 day 7 dose

Day	Drug	Dose	Route
1 & 15	Talquetamab	0.8mg/kg	SC injection

A minimum of 12 days should be maintained between biweekly maintenance doses. For dose delays, see 'administration' section.

Cycle frequency

28 days (after initial step-up dosing)

Number of cycles

Until disease progression or unacceptable toxicity

Pre-medication

During step up dosing, 1-3 hours prior to talquetamab:

- Dexamethasone 16mg IV or PO
- Chlorphenamine 10mg IV or 4mg PO
- Paracetamol 1g IV or PO

Continue premedication for subsequent doses of talquetamab in patients who:

- Require repeat doses of the step up schedule due to dose delays
- Experience cytokine release syndrome (CRS) with previous doses

Supportive medication

Cycle 1 days 1-8: Omeprazole 20mg OD, consider ongoing treatment as indicated.
Cycle 1 only days 1-7: Allopurinol 300 mg OD (100mg OD if CrCl < 20mL/min)
Cycle 1 only days 1-14: Paracetamol 1g QDS PRN
Cycles 1-3: Levofloxacin 500mg OD (reduced dose if CrCl <50mL/min)
All cycles: Antiviral prophylaxis as per local policy and continue until off treatment for > 3 months
All cycles: Prophylactic co-trimoxazole 480mg BD on Mon, Weds, Fri until CD4 count >200/microL
All cycles: Metoclopramide 10mg TDS PRN
Hep B virus treatment entecavir: screen for virus prior to treatment and start if positive hep B PCR.
Ganciclovir/valganciclovir: if positive CMV PCR with CMV related organ disease. Monitor the viral load.
Bisphosphonates as per SWAG 'Bone Protection Myeloma' protocol
IVIg monthly when total IgG <4g/L. Recommended dose of IVIg: 0.4-0.6g/kg/month to achieve a trough level of at least the lower limit of the age-specific reference range. Continue when off treatment until IgG >4g/L as per NHSE policy

Emetogenicity

Low risk

Administration

Inject into the subcutaneous tissue of the abdomen (preferred) or, alternatively, it may be injected into the subcutaneous tissue at other sites (e.g. thigh). Each injection volume should not exceed 2mL, doses greater than 2 mL should be divided equally between multiple syringes. If multiple injections are required, injections should be administered at least 2 cm apart. Do not press or rub the site of injection. Do not inject into areas where the skin is red, bruised, tender, hard or not intact.

If a dose is delayed, treatment should be restarted according to the table below, based on last dose administered and length of delay:

Last dose administered	Duration of delay from last dose administered	Action
Step-up dose 1 (0.01mg/kg)	> 7 days	Restart step-up dosing schedule at step-up dose 1 (0.01mg/kg)
Step-up dose 2 (0.06mg/kg)	8 - 28 days	Repeat step-up dose 2 (0.06mg/kg) and continue step-up schedule
	> 28 days	Restart step-up dosing schedule at step-up dose 1 (0.01mg/kg)
Step-up dose 3 (0.4mg/kg)	8 - 35 days	Continue with maintenance dose (0.4mg/kg) at previous schedule
	36 – 56 days	Repeat step-up dose 2 (0.06mg/kg) and continue step-up schedule
	> 56 days	Restart step-up dosing schedule at step-up dose 1 (0.01mg/kg)
Any maintenance doses (0.8mg/kg)	14 – 35 days	Continue with maintenance dose (0.8mg/kg) at previous schedule
	36 – 56 days	Repeat step-up dose 3 (0.4mg/kg) and continue step-up schedule
	> 56 days	Restart step-up dosing schedule at step-up dose 1 (0.01mg/kg)

Extravasation

N/A

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, albumin)	14 days
Clotting screen	14 days
Virology (Hep B/C, HIV, CMV (inc PCR), EBV inc PCR))	3 months
Immunoglobulins	14 days

Additional investigations advised pre-first cycle

- HBA1C
- Serum protein electrophoresis
- Serum free light chains
- β2 microglobulin
- Bone profile (Calcium, phosphate, magnesium)
- CRP
- LDH
- Serum free light chains (SFLC)/Paraprotein (PP)
- Urine protein/creatinine ratio
- Bone marrow examination for cytogenetic analysis FISH
- Imaging as per local guidelines
- ECG/ECHO (if indicated)
- Blood pressure
- Baseline ICE score
- Annual flu, Covid-19 and pneumococcal vaccination

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
Immunoglobulins	7 days

Additional investigations advised pre subsequent cycles

- SFLC, PP – results are not required prior to administration of cycle
- Bone profile (Calcium, phosphate, magnesium)
- Viral PCRs inc EBV, CMV (every 3 months)
- Blood pressure

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	≥ 0.5 x 10^9/L
Platelets	≥ 25 x 10^9/L
Haemoglobin (Hb)	≥ 80g/L
Creatinine clearance (CrCl)	> 30 mL/min
Bilirubin	< 1.5 x ULN
ALT/AST	< ULN (see below)

Dose modifications

Dose modifications are not recommended. Dose delays may be required to manage toxicities.

Haematological toxicity

Toxicity	Action
Hb <80g/L	Withold dose until Hb≥80g/L or consider transfusion if disease related.
Neutrophils <0.5 x 10^9/L or febrile neutropenia	Withold dose until count ≥ 0.5 x 10^9/L (or > 1.0 x 10^9/L and resolution of fever if febrile neutropenia). Consider GCSF if disease related.
Platelets <25 x 10^9/L or Platelets 25 -50 x 10^9/L with bleeding	Withold dose until count ≥ 25 x 10^9/L and no evidence of bleeding

Renal impairment

No dose adjustment is recommended in mild to moderate renal impairment (>30mL/min). No data is available in patients with severe renal impairment (<30mL/min).

Hepatic impairment

No dose adjustment is recommended in mild hepatic impairment (bilirubin <1.5 x ULN with any ALT). There is insufficient data available in patients with moderate or severe hepatic impairment.

Other toxicities

Toxicity	Definition	Action/Dose adjustment
Cytokine release syndrome (CRS)	Any grade	If CRS is suspected, treatment should be withheld until adverse reaction resolves. For recurrent or persistent (>48 hrs) Grade 3 or any Grade 4 CRS permanently discontinue talquetamab For management of CRS see below.
Immune effector cell-associated neurotoxicity syndrome (ICANS)	Any grade	If ICANS is suspected, treatment should be withheld until adverse reaction resolves. • For first occurrence Grade 3 ICANS, patient must be monitored for 48 hours following the next dose of talquetamab. Patients should remain within the proximity of a healthcare facility or be treated as an inpatient during this period. • For recurrent Grade 3 or any Grade 4 ICANS permanently discontinue talquetamab For management of ICANS see below.

Toxicity	Definition	Action/Dose adjustment
Neurologic toxicity (excluding ICANS)	Grade 1	Withhold talquetamab until neurologic toxicity symptoms resolve or stabilise.
	Grade 2 or 3 with first occurrence	Withhold talquetamab until neurologic toxicity symptoms improves to ≤ Grade 1 and provide supportive therapy.
	Grade 3 (recurrent) or 4	Permanently discontinue talquetamab and provide supportive therapy which may include intensive care.
Infections	Any grades	For patients on step-up dosing schedule, DO NOT administer, restart on resolution of active infection.
	≥grade 3	Withhold subsequent maintenance doses of talquetamab until infection resolves to ≤ Grade 2.
Oral toxicity, including weight loss	≥grade 2	Interrupt talquetamab until stabilisation or improvement, and consider restarting on modified schedule as follows: • If current dose is 0.4 mg/kg every week, change to 0.4 mg/kg every two weeks • If current dose is 0.8 mg/kg every two weeks, change to 0.8 mg/kg every four weeks
Skin reactions, including nail disorders	≥grade 3	Withold talquetamab until adverse reaction resolves to ≤ Grade 1.
Any other non-haematological toxicity	≥grade 3	Withold talquetamab until adverse reaction resolves to ≤ Grade 1.

Side Effects

MonumenTAL-1 study:

Toxicity		0.8mg/kg Biweekly	
		Any grade (%)	Grade 3 or 4 (%)
Haematological	Anaemia	43	17
	Neutropenia	29	22
	Lymphopenia	30	26
	Thrombocytopenia	29	18
	Leukopenia	19	12
Non-haematological	Cytokine release syndrome	75	1
	Immune Effector Cell Neurotoxicity Syndrome (ICANS)	10	4
	Taste-related changes	71	N/A
	Non-rash skin-related adverse events	74	1
	Dysgeusia	72.1	2
	Infection (incl COVID-19)	68.2	18.2
	Nail-related adverse events	53	0
	Weight decreased	41	5
	*Rash-related adverse events	34	5
	Dry mouth	39	0
	Pyrexia	27	1
	Diarrhoea	27	1
	Fatigue	28	1

	Decreased appetite	28	1
	Dysphagia	25	2
	Cough	21	0
	Headache	21	1
	Nausea	19	0
	Arthralgia	18	0
	Asthenia	11	1
	Constipation	20	0
	COVID-19	26	3

*Median time to onset from the first treatment dose was 22 days.

Specific drug related side effects:

Cytokine Release Syndrome (CRS)

Cytokine release syndrome (CRS), including life-threatening or fatal reactions, may occur in patients receiving talquetamab. The median time to onset is 2 days (range 1-6 days) and the median time to resolution is 2 days (range 1-9 days). Clinical signs and symptoms may include fever, hypoxia, chills, hypotension, tachycardia, headache and elevated liver enzymes. If CRS is suspected treatment should be withheld and the following investigations should be performed:

- FBC, U&Es, LFTs, bone profile, CRP, ferritin and coagulation screen, CXR and ECG

Management of CRS should be as the table below:

Grade	Symptoms	Management
1	Temp >38 °C **AND** no hypoxia or hypotension	• Monitor vital signs every 4 hours • Treat as per neutropenic sepsis guidelines • Consider early tocilizumab use • If persistent fevers (>24-48 hrs), consider IV tocilizumab 8mg/kg (max 800mg) over 1 hr* •
2	Temp >38 °C **WITH** hypotension responsive to fluids **OR** hypoxia requiring <6L/min O2	• Monitor vital signs every 4 hours • Treat as per neutropenic sepsis guidelines • Administer IV tocilizumab 8mg/kg (max 800mg) over 1 hr, repeat every 8 hours as needed* • Consider IV methylprednisolone 1mg/kg bd • Inform ICU/consider transfer • Administer O2 and fluids •
3	Temp >38 °C **WITH** hypotension requiring vasopressors **OR** hypoxia requiring >6L/O2	**TRANSFER TO ITU** • Treat as per neutropenic sepsis guidelines • Perform continuous cardiac monitoring and echo • Administer vasopressors as required • Administer O2 as required • Administer IV tocilizumab 8mg/kg (max 800mg) over 1 hr, repeat every 8 hours as needed* • Administer IV methylprednisolone 1mg/kg bd • If refractory, consider IV methylprednisolone 1g OD and/or alternative immunosuppressive agents (e.g. anakinra) • For recurrent or duration ≥48 hours grade 3 CRS, permanently discontinue talquetamab.

Grade	Symptoms	Management
4	Temp >38 **WITH** hypotension requiring multiple vasopressors **OR** hypoxia requiring CPAP/BiPAP/ventilation	**TRANSFER TO ITU** • Treat as per neutropenic sepsis guidelines • Perform continuous cardiac monitoring and echo • Administer vasopressors • Administer O2 • Administer IV tocilizumab 8mg/kg (max 800mg) over 1 hr, repeat every 8 hours as needed* • Administer IV methylprednisolone 1g OD and/or alternative immunosuppressive agents (e.g. anakinra) • Permanently discontinue talquetamab.

*Max 3 doses in a 24 hour period, maximum total of 4 doses.

Immune Effector Cell Neurotoxicity Syndrome (ICANS)

Immune effector cell neurotoxicity syndrome (ICANS) is a potential neurological complication seen in patients receiving talquetamab. 3% of patients experienced >1 ICANS event. Clinical signs of ICANS can include a change in cognitive state, fall in GCS and seizures.

ICANS monitoring

- Check Immune effector Cell Encephalopathy (ICE) score using ICE assessment tool, prior to receiving talquetamab
- Check ICE score twice a day whilst an inpatient and twice a day for 48 hours as an outpatient during step up dosing
- If grade 2 or higher ICANS experienced, patients should be monitored as an inpatient for 48 hours following the next dose.
- If ICANS is suspected a neurological examination should be performed, in addition to the following investigations:
  - ECG
  - Three times a day ICE assessment
  - MRI brain/CT brain
  - Consider diagnostic lumbar puncture

ICE assessment tool

	Question	Points
1	Which year is it?	1
2	Which month is it?	1
3	Which city/town are we in?	1
4	Which hospital are we in?	1
5	Follow an instruction e.g. touch your nose, lift your right arm, shrug your shoulders	1
6	Name 3 objects Point to three different objects	3
7	Write a sentence	1
8	Count backwards from 100 in 10's	1

Management of ICANS should be as the table below, with grading based on score from the ICE assessment:

ICE score and symptoms	Management	
	Monitoring/Investigations	**Treatment**
Score 10	No ICANS present	
Grade 1 - Score 7-9 Awakes spontaneously	**Score 3-9** • Three times a day ICE score • Regular neurological observations • Consider tocilizumab if concurrent CRS	**Score 7-9** • If persistent symptoms (>48 hrs), consider IV dexamethasone (10mg QDS) until resolution, then taper • Consider seizure prophylaxis*
Grade 2 - Score 3-6 Awakes to voice		**Score 3-6** • Administer IV dexamethasone (10mg QDS) until resolution to grade 1 or less, then taper • Administer antiepileptics • Consider EEG and imaging
Grade 3 - Score 0-2 AND Awakes to tactile stimuli Seizures resolve rapidly Focal cerebral oedema on imaging	**Score 0-2** **TRANSFER TO ICU** • Regular neurological observations • Three times a day ICE score • Perform neuroimaging and EEG • Administer antiepileptics • Consider CSF evaluation for other causes/pressure measurement • Consider tocilizumab if concurrent CRS	**Score 0-2 and rousable** • Administer IV dexamethasone (10mg QDS) until resolution to grade 1 or less, then taper • If refractory consider IV methylprednisolone 1g daily for 3 days. Taper when symptoms improve
Grade 4 - Score 0 AND Unrousable, prolonged (>5 min) or frequent seizures, motor weakness, diffuse cerebral oedema on imaging		**Score 0 and unrousable** • Administer IV methylprednisolone 1g daily for 3 days. Taper when symptoms improve • For refractory patients consider alternative therapies (e.g. anakinra)

*Seizure prophylaxis includes levetiracetam 500mg po/IV bd, up to 2000mg bd

Additional information

N/A

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

No formal drug interactions have been identified. Based on in vitro and clinical data, there is a low risk of pharmacokinetic or pharmacodynamic drug interactions.

CYP450 substrates with narrow therapeutic index: transient elevation of proinflammatory cytokines when starting treatment with talquetamab may suppress CYP450 activities, consider therapeutic monitoring of substrate if narrow therapeutic index.

References

- National Institute for Health and Care Excellence (NICE), TA1114 accessed: 17th December 2025 via www.nice.org.uk
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- Chari, A. et al. Safety and activity of talquetamab in patients with relapsed or refractory multiple myeloma (MonumenTAL-1): a multicentre, open-label, phase 1-2 study. Lancet Haematol. 2025;12: e269-81.
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Version	Issue date	Review date	Revision	Written/Checked/Authorised
1	December 2025	December 2028	New protocol	Written: Dr S Moore (Consultant Haematologist, UHBW NHS Trust), Dr A Whiteway (Consultant Haematologist, North Bristol NHS Trust) and Dr J Crowe (Consultant Haematologist, RUH 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)