SMC2863

talquetamab solution for injection (Talvey®)

Johnson & Johnson Innovative Medicine

08 May 2026

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and, following review by the SMC executive, advises NHS Boards and Area Drug and Therapeutic Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

ADVICE: following a full submission

talquetamab (Talvey®) is accepted for use within NHSScotland.

Indication under review: as monotherapy for the treatment of adult patients with relapsed and refractory multiple myeloma, who have received at least 3 prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy.

In an uncontrolled phase I/II study, patients with relapsed and refractory multiple myeloma who had at least 3 prior therapies (including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody), and received talquetamab 0.8 mg/kg every two weeks, achieved an objective response rate of 70%.

This advice applies only in the context of an approved NHSScotland Patient Access Scheme (PAS) arrangement delivering the cost-effectiveness results upon which the decision was based, or a PAS/ list price that is equivalent or lower.

Chair
Scottish Medicines Consortium

1. Clinical Context

1.1. Medicine background

Talquetamab is an immunoglobulin G4 (IgG4) bispecific antibody that targets the CD3 receptor complex expressed on T cells and the G protein-coupled receptor class 5D (GPRC5D) expressed on multiple myeloma cells. This leads to the activation of T cells and induces subsequent lysis of GPRC5D-expressing multiple myeloma cells.[1, 2]

The recommended dose of talquetamab is 0.4 mg/kg once a week or 0.8 mg/kg once every two weeks, administered subcutaneously. This is preceded by step-up doses of 0.01 mg/kg on day 1, 0.06 mg/kg on day 3 and 0.4 mg/kg on day 5; an additional dose of 0.8 mg/kg is given on day 7 of the biweekly (every two weeks) dosing schedule. Treatment should continue until disease progression or unacceptable toxicity. See the summary of product characteristics (SPC) for further information.[1]

1.2. Disease background

Multiple myeloma is a rare haematological cancer which mostly affects people over 60 years of age and is caused by the abnormal proliferation of monoclonal plasma cells in the bone marrow. Common symptoms and presenting features include anaemia, bone pain, hypercalcaemia, renal impairment, increased susceptibility to infections and neurological complications. Despite advances in therapy improving outcomes, the disease is incurable and almost all patients eventually relapse as they acquire resistance to treatment. The period between response and relapse shortens with each successive treatment and patients often receive multiple lines of therapy. Relapsed and refractory myeloma is defined as disease that progresses on therapy or progresses within 60 days of the last treatment in patients who previously achieved at least a minimal response. Patients with triple class refractory disease (that is, refractory to a proteasome inhibitor, an immunomodulatory drug, and an anti-CD38 antibody) have a poor prognosis with limited overall survival (OS). [2-5]

1.3. Treatment pathway and relevant comparators

The treatment pathway for multiple myeloma is patient specific; pharmacological options depend on fitness, response to previous treatment, the number of prior lines of therapy and patient choice. Most patients early in the treatment pathway will receive a combination regimen that includes at least one of a proteasome inhibitor (for example, bortezomib), an immunomodulatory agent (for example, lenalidomide) and an anti-CD38 monoclonal antibody (for example, daratumumab). Other available options used in combination regimens for relapsed or refractory multiple myeloma include the antibody-drug conjugate, belantamab mafodotin, and the histone deacetylase inhibitor, panobinostat. Chimeric antigen receptor T-cell (CAR-T) therapies (ciltacabtagene autoleucel and idecabtagene vicleucel) are also licensed in this setting. However they have not been launched in the UK and therefore SMC has not issued advice on these treatments. Experts indicated use of CAR-T therapies across Scotland is low, mainly through clinical trials. Guidelines recommend a different backbone agent to the most recent regimen unless there has been a long treatment-free interval and therefore there are multiple different treatment options for patients who have progressed following at least three prior therapies

(including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody) and have demonstrated disease progression on the last therapy.[2, 6]

Teclistamab and elranatamab are both bispecific antibodies that target CD3 and B-cell maturation antigen (BCMA) receptors and, in September 2024 were accepted for use within NHS Scotland for patients with relapsed and refractory multiple myeloma who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody (SMC2668 and SMC2669). In October 2024, selinexor (a first in class selective inhibitor of nuclear export [SINE] compound that inhibits XPO1) was accepted for use within NHS Scotland in combination with dexamethasone for patients with multiple myeloma who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, two immunomodulatory agents and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy (SMC2673). Clinical experts consulted by SMC considered teclistamab and elranatamab the most relevant comparators in the fourth-line setting, with selinexor plus dexamethasone a less relevant comparator later in the treatment pathway. Some SMC experts also highlighted pomalidomide, isatuximab and dexamethasone if patients are not anti-CD38 antibody refractory or pomalidomide and dexamethasone as additional treatment options which may also be displaced by talquetamab.

1.4. Category for decision-making process

Eligibility for interim acceptance

Talquetamab has conditional marketing authorisation from the Medicines and Healthcare products Regulatory Agency (MHRA).

Eligibility for a PACE meeting

Talquetamab meets SMC end of life and orphan equivalent criteria for this indication.

2. Summary of Clinical Evidence

2.1. Evidence for the licensed indication under review

Evidence to support the efficacy and safety of talquetamab for the indication under review is from the MonumenTAL-1 study. The submitting company have focussed this submission on patients who received talquetamab 0.8 mg/kg every two weeks. See Table 2.1 for details.

Table 2.1. Overview of relevant studies[2, 7]

Criteria	MonumenTAL-1
Study design	A multicentre, open-label single-arm, phase I/II study. Phase I included dose escalation (part 1) and dose expansion (part 2). Phase II included treatment at the recommended phase 2 doses (part 3).
Eligible patients	• Adults ≥18 years of age. • A diagnosis of measurable multiple myeloma according to International Myeloma Working Group (IMWG). • Documented progressive disease based on IMWG 2016 criteria. • ≥3 previous lines of therapy that included a proteasome inhibitor, immunomodulatory drug, and anti-CD38 antibody (phase II). • An Eastern Cooperative Oncology Group performance status (ECOG PS) of 0 to 1 (parts 1 and 2) or 0 to 2 (part 3).

	• Patients who had prior exposure to T-cell redirecting (TCR) therapy (including bispecific antibody or chimeric antigen receptor T-cell (CAR-T) therapy) were excluded from Cohorts A and C (see treatments below) but included in Cohort B.
Treatments	Talquetamab was administered by subcutaneous injection at the following doses to three groups of patients. • 0.4 mg/kg on day 1, 8, 15 and 22 of a 28-day cycle, preceded by step-up dosing of 0.01 mg/kg and 0.06 mg/kg each separated by 2 to 4 days and to be completed 2 to 4 days before the first treatment dose (Cohort A). • 0.8 mg/kg on day 1 and 15 of a 28-day cycle, preceded by step-up dosing of 0.01 mg/kg, 0.06 mg/kg and 0.3 mg/kg each separated by 2 to 4 days and to be completed 2 to 4 days before the first treatment dose (Cohort C). • 0.4 mg/kg or 0.8 mg/kg according to the dosing regimens above (previous TCR therapy group) (Cohort B). Patients received treatment until disease progression, unacceptable toxic effects, withdrawal of consent, or end of study.
Randomisation	Not applicable.
Primary outcome	Overall response rate (ORR), defined as the proportion of patients who had a partial response or better assessed by independent committee review based on IMWG 2016 criteria.
Selected secondary outcomes	Duration of response, time to response, minimal residual disease negativity, progression free survival and OS.
Statistical analysis	Safety and activity were analysed in patients who received at least one dose of talquetamab in phase I (at the recommended phase II dose) and II (all-treated analysis set). The primary efficacy analyses evaluated the null hypothesis that the ORR was ≤ 30% in the 0.4 mg/kg weekly and 0.8 mg/kg every two weeks groups and ≤15% in the previous TCR group.

Key efficacy results from the data cut (September 2024) have been presented in Table 2.2. After a median follow-up of 31.2 months, the ORR was 70% in the 0.8 mg/kg every two weeks group. Supportive evidence is available from a group of patients that received talquetamab at a dose of 0.4 mg/kg once weekly. This dosing regimen is also licensed but was considered less relevant by the submitting company as they anticipate most patients will receive talquetamab every two weeks. An additional group of patients had previous T-cell redirecting (TCR) therapy targeting BCMA and included 33% (26/78) with previous exposure to a bispecific antibody (for example, teclistamab or elranatamab) and 73% (57/78) with previous exposure to CAR-T therapy (not currently available in Scotland). Patients in this group had either talquetamab weekly or every two weeks.[1, 7] The ORR is similar in all three groups however the duration of response was longer in the 0.8 mg/kg every two weeks group and previous TCR therapy group. Median progression free survival (PFS) was longer in the 0.8 mg/kg every two weeks group compared with the other groups.

Table 2.2. Key efficacy results for MonumenTAL-1 (data cut: September 2024) (all-treated analysis set).[8, 9]

	Talquetamab 0.8 mg/kg every two weeks (Cohort C) (n=154)	Talquetamab 0.4 mg/kg every week (Cohort A) (n=143)	Talquetamab 0.4 mg/kg every week or 0.8 mg/kg every two weeks[a] (Cohort B) (n=78)
Previous TCR therapy	**No**	**No**	**Yes**
Median follow-up	31.2 months	38.2 months	30.3 months
Primary outcome: ORR assessed by IRC per IMWG criteria			
ORR	70%	74%	67%
Stringent CR	31%	23%	33%
CR	9.1%	9.8%	9.0%
Very good PR	19%	27%	13%
PR	10%	15%	12%
Secondary outcome: median DOR assessed by IRC per IMWG criteria			
Median DOR[b]	17.5 months	9.5 months	19.2 months
Secondary outcome: PFS assessed by IRC per IMWG criteria			
Median PFS	11.2 months	7.5 months	7.7 months
Secondary outcome: overall survival			
Median OS	NE	34.0 months	28.3 months
OS rate at 36 months	61%	49%	45%

Abbreviations: CR = complete response; DOR = duration of response; IMWG = International Myeloma Working Group; IRC = independent review committee; NE = not estimable; ORR = overall response rate; OS = overall survival; PFS = progression free survival; PR = partial response; TCR = T-cell redirecting. [a]n=70 received 0.4 mg/kg once weekly and n=8 received 0.8 mg/kg every two weeks. [b] Assessed in 107 (0.8 mg/kg every two weeks), 106 (0.4 mg/kg once weekly) and 52 (previous TCR therapy) patients who achieved a response.

*Other data were also assessed but remain confidential.**

2.2. Health-related quality of life outcomes

Health-related quality of life was assessed using European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 (EORTC QLQ-C30), EuroQol 5-Dimension 5-Level (EQ-5D-5L) and the Patient Global Impression scale - Severity (PGI-S). For patients in MonumenTAL-1 in the 0.8 mg/kg every two weeks group, after an initial worsening from baseline to cycle 1, most patient-reported outcomes either returned to baseline and stabilised or demonstrated an improvement throughout treatment. There were notable improvements in the EORTC QLQ-C30 emotional functioning (least squares [LS] mean change 12.5 points) and pain (LS mean change 11.4) from baseline to cycle 21.[10]

2.3. Indirect evidence to support clinical and cost-effectiveness comparisons

In the absence of direct evidence, the submitting company presented indirect evidence that compared talquetamab to teclistamab and selinexor plus dexamethasone. Survival and safety results have been used to inform the cost-effectiveness analysis.

Table 2.3: Summary of indirect treatment comparison

Criteria	Overview	
Comparators	Teclistamab	Selinexor plus dexamethasone
Design	Adjusted indirect treatment comparison (ITC), and naïve comparison.	Unanchored matched adjusted indirect comparison (MAIC)
Population	Adults with relapsed or refractory multiple myeloma, who have received at least 3 prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy.	Adult patients with penta-refractory triple class exposed relapsed or refractory multiple myeloma.
Studies included	MonumenTAL-1[8, 9] and MajesTEC-1[11]	MonumenTAL-1[8, 9] and STORM[12]
Outcomes	OS and PFS. Adverse events (AEs) for teclistamab comparison only.	
Results	The results of the ITC suggest that talquetamab is superior to teclistamab for OS. There was no evidence of a difference between treatments for PFS. The results of a naïve comparison of safety outcomes suggested grade 3 or 4 infections were more frequently reported with teclistamab. Immune effector cell-associated neurotoxicity syndrome (ICANS) and GPRC5D-related adverse events were more common with talquetamab. Other safety outcomes were similar in both groups. Results for indirect comparisons were considered confidential by the company.	The results of the MAIC suggest that talquetamab is superior to selinexor plus dexamethasone for PFS and OS. Results for indirect comparisons were considered confidential by the company.

*Other data were also assessed but remain confidential.**

3. Summary of Safety Evidence

Evidence from the MonumenTAL-1 study supports the safety of talquetamab for the treatment of patients with multiple myeloma. There are no direct comparative safety data available, however, an indirect unadjusted (naïve) comparison for selected outcomes was provided by the company. Published safety data from MonumenTAL-1 are available from an October 2023 (post hoc) data cut with a median duration of follow-up of 19.4 months. In the 0.8 mg/kg every two weeks group, treatment-emergent adverse events (TEAEs) resulted in 9.1% (14/154) of patients discontinuing treatment, a dose reduction was required by 8.4%, and 53% reported at least one serious adverse event. The most common grade 3 or 4 haematological TEAEs were anaemia (26%), lymphopenia (26%), neutropenia (21%), thrombocytopenia (18%) and leukopenia (12%). These were generally reversible and limited to the first few treatment cycles. Other common AEs included non-rash skin-related (74%), taste changes (71%), nail-related adverse (53%) and rash-related (34%) events. These are considered on-target, off-tumour AEs and were mainly low-grade in severity.[7]

Cytokine release syndrome (CRS) was the most frequently reported TEAE of any grade (75% [115/154]). Most events occurred during the step-up or first full doses. Supportive treatments were required by 71% including 37% who required tocilizumab. ICANS of any grade was reported

by 10% (12/118) of patients with 3.4% grade 3 or 4 in severity. Most events occurred concurrently with CRS. Infections were also common and occurred in 68% of patients with 18% reported as grade 3 or 4 in severity.[7]

The regulator noted that the safety profile could be considered manageable with appropriate risk minimisation measures, however severe CRS and ICANS toxicity remain serious issues that should be considered. The limited follow-up and overall size of the safety database, particularly for patients with previous TCR therapy limited comprehensive assessment and therefore longer-term safety data, including from controlled studies has been requested as part of the conditional marketing authorisation. See the SPC for further information.[1, 2]

4. Summary of Clinical Effectiveness Considerations

4.1. Key strengths

- Talquetamab is the first bispecific antibody that targets the GPRC5D receptor on myeloma cells. This is a distinct mechanism of action from other bispecific antibodies licensed for the same indication which target BCMA.[7]
- In the MonumenTAL-1 study (September 2024 data cut), the ORR of patients with relapsed or refractory multiple myeloma who had least three previous lines of therapy and received talquetamab monotherapy 0.8 mg/kg every two weeks was 70%. This was supported by deep and durable responses. Similar results from an earlier data cut-off were considered clinically relevant by the regulator in the context of a heavily pre-treated population characterised by treatment resistance.[2, 8]

4.2. Key uncertainties

- In the absence of direct or indirect evidence versus elranatamab, the submitting company assumed a similar efficacy and safety profile with teclistamab, although there may be some uncertainty as inconsistent results have been reported in real-world studies and indirect comparisons.[13-17] SMC clinical experts generally agreed this was a reasonable assumption and indicated elranatamab was the preferred bispecific antibody used in clinical practice in Scotland which was confirmed with the Cancer Medicines Outcome Programme Public Health Scotland (CMOP-PHS) report.[18] Some clinical experts identified additional potential comparators including pomalidomide and dexamethasone with or without isatuximab depending on anti-CD38 antibody refractory status. There are no direct or indirect data versus these treatments.
- The indirect evidence was associated with several limitations. Both comparisons use data from small single-arm phase II studies with no common comparator. For the comparison versus teclistamab, there is an early and sustained separation of the OS Kaplan-Meier curves which is inconsistent with the PFS results, increasing uncertainty regarding the suggested survival benefit. The submitting company suggest the reasons for early and sustained separation of the OS curve is because of a reduction in early deaths due to progressed disease, and lower risk of infection-related mortality and T-cell exhaustion with talquetamab. For the comparison versus selinexor plus dexamethasone, not all identified prognostic covariates could be matched and the effective sample size was substantially reduced. Due to these limitations the results for the

comparison versus teclistamab are uncertain and versus selinexor plus dexamethasone are highly uncertain.

- SMC experts indicated that talquetamab may be used in patients who have received prior BCMA-directed treatments, including after other bispecific antibodies. However, the 0.8 mg/kg every two weeks and 0.4 mg/kg once weekly groups in MonumenTAL-1 excluded patients with prior exposure to bispecific antibodies or CAR-T therapy and only 11% and 15% in the respective groups had received belantamab mafodotin (an antibody-drug conjugate targeting BCMA). The previous TCR therapy group provides limited evidence in this population, however most patients received CAR-T therapy which is not available in this setting in Scotland.[7]
- The company focussed this submission on a group of patients who were naïve to T-cell redirecting therapy and received talquetamab at a dose of 0.8 mg/kg every two weeks as they anticipated that most patients (~90%) would receive this regimen. SMC clinical experts broadly agreed with this assumption. At the latest data cut-off, survival data remained immature and median OS has not yet been reached. As a substantial proportion of surviving patients had started at least one subsequent treatment, it is likely that longer term OS events will be confounded.[8, 9]
- The open-label study design may bias subjective efficacy, quality of life and safety outcomes. This risk was minimised for response and PFS outcomes which were assessed by independent review committee.
- There were some limitations that may affect the generalisability of results to patients in Scotland. Patients with severe anaemia (<8 g/dL), severe renal failure (glomerular filtration rate <40 mL/min) and high serum calcium levels (>14 mg/dL) were excluded from the MonumenTAL-1 study. This is relevant as these are common complications that can present with multiple myeloma.[2, 19]

4.3. Clinical expert input

Clinical experts consulted by SMC considered that talquetamab fills an unmet need and is a therapeutic advance due to its distinct GPRC5D target compared with other bispecific antibodies used in this setting which target BCMA. They indicated it may be used in patients who have received prior BCMA-targeted treatments or in those with a particularly high infection risk.

4.4. Service implications

The introduction of talquetamab could have substantial service and resource implications as an inpatient stay is required during the step-up dosing in most treatment centres to closely monitor for CRS and ICANS.

5. Summary of Patient and Carer Involvement

The following information reflects the views of the specified Patient Group.

- We received a patient group submission from Myeloma UK, which is a registered charity.
- Myeloma UK has received 2.03% pharmaceutical company funding in the past two years, including from the submitting company.

- Myeloma is an incurable blood cancer which can be treated with sequential lines of combination treatments. Patients relapse after every line of treatment as their myeloma becomes resistant. The complications of myeloma can be debilitating and painful; they include severe bone pain, bone destruction, kidney damage, fatigue and a depleted immune system.
- There is a need for anti-myeloma treatments with novel mechanisms of action which will deliver deeper responses and be clinically effective for patients who have failed previous lines of treatment. Talquetamab is a GPRC5D targeted bispecific antibody. There is currently no treatment with this mechanism of action approved for use in the NHS in Scotland.
- Patient interviews conducted by the patient group showed that patients who had received talquetamab would recommend it for approval on the NHS. They reported that side-effects occurred but were manageable.
- Talquetamab can deliver benefits which are important to patients such as good response rates, deep remission, and improved quality of life. The administration through fortnightly subcutaneous injections was also considered an advantage. In addition, fortnightly dosing can be considered from the fourth dose giving patients more freedom and flexibility at an earlier stage in treatment than other treatments.

6. Summary of Comparative Health Economic Evidence

6.1. Economic case

An economic case was presented and is summarised in Table 6.1.

Table 6.1 Description of economic analysis

Criteria	Overview
Analysis type	Cost-utility analysis.
Time horizon	A lifetime time horizon of 40 years was used.
Population	The submitting company requested SMC consider talquetamab for the treatment of adult patients with relapsed and refractory multiple myeloma, who have received at least 3 prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy.
Comparators	Teclistamab, elranatamab, and selinexor plus dexamethasone were comparators in the analysis. The main economic evaluation was conducted versus teclistamab, with supportive evaluations provided versus elranatamab and selinexor plus dexamethasone. Based on SMC expert responses, elranatamab and teclistamab were considered the main comparators, with selinexor plus dexamethasone considered a minor comparator.
Model description	A three-state partitioned survival model was used with three mutually exclusive health states of progression free, progressed disease, and death. Patients enter the model in the progression free health state, receiving either talquetamab or a comparator treatment. Within the progression free health state, patients can be on or off treatment. In this health state patients may either remain progression free, transition to progressed disease, or transition directly to death. Patients in the progressed disease health state either remain in this health state or transition to death. Subsequent treatments were administered in this health state. Death was an absorbing health state.
Clinical data	Talquetamab OS, PFS, time to treatment discontinuation (TTD) and AE data were from MonumenTAL-1 (Cohort C (0.8 mg/kg every two weeks)), using the September 2024 data cut.[8, 9] Teclistamab OS, PFS, TTD and AE data were from MajesTEC-1.[11] Data from MonumenTAL-1 and MajestTEC-1 were used in the ITC of talquetamab versus teclistamab. Selinexor plus dexamethasone OS, PFS, and AE data were from STORM.[12] STORM and

	MonumenTAL-1 data were used in the MAIC of talquetamab versus selinexor plus dexamethasone. No clinical data were included for elranatamab, as its efficacy and safety were assumed to be equivalent to teclistamab.
Extrapolation	In the teclistamab economic evaluation, the data underpinning extrapolations were informed by the ITC. The teclistamab MajesTEC-1 OS, PFS, and TTD Kaplan-Meier curves were adjusted using inverse probability treatment weights (IPTW), applying average treatment effect for the treated (ATT) weights from the ITC. In addition, OS data in the ATT ITC were adjusted to account for subsequent treatments not routinely available in NHS Scotland clinical practice. Teclistamab OS, PFS and TTD data were extrapolated using log-normal distributions, calibrated to company clinical expert estimates at 10 and 15 years. Talquetamab OS, PFS and TTD were extrapolated by applying the ATT ITC hazard ratios to the teclistamab extrapolations. In the elranatamab economic evaluation, elranatamab extrapolations were assumed to be equivalent to those applied for teclistamab. Talquetamab extrapolations also remained identical to those in the teclistamab analysis. In the selinexor plus dexamethasone economic evaluation, the data underpinning extrapolations were informed by the MAIC, which adjusted the talquetamab MonumenTAL-1 OS, PFS, and TTD data. Selinexor plus dexamethasone OS and PFS data were extrapolated using log-normal distributions. Selinexor plus dexamethasone TTD was extrapolated by applying the talquetamab PFS to TTD hazard ratio to the selinexor plus dexamethasone PFS curve. Talquetamab OS, PFS, and TTD were extrapolated from the MAIC-adjusted analysis using log-normal distributions.
Quality of life	Talquetamab health state utility values were derived from EQ-5D-5L data from MonumenTAL-1. Teclistamab and elranatamab were assumed to have equivalent health state utility values. Selinexor plus dexamethasone health state utility values were sourced from SMC2673. AE disutilities were included.
Costs and resource use	Medicine acquisition, administration, pre-treatment, subsequent treatment, intravenous immunoglobulin (IVIg), AE costs, monitoring and resource use, end of life care.
PAS	A Patient Access Scheme (PAS) was submitted by the company and assessed by the Patient Access Scheme Assessment Group (PASAG) as acceptable for implementation in NHSScotland. Under the PAS, a discount was offered on the list price. PAS discounts are in place for teclistamab, elranatamab and selinexor, and these were included in the results used for decision-making by using estimates of the comparator PAS price.

6.2. Results

SMC considered results for decision-making that took into account all relevant PAS. SMC is unable to present these results due to competition law issues.

*Other data were also assessed but remain confidential.**

6.3. Sensitivity analyses

A range of sensitivity and scenario analyses were considered, and descriptions of these key scenarios are provided in tables below.

Table 6.3.1: Teclistamab and elranatamab scenario analysis results

	Parameter	**Base case**	**Scenario**
1	Time horizon	40 years	10 years
2a	MonumenTAL-1 cohort	MonumenTAL-1 Cohort C	MonumenTAL-1 Pooled Cohort A and C
2b			MonumenTAL-1 Pooled Weighted 10% Cohort A and 90% Cohort C

3	Talquetamab PFS/OS/TTD extrapolations	ITC derived hazard ratios	Individually fitted - Log-normal
4a	Talquetamab OS hazard ratio	ITC point estimate	Lower bound
4b			Upper bound
5a	Talquetamab PFS hazard ratio	ITC point estimate	Lower bound
5b			Upper bound
6a	Talquetamab TTD hazard ratio	ITC point estimate	Lower bound
6b			Upper bound
7a	Teclistamab OS and PFS and TTD long-term clinical calibration	Base case values	Lower bounds
7b			Upper bounds
7c			Calibration removed
8	Teclistamab OS/PFS/TTD extrapolation	Log-normal	Weibull
9a	Subsequent treatment OS adjustment	Teclistamab included following talquetamab	Teclistamab excluded following talquetamab
9b			Talquetamab also included following teclistamab
10	Utility values	MonumenTAL-1	MajesTEC-1

Abbreviations: HR = hazard ratio; OS = overall survival; PFS = progression free survival; TTD = time to treatment discontinuation.

Table 6.3.2: Selinexor plus dexamethasone scenario analysis results

	Parameter	**Base case**	**Scenario**
1	Time horizon	40 years	10 years
2	SelDex OS/PFS	Independent extrapolation	HR approach using SelDex as a reference curve
3a	Talquetamab PFS/OS/TTD	Individually fitted log-normal to MAIC-adjusted data	Individually fitted Weibull to MAIC-adjusted data
3b			Individually fitted Gamma to MAIC-adjusted data
4a	SelDex PFS/OS	Log-normal	Gen-gamma
4b		Log-normal	Gompertz
5	SelDex TTD	PFS to TTD HR from talquetamab	PFS=TTD
6	Utility values	Sourced from SMC2673	Sourced from MonumenTAL-1

Abbreviations: HR = hazard ratio; MAIC = matching-adjusted indirect comparison; OS = overall survival; PFS = progression free survival; SelDex = selinexor plus dexamethasone; TTD = time to treatment discontinuation.

6.4. Key strengths

- The three-state partitioned survival model was appropriate.
- Utility data for talquetamab were derived from EQ-5D data in the MonumenTAL-1 study.
- The sources used to value medicine costs and resource use were appropriate.
- Parameters in one-way deterministic sensitivity analysis were varied using an appropriate range.

6.5. Key uncertainties

- There was uncertainty in the early and sustained separation of the OS Kaplan-Meier curves, which was inconsistent with the PFS results, in the comparison of talquetamab with

teclistamab. This may introduce favourable bias into the overall-survival extrapolations for talquetamab, which is notable given that the majority of incremental QALYs were accrued in the progressed-disease health state. The submitting company suggested that the early separation was due to factors such as a lower risk of infection-related mortality and reduced T-cell exhaustion with talquetamab. To consider this uncertainty scenario analyses were considered. Firstly, the time horizon was reduced to 10 years to limit the accrual of long-term post-progression survival gains (See Scenario 1, Table 6.3.1). Secondly, as a most conservative consideration the upper bound of the OS hazard ratio was applied (Scenario 4b, Table 6.3.1). These scenarios increased the incremental cost-effectiveness ratio (ICER).

- There were uncertainties regarding the choice of comparators in the economic evaluation. While elranatamab and teclistamab were identified as relevant comparators by SMC clinical experts, pomalidomide and dexamethasone with or without isatuximab (if not anti-CD38 refractory) were also identified as alternative comparators. No further supportive economic evaluations were provided, and the submitting company noted it expects the relevance of these comparators to be small and to diminish over time.
- The clinical calibration process used for OS, PFS, and TTD outcomes in the teclistamab arm was subject to uncertainty. Scenario analyses considered the lower and upper bounds of the 10- and 15-year targets, as well as their full removal (Scenarios 7a, 7b and 7c, Table 6.3.1). In addition, although the submitting company selected the log-normal curve in its base case, the Weibull curve represented a plausible alternative (Scenario 8, Table 6.3.1). The ICER impact of these scenarios was modest.

7. Conclusion

After considering all the available evidence, the Committee accepted talquetamab for use in NHSScotland.

8. Guidelines and Protocols

The British Society for Haematology published " Management of relapsed multiple myeloma: a British Society for Haematology/UK Myeloma Forum Guideline" in October 2025.[6]

The European Society for Medical Oncology (ESMO) and the European Haematology Association (EHA) published "Multiple myeloma: EHA-ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up" in February 2021.[20]

9. Additional Information

9.1. Product availability date

October 2023

Table 9.1 List price of medicine under review

Medicine	Dose regimen	Cost per 28 days (£)
Talquetamab	**0.4 mg/kg once weekly or 0.8 mg/kg once every two weeks by subcutaneous injection, preceded by step-up doses of 0.01 mg/kg on day 1, 0.06 mg/kg on day 3 and 0.4 mg/kg on day 5; an additional dose of 0.8 mg/kg is given on day 7 of the biweekly (every two weeks) dosing schedule.**	**17,408 (not including step-up doses)**

Costs from BNF online on 09 March 2026. Costs calculated using the full cost of vials/ampoules assuming wastage. Costs assume a body weight of 70 kg. Costs do not take any patient access schemes into consideration.

10. Company Estimate of Eligible Population and Estimated Budget Impact

The submitting company estimated there would be 44 patients eligible for treatment with talquetamab each year. The estimated uptake rate was 20% in year 1 and 32.5% in year 3. This resulted in 9 patients estimated to receive treatment in year 1 rising to 14 in year 3. SMC clinical expert responses indicated the number of patients eligible for treatment is likely to be higher than estimated by the submitting company.

SMC is unable to publish the with-PAS budget impact due to commercial in confidence issues. A budget impact template is provided in confidence to NHS health boards to enable them to estimate the predicted budget with the PAS. This template does not incorporate any PAS discounts associated with comparator medicines or PAS associated with medicines used in a combination regimen.

*Other data were also assessed but remain confidential.**

References

1. Janssen-Cilag Ltd (a Johnson & Johnson Company). Talquetamab solution for injection (Talvey®) Summary of product characteristics. Electronic Medicines Compendium www.medicines.org.uk/emc/ Last updated: 16/01/2026.
2. The European Medicines Agency (EMA) European Public Assessment Report. Talquetamab (Talvey®). 20/07/23, EMA/365426/2023. www.ema.europa.eu.
3. Elbahoty MH, Papineni B, Samant RS. Multiple myeloma: clinical characteristics, current therapies and emerging innovative treatments targeting ribosome biogenesis dynamics. Clin Exp Metastasis. 2024;41(6):829–42. Epub 20240820.
4. Chari A, Minnema MC, Berdeja JG, Oriol A, van de Donk N, Rodriguez-Otero P*, et al.* Talquetamab, a T-Cell-Redirecting GPRC5D Bispecific Antibody for Multiple Myeloma. New England Journal of Medicine. 2022;387(24):2232–44.
5. BMJ Best Practice. Multiple myeloma. Topic last updated 12 September 2025. Available from: https://bestpractice.bmj.com/topics/en-gb/179.
6. Jenner M, Boyd K, Choudhuri S, Parrish C, Garg M, Stern S*, et al.* Management of relapsed multiple myeloma: A British Society of Haematology and UK Myeloma Society guideline. British Journal of Haematology. 2025;207(6):2322–54.
7. Chari A, Touzeau C, Schinke C, Minnema MC, Berdeja JG, Oriol 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(4):e269–e81. Epub 20250313.
8. Rasche L, Schinke CD, Touzeau C, Minnema M, Donk NWCJvd, Rodríguez-Otero P, et al. Efficacy and safety from the phase 1/2 MonumenTAL-1 study of talquetamab, a GPRC5D×CD3 bispecific antibody, in patients with relapsed/refractory multiple myeloma: Analyses at an extended median follow-up. Journal of Clinical Oncology. 2025;43(16_suppl):7528–7528.
9. Medicine J, Johnson I. [Data on file] MonumenTAL-1 Clinical Study Report. September 2024.
10. Schinke C, Touzeau C, Oriol A, Mateos MV, Stevens D, Rasche L*, et al.* Talquetamab improves patient-reported symptoms and health-related quality of life in relapsed or refractory multiple myeloma: Results from the phase 1/2 MonumenTAL-1 study. Cancer. 2025;131(14):e35927.
11. Medicine J, Johnson I. [Data on file] MajesTEC-1 Clinical Study Report. August 2023.
12. Chari A, Vogl DT, Gavriatopoulou M, Nooka AK, Yee AJ, Huff CA, et al. Oral Selinexor-Dexamethasone for Triple-Class Refractory Multiple Myeloma. N Engl J Med. 2019;381(8):727–38.
13. Tan CR, Asoori S, Nemirovsky D, Derkach A, Brunaldi L, Popat R*, et al.* Long-Term Follow-up of Real-World Teclistamab Therapy for Relapsed/Refractory Multiple Myeloma from the IMWG Immunotherapy Working Group Committee. Blood. 2024;144(Supplement 1):5166–8.
14. Portuguese A, Davis J, Raza S, Castaneda Puglianini OA, Freeman CL, Alsina M*, et al.* Real-world outcomes with elranatamab in multiple myeloma: A multi-center analysis from the United States multiple myeloma immunotherapy consortium. Blood. 2025;146(Supplement 1):136–7.
15. Tomkins O, Tenorio Feixas P, Willis F, De-silva D, Ziller C, Gunawan A, et al. Single agent elranatamab for relapsed/refractory multiple myeloma (R/R MM) - Multi-centre real-world outcomes from 5 United Kingdom (UK) sites. Presented at EHA2025; 12–15 June; Milan, Italy.
16. Mol I, Hu Y, LeBlanc TW, Cappelleri JC, Chu H, Nador G*, et al.* Matching-Adjusted Indirect Comparison of Elranatamab versus Teclistamab in Patients with Triple-Class Exposed/Refractory Multiple Myeloma: Updated Results. J Blood Med. 2025;16:233–9. Epub 20250514.
17. Mol I, Hu Y, LeBlanc TW, Cappelleri JC, Chu H, Nador G*, et al.* A matching-adjusted indirect comparison of the efficacy of elranatamab versus teclistamab in patients with triple-class exposed/refractory multiple myeloma. Leuk Lymphoma. 2024;65(5):660–8. Epub 20240212.

18. Public Health Scotland. Cancer Medicines Outcomes Programme-Public Health Scotland (CMOP-PHS) report for the Scottish Medicines Consortium (SMC). Bispecific antibody treatment of adults with relapsed and refractory multiple myeloma: SMC2863. Published 31 March 2026. Available at: https://publichealthscotland.scot/publications/cancer-medicines-outcomes-programme-public-health-scotland-cmop-phs-report-for-the-scottish-medicines-consortium-smc/bispecific-antibody-treatment-of-adults-with-relapsed-and-refractory-multiple-myeloma-smc2863/.
19. Cancer Research UK. Myeloma incidence (2017 - 2019). Last reviewed: September 2025. Available at: https://crukcancerintelligence.shinyapps.io/CancerStatsDataHub/_w_581e61d1d0b94ec694063c2246fe0d54/?_inputs_&nav=%22Incidence%20Breakdowns%20and%20Trends%22&app_select_CancerSite=%22Myeloma%22&app_select_Country=%22United%20Kingdom%22.
20. Dimopoulos MA, Moreau P, Terpos E, Mateos MV, Zweegman S, Cook G*, et al.* Multiple myeloma: EHA-ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2021;32(3):309–22. Epub 20210203.

This assessment is based on data submitted by the applicant company up to and including 17 April 2026.

**Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal:*https://www.scottishmedicines.org.uk/about-us/policies-publications/

Medicine prices are those available at the time the papers were issued to SMC for consideration. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document. Area Drug and Therapeutics Committees and NHS Boards are therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

Patient Access Schemes (PAS): A PAS is a scheme proposed by a pharmaceutical company in order to improve the cost-effectiveness of a medicine and enable patients to receive access to cost-effective innovative medicines. The Patient Access Scheme Assessment Group (PASAG), established under the auspices of Public Services Delivery Scotland, reviews and advises NHS Scotland on the feasibility and acceptability on implementing proposed schemes. PASAG operates separately from SMC to maintain the integrity and independence of the assessment process of the SMC. When SMC accepts a medicine for use in NHS Scotland on the basis of a PAS that has been considered acceptable for implementation by PASAG, a set of guidance notes on the operation of the scheme will be circulated to health boards' Area Drugs and Therapeutics Committees prior to publication of SMC advice.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the

considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.