Record of the Cancer Treatments Advisory Committee Meeting held on 2 May 2025

Cancer Treatments Advisory Committee records are published in accordance with the Terms of Reference for the Specialist Advisory Committees 2021.

Note that this document is not necessarily a complete record of the Cancer Treatments Advisory Committee meeting; only the relevant portions of the meeting record relating to Cancer Treatments Advisory Committee discussions about an application or Pharmac staff proposal that contain a recommendation are generally published.

The Cancer Treatments Advisory Committee may:

(a) recommend that a pharmaceutical be listed by Pharmac on the Pharmaceutical Schedule and the priority it gives to such a listing;

(b) defer a final recommendation, and give reasons for the deferral (such as the supply of further information) and what is required before further review; or

(c) recommend that Pharmac decline to list a pharmaceutical on the Pharmaceutical Schedule.

Pharmac Advisory Committees make recommendations, including priority, within their therapeutic groups of interest.

The record of this Advisory Committee meeting will be reviewed by PTAC at an upcoming meeting.

Specialist Advisory Committees and PTAC may differ in the advice they provide to Pharmac, including recommendations' priority, due to the committees' different, if complementary, roles, expertise, experience, and perspectives.

Pharmac is not bound to follow the recommendations made below. Applications are prioritised by Pharmac against other funding options and progressed accordingly. The relative priority of any one funding choice is dependent on a number of factors, including (but not limited to) the recommendation of PTAC and/or Specialist Advisory Committees, the mix of other applications being assessed, the amount of funding available, the success of commercial negotiations and/or the availability of clinical data.

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1. Attendance

Present
Stephen Munn - Chair
Alanah Kilfoyle
Alice Loft
Alice Minhinnick
Chris Frampton
Lochie Teague
Michelle Wilson
Oliver Brake
Richard Isaacs

Apologies
Scott Babington
Vidya Mathavan

2. Summary of recommendations

	Pharmaceutical and Indication	Recommendation
7.3.	Bevacizumab for the treatment of recurrent ovarian cancer	Medium Priority
8.2.	Bevacizumab with/without lomustine for the treatment of high-grade, relapsed or recurrent glioma, within the context of treatment of malignancy	Decline
9.3.	Trastuzumab deruxtecan in the context of treatment of malignancy, subject to Special Authority criteria	High Priority
10.3	Widened access to azacitidine to include people with VEXAS syndrome with myelodysplastic syndrome, within the context of treatment of malignancy, subject to Special Authority criteria	High Priority
10.4	Widened access to ruxolitinib to include people with VEXAS syndrome without myelodysplastic syndrome, within the context of treatment of malignancy, subject to Special Authority criteria	High Priority
10.5	Widened access to tocilizumab to include people with VEXAS syndrome without myelodysplastic, within the	High Priority

	context of treatment of malignancy, either subject to Special Authority criteria or funded via the Named Patient Pharmaceutical Assessment Policy (NPPA) pathway (as appropriate)

3. The role of Specialist Advisory Committees and records of meetings

3.1. This meeting record of the Cancer Treatments Advisory Committee is published in accordance with the Terms of Reference for the Pharmacology and Therapeutics Advisory Committee (PTAC) 2021 and Specialist Advisory Committees 2021.Terms of Reference describe, *inter alia*, the establishment, activities, considerations, advice, and the publication of such advice of Specialist Advisory Committees and PTAC.

3.2. Conflicts of Interest are described and managed in accordance with section 6.4 of the SAC Terms of Reference.

3.3. The Cancer Treatments Advisory Committee is a Specialist Advisory Committee of Pharmac. The Cancer Treatments Advisory Committee and PTAC and other Specialist Advisory Committees have complementary roles, expertise, experience, and perspectives. The Cancer Treatments Advisory Committee and other Specialist Advisory Committees may therefore, at times, make recommendations for treatments for Cancer that differ from PTAC's, including the priority assigned to recommendations, when considering the same evidence. Likewise, PTAC may, at times, make recommendations for treatments for Cancer that differ from the Cancer Treatments Advisory Committee's, or Specialist Advisory Committees may make recommendations that differ from other Specialist Advisory Committees'.

Pharmac considers the recommendations provided by both the Cancer Treatments Advisory Committee and PTAC and any other relevant Specialist Advisory Committees when assessing applications for treatments for Cancer.

4. Welcome and introduction

4.1. The Chair welcomed the committee with a karakia followed by whakawhanaungatanga.

5. Pharmac Update

5.1. The Committee noted the Pharmac Update.

6. Correspondence and Matters Arising

6.1. Calcium folinate injection supply issues

Discussion

Background

6.1.1. The Committee noted that the contracted supplier of calcium folinate injection notified of a global discontinuation of the Medsafe approved Sandoz branded product, with stock expected to be depleted in March 2025. Following notification, Pharmac staff sought continuity of supply through their Annual Tender process, however no bids were received, and no other suppliers have Medsafe approval for calcium folinate injections.

6.1.2. The Committee noted that, following the discontinuation of the Sandoz branded calcium folinate injection, Pharmac secured a fixed quantity of stock and listed three strengths (50, 100 and 1000 mg) of an unapproved (Section 29) alternative calcium folinate injection (brand name Eurofolic), and that further supply has not yet been negotiated.

General

6.1.3. The Committee noted that calcium folinate injection is an essential medicine which is used in chemotherapy regimens that utilise high dose methotrexate, where it is used to reverse the toxicity associated with methotrexate use. The Committee noted that there is no medicine available that may be substituted in place of calcium folinate for this purpose.

6.1.4. The Committee noted that calcium folinate injection is also used to potentiate the effect of fluorouracil when used in chemotherapy regimens to treat colon cancer, where it is used in lower doses compared to when it is used to treat methotrexate toxicity.

6.1.5. The Committee noted that without calcium folinate injection being available, it would not be safe to administer chemotherapy regimens containing high dose methotrexate and this would have an impact on the treatment of multiple different malignancies across both oncology and haematology settings. The Committee noted that regimens using calcium folinate to potentiate the effect of fluorouracil would also be compromised.

6.1.6. The Committee considered there is work being done through the Anti-Cancer Therapy - Nationally Organised Workstreams (ACT-NOW) programme to review the dosing of calcium folinate that is used across different regimens, and it may be useful for Pharmac to engage with those involved with the ACT-NOW programme to further inform which presentations of calcium folinate are required.

6.2. **Oncology agent brand changes**

Discussion

Background

6.2.1. The Committee noted that at the March 2025 Tender Clinical Advisory Committee (TCAC) meeting, it was recommended for Pharmac to seek further advice from CTAC regarding potential product brand changes affecting nilotinib, fulvestrant and mitomycin that could occur as a result of the Tender.

Nilotinib

6.2.2. The Committee noted that nilotinib has been funded for the treatment of chronic myeloid leukaemia (CML) since 1 November August 2014.

6.2.3. The Committee noted that Pharmac sought advice regarding the outcome of a competitive process for nilotinib that could result in a brand change for this patient group.

6.2.4. The Committee noted that similar to imatinib and dasatinib, nilotinib is a small molecule medicine and considered it to be fully replicable in the context of alternative brands due to bioequivalence.

6.2.5. The Committee considered that there is no evidence to indicate any clinical risk associated with a transition to a generic tyrosine kinase inhibitor (TKI). The

Committee noted that the previous transition to a generic TKIs (imatinib & dasatinib) for a similar patient group was successful.

6.2.6. The Committee noted that brand changes would likely only occur greater than every three years, unless there were supply issues that necessitated an earlier change. Members noted that this was likely clinically acceptable if this were to occur.

6.2.7. The Committee considered it unlikely for a person to experience any adverse reactions from a generic nilotinib if they are tolerating the currently funded brand. The Committee considered if an adverse reaction were to occur, then exceptional circumstances would be the appropriate pathway to proceed.

6.2.8. The Committee considered that resource implications would be similar to the dasatinib brand change with no additional impact expected.

6.2.9. The Committee considered nilotinib is often used when there is treatment resistance to other TKIs due to disease mutation or treatment intolerance. The Committee considered widening of access to other indications wouldn't be required at this time.

Fulvestrant

6.2.10. The Committee noted that Pharmac sought advice regarding the outcome of a competitive process for fulvestrant that could result in a brand change for this patient group.

6.2.11. The Committee considered there appeared to be no clinical risk to a fulvestrant brand change.

6.2.12. The Committee noted that it would be important to consider the excipients of the generic as there could be something that would result in discomfort or pain to the patient when being administered with the injection, in which case a brand switch for fulvestrant may be seen as troublesome by patients. The Committee noted that a similar issue was seen when there was a brand change with goserelin, where patients reported marked experiences of pain during administration despite the clinical profile of the generic being identical to the innovator.

6.2.13. The Committee noted that there was a lack of data on the tolerance of a generic product however it may be beneficial to consider the generic fulvestrant products listed in Australia and any feedback that may have been received following the administration of them.

Mitomycin

6.2.14. The Committee noted that Pharmac staff sought advice regarding a potential brand change affecting mitomycin injection that could result from a competitive process.

6.2.15. The Committee noted that Pharmac currently list multiple brands of mitomycin 20 mg and 5 mg injection (as vials) on the Pharmaceutical Schedule due to previous supply issues affecting this product. The Committee noted that, of the brands listed, only the 20 mg injection supplied by Teva has received Medsafe approval.

6.2.16. The Committee noted that the Medsafe approved product supplied by Teva has been approved for multiple indications in the palliative setting when administered intravenously and for the treatment of superficial bladder cancer when administered via the intravesicular route. The Committee noted that

mitomycin may also be used off-label for other indications, including use in ophthalmology.

6.2.17. The Committee considered that as mitomycin is a cytotoxic medicine, the injection is aseptically compounded into the final dose form for administration either by a hospital pharmacy or third-party manufacturer. The Committee noted that depending on the final dose required for the individual, there may be wastage associated with compounding depending on the vial size used, and that having a lower dose vial available and funded may help to reduce wastage associated with compounding.

6.2.18. The Committee considered that there would not be a clinical need for Pharmac to continue listing a mitomycin 5 mg injection product, provided that both a 2 mg and 20 mg mitomycin injection product is listed on the Pharmaceutical Schedule.

7. Bevacizumab funding criteria for ovarian cancer

Application

7.1. The Committee reviewed a request from Pharmac staff to review feedback received from the New Zealand Gynaecological Cancer Group (NZGCG) and provide advice on the eligibility criteria for bevacizumab for advanced or metastatic ovarian cancer.

7.2. The Committee took into account, where applicable, Pharmac's relevant decision-making framework when considering this agenda item.

Recommendation

7.3. The Committee recommended that bevacizumab for the treatment of recurrent ovarian cancer be funded with a **medium priority**.

7.4. The Committee recommended that the Special Authority criteria for advanced or metastatic ovarian cancer be amended as follows:

Initial application – (advanced or metastatic ovarian cancer) from any relevant practitioner. Approvals valid for 4 months for applications meeting the following criteria:
All of the following:
1. Any of the following:
    1.1. The patient has FIGO Stage IV epithelial ovarian, fallopian tube or peritoneal cancer; or
    1.2. Both:
        1.2.1. The patient has FIGO Stage IIIB or IIIC epithelial ovarian, fallopian tube or peritoneal cancer; and
        1.2.2. Either:
            1.2.2.1. Debulking surgery is inappropriate; or
            1.2.2.2. The cancer is sub-optimally debulked (maximum diameter of any gross residual disease greater than 1cm); or
    1.3. The patient has recurrent epithelial ovarian, fallopian tube or peritoneal cancer and has not received bevacizumab previously; and
2. Bevacizumab to be administered at a maximum dose of 15 mg/kg every three weeks.

Renewal – (advanced or metastatic ovarian cancer) from any relevant practitioner. Approvals valid for 4 months for applications meeting the following criteria:
Either:
1. All of the following:
    1.1. The patient is receiving bevacizumab for first-line treatment of stage IIIB, IIIC or IV epithelial ovarian, fallopian tube or peritoneal cancer; and
    1.2. There is no evidence of disease progression; and
    1.3. Either:
        1.3.1. Bevacizumab is to be administered for a maximum of 15-months; or
        1.3.2. Bevacizumab is to be administered for a maximum of 24-months if administered in combination with olaparib; or
2. Both:

2.1. The patient is receiving bevacizumab for treatment of recurrent epithelial ovarian, fallopian tube or peritoneal cancer; and
2.2. There is no evidence of disease progression.

7.5. In making this recommendation, the Committee considered:

7.5.1. the available evidence that treatment with bevacizumab improves progression-free survival (PFS) and health related quality of life (HRQoL) in those with recurrent ovarian cancer

7.5.2. that the use of bevacizumab for recurrent disease may be a preferred treatment option over its use in the first-line setting for many individuals with ovarian cancer.

Discussion

Background

7.6. The Committee noted that from 1 March 2025, as a result of a Request for Tender for the supply of bevacizumab, the Vegzelma brand of bevacizumab was listed on the Pharmaceutical Schedule and funded access to bevacizumab was widened to include people with advanced or metastatic ovarian cancer, subject to eligibility criteria.

7.7. The Committee noted that this decision followed clinical advice from the Pharmacology and Therapeutics Advisory Committee (PTAC) in May 2022. At that meeting, PTAC recommended bevacizumab be funded for the first-line treatment of high-risk advanced ovarian a cancer. PTAC also recommended that bevacizumab, as a second-line treatment for high-risk advanced ovarian a cancer (i.e. for treatment of recurrent disease), be declined due to there being only small PFS benefit and no (or at best only very limited) overall survival (OS) benefit in this setting.

7.8. The Committee considered that the eligibility criteria for bevacizumab for ovarian cancer, implemented from 1 March 2025, limit access to first-line treatment only for individuals with FIGO Stage IIIB or IIIC disease. However, the Committee considered the criteria do not restrict access to individuals with FIGO Stage IV ovarian cancer to only those with previously untreated disease.

7.9. The Committee noted that Pharmac, as a result of consultation feedback and further clinical advice, amended the bevacizumab eligibility criteria for ovarian cancer to enable access to bevacizumab until disease progression, and removed the 12-month treatment duration limit. Members noted that Pharmac had also amended the criteria to enable bevacizumab to be used in combination with a poly ADP-ribose polymerase (PARP) inhibitor.

7.10. The Committee noted that, following feedback and clinical advice received post-decision, Pharmac amended bevacizumab eligibility criteria for ovarian cancer from 1 April 2025 to allow up to 15 mg/kg dosing every three weeks, allowing treatment with dosing regimens that are more representative of those used across relevant clinical trials and treatment settings.

7.11. The Committee noted that Pharmac received additional feedback post-decision from the New Zealand Gynaecological Cancer Group (NZGCG), highlighting several limitations with the current criteria and that there is confusion around the group intended for funding and whether the criteria intend to include individuals with recurrent disease.

General

7.12. The Committee considered that the current eligibility criteria, specifically regarding the wording of disease staging, may be causing confusion and variation in how clinicians are interpreting the criteria, and this is evident from the feedback provided by NZGCG.

7.13. The Committee considered that for staging of ovarian cancer, staging occurs upon initial diagnosis and within the first-line treatment setting. Once disease recurs, the disease is referred to as recurrent disease, regardless of initial staging. As the current criteria specify that individuals with FIGO Stage IV disease do not require previously untreated disease to be eligible to receive bevacizumab, this may be interpreted as meaning Stage IV disease is intended to mean recurrent disease.

7.14. The Committee considered that the criteria may be being interpreted differently across the country with respect to the eligibility of individuals with recurrent disease. The Committee considered that clinicians specialising in gynaecological cancers do see that the criteria were intended for first-line treatment, however, the practice of using bevacizumab for ovarian cancer has now largely moved away from first-line treatment, particularly following the funding of niraparib and olaparib, and is now used internationally and in private largely for the treatment of recurrent disease.

7.15. The Committee noted that the current eligibility criteria specify that 18-weeks concurrent treatment with chemotherapy is planned. Members considered that this is not always feasible in the first-line setting, as chemotherapy is typically initiated prior to surgery. Therefore, once it is known that the cancer has been sub-optimally debulked post-operatively and the individual therefore becomes eligible for bevacizumab under the current criteria, concurrent therapy will only occur for the remaining duration of chemotherapy, which at that point will be less than 18 weeks. The Committee considered that the eligibility criteria be amended to remove specific criteria around the timing of concurrent chemotherapy.

7.16. The Committee estimated that if bevacizumab was to be funded for recurrent ovarian cancer, up to 80% of patients with recurrent disease may receive treatment, due to either a proportion of the overall group having contraindications to treatment or for other reasons such as patients declining treatment.

7.17. The Committee considered that if there were a choice for individuals to be treated with bevacizumab at one stage in the natural history of the disease for ovarian cancer, there would be a preference to utilise bevacizumab in the recurrent setting as opposed to first-line treatment for most patients.

7.18. Committee members considered that if bevacizumab was to be funded for recurrent ovarian cancer, the treatment would occur until disease progression, consistent with the data from the OCEANS, GOG-0213 and AURELIA clinical trials that were previously reviewed by the Committee (Aghajanian et al. J Clinical Oncol 2012;30:2039-45; Coleman et al. Lancet Oncol. 2017;18:779-91; Pujade-Lauraine et al. J Clinical Oncol 2014;32:1302-8). Committee members considered that average time on bevacizumab would be shorter for treatment of recurrent disease, compared with first-line treatment.

7.19. Committee members considered that, with respect to concurrent therapy with bevacizumab and a PARP inhibitor, there is only evidence to support the use of concurrent therapy with olaparib and that this was in a cohort of patients with homologous recombination deficient (HRD) disease. The Committee noted that there is currently no funded test for this in New Zealand. Committee members considered that, if funded, there may be a small number of patients with BRCA gene mutations who would receive combination treatment with bevacizumab and olaparib.

7.20. The Committee noted PTAC's May 2022 recommendation to decline the second line use of bevacizumab for ovarian cancer for recurrent disease. Committee members considered that although no new data supporting the use of bevacizumab in ovarian cancer have been published, within the private care setting in New Zealand and internationally, bevacizumab for treatment of ovarian cancer has been accepted as standard of care, particularly in the recurrent disease setting, and this may have contributed to the lack of additional published data.

7.21. The Committee considered that the eligibility criteria do not strictly prohibit use of bevacizumab in the recurrent setting for those with stage IV ovarian cancer. However, as people are not restaged upon disease recurrence, this wording is causing confusion among clinicians, and this is creating inequity in interpretation and use of bevacizumab for ovarian cancer across the country.

7.22. The Committee noted that bevacizumab demonstrates a significant progression-free survival (PFS) benefit in the treatment of recurrent ovarian cancer (OCEANS; AURELIA). The Committee noted that this benefit is considered comparable to that noted in first-line treatment and may be particularly meaningful for individuals with recurrent disease, where delaying progression can have a substantial impact on quality of life. The improvement in health-related quality of life (HRQoL) gained from bevacizumab in recurrent disease, as shown in AURELIA and from real-world observational experience, that includes greater comfort and the ability to engage in daily activities, further supports the clinical value of bevacizumab in this setting.

7.23. The Committee considered that while no new clinical trial data has emerged recently, the existing evidence provides a strong rationale for funding bevacizumab for recurrent ovarian cancer. The Committee considered that the available evidence supporting the health benefits gained from the use of bevacizumab in this setting has been further substantiated from real-world observational experience and its adoption as standard of care. The Committee considered that this provides further justification for bevacizumab for recurrent ovarian cancer to be funded as another treatment option, in addition to first-line treatment.

8. Bevacizumab for relapsed or recurrent glioma - consultation feedback

8.1. The Committee took into account, where applicable, Pharmac's relevant decision-making framework when considering this agenda item.

Recommendation

8.2. The Committee reiterated its previous **recommendations** that bevacizumab with/without lomustine for the treatment of high-grade, relapsed or recurrent glioma, within the context of treatment of malignancy, be **declined**.

8.3. In reiterating these recommendations, the Committee:

8.3.1. recognised the high health needs of people with relapsed or recurrent high-grade glioma and the inequity experienced in health outcomes for priority populations

8.3.2. recognised that some people and their partners, loved ones, caregivers, families and whānau experience meaningful benefits from treatment with bevacizumab for high-grade, relapsed or recurrent glioma (e.g. improvement in quality of life due to corticosteroid sparing effect)

8.3.3. considered that there remains a lack of clinical evidence supporting health benefits at a population level from bevacizumab with/without lomustine in the treatment of relapsed or recurrent high-grade glioma

8.3.4. considered that whilst international guidelines suggest the use of bevacizumab for some relapsed or recurrent high-grade gliomas, these are not supported by high quality clinical evidence.

Discussion

Priority populations

8.4. The Committee discussed the impact of funding bevacizumab with/without lomustine for the treatment of high-grade, relapsed or recurrent glioma on Māori health areas of focus | Hauora Arotahi and Māori health outcomes. The Committee acknowledged the high health needs of Māori, Pacific peoples, and people with disabilities, and inequity experienced in health outcomes. The Committee did not have any new advice to provide regarding the needs of these groups in relation to bevacizumab for the treatment of relapsed or recurrent high-grade glioma.

Background

8.5. The Committee noted previous discussion on the clinical evidence for bevacizumab with/without lomustine by itself (the Cancer Treatment Advisory Committee (CTAC)) in April 2023 and October 2024, preceded by that of the Pharmacology and Therapeutics Advisory Committee (PTAC) in February 2016. The Committee noted that CTAC had most recently recommended the applications for bevacizumab with/without lomustine for the treatment of high-grade, relapsed or recurring glioma be declined in October 2024 in the context of restored lomustine supply.

Health need

8.6. The Committee noted and agreed with BTSNZ and NANOS regarding the high unmet need of people with glioma, specifically that glioma is a particularly aggressive cancer with a lack of treatment options and poor prognosis. The Committee also acknowledged the need of this population in terms of symptom relief, salvage for oedema reduction and improved quality of life (QoL), as well as improvements in progressive-free survival and overall survival. However, the Committee considered the restoration of lomustine supply would partly mitigate this need.

8.7. The Committee considered that the functional performance status of the person is a critical clinical factor affecting caregiver burden and quality of life.

Health benefit

8.8. The Committee noted that the clinical evidence submitted by BTSNZ and NANOS had previously been considered by CTAC and/or PTAC. The Committee considered that, in line with previous advice on bevacizumab for glioma, the evidence base does not support a large health benefit to the individual, their family, whānau or wider society.

8.9. The Committee noted the previously reviewed trials:

8.9.1. Friedman et al. J Clin Oncol. 2009;27(28):4733-40 and Kreisl et al. J Clin Oncol. 2009;27(5):740-5 trials that contributed to FDA approval of bevacizumab for the treatment of high-grade recurrent or relapsed glioma. The Committee considered that approximately a third of participants experienced responses, but that the Kreisl et al (2009) trial was a single arm trial in a heavily pretreated population, thereby decreasing the validity of reported results.

8.9.2. Taal et al. Lancet Oncol. 2014;15(9):943-53 in which the study authors considered phase 3 investigation of bevacizumab with lomustine was warranted

but further study in bevacizumab monotherapy for the treatment of high-grade recurrent or relapsed glioma was not justified.

8.9.3. Wick et al. N Engl J Med. 2017;377(20):1954-63 in which the addition of bevacizumab to lomustine was not associated with changes in reported HRQoL, neurocognitive function, or requirement of glucocorticoid. There was also no overall survival advantage found to be associated with combination (bevacizumab plus lomustine) therapy in comparison to bevacizumab monotherapy.

8.10. The Committee noted it had previously reviewed the Chinot et al. N Engl J Med 2014;370:708-22 phase 3 study that investigated the steroid-sparing effect of bevacizumab in the first-line setting as an exploratory endpoint. The authors reported that bevacizumab first-line may have a steroid-sparing effect. However, the Committee considered that there was clinical uncertainty in whether this was able to be extrapolated to second-line use, in high-grade recurrent or relapsed glioma due to these being different points in the disease course.

8.11. The Committee noted the use of bevacizumab with/without lomustine for high-grade, relapsed or recurrent glioma is suggested in international guidelines as an option for treatment, but considered there remains a lack of clinical evidence to support the use of bevacizumab as recommended in these guidelines

8.11.1. The US National Comprehensive Cancer Network (NCNN) guidelines (not in public domain) for bevacizumab in the treatment of glioma are premised upon evidence that has previously been considered by the Committee. In the case of glioma treatment with bevacizumab and systemic therapies, the Committee noted that the recommended continuation of bevacizumab after disease progression, solely for obtaining corticosteroid-sparing effects, is not supported by evidence. The Committee noted that the NCNN guideline regarding the use of bevacizumab in relapsed or recurrent glioma is formed from a consensus of expert opinion that the treatment is appropriate (more than 85% support from the NCNN panel), and the evidence used to support the guideline is lower-level.

8.11.2. The European Association of Neuro-Oncology (EANO) guidelines specify the use of bevacizumab as symptom control in the treatment of glioma, and do not provide evidence to support the use of bevacizumab with systemic therapy.

8.11.3. In England and Wales, the National Institute for Health and Care Excellence (NICE) suspended its initial appraisal pending final result availability from the pivotal EORTC trial. After the trial failed to reach its primary endpoint, the appraisal was discontinued.

8.11.4. Australia's Pharmaceutical Benefits Advisory Committee (PBAC) listed bevacizumab as a targeted therapy in the treatment of glioma in May 2019. CTAC noted that the recommendation is not supported by specified evidence of efficacy in this population.

8.12. The Committee noted that bevacizumab with/without lomustine is not a life-extending treatment for high-grade glioma and that health benefit is primarily relative to the reduction of cerebral oedema. The Committee also considered that within the context of privately accessed treatment in New Zealand (NZ), bevacizumab is used either as monotherapy or in combination with lomustine for cerebral oedema with anecdotal reports of a small number of individual patients experiencing increased overall survival, progressive-free survival, corticosteroid-sparing effects and quality of life. At an individual level the Committee recognised that there may be treatment benefit(s) but considered that the evidence does not support use and improved health benefits and outcomes, especially in the NZ population.

Suitability

8.13. The Committee noted that if implemented in the NZ health system, bevacizumab treatment for glioma would likely be given by the protocol of 10mg/kg fortnightly infusion over 90 minutes, then reduced to 60 minutes if well tolerated, and further reduced to 30 minutes ongoing, provided no issues (side effects, site reactions) arose. In the context of current, constrained infusion resource capacity, increasing demand by funding this treatment without high quality evidence would cause resource impacts.

8.14. The Committee noted that clinical preference is for treatments with evidenced, high efficacy to take resource priority over lower efficacy treatments, to help ensure NZ achieves the best possible health outcomes given our resource constraints and capacity.

Cost and savings

8.15. The Committee considered that no significant savings to the NZ health system would be expected if bevacizumab were funded for high-grade recurrent or relapsed glioma. However, the Committee acknowledged that the scarcity of clinical evidence means that this consideration is not definitive.

General

8.16. The Committee noted the submission included published case reports and consumer comments and acknowledged that bevacizumab provides some benefit(s) for some individuals including QoL benefit due to corticosteroid sparing. However, the Committee considered that there remained low quality and insufficient clinical trial etc. evidence of population-level benefits from bevacizumab, with not all individuals being anticipated to benefit, and unfortunately the submission did not provide new information to change the Committee's previous recommendations.

9. Trastuzumab deruxtecan for HER-2 low, unresectable or metastatic breast cancer

Application

9.1. The Committee reviewed the application for trastuzumab deruxtecan (T-DXd) for human Epidermal Growth Factor 2 (HER2) low unresectable or metastatic breast cancer (mBC).

9.2. The Committee took into account, where applicable, Pharmac's relevant decision-making framework when considering this agenda item.

Recommendation

9.3. The Committee recommended that trastuzumab deruxtecan be listed with a **high priority** in the context of treatment of malignancy, subject to the following Special Authority criteria:

> **Initial application** (**HER2-low unresectable or metastatic breast cancer**) – from any relevant practitioner. Approvals valid for 6 months if the following criteria are met:
> All of the following:
> 1. Patient has metastatic or unresectable breast cancer expressing HER2 IHC1+ or IHC2+ and ISH negative; and
> 2. Either
> 2.1. Patient has received prior chemotherapy in the metastatic setting; or
> 2.2. Patient has developed disease recurrence during, or within 6 months of completing adjuvant chemotherapy; and
> 3. Patient has received, or is ineligible for endocrine therapy in the metastatic setting, if hormone receptor positive; and

4. Patient has good performance status (ECOG 0-1); and
5. Patient has not received prior trastuzumab deruxtecan treatment; and
6. Treatment to be discontinued at disease progression

Renewal application (**HER2-low unresectable or metastatic breast cancer**) – from any relevant practitioner. Approvals valid for 6 months if the following criteria are met:
Both:
1. The cancer has not progressed at any time point during the previous approval period whilst on trastuzumab deruxtecan; and
2. Treatment to be discontinued at disease progression

9.4. In making this recommendation, the Committee considered:

9.4.1. The unmet health need of people with unresectable or metastatic HER2-low breast cancer, specifically for effective treatments that improve both length and quality of life. As individuals with HER2-positive disease already have access to HER2-targeted therapies, this unmet need was considered as being additional and specific to the HER2-low population.

9.4.2. The high-quality clinical evidence supporting the meaningful health benefit offered by T-DXd for people with HER2-low mBC

9.4.3. The diagnostic challenges associated with consistent immunohistochemistry (IHC) HER2 grading, especially when differentiating between HER2-low and HER2-ultralow or HER2-zero mBC.

Discussion

Māori impact

9.5. The Committee discussed the impact of funding T-DXd for the treatment of HER2-low mBC on Māori health outcomes. The Committee noted breast cancer | mate pukupuku is a Pharmac | Te Pātaka Whaioranga Hauora Arotahi | Māori health area of focus.

Populations with high health needs

9.6. The Committee discussed the health need(s) of Māori, Pacific peoples, disabled peoples including tāngata whaikaha Māori, and other populations with HER2-low mBC, identified by the Government Policy Statement on Health 2024-27 to have high health needs. The Committee discussed the impact of funding T-DXd and considered that:

9.6.1. Māori and Pacific peoples continue to present with more advanced disease, and, as such, are expected to particularly benefit if access to T-DXd is expanded to include HER2-low mBC.

9.6.2. Once a diagnosis is made, the benefit a patient may derive from T-DXd is determined by their disease biology, which is the focus of investigation in randomised controlled trials (RCTs). However, there is a lack of priority population representation in clinical trials. Specifically, the Committee considered that the key international trial (DESTINY-Breast 04, see Health Benefit) of T-DXd in the assessed population was conducted in predominantly Caucasian and Asian populations, therefore there was uncertainty over health outcomes for Māori and Pacific peoples, including the likelihood of severe adverse events, such as interstitial lung disease.

9.6.3. Outcomes are also affected by social support and access to care.

9.6.4. That the health need of people with mBC in these priority populations was documented in the Committee's previous consideration of T-DXd for mBC (PTAC Record: April 2023).

Background

9.7. The Committee noted that HER2-low breast cancer is defined as a score of 1+ on immunohistochemical (IHC) analysis or as an IHC score of 2+ and negative results on in situ hybridization (ISH). This differs from HER2-positive disease, characterised by HER2 overexpression (IHC score of 3+ or 2+ and ISH positive), and from HER2-negative or ultra-low phenotypes (IHC score of 0).

9.8. The Committee noted that no targeted pharmaceutical agents specified for the treatment of HER2-low mBC had previously been considered by an advisory committee at Pharmac.

9.9. The Committee noted that T-DXd was previously considered in April 2023 for the second line treatment of HER2-positive metastatic or unresectable breast cancer, after HER2 therapy in metastatic setting, or first line if disease had progressed within 6 months of HER2 treatment in the adjuvant setting. T-DXd was recommended for funding with a high priority and was funded in December 2024.

9.10. The Committee considered that the prognostic significance of HER2-low expression, relative to HER2-negative disease, remains uncertain. Members considered that the evidence suggesting a clinically significant difference between HER2-low and HER2-negative to be conflicting, and expressed uncertainty over the distinction between these two groups. The Committee noted:

9.10.1. Baez-Navarro et al. Mod Pathol. 2023;36:100087, a longitudinal follow-up study of 65,035 people with breast cancer in the Netherlands which reported no substantial absolute clinicopathologic differences between HER2-low and HER2 negative (IHC 0) phenotypes in any of the cohorts, including no statistically significant differences in overall survival, irrespective of oestrogen receptor (ER) status.

9.10.2. Shirman et al. Breast Cancer Dove Med Press. 2023;15:605-16 reported individuals with HER2-low mBC had a slightly better prognosis than those with HER2-negative status in a study involving more than 15,000 people.

Health need

9.11. The Committee noted that cancer treatments are a Government Health priority, and breast cancer specifically is the most diagnosed cancer in women and remains the leading cause of cancer-related mortality.

9.12. The Committee previously noted that the 5-year survival for people diagnosed with mBC is 29% and 10-year survival is 16%, compared with 99% and 97%, respectively for people diagnosed with Stage 1 disease (Breast Cancer New Zealand. 2022). The Committee considered the significant physical, emotional, psychological, and practical burden associated with mBC, not only for those diagnosed with the disease but also for their family, whānau, and loved ones, who are often profoundly impacted by the demands of caregiving and the many ongoing uncertainties surrounding the illness. The Committee considered the health needs of those with mBC to be well documented in the Committee's previous consideration of T-DXd for HER2-positive mBC in April 2023.

9.13. The Committee considered that compared to HER2-positive mBC, HER2-low disease may present with a more indolent clinical course, potentially with fewer brain metastases. The Committee considered that regardless of HER phenotype, health-related quality of life (HRQoL) for those with mBC would be expected to improve with

response to treatment. The Committee considered that once the disease progresses, HRQoL is unlikely to differ significantly between HER2-low and HER2-positive patients, or based on prior treatment history. Members also considered that regardless of HER2 status, people with mBC require care matching the severity their symptoms.

9.14. The Committee noted a NZ retrospective cohort study on breast cancer (Lasham et al. Cancers. 2024;16:3204) which reported that for advanced-stage disease, irrespective of hormone receptor (HR) status, 38% of those formerly classified as HER2-negative were reclassified as HER2-low. Including those with HER2-positive disease, 60% of all individuals with mBC were reported to potentially benefit from HER2 targeted antibody drug conjugates, such as T-DXd.

9.15. The Committee considered that approximately 300 women are diagnosed with mBC each year in NZ, with an estimated 400 individuals eligible for treatment at any given time. Based on the incidence of HER2-low phenotypes in the NZ population (Lasham et al. Cancers. 2024;16:3204), the Committee estimated that a minimum of 140 individuals would be HER2 low and potentially eligible for treatment with T-DXd. The Committee reviewed the applicant's estimate of 121 individuals expected to receive treatment in the first year and considered this figure to be low, depending on how factors such as line of therapy, performance status and treatment uptake were accounted for in the calculation.

9.16. The Committee considered the current and proposed treatment paradigms for those with HER2-low mBC as provided in the application to be accurate. The Committee noted that treatment strategies depend on ER status. Components of the paradigms included:

9.16.1. in ER+/HER2-low mBC, first-line treatment typically involves a cyclin-dependent kinase (CDK) 4/6 inhibitor (eg palbociclib or ribociclib) combined with endocrine therapy. When there is a large disease burden, chemotherapy may be given ahead of CDK4/6 inhibitors and hormonal therapy for a more rapid response. This may be followed by a second-line endocrine therapy, such as a selective estrogen receptor degrader (SERD) like fulvestrant, depending on the rate of disease progression, disease burden and performance status of the patient. When the cancer becomes refractory to endocrine therapy, systemic chemotherapy may be introduced sequentially. Chemotherapy options include combination regimens for patients with high-risk disease (e.g. mitoxantrone, mitomycin C and methotrexate (MMM) OR epirubicin with cyclophosphamide (EC)) or single agent chemotherapy (eg taxanes, capecitabine, or vinorelbine).

9.16.2. in ER-/HER2-low mBC first-line treatment typically involves carboplatin and gemcitabine, potentially in combination with immunotherapy. In subsequent lines of treatment, systemic single-agent chemotherapy, such as taxanes, capecitabine, or vinorelbine, may be used.

9.17. The Committee noted that funding T-DXd in accordance with the supplier's application would introduce an additional treatment option following chemotherapy.

Health benefit

9.18. The Committee noted that T-DXd is an antibody-drug conjugate consisting of the humanised HER2-targeted antibody, trastuzumab and the cytotoxic payload, deruxtecan.

9.19. The Committee noted that T-DXd is Medsafe approved for the treatment of unresectable or metastatic HER2-low (IHC 1+ or IHC 2+/ISH-negative) breast cancer who have received prior chemotherapy in the metastatic setting or developed disease recurrence during or within 6 months of completing adjuvant chemotherapy.

9.20. The Committee noted that Australia (PBAC), Canada (CADTH), and Scotland (SME) recommended funding T-DXd for HER2-low mBC. Members noted that England (NICE) declined funding T-DXd for this indication as the treatment's estimated cost-effectiveness is above what NICE considers an acceptable use of resource.

9.21. The Committee noted the DESTINY-Breast04 trial as the main evidence for this application (Modi et al. N Engl J Med. 2022;387:9-20). This open-label, randomised, phase III trial investigated T-DXd (n=373) versus physician's choice (PC) of chemotherapy (n=184) for treating HER2-low metastatic breast cancer.

9.21.1. Participants had HER2-low (IHC1+ or IHC2+ and ISH negative) metastatic breast cancer. Eligible patients must have received chemotherapy for metastatic disease or have had disease recurrence during or within 6 months after completing adjuvant chemotherapy; patients with ER+ disease must have received at least one line of endocrine therapy.

9.21.2. The Committee noted the PC arm to consist of eribulin (51%), capecitabine (20%), nab-paclitaxel (10%), gemcitabine (10%) and paclitaxel (8%). Members considered this treatment arm to be comparable to the benefit and risk profile of the current treatment setting in NZ, noting that eribulin and nab-paclitaxel are not currently funded.

9.21.3. The Committee noted the significant increase in median progression-free survival (PFS) for participants in the T-DXd arm (9.9 months T-DXd vs 5.1 months PC; Hazard Ratio: 0.50; P<0.001). Members noted the improvement in overall survival (23.4 months T-DXd vs 16.8 months PC; Hazard Ratio: 0.64; P=0.001), and considered their overlapping 95% confidence intervals (20.0-24.8 months vs 14.5-20.0 months, respectively) to be indicative of an evolving difference that may not have been fully captured considering the follow-up duration. The Committee further noted that while complete response rates were of a similar magnitude between arms, partial responses were markedly greater in the T-DXd arm (49.1%) vs chemotherapy (15.2%) as were those who experienced a clinical benefit (70.2% T-DXd vs 33.7% PC).

9.21.4. The Committee noted significant nausea (73%) and fatigue (48%) in the T-DXd arm, as well as alopecia (38%), pneumonitis (12%), and seven deaths that were ruled to be drug-related. Adverse events of grade 3 or higher occurred in 52.6% of the patients who received T-DXd and 67.4% of those in the PC arm. Overall, members considered T-DXd to have the potential for uncommon but significant toxicity, particularly lung toxicity (risk of severe pneumonitis).

9.22. The Committee noted the DESTINY-Breast06 trial (Bardia et al. N Engl J Med. 2024;391: 2110-22), an open-label, randomised, phase III investigation of T-DXd vs PC of chemotherapy in patients with HR+/HER2-low and HR+/HER2-ultralow mBC. Participants were eligible who had received one or more lines of endocrine therapy and no previous chemotherapy. While the DESTINY-Breast06 study population does not align directly with the population assessed in this application, the trial provides insight into the potential benefit of T-DXd in a relevant subgroup (HR+/HER2-low) and separate mBC population (HER2-ultralow).

9.22.1. The Committee noted the PC arm consisted of capecitabine (60%), nab-paclitaxel (24%), and paclitaxel (16%). Members considered this regimen to be comparable to the benefit and risk profile of the treatments currently available in NZ, despite including nab-paclitaxel (not currently funded).

9.22.2. The Committee noted the significantly improved progression free survival of 13.2 months T-DXd (95% CI, 11.4 to 15.2) vs 8.1 months PC (95% CI, 7.0 to 9.0); HR:0.62; 95% CI, 0.52 to 0.75 P<0.001). The Committee considered that the additional benefit observed in DESTINY-Breast06 vs DESTINY-Breast04

may be the result of participants being chemotherapy naïve vs experienced, respectively. The data for overall survival in the DESTINY-Breast06 trial was noted to be immature.

9.22.3. The Committee noted primary results from DESTINY-Breast06, presented at the 2024 ASCO Annual Meeting (Curigliano et al. JCO.2024.42.17_suppl.LBA1000). Although the OS data were still immature, it indicated a non-significant difference in median OS between T-DXd and PC in the HER-low and HER2-ultralow populations (Curigliano et al. 2024).

9.22.4. The Committee noted the common occurrences of nausea (66%), fatigue (47%), and alopecia (45%) in the T-DXd arm. Members noted that pneumonitis occurred in 11.3% the T-DXd arm, including three cases which resulted in death. Adverse events of grade 3 or higher occurred in 52.8% of the patients in the T-DXd arm and in 44.4% of those in the PC arm. As with DESTINY-Breast04, the Committee considered T-DXd to be associated with uncommon but potentially significant toxicity.

9.22.5. The Committee concluded that a separate application is required to evaluate the benefit of T-DXd for either of the populations described in DESTINY-Breast06, once further data are available.

9.23. Overall, the Committee considered that T-DXd demonstrated superior health benefits compared to the chemotherapy regimens used in DESTINY-Breast04 . The Committee also noted emerging evidence suggesting that T-DXd may have activity in treating brain and meningeal metastases, which is not commonly observed with standard comparator chemotherapy. However, the Committed considered the adverse events associated with T-DXd (e.g. neutropenia, nausea, vomiting, alopecia, pneumonitis) to be significant, and noted the uncommon but potentially severe risks of treatment. Members also considered the significant physical and emotional burden of these treatment-related adverse events.

9.24. The Committee considered that DESTINY-Breast 04 was a high quality randomised controlled trial, which utilised appropriate comparators, predetermined endpoints, and reported significant outcomes which were reproduced across studies. While the Committee considered the evidence relevant to the New Zealand context, the Committee expressed concern about the distinction between HER2-low and ultralow classifications, which rely heavily on pathology reporting.

9.25. The Committee noted the findings of DESTINY-Breast 04 was supported by a systematic review and meta-analysis, using PRISMA guidelines, of seven studies and 2200 people up to January 2024 (Qureshi et al. Am J Clin Oncol. 2024;47:535-41). The pooled analysis revealed that T-DXd significantly improved PFS (OR=0.37, 95% CI: 0.27-0.52), indicating a robust efficacy in slowing disease progression. However, treatment was associated with an increased risk of anaemia (OR=2.10, 95% CI: 1.36-3.25), fatigue (OR=1.56, 95% CI: 1.21-2.02), nausea (OR=6.42, 95% CI: 4.37-9.42), vomiting (OR=6.21, 95% CI: 3.14-12.25), constipation (OR=2.26, 95% CI: 1.53-3.34), and notably, drug-related interstitial lung disease (OR=10.89, 95% CI: 3.81-31.12).

9.26. The Committee noted that the participants in DESTINY-Breast 04 were limited to individuals with relatively good performance status (ECOG 0 or 1). The Committee considered that many patients in real-world settings may have greater comorbidity. Members considered there to be high variability and uncertainty surrounding the proportion of New Zealanders with HER2-low mBC with a good performance status (ECOG 0 or 1) but estimated it could be up to 70% for those receiving first-line treatment.

9.27. The Committee noted the evidence for the benefits of T-DXd to be much less definitive in people with HER2-ultralow disease. The Committee was made aware of

the findings of the DAISY 2 trial (Mosele et al. Nat Med. 2023;29(8):2110-20), which provided evidence that the efficacy of T-DXd varied according to HER2 expression.

9.28. The Committee was made aware of a European Society for Medical Oncology (ESMO) consensus statement on HER2-low breast cancer (Tarantino et al. Ann Oncol. 2024;34,8:645-59), which included a discussion on the challenges of determining HER2 status. The Committee considered the dynamic and variable nature of HER2 expression, noting that tumour HER2 phenotype can change between an initial biopsy and definitive resection following neoadjuvant therapy. Additionally, members noted that biopsy location can influence results due to tumour heterogeneity. The Committee also noted the variability in HER2 scoring among pathologists among other analytical variables that may contribute to scoring discordance. Members considered these factors to be particularly relevant when differentiating a HER2-low phenotype from HER2-ultralow/negative, and that there would potentially be upward drift of tumours with very low ICH staining being classed as HER2-low. This could lead to more patients receiving treatment who may derive limited benefit, as reported in the DAISY 2 trial (Mosele et al. 2023).

9.29. The Committee noted that within HER2-low mBC, various studies have reported no clear differences in outcomes/prognosis between ER positive and negative disease and considered this suggests that treatment benefits may be extrapolated irrespective of ER status.

Cost & Savings

9.30. The Committee considered that given the size of the HER2 low population, there would be a substantial impact to the medicines budget. Members also considered that funding T-DXd for people with HER 2 low mBC would add significant health resource demands on an already strained public healthcare system (e.g. additional medical and nursing staff, IHC scoring, managing expected adverse events, infusion time, treatment monitoring frequency).

9.31. The Committee did not consider it likely that there is a subgroup of individuals with HER2-low metastatic breast cancer who are not currently receiving chemotherapy but would receive T-DXd if it were funded. This is due to the significant toxicities associated with T-DXd, which are expected to be at least comparable to those of existing chemotherapy options.

9.32. The Committee noted that clinical practice is increasingly moving away from the routine use of adjuvant chemotherapy in many individuals with ER-positive disease, supported by tools such as gene expression assays (where available) and NHS Predict. As a result, many patients who experience disease recurrence during or within six months of completing adjuvant therapy may not have received chemotherapy. The proportion of the HER2-low population experiencing recurrence for this disease type within this timeframe who did receive chemotherapy (mainly people with high-risk disease) is uncertain, but the committee considered a reasonable estimate to be less than 10%.

9.33. The Committee noted a preference for current histology to be obtained, ideally with central scoring, but acknowledged the prohibitive resource constraints and equity considerations associated with implementation.

9.34. The Committee considered that with the likely monitoring frequency of people being treated with T-DXd that:

9.34.1. prior to disease progression, a person would visit an oncology consultant once every 3-4 weeks and would be unlikely to have regular GP and/or nurse treatment-related visits

9.34.2. while on comparator chemotherapies, patients would be likely to see an oncology consultant every three weeks

9.34.3. echocardiographic left ventricular ejection fraction (LVEF) measurement, not simply electrocardiography (ECG), would be performed every three months while on treatment

9.34.4. post-disease progression, monitoring frequency would depend on whether the person continued to another treatment. People on other treatments would likely be monitored every 3-4 weeks. Extensive ongoing monitoring of for example heart function after disease progression is not expected.

9.34.5. for those no longer receiving active treatment, care would transition to palliative services, with support mostly provided by local hospice teams rather than general practitioners.

Funding criteria

9.35. The Committee considered that the eligibility criteria should only include people who meet the DESTINY-Breast04 eligibility criteria.

Summary for assessment

9.36. The Committee considered that the below summarises its interpretation of the most appropriate PICO (population, intervention, comparator, outcomes) information for T-DXd if it were to be funded in New Zealand for HER2-low mBC. This PICO captures key clinical aspects of the proposal and may be used to frame any future economic assessment by Pharmac staff. This PICO is based on the Advisory Committee's assessment at this time and may differ from that requested by the applicant. The PICO may change based on new information, additional clinical advice, or further analysis by Pharmac staff.

Population	Adult patients with unresectable or metastatic HER2-low (IHC 1+ or IHC 2+ and ISH-negative) breast cancer who have received prior chemotherapy in the metastatic setting or developed disease recurrence during or within 6 months of completing adjuvant chemotherapy. This population includes both hormone-receptor positive and negative breast cancer. Patients with hormone receptor positive (HR+) breast cancer should additionally have received or be ineligible for endocrine therapy.
Intervention	Trastuzumab deruxtecan (5.4mg/kg administered as an IV infusion every 3 weeks) until disease progression, unacceptable toxicity, or death.
Comparator(s)	Comparator treatments are most likely to be single-agent chemotherapy in the following sequence: capecitabine, vinorelbine, and taxanes. Some patients with high-risk, HR+ mBC may receive combination chemotherapy regimens such as MMM (mitomycin C, methotrexate, and mitoxantrone) or EC (epirubicin and cyclophosphamide). However, as these regimens are typically used as the first systemic chemotherapy in the metastatic setting, they are not considered appropriate comparators. This is because patients would only become eligible for T-DXd after receiving their initial chemotherapy treatment.

Outcome(s)	*Supplier clinical claim*: In previously treated individuals with HER2-low unresectable or metastatic BC, T-DXd has superior efficacy and a different but non-inferior safety profile, compared with TPC based on DESTINY-Breast04 data (Modi et al. N Engl J Med. 2022;387(1):9-20). Treatment outcomes for all HER2-low patients (HR+ and HR-): • Increased median progression free survival (mPFS) (9.9 months vs 5.1 months, hazard ratio 0.5, p<0.001) • Increased median overall survival (mOS) (23.4 months versus 16.8 months, hazard ratio 0.64, p=0.001) with median duration of follow up 18.4 months. • Lower adverse event rates of grade 3 or higher (52.6% (195 events) vs. 67.4% (116 events)) with exposure adjusted incidence rates of 0.69 and 1.82 respectively. • Higher rates of adjudicated, drug-related interstitial lung disease or pneumonitis (12.1% of T-DXd group) • Increased median time to definitive deterioration of EuroQol 5-dimension, 5-level (EQ-5D-5L) visual analogue scale (VAS) (8.8 months vs 4.7 months, hazard ratio 0.70 [0.54-0.91]) (Ueno et al. 2022).
Table definitions: Population, the target population for the pharmaceutical; Intervention, details of the intervention pharmaceutical; Comparator, details the therapy(s) that the patient population would receive currently (status quo – including best supportive care); Outcomes, details the key therapeutic outcome(s) and source of outcome data.	

10. Azacitidine, ruxolitinib and tocilizumab for VEXAS syndrome

Application

10.1. The Committee reviewed the Pharmac-initiated application for azacitidine, ruxolitinib and tocilizumab for VEXAS (Vacuoles, E1 enzyme, X-linked, Autoinflammatory, Somatic) syndrome ("VEXAS").

10.2. The Committee took into account, where applicable, Pharmac's relevant decision-making framework when considering this agenda item.

Recommendation

10.3. The Committee **recommended** that access to azacitidine be widened to include people with VEXAS syndrome with myelodysplastic syndrome with a **high priority**, within the context of treatment of malignancy, subject to the following Special Authority criteria:

> AZACITIDINE – VEXAS syndrome
> Initial application
> Applications from any relevant practitioner. Approvals valid without further renewal unless notified.
> All of the following:
> 1. Diagnosis of VEXAS syndrome with somatic *UBA1* mutation and clinical signs of VEXAS, and
> 2. Either:
> 2.1. Disease is uncontrolled despite treatment with high-dose corticosteroids or
> 2.2. High-dose corticosteroids are contraindicated or no longer able to be tolerated, and
> 3. Concurrent diagnosis of myelodysplastic syndrome (MDS).

10.4. The Committee **recommended** that access to ruxolitinib be widened to include people with VEXAS syndrome without myelodysplastic syndrome with a **high**

priority, within the context of treatment of malignancy, subject to the following Special Authority criteria:

RUXOLITINIB – VEXAS syndrome
Initial application
Applications from any relevant practitioner. Approvals valid for 3 months.
1. Diagnosis of VEXAS syndrome with somatic *UBA1* mutation and clinical signs of VEXAS, and
2. Either:
    2.1. Disease is uncontrolled despite treatment with high-dose corticosteroids or
    2.2. High-dose corticosteroids are contraindicated or no longer able to be tolerated.

Renewal
Applications from any relevant practitioner. Approvals valid for 3 months.
1. Ruxolitinib has been associated with new or ongoing improvement in the person's VEXAS clinical manifestations and/or a reduction in their corticosteroid use.

10.5. The Committee **recommended** that access to tocilizumab be widened to include people with VEXAS syndrome without myelodysplastic syndrome with a **high priority**, within the context of treatment of malignancy, either subject to the following Special Authority criteria or funded via the Named Patient Pharmaceutical Assessment Policy (NPPA) pathway (as appropriate):

TOCILIZUMAB – VEXAS syndrome
Initial application
Applications from any relevant practitioner. Approvals valid for 3 months.
1. Diagnosis of VEXAS syndrome with somatic *UBA1* mutation and clinical signs of VEXAS, and
2. Either:
    2.1. Disease is uncontrolled despite treatment with high-dose corticosteroids or
    2.2. High-dose corticosteroids are contraindicated or no longer able to be tolerated, and
3. Azacitidine and/or ruxolitinib has/have not been associated with sufficient improvement in VEXAS clinical signs and/or reduction in corticosteroid use.

Renewal
Applications from any relevant practitioner. Approvals valid for 3 months.
1. Tocilizumab has been associated with new or ongoing improvement in the person's VEXAS clinical manifestations and/or a reduction in their corticosteroid use

10.6. In making these recommendations, the Committee considered

10.6.1. The very high health need of people with VEXAS syndrome, who have few effective and appropriate treatment options and are at risk of higher mortality than those with the same clinical manifestations without VEXAS

10.6.2. The uncertain incidence and prevalence of VEXAS in New Zealand, which are likely lower than estimated from previous expert advice obtained by Pharmac staff

10.6.3. The evidence of benefit from treatment with azacitidine, ruxolitinib and tocilizumab including reductions in the extent, frequency and/or severity of the clinical effects of VEXAS, reductions in needed corticosteroid doses (a sparing effect reasonably likely to be a surrogate associated with HRQoL improvement), and reductions in blood transfusion dependence.

10.7. The Committee considered that the Dermatology, Rheumatology and Rare Disorders Advisory Committees should each receive a copy of the record of this discussion, alongside PTAC.

Discussion

Māori impact

10.8. The Committee discussed the impact of funding azacitidine, ruxolitinib and tocilizumab for the treatment of VEXAS on Māori health areas of focus and Māori health outcomes. The Committee considered that the prevalence, incidence and impact of VEXAS in Māori was unable to be confirmed based on the evidence available to date, noting there is a lack of good data on the syndrome's true incidence and prevalence overall.

Populations with high health needs

10.9. The Committee discussed the health need(s) of those with VEXAS among Māori, Pacific peoples, disabled peoples including tāngata whaikaha Māori, and other populations identified by the Government Policy Statement on Health 2024-2027 to have high health needs. The Committee discussed the impact of widening access to azacitidine, ruxolitinib and tocilizumab for VEXAS and considered that:

10.9.1. There is no evidence to indicate whether there is disproportionate VEXAS syndrome disease severity and/or differences in VEXAS health outcomes for priority groups.

10.9.2. There is no data to inform whether priority populations would be overrepresented in this therapeutic setting or experience differences in access to or benefit from treatment with azacitidine (AZA), ruxolitinib (RUX) or tocilizumab (TOCI) compared with other groups.

Background

10.10. The Committee noted that Pharmac staff sought advice from the Committee regarding widening access to three funded treatments for the treatment of VEXAS:

10.10.1. azacitidine, a DNA hypomethylating agent used primarily in the treatment of myelodysplastic syndromes (MDS) and certain types of leukaemia

10.10.2. ruxolitinib, a Janus kinase (JAK) inhibitor used to treat conditions like myelofibrosis and polycythemia vera

10.10.3. tocilizumab, an anti-IL6 receptor monoclonal antibody used to treat rheumatoid arthritis, cytokine release syndrome and some other inflammatory diseases.

10.11. The Committee noted that Pharmac has funded some treatments for VEXAS via the Named Patient Pharmaceutical Assessment (NPPA) pathway based on advice received in November 2022 indicating that people with VEXAS would be able to be considered exceptional through this funding stream. The Committee noted that some NPPA applications were for individuals requiring second- or later line treatments for VEXAS following a poor response to first-line therapy (predominantly corticosteroids).

10.12. The Committee noted that since 2023, Pharmac has received an increasing number of NPPA applications for various treatments for VEXAS and this prompted a request for updated advice, which now indicates that there is an appreciable number of patients with VEXAS in New Zealand. The Committee noted that Pharmac staff have subsequently initiated a Pharmaceutical Schedule funding application to consider funding azacitidine, ruxolitinib and tocilizumab for VEXAS.

Health need

10.13. The Committee noted that VEXAS is a relatively new disease whose aetiology was first described in 2020 in a cohort of adults with unexplained fever or inflammation, who were all found to have somatic mutations in the *UAB1* gene (Beck et al. N Engl J Med. 2020;383:2628-38). The Committee noted that the broad range of possible clinical manifestations of VEXAS are driven by the somatic mutation and include haematologic or autoinflammatory (eg rheumatologic and dermatologic) features. The Committee noted that this widespread systemic disease often includes deep vein

thrombosis (DVT), skin lesions, fever, systemic features, significant lung involvement, and ocular problems (Kouranloo et al. Rheumatol Int. 2024;44:1219-32).

10.14. The Committee noted that myelodysplastic syndrome (MDS) is reported in roughly 45-50% of cases of VEXAS, although some estimates are as low as 25% (Grayson et al. Blood. 2021;137:3591-4). The Committee noted that cytopaenias lead to transfusion dependency in many with MDS in VEXAS. The Committee noted that, compared with 'classical' MDS in individuals without VEXAS, those with low risk MDS and VEXAS have other systemic symptoms and higher mortality rates from the syndrome. The Committee considered this to have a more significant impact on an individual and their quality of life than non *UAB1*-mutated MDS.

10.14.1. The Committee noted that people with intermediate risk MDS can access funded azacitidine, although the funded group with intermediate risk has specific features that would encompass only 6-10% of those with VEXAS and MDS. Members considered that this number would increase with increasing awareness of the syndrome and its clinical manifestations.

10.14.2. The Committee considered that those with VEXAS and MDS who are unable to access azacitidine have a higher health need than the funded group's, especially noting that MDS in VEXAS is associated with other inflammatory symptoms even if MDS is low risk.

10.15. The Committee noted that retrospective observational analysis has added to the understanding of VEXAS overall including its very high mortality, the generally poor efficacy of treatments including high-dose corticosteroids, and the very high health need of people with the syndrome.

10.15.1. The Committee noted that infections are the major cause of death and prognosis is poor, with a five-year mortality rate of 18-40% (de Valence et al. Ann Rheum Dis. 2024;83:372-81; Kötter et al. Curr Opin Rheumatol. 2025;37:21-31). The Committee considered it hard to derive the true mortality of the disease from the retrospective evidence involving many differing treatments, and considered it influenced by patient selection.

10.15.2. The Committee noted that stem cell transplant (SCT) is the only potentially curative treatment for VEXAS, although this is based on a limited number of cases including a randomised prospective trial of SCT for people with VEXAS who generally received good outcomes (Shahzad et al. Blood. 2023;142 (Suppl 1):7085). The Committee considered that SCTs in this age group would be expected to be associated with about a 15% mortality rate, and that the outcomes in VEXAS were in keeping with this literature.

10.15.3. The Committee considered that symptom control and extension of life were the most important outcomes for people with VEXAS given there is a lack of potentially curative treatments other than SCT. The Committee considered that corticosteroids are the first line of treatment for VEXAS in New Zealand, however, higher doses (ie more than 20mg daily) are needed to attain disease control in VEXAS and these patients would have a high likelihood of steroid toxicity. The Committee also noted that some patients experience disease progression despite treatment with corticosteroids. The Committee considered that while ruxolitinib and tocilizumab are both currently on the Pharmaceutical Schedule for specific indications, these treatments' eligibility criteria would likely apply to very few people with VEXAS.

10.15.4. The Committee considered that those with VEXAS whose physical state meant SCT would be too gruelling for them would receive best supportive care (BSC) including high dose corticosteroids, vaccinations against *Pneumocystis jirovecii* pneumonia (PJP), prophylaxis against venous thromboembolism (VTE)

and antithrombotic treatment given the risk of venous rather than arterial thrombosis (which may be helped by VTE prophylaxis), erythropoietin and transfused red blood cells and/or platelets. Members considered that the transfusion burden can be significant, for example, weekly in those with severe symptomatic thrombocytopaenia.

10.15.5. The Committee considered that the population with VEXAS would generally have either uncontrolled or steroid-dependent disease. The Committee considered that the health need of these individuals would be higher than that of those with the same dermatological or rheumatological issues without VEXAS, as survival is better in those other conditions compared with VEXAS. The Committee noted that higher doses of corticosteroids are required in VEXAS, which come with a higher risk of steroid toxicity, and that some patients experience intolerable toxicity from corticosteroids or experience disease progression despite corticosteroids.

10.16. The Committee noted that CADTH (Canada) had reviewed treatments for VEXAS in 2022 (CADTH Health Technology Review Treatment Options for VEXAS Syndrome [November 2022]) and had noted that there were no reliable data to inform true incidence and prevalence of VEXAS at that time. The Committee noted the subsequent retrospective observational study by Beck et al. (JAMA. 2023;329:318-24), although it was unclear whether this was community-based. The Committee considered that the estimate of an incident population of 340-400 people with VEXAS in New Zealand was likely an overestimate, although true numbers would be difficult to confirm given clinical heterogeneity and phenotypic differences. The Committee considered that in New Zealand, there would be very few cases in women however there could include some undiagnosed but symptomatic cases.

10.17. The Committee noted that VEXAS is an emerging disease entity and considered that diagnoses made to date were for patients whose disease was more severe, hence future consideration of the patient group would need to take into account severity. The Committee noted that a publication by Georgin-Lavialle et al. (Br J Dermatol. 2022;186:564–74) suggested patients with VEXAS might be able to be stratified into one of three subgroups. However, the Committee considered that people with VEXAS could not be differentiated for the purposes of targeting a group(s) for treatment funding at this stage, given there was significant overlap between presentations among the three subgroups and this had not been further validated.

Health benefit

10.18. The Committee noted the body of evidence provided by NPPA applicants and identified during Pharmac staff literature searches, which consisted predominantly of small retrospective studies, some including retrospective diagnoses, which included small patient cohorts, case series or individual cases. The Committee considered this currently provides the best evidence to inform how outcomes differ among these different treatments when used for VEXAS and raised comments about specific evidence as described below.

Azacitidine

10.19. The Committee noted the prospective open-label, single-arm multicentre, phase II study of 29 individuals, including 12 with VEXAS, who received azacitidine for at least six cycles (Mekinian et al. Leukemia. 2022;36:2739-42). Participants had corticosteroid-dependent or refractory systemic autoimmune/inflammatory disorders and VEXAS syndrome associated with myelodysplastic neoplasms (MDS) and chronic myelomonocytic leukaemia (CMML).

10.19.1. The Committee noted that 9/12 (75%) of the participants with VEXAS experienced a treatment response after six cycles, and overall, they received a

median of 16 cycles. Median follow-up was 19 months and their overall survival (OS) at one year was 82% (95% CI: 69,98]). The Committee considered both this treatment duration was longer and survival better than expected, and that the response rate was good in this context.

10.20. The Committee noted evidence regarding outcomes for 11 patients with concomitant MDS included in the French VEXAS registry who received at least one cycle of azacitidine (Comont et al. Br J Haemat. 2022;196: 969-74). Clinical response to azacitidine was experienced by five patients (46%) and corticosteroid doses were reduced or withdrawn for them. The Committee noted that patients received a median of 11 cycles of azacitidine (range two to 35), and several proceeded to SCT.

10.21. Members considered it was unclear from the evidence whether benefits from azacitidine would differ between patients with low risk MDS with VEXAS and those with low risk MDS without VEXAS, but that it would be reasonable to make such an assumption.

Ruxolitinib

10.22. The Committee noted that the key evidence for ruxolitinib for VEXAS was from a retrospective open-label multicentre study (effectively a retrospective case series) reported by Heiblig et al. (Blood. 2022 ;140:927-31). The Committee noted that 30 individuals received a Janus kinase inhibitor (JAKi) of whom 12 received ruxolitinib, and 14 (40%) had concomitant myeloid dysplasia (12 of whom had MDS).

10.22.1. The Committee noted that after median follow-up of 6.9 (range 1-41) months, higher response rates were reported in patients treated with ruxolitinib than with other JAKi, at one (complete response [CR], 67% vs 38%; P =0.13), three (CR, 83 vs 18%; P =0.001), and six months (CR, 87% vs 11%; P =0.002), respectively. The Committee noted that similar responses to ruxolitinib were reported for those with and without myeloid neoplasms (MN) such as MDS.

10.22.2. The Committee noted that among those still on treatment at six months, the median corticosteroid dose reduction was 83.6% with ruxolitinib vs 75% with other JAKi, and at the last follow up two ruxolitinib patients had discontinued corticosteroids.

10.22.3. The Committee noted that of the 14 patients with MN, seven were RBC transfusion-dependent at JAKi onset, and four (all treated with ruxolitinib) experienced RBC transfusion independence after one month (a reduction of 57%).

10.22.4. The Committee considered that despite including small numbers, the study suggested a reasonable response with ruxolitinib of at least 40% with significant and meaningful reductions in corticosteroid use and transfusion dependency.

Tocilizumab

10.23. The Committee noted several publications reporting outcomes with tocilizumab in small series or individual cases of patients with VEXAS:

- Heiblig et al. Semin Hematol. 2021;58:239-46
- Bourbon et al. Blood. 2021;137:3682-4
- van der Made et al. J Allergy Clin Immunol. 2022;149:432-9
- Kunishita et al. Front Immunol. 2022;13:901063
- Goyal et al. JAAD Case Rep. 2022:23:15-19

10.24. The Committee considered that this evidence overall indicated a proportion of people experienced a response to tocilizumab, although this proportion was less than seen with azacitidine or ruxolitinib.

General

10.25. The Committee noted the systematic review (n=116) reported by Boyadzhieva et al. (Rheumat. 2023; 62:3518-25), which reported the following responses with the treatments of interest in people with VEXAS:

- azacitidine: CR 9/36, 25%; partial response (PR) 14/36, 38.9%
- ruxolitinib: CR 7/13, 53.8%; PR 5/13, 38.5%
- tocilizumab: CR 3/15, 20%; PR 6/15, 40%
- allogeneic SCT: CR 6/7, 85.7% (one patient died)

10.26. The Committee also noted the retrospective multicentre study within the French national registry (n=110) reported by Hadjadj et al. (Ann Rheum Dis. 2024;83:1358-67) and noted the CADTH Health Technology Review Treatment Options for VEXAS Syndrome (November 2022) which reviewed evidence from five non-randomised studies that the Committee had noted individually in its review.

10.27. The Committee considered the evidence base had not substantially changed since the 2022 CADTH review, and limitations of study designs, retrospective diagnoses, sample sizes, geographic invariability, and standardisation of therapy remained significant issues. The Committee considered that there was no evidence to suggest the evidence for azacitidine (AZA), ruxolitinib (RUX) and tocilizumab (TOCI) for VEXAS would not be generalisable or relevant to the New Zealand setting. The Committee considered that prospective studies for VEXAS would take a long time to eventuate and be published.

10.28. The Committee considered that there are some potential clinically significant risks when using AZA/RUX/TOCI for VEXAS compared with funded treatments (ie corticosteroids). Members considered it can be difficult to distinguish between disease progression (such as in MDS) and side effects of treatment, given that these medicines can be associated with cytopaenias and would result in a high requirement for prophylaxis against VTE.

10.29. The Committee noted that some studies reported fewer deaths for patients who received these treatments for VEXAS (eg Mekinian et al. 2022) although the range of reported mortality rates rendered the magnitude of survival benefits uncertain. The Committee considered that the evidence suggests a survival benefit from AZA/RUX/TOCI for VEXAS manifestations for some people with VEXAS, which the Committee considered meaningful given the very poor prognosis of the disease.

10.30. Overall, the Committee considered that despite clear limitations in predominantly retrospective evidence base of small studies, and weaker evidence of a smaller proportion who would respond to tocilizumab, the available evidence for AZA/RUX/TOCI for VEXAS supports a consistent benefit in terms of VEXAS symptom management and corticosteroid sparing. However, the Committee noted that these treatments would not be curative, and some patients might not experience a treatment response, might experience disease progression, or may receive toxicity from therapy.

10.31. The Committee considered that the relationship between response rates and clinical outcomes such as health-related quality of life (HRQoL) and survival was probable but unconfirmed. The Committee noted that HRQoL was not reported but could be reasonably extrapolated from response rates and corticosteroid dose reductions, with a substantial reduction in corticosteroid dose also avoiding the most severe toxicities

associated with this treatment. The Committee considered that the time to next treatment is probably a reasonable a surrogate for efficacy in this context also, derived from retrospective analysis.

10.32. The Committee considered that there were no other treatments with emerging evidence that Pharmac should consider, or seek applications for, for VEXAS at this time.

Proposed treatment paradigm

10.33. The Committee considered the proposed treatment paradigm for VEXAS by Khitri et al. 2024, which was a pragmatic expert opinion with recommendations for first-line therapy to consist of high-dose corticosteroids (ie prednisone) for all with VEXAS; second-line treatment with a JAK-2 inhibitor such as ruxolitinib if no or low-risk concurrent MDS, otherwise tocilizumab; and third-line options including azacitidine. If MDS was present, then second-line treatment could consist of azacitidine if disease symptoms were mainly haematological, or a JAK-2 inhibitor if symptoms were mainly rheumatological (ie did not have cytopaenia and did not require transfusions).

10.34. The Committee noted that the paradigm offered by Koster et al. (Am J Hematol. 2024;99:284-99) was similar, however, with a distinction that those eligible for SCT would receive this, while those whose physical state made transplant untenable would undergo medical treatment tailored to the specific disease manifestations (eg VEXAS with a plasma cell disorder such as myeloma would be treated according to myeloma treatment protocols). Members considered that some cases would commence either a JAKi or azacitidine alongside first-line prednisone, due to the inflammatory impact of the disease, presence of significant pathology, and predicted transient duration of benefit from high-dose corticosteroids (eg in cases presenting with significant pulmonary pathology). Members considered that both approaches were consistent with the NPPA applications received prior to closure of the NPPA funded group.

10.35. The Committee noted that there was no strong evidence to support sequencing of these treatments for VEXAS, although considered it appropriate for tocilizumab to be considered for use at a later point in the New Zealand paradigm given the weaker evidence for its lesser benefit. The Committee considered it appropriate for clinical management to be driven by symptoms and for subsequent lines of therapy to be recommended based on response monitoring.

10.36. The Committee noted that there was also an absence of data to inform whether or not, if a specific treatment were discontinued, it would be reasonable to allow for retreatment post-discontinuation or after other treatments (eg on inflammatory flare).

Cost and savings

10.37. The Committee considered that the duration of use for each treatment for VEXAS was difficult to confirm based on current evidence.

10.38. The Committee considered that widening access to these treatments for VEXAS would be associated with an increase in the use of prophylaxis against VTE due to cytopaenia associated with these treatments, and possibly some increase in prophylaxis against PJP infection. The Committee reiterated that it could be difficult to tease out what are side effects from treatment and what is normal disease progression, and noted that prophylaxis of these infections was also considered as part of best supportive care (BSC) treatment.

10.39. The Committee considered that the comparator is BSC consisting of high dose corticosteroids alone and noted that this is known to be less effective and less suitable treatment associated with toxicity and mortality.

10.40. The Committee considered that the transfusion dependency burden would be largely addressed by widening access to these treatments for VEXAS. The Committee considered that reductions in blood transfusion frequency would occur in all patients who are responsive to these treatments, noting that the study by Heiblig et al. (2022) reported reductions in transfusions with ruxolitinib within one month, which is considered a highly meaningful impact from this treatment.

Funding criteria

10.41. The Committee considered that the evidence supported widening access to azacitidine for those with VEXAS and MDS and widening access to ruxolitinib and tocilizumab for people with VEXAS without MDS. However, the Committee considered that tocilizumab should be accessed after azacitidine and/or ruxolitinib has been trialled first, as clinically appropriate, based on the low level of evidence for tocilizumab for VEXAS.

10.42. The Committee considered that if feasible and preferable from Pharmac's perspective, funded access to tocilizumab for VEXAS could be reasonably managed by clinicians via the NPPA pathway instead of the Pharmaceutical Schedule.

10.43. Members considered that there might be a desire for retreatment with azacitidine, ruxolitinib or tocilizumab post-discontinuation of that treatment, or after other treatments for VEXAS syndrome (eg on inflammatory flare). Members considered that this would be clinically appropriate to permit within future funding criteria, targeting those who received benefit but discontinued for other reasons and subsequently might benefit again at the time of disease progression or symptomatic recurrence.

10.44. The Committee considered it reasonable to have an early requirement for assessment of benefit to inform renewal of approval for ruxolitinib and tocilizumab, given their price and the low level of evidence for tocilizumab for VEXAS. The Committee considered that no renewal should be required for azacitidine for VEXAS and noted that clinical responses would be expected to develop over a long time (eg following six cycles in standard cases of MDS).

Summary for assessment

10.45. The Committee considered that the below summarises its interpretation of the most appropriate PICO (population, intervention, comparator, outcomes) information for azacitidine, ruxolitinib and tocilizumab if access to these medicines was widened in New Zealand for the treatment of VEXAS syndrome. This PICO captures key clinical aspects of the proposal and may be used to frame any future economic assessment by Pharmac staff. This PICO is based on the Committee's assessment at this time and may differ from that requested by the applicant. The PICO may change based on new information, additional clinical advice, or further analysis by Pharmac staff.

Population	Uncontrolled and/or corticosteroid dependent VEXAS syndrome with myelodysplastic syndrome (MDS)	Uncontrolled and/or corticosteroid-dependent VEXAS with no or low-risk MDS	Uncontrolled and/or corticosteroid-dependent VEXAS with no or low-risk MDS Trialled azacitidine and/or ruxolitinib previously
Intervention	**Azacitidine** 75 mg/m2 SC QD for 7 days, 4-weekly.	**Ruxolitinib** starting dose 10mg twice daily (TD) or 5mg TD if elderly or neutropenic. Dose increase based on clinical and biological response progressively up to 20mg TD, until clinical	**Tocilizumab** 8mg/kg IV Q4w OR 162mg SC wkly, then every 10 days.

		response and eventually biological response are reached. Recommended tapering corticosteroids after at least 3 months of stable clinical response at fixed dosage.	
	All with corticosteroids and best supportive care (BSC) as required.		
Comparator(s)	Corticosteroids and BSC as required		
Outcome(s)	• Response to VEXAS clinical features • Reduction in corticosteroid use • Increased time to next therapy		
Table definitions: Population, the target population for the pharmaceutical; Intervention, details of the intervention pharmaceutical; Comparator, details the therapy(s) that the patient population would receive currently (status quo – including best supportive care); Outcomes, details the key therapeutic outcome(s) and source of outcome data.			

11. Other Business

11.1. The Chair acknowledged the resignation of Dr Alice Loft (Medical Oncologist) who joined the committee in January 2023.