MSAC Application

Integrated, closed-system, extracorporeal photopheresis and methoxsalen (UVADEX®) for cutaneous T-cell lymphoma, update to MBS and PBS items

PICO Set (2)

Table of Abbreviations

ALLG	Australasian Leukaemia and Lymphoma Group
ANZTCT	Australia and New Zealand Transplant and Cellular Therapies
ARTG	Australian Register of Therapeutic Goods
BV	Brentuximab vedotin
CTCL	Cutaneous T-cell lymphoma
CTL	Cytotoxic T-lymphocytes
ECP	Extracorporeal photopheresis
EDF	European Dermatology Forum
EORTC	European Organisation of Research and Treatment of Cancer
ESC	Evaluation Subcommittee
HSANZ	Haematology Society of Australia and New Zealand
ISCL	International Society for Cutaneous Lymphomas
MBS	Medicare Benefits Schedule
MF	Mycosis fungoides
MSAC	Medical Services Advisory Committee
NHS	National Health Service
PBS	Pharmaceutical Benefits Scheme
PUVA	Psoralen plus ultraviolet A radiation
RBC	Red blood cells
TSEB	Total skin electron beam
TSEBT	Total skin electron beam therapy
TTNT	Time to next treatment
UK	United Kingdom
UV	Ultraviolet
UVA	Ultraviolet A
WBC	White blood cells

Population

Describe the population in which the proposed health technology is intended to be used:

Due to the nature of this application, the population is unchanged from those currently approved for treatment with extracorporeal photopheresis (ECP) under Medicare Benefits Schedule (MBS) items 14247 and 14249.

In summary, the proposed health technology is intended for use in Australian adults with a confirmed diagnosis of erythrodermic stage III–IVa T_4 M_0 cutaneous T-cell lymphoma (CTCL) who are:

- aged 18 years or older
- refractory* to one or more prior systemic treatments for this condition
- receiving the treatment in combination with use of ex-vivo injectable methoxsalen

*Refractory implies the individual has had either disease recurrence while on treatment or has experienced intolerance or unacceptable toxicity to treatment (MSAC Application 1420.1 PSD).

Specify any characteristics of patients with, or suspected of having, the medical condition, who are proposed to be eligible for the proposed health technology, describing how a patient would be investigated, managed and referred within the Australian healthcare system in the lead up to being considered eligible for the technology:

CTCL is a rare heterogeneous group of diseases comprised of non-Hodgkin lymphomas involving malignant T-cell clones that accumulate in the skin (Knobler et al. 2014; Raphael et al. 2011). CTCL has an annual age-standardised incidence of 0.77 per 100,000 (95% CI 0.74–0.79) in Australia (Campbell et al. 2025) and occurs most commonly in adults of all races aged 40–60 years, with males affected approximately twice as often as females. The two most common CTCL variants are mycosis fungoides (MF) and Sézary syndrome (SS). MF accounts for around 60% (Knobler et al. 2014) of all CTCL patients and is characterised by clonal T-cells in the cutaneous environment that present early on as plaques and patches on the skin (which can resemble eczema or psoriasis), and eventually result in lesions, pruritus, and tumours (Knobler et al. 2014; Raphael et al. 2011). SS accounts for around 5% (Knobler et al. 2014) of all CTCL and is a leukaemic form of MF, where T-cells circulate in the peripheral blood and affect internal organs such as the spleen and lungs (Knobler et al. 2014; Raphael et al. 2011).

Presentation and investigation

Diagnosing CTCL requires correlation of clinical and pathological findings, and consultation with an experienced pathologist (Prince et al. 2009). Tests used to determine disease severity include a complete physical examination, skin biopsy, blood tests, radiologic imaging, and lymph-node biopsy (Olsen et al. 2007). The results of these investigations are then used by the treating clinician to establish the person's disease stage (Olsen et al. 2007). The most commonly used staging criteria is the International Society for Cutaneous Lymphomas (ISCL) and European Organisation of Research and Treatment of Cancer's (EORTC) revision to the staging of MF and SS, which is outlined in Table 1 (Olsen et al. 2007; Prince et al. 2009). Based on this criterion, MSAC supported listing of ECP for patients with erythrodermic (stage T_4 M_0) CTCL.

Table 1 ISCL/EORTC Revision to the staging of mycosis fungoides and Sézary syndrome

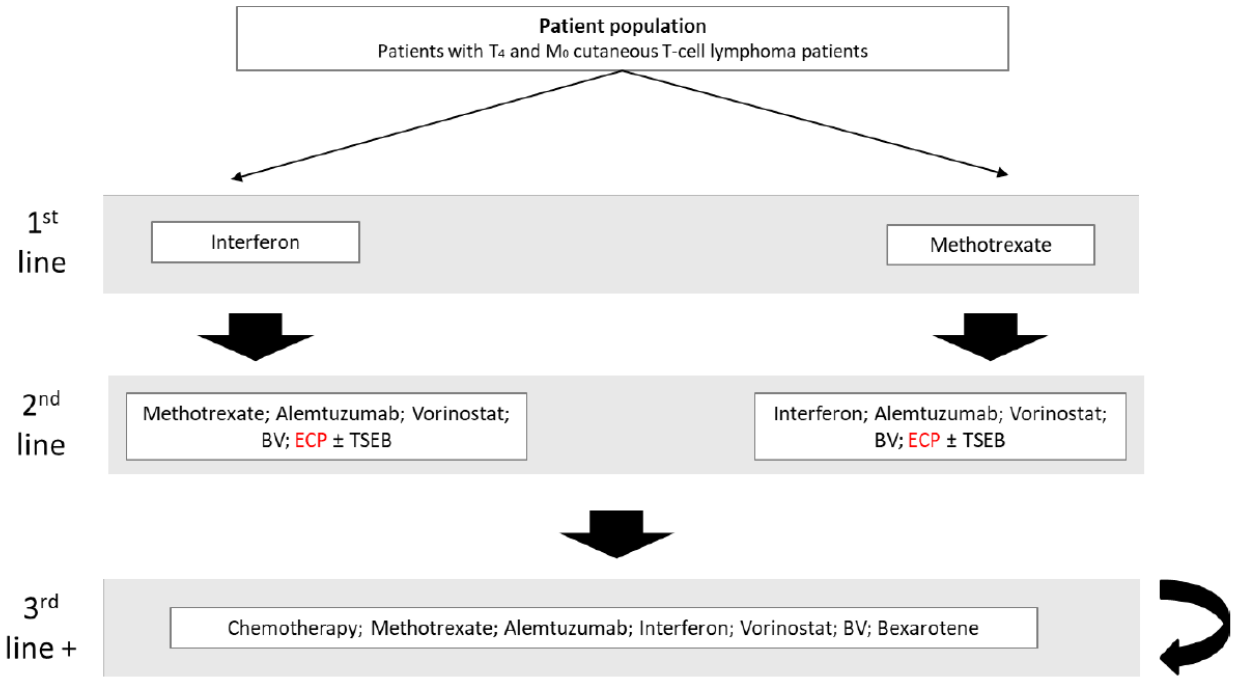
	T	N	M	B
Early-stage disease				
IA	1	0	0	0, 1
IB	2	0	0	0, 1
IIA	1, 2	1, 2	0	0, 1
Advanced-stage disease				
IIB	3	0-2	0	0, 1
III	4	0-2	0	0, 1
IIIA	4	0-2	0	0
IIIB	4	0-2	0	1
IVA_1	1-4	0-2	0	2
IVA_2	1-4	3	0	0-2
IVB	1-4	0-3	1	0-2

Source: Adapted from Prince et al. (2009)
Abbreviations: B, blood – blood involvement; EORTC, European Organisation for Research and Treatment of Cancer; ISCL, International Society for Cutaneous Lymphomas; M, metastasis – visceral involvement; N, node – node involvement; T, tumour – skin involvement.

Management and referral within the Australian healthcare system

Disease staging guides treatment selection and identifies people with advanced or erythrodermic disease (stage III–IVa T_4 M_0) who are eligible for systemic therapy. Currently approved systemic options for erythrodermic (T_4 M_0) CTCL include methotrexate, interferon-α, vorinostat, brentuximab vedotin and ECP. Each of these treatments are often used in combination with total skin electron beam therapy (TSEBT) (Campbell 2016). Interferon-α or methotrexate are used first-line, with interferon-α preferred unless not tolerated. No curative therapies exist for CTCL, so individuals with refractory disease progress through multiple lines of treatment, with movement between treatments dependent on individual response with respect to inducing and maintaining long-term remissions (Knobler et al. 2014). Once a therapy is ineffective, it is not re-used within the treatment pathway, and chemotherapy is reserved as a last-line option. The current clinical management algorithm (Figure 1) for CTCL positions ECP as a second-line therapy (MSAC Application 1420.1 PSD), and no change is being sought regarding this sequencing.

Figure 1 Clinical management algorithm in T_4 M_0 cutaneous T-cell lymphoma patients that are refractory to initial therapy



Abbreviations: BV, brentuximab vedotin; TSEB, total skin electron beam therapy
*Alemtuzumab is not listed on the Pharmaceutical Benefits Scheme (PBS) for CTCL, and thus not listed as a comparator. However, it is occasionally used to treat CTCL in Australia and thus included in the clinical management algorithm.
Source: Adapted from MSAC Application 1420.1 PSD Figure 1 p8

Provide a rationale for the specifics of the eligible population:

The Medical Services Advisory Committee (MSAC) previously accepted the high clinical need in patients with erythrodermic T_4 M_0 CTCL, and acknowledged that integrated, closed-system ECP has an established place in the clinical management algorithm as a second-line therapy (MSAC Application 1420.1 PSD Figure 1 p8). This application does not seek to change the eligibility criteria for ECP, but to extend the current prescriber restriction which states that the service must be supervised by a specialist or consultant physician in the speciality of haematology, to allow dermatologists to also supervise this service. This change would reflect contemporary practice in Australia, where national standards for CTCL care recognise dermatologists as integral members of multidisciplinary management teams (Leukaemia Foundation 2023). The original restriction was informed by clinical practice at the time of the initial MSAC submission, when ECP was only available at two centres in Australia: The Peter MacCallum Cancer Centre and the Royal Prince Alfred Hospital. Both services operated within apheresis units and were primarily staffed by haematologists. Accordingly, expert consultation for the original application came predominantly from the haematology field. However, this limitation was not a central requirement of the MSAC submission, and it does not reflect current clinical practice or international standards.

In other jurisdictions, dermatologists are involved in the delivery of ECP. The European Dermatology Forum published clinical guidelines in 2013, which were updated in 2020 (Knobler et al. 2020; Knobler et al. 2014). Developed through consultation both within and outside the field of dermatology, these guidelines currently represent the most comprehensive expert recommendations for the use of ECP, based on published literature and consensus opinion. In the United Kingdom (UK), ECP is formally endorsed by both the Joint British Association of Dermatologists and the UK Photopheresis Society for CTCL. ECP services are delivered through specialised NHS centres located in regions throughout the UK. All designated centres assess and manage patients with CTCL, with dermatologists routinely involved in both referral and longitudinal clinical care. In Germany, ECP is predominantly delivered within hospital-based settings, typically with departments of dermatology, haematology, or transfusion medicine. Access is enabled through established procedural codes, allowing dermatologists to initiate, coordinate, and oversee ECP therapy as part of multidisciplinary inpatient services.

More recently in Australia, the optimal care pathway for CTCL management has positioned dermatologists as leading contributors within multidisciplinary care teams (Leukaemia Foundation 2023). Given their recognised expertise in assessing the characteristic cutaneous manifestations of CTCL, dermatologists play an integral role in the clinical evaluation and coordination of care for these patients. Their established experience with phototherapy and ultraviolet (UV) interventions similarly supports their capacity to supervise light-based therapies such as ECP for the management of CTCL (Tan and GeBauer 2025).

While availability of ECP in Australia has expanded since the initial MSAC submissions, it remains limited, with services currently available at one hospital in each of New South Wales, South Australia, and Queensland, and three hospitals in Victoria. Expert clinical opinion indicates that expanding prescribing rights to dermatologists would facilitate the establishment of additional sites, improving equity of access for this small but high-need patient population. Given that MSAC has accepted the Evaluation Subcommittee's (ESC) advice that ECP is likely safer than, and at least as effective as, all four identified comparators (Figure 1) for stage T_4 M_0 CTCL (MSAC Application 1420.1 PSD), increasing access to this validated treatment – while maintaining the safety, efficacy, and cost-effectiveness parameters that MSAC has already endorsed – would represent a pragmatic and patient-centred change.

Are there any prerequisite tests?

No

Are the prerequisite tests MBS funded?

Not applicable

Provide details to fund the prerequisite tests:

Not applicable

Intervention

Name of the proposed health technology:

Integrated, closed-system, extracorporeal photopheresis (ECP)

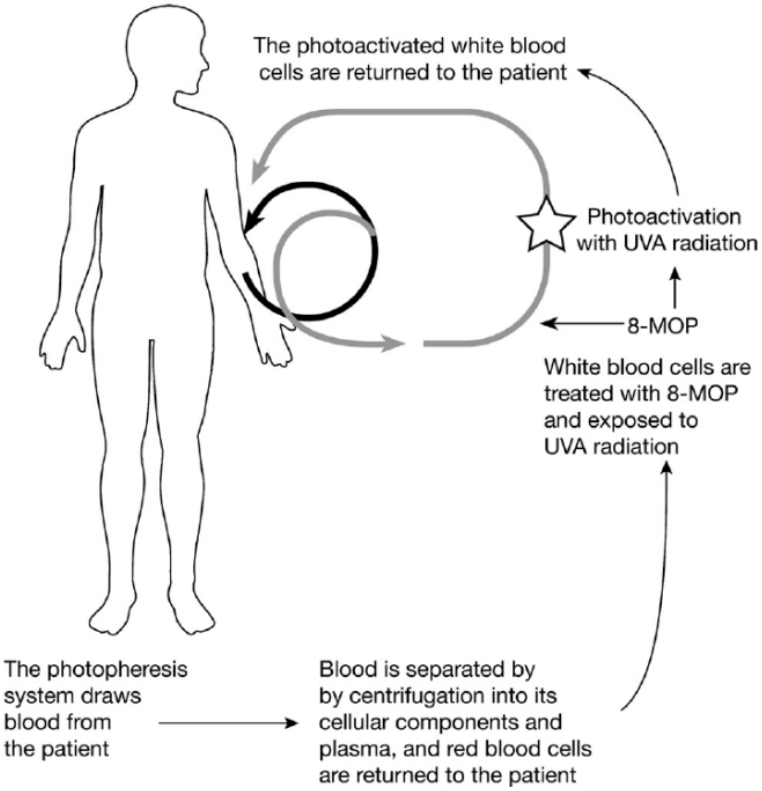
Methoxsalen (UVADEX®)

Describe the key components and clinical steps involved in delivering the proposed health technology:

Extracorporeal photopheresis

ECP is a leukapheresis-based, immunomodulatory therapy in which a patient's leukocytes are collected and treated ex-vivo with methoxsalen and UVA light and then returned to the patient (Figure 2). Integrated, closed ECP systems complete the processes of cell separation, photo activation of methoxsalen (UVADEX®), and reinfusion of the treated cells back into the patient within an automated and fully integrated process (Knobler et al. 2014). All components of the treatment are validated for use together. Treatment of CTCL with integrated ECP systems is well established, with a large body of international (Bouwhuis et al. 2002; Duvic et al. 1996; Edelson et al. 1987; Heald et al. 1989; Jiang et al. 1999; Knobler et al. 2012; Prinz et al. 1995; Siakantaris et al. 2012; Stevens et al. 2002) and Australian studies (Arulogun et al. 2008; Hughes et al. 2015) supporting use of the intervention.

Figure 2 Overview of ECP



Abbreviations: 8-MOP, methoxsalen; UVA, ultraviolet A
Note: Blood is removed from the patient, and the red blood cells (RBC) and white blood cells (WBC) are separated. RBC are immediately returned to the patient, whereas WBC are treated with methoxsalen (8-MOP) and ultraviolet A (UVA) radiation to photoactivate the drug; photoactivated WBC are then returned to the patient.
Source: Worel and Leitner (2012)

Photopheresis is also performed with open systems, also known as two-step methods, which are characterised by different devices for cell separation and drug photo activation (Knobler et al. 2014). In these systems the combination of the device for separation and the device for photoactivation has not been approved for use together or specifically approved for photopheresis (Knobler et al. 2014). The two-step approach also increases the potential risk of patient reinfusion error, infection and cross-contamination (Knobler et al. 2014). Open systems are only recommended for use in centres that have approval for handling blood components separately (Knobler et al. 2014). MSAC has not assessed the efficacy or cost-effectiveness of open systems for the treatment of CTCL.

Methoxsalen

Methoxsalen is a naturally occurring photoactive substance found in the seeds of the Ammi majus (Umbelliferae) plant and in the roots of Heracleum Candicans. It belongs to a group of compounds known as psoralens, or furocoumarins. Methoxsalen is pharmacologically active only when exposed to ultraviolet light in the UVA range (320 to 400 nm). Methoxsalen is commonly used in combination with UVA radiation, known as PUVA. This activity has been exploited for many years and PUVA has been shown to be effective for the skin lesions of psoriasis and in the treatment of patients with CTCL.

The ECP procedure involves chemical treatment of WBC with a drug that is activated by light (e.g. methoxsalen), exposing this mix to ultraviolet light and returned to the patient. While the mechanism of action of ECP in CTCL is still not fully understood, it is believed that the combination of ultraviolet light and methoxsalen induces apoptosis (programmed cell death) in treated T-lymphocytes. Following reinfusion the treat cell stimulates antitumor responses mediated by cytotoxic T-lymphocytes (CTL) (Edelson 2001)

Identify how the proposed technology achieves the intended patient outcomes:

ECP is used in combination with PBS reimbursed methoxsalen to treat patients with CTCL. MSAC has previously accepted that ECP is safer than, and at least as effective as the comparators methotrexate, interferon-α, brentuximab vedotin, and vorinostat, for the treatment of stage T_4, M_0 CTCL.

CTCL is a chronic condition in which patients may live for many years with persistent and debilitating symptoms. As such, treatment typically requires multiple lines of therapy aimed at providing sustained symptom relief. Time to next treatment (TTNT) is an important clinical and functional measure of therapeutic benefit, as it reflects the duration of symptom control and disease stability. Accordingly, TTNT was considered a key clinical outcome in MSAC's previous assessment.

The median TTNT when ECP was used alone was 14 months. This was significantly greater than IFN-α (8 months, p = 0.0067), vorinostat (4 months, p < 0.0011), antibody/ADC/FT/bexarotene vedotin therapy (n = 20; 6.5 months, p = 0.028), chemotherapy (3 months, p < 0.0001), and low-dose methotrexate (n = 35; 2.5 months, p<0.0001). Compared to biological agents including brentuximab vedotin (n=1 of 20), TTNT was also considerably greater (n = 20, 7 months, p-value not reported) (Gao et al. 2019).

MSAC has also accepted that ECP is a safe and well tolerated intervention further supporting its role in achieving sustained clinical benefit and improving patient outcomes in CTCL.

Does the proposed health technology include a registered trademark component with characteristics that distinguishes it from other similar health components?

Yes

Explain whether it is essential to have this trademark component or whether there would be other components that would be suitable:

Both methoxsalen and the photopheresis system are registered components. Methoxsalen (ARTG 38832) was approved for listing on the ARTG in September 2019 for the following therapeutic use:

'*Uvadex (methoxsalen) is indicated for extracorporeal administration with the Therakos Cellex Photopheresis System for the palliative treatment of the skin manifestations of cutaneous T-cell lymphoma (CTCL) that is unresponsive to other forms of treatment.*'

As such methoxsalen is only indicated for use with the THERAKOS® CELLEX® Photopheresis System Instrument systems. Therefore, substituting this system with another component or device would not align with the ARTG-approved indication. Alternative components have not been evaluated or approved for use with methoxsalen in this context.

Are there any proposed limitations on the provision of the proposed health technology delivered to the patient (For example: accessibility, dosage, quantity, duration or frequency):

Yes

Provide details and explain:

This submission proposes no changes to the dosage, quantity, duration, or frequency of ECP administration compared with MSAC's previous consideration. The safety, efficacy, and cost-effectiveness parameters endorsed by MSAC in 2020 remain unchanged (MSAC Application 1420.1 PSD).

The application seeks to extend the current prescriber restriction, which currently requires that the service be supervised by a specialist or consultant physician in the specialty of haematology, to also allow dermatologists to supervise the service.

As previously described, this change will address existing accessibility barriers impacting access to ECP services as ECP services in Australia remain limited to a small number of hospital sites. Allowing dermatologists to supervise the service will facilitate the establishment of additional treatment centres, improving geographical accessibility and equity of access for this small but high-need patient population.

If applicable, advise which health professionals will be needed to provide the proposed health technology:

The current MBS items for ECP for the treatment of CTCL, items 14247 and 14249, state that the service must be supervised by a specialist or consultant physician in the speciality of haematology. This is consistent with the PBS restriction for methoxsalen for the treatment of CTCL (items 12154Q, 12156T, 12162D, 12173Q), which contain treatment criteria which state that the patient must be treated by a haematologist, or must be treated by a medical physician working under the supervision of a haematologist. This application seeks to extend the current treatment restrictions to include dermatologists reflecting contemporary multidisciplinary practice in the management of CTCL.

If applicable, advise whether delivery of the proposed health technology can be delegated to another health professional:

ECP delivery requires a multidisciplinary clinical team to support the management of patients with CTCL. This team may include dermatologists, haematologists, specialist nurses, apheresis technicians, and transfusion medicine staff. Haematologists and dermatologists are responsible for clinical oversight and patient management, while trained nursing and technical staff perform the photopheresis procedure and monitor treatment safety.

This application proposes that the current restriction on specialist supervision be expanded to also allow oversight by dermatologists, reflecting contemporary multidisciplinary practice and improving accessibility to ECP services.

If applicable, advise if there are any limitations on which health professionals might provide a referral for the proposed health technology:

Not applicable

Is there specific training or qualifications required to provide or deliver the proposed service, and/or any accreditation requirements to support delivery of the health technology?

No

Provide details and explain:

Not applicable

Indicate the proposed setting(s) in which the proposed health technology will be delivered:

☐ Consulting rooms
☐ Day surgery centre
☐ Emergency Department
☒ Inpatient private hospital
☒ Inpatient public hospital
☐ Laboratory
☐ Outpatient clinic
☐ Patient's home
☐ Point of care testing
☐ Residential aged care facility
☐ Other (please specify)

Is the proposed health technology intended to be entirely rendered inside Australia?

Yes

Provide additional details on the proposed health technology to be rendered outside of Australia:

Not applicable

Comparator

Nominate the appropriate comparator(s) for the proposed medical service (i.e., how is the proposed population currently managed in the absence of the proposed medical service being available in the Australian healthcare system). This includes identifying healthcare resources that are needed to be delivered at the same time as the comparator service:

Not applicable

List any existing MBS item numbers that are relevant for the nominated comparators:

Not applicable

Provide a rationale for why this is a comparator:

Not applicable

Pattern of substitution – Will the proposed health technology wholly replace the proposed comparator, partially replace the proposed comparator, displace the proposed comparator or be used in combination with the proposed comparator?

☐ None (used with the comparator)
☐ Displaced (comparator will likely be used following the proposed technology in some patients)
☐ Partial (in some cases, the proposed technology will replace the use of the comparator, but not all)
☐ Full (subjects who receive the proposed intervention will not receive the comparator)

Outline and explain the extent to which the current comparator is expected to be substituted:

Not applicable

Outcomes

List the key health outcomes (major and minor – prioritising major key health outcomes first) that will need to be measured in assessing the clinical claim for the proposed medical service/technology (versus the comparator):

☒ Health benefits
☒ Health harms
☐ Resources
☐ Value of knowing

Outcome description – include information about whether a change in patient management, or prognosis, occurs as a result of the test information:

The MSAC has accepted that treatment with ECP is likely safer than, and at least as effective as, all four identified comparators (methotrexate, interferon-α, vorinostat, and brentuximab vedotin) for stage T_4 M_0 cutaneous T-cell lymphoma (MSAC Application 1420.1 PSD).

The outcomes assessed by MSAC in the April 2020 submission were:

a) Quality of life/itch improvement/pruritus score
b) Reduction in erythroderma/skin response/skin examination
c) Time to next systemic treatment
d) Overall survival
e) Response rate
f) Safety

This submission requests that the current restriction for supervision of ECP be expanded to include dermatologists, in addition to haematologists. This proposed change is not expected to alter the clinical

outcomes previously accepted by MSAC, as it does not modify the treatment indication, delivery method, dosage, or duration of therapy.

Proposed MBS items

How is the technology/service funded at present? (e.g., research funding; State-based funding; self-funded by patients; no funding or payments):

In April 2020, MSAC supported an application for public funding of ECP by the MBS. The service is currently funded on the MBS under items 14247 and 14249. Methoxsalen is reimbursed on the PBS under items 12154Q, 12156T, 12162D, and 12173Q.

Provide at least one proposed item with their descriptor and associated costs, for each Population/Intervention:

Two MBS items exist for the delivery of ECP for CTCL; one for initial treatment and one for continued use after a confirmed response to initial treatment. Under the proposed change, point (f) of the existing MBS item descriptor has been amended to include dermatology, such that the service may be supervised by a specialist or consultant physician in the speciality of haematology or dermatology.

MBS item number (where used as a template for the proposed item)	**14247**
Category number	3
Category description	Therapeutic procedures
Proposed item descriptor	Extracorporeal photopheresis for the treatment of erythrodermic stage III-IVa T4 M0 cutaneous T-cell lymphoma; if a) the service is provided in the initial six months of treatment; and b) the service is delivered using an integrated, closed extracorporeal photopheresis system; and c) the patient is 18 years old or over; and d) the patient has received prior systemic treatment for this condition and experienced either disease progression or unacceptable toxicity while on this treatment; and e) the service is provided in combination with the use of Pharmaceutical Benefits Scheme-subsidised methoxsalen; and f) the service is supervised by a specialist or consultant physician in the speciality of haematology ***or dermatology.*** Applicable once per treatment cycle (H)
Proposed MBS fee	Fee: $2,158.85 Benefit: 75% = $1,619.15
Indicate the overall cost per patient of providing the proposed health technology	$2,158.85
Please specify any anticipated out of pocket expenses	No additional out of pocket costs are expected
Provide any further details and explain	The application does not propose any change to the MBS fee for ECP services for CTCL.

MBS item number (where used as a template for the proposed item)	**14249**
Category number	3
Category description	Therapeutic procedures
Proposed item descriptor	Extracorporeal photopheresis for the continuing treatment of erythrodermic stage III-IVa T4 M0 cutaneous T-cell lymphoma; if a) in the preceding 6 months: i. a service to which item 14247 applies has been provided; and ii. the patient has demonstrated a response to this service; and iii. the patient requires further treatment; and b) the service is delivered using an integrated, closed extracorporeal photopheresis system; and c) the patient is 18 years old or over; and d) the service is provided in combination with the use of Pharmaceutical Benefits Scheme-subsidised methoxsalen; and e) the service is supervised by a specialist or consultant physician in the speciality of haematology ***or dermatology.*** Applicable once per treatment cycle (H)
Proposed MBS fee	Fee: $2,158.85 Benefit: 75% = $1,619.15
Indicate the overall cost per patient of providing the proposed health technology	$2,158.85
Please specify any anticipated out of pocket expenses	No additional out of pocket costs are expected
Provide any further details and explain	The application does not propose any change to the MBS fee for ECP services for CTCL.

Algorithms

PREPARATION FOR USING THE HEALTH TECHNOLOGY

Define and summarise the clinical management algorithm, including any required tests or healthcare resources, before patients would be eligible for the proposed health technology:

The clinical management algorithm is unchanged from the algorithm which was supported by MSAC in the April 2020 submission and is displayed in Figure 3. Individuals with T_4 M_0 CTCL are typically treated with interferon-α or methotrexate first-line, with interferon-α preferred unless not tolerated. As no curative therapies exist for CTCL, those with refractory disease progress through multiple lines of treatment, dependent on individual response with respect to inducing and maintaining long-term remissions (Knobler et al. 2014). Resource and adverse event costs are expected to remain consistent as the clinical algorithm is unchanged. However, extending prescriber restrictions to include dermatologists may streamline the treatment pathway, as dermatologists managing individuals with CTCL would be able to directly supervise ECP treatment without further referral to a haematologist.

Is there any expectation that the clinical management algorithm before the health technology is used will change due to the introduction of the proposed health technology?

No

Describe and explain any differences in the clinical management algorithm prior to the use of the proposed health technology vs. the comparator health technology:

Not applicable

USE OF THE HEALTH TECHNOLOGY

Explain what other healthcare resources are used in conjunction with delivering the proposed health technology:

Methoxsalen (UVADEX®)

Explain what other healthcare resources are used in conjunction with the comparator health technology:

Not applicable

Describe and explain any differences in the healthcare resources used in conjunction with the proposed health technology vs. the comparator health technology:

Not applicable

CLINICAL MANAGEMENT AFTER THE USE OF HEALTH TECHNOLOGY

Define and summarise the clinical management algorithm, including any required tests or healthcare resources, after the use of the proposed health technology:

The clinical management algorithm will remain unchanged as ECP is currently funded for CTCL via MBS items 14247 and 14249. As such, healthcare resourcing costs are expected to remain consistent with current practice. After the use of ECP in the algorithm (if an individual has refractory disease progress), they will progress to third-line treatment (Figure 3).

Define and summarise the clinical management algorithm, including any required tests or healthcare resources, after the use of the comparator health technology:

After the use of a comparator in the algorithm (if an individual has refractory disease progress), they will progress to third-line treatment (Figure 3).

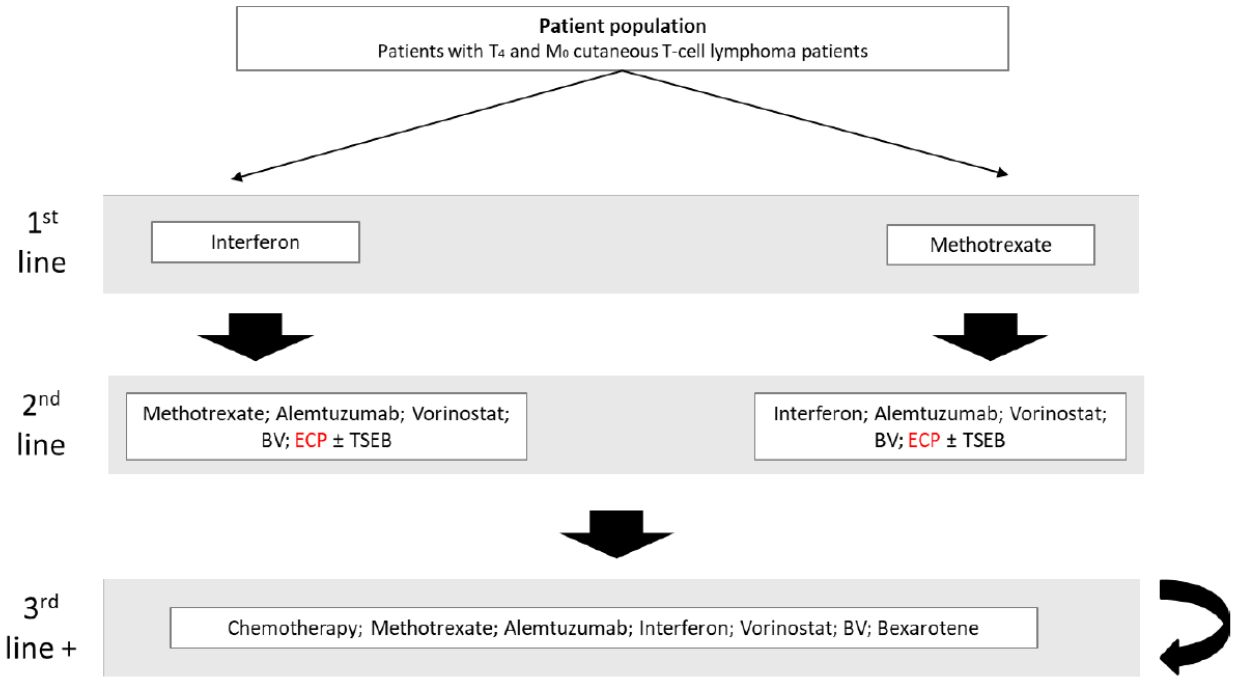
Describe and explain any differences in the healthcare resources used after the proposed health technology vs. the comparator health technology:

Due to the non-curative nature of CTCL, and that individuals with refractory disease progress through multiple lines of treatment once a therapy is ineffective, the difference is only one of treatment sequencing. As such, resource use is not expected to change.

Insert diagrams demonstrating the clinical management algorithm with and without the proposed health technology:

Figure 3 shows the clinical management algorithm with ECP as a second-line therapy. No change is being requested to this clinical management algorithm.

Figure 3 Clinical management algorithm in T_4 M_0 cutaneous T-cell lymphoma patients that are refractory to initial therapy



Abbreviations: BV, brentuximab vedotin; ECP, extracorporeal photopheresis; TSEB, total skin electron beam therapy
*Alemtuzumab is not listed on the Pharmaceutical Benefits Scheme (PBS) for CTCL, and thus not listed as a comparator. However, it is occasionally used to treat CTCL in Australia and thus included in the clinical management algorithm.
Source: Adapted from MSAC Application 1420.1 PSD Figure 1 p8

Claims

In terms of health outcomes (comparative benefits and harms), is the proposed technology claimed to be superior, non-inferior or inferior to the comparator(s)?

☐ Superior
☒ Non-inferior
☐ Inferior

Please state what the overall claim is, and provide a rationale:

The clinical claim is unchanged from the April 2020 submission; ECP has superior safety and at least non-inferior effectiveness compared to its comparators. The MSAC accepted the claim of improved comparative safety and confirmed that ECP is associated with fewer adverse events than its comparators (MSAC Application 1420.1 PSD). Regarding comparative effectiveness, MSAC accepted that although the evidence is limited, ECP is at least as effective as the four identified comparators (MSAC Application 1420.1 PSD). Expanding treatment criteria for the service to allow supervision by dermatologists is not expected to affect this claim.

Why would the requestor seek to use the proposed investigative technology rather than the comparator(s)?

Not applicable

Identify how the proposed technology achieves the intended patient outcomes:

ECP is used in combination with PBS reimbursed methoxsalen to treat patients with CTCL. MSAC has previously accepted that ECP is safer than, and at least as effective as the comparators methotrexate, interferon-α, brentuximab vedotin, and vorinostat, for the treatment of stage T_4 M_0 CTCL.

CTCL is a chronic condition in which patients may live for many years with persistent and debilitating symptoms. As such, treatment typically requires multiple lines of therapy aimed at providing sustained

symptom relief. Time to next treatment (TTNT) is an important clinical and functional measure of therapeutic benefit, as it reflects the duration of symptom control and disease stability. Accordingly, TTNT was considered a key clinical outcome in MSAC's previous assessment.

The median TTNT when ECP was used alone was 14 months. This was significantly greater than IFN-α (8 months, p = 0.0067), vorinostat (4 months, p < 0.0011), antibody/ADC/FT/bexarotene vedotin therapy (n = 20; 6.5 months, p = 0.028), chemotherapy (3 months, p < 0.0001), and low-dose methotrexate (n = 35; 2.5 months, p<0.0001). Compared to biological agents including brentuximab vedotin (n=1 of 20), TTNT was also considerably greater (n = 20, 7 months, p-value not reported) (Gao et al. 2019).

MSAC has also accepted that ECP is a safe and well tolerated intervention further supporting its role in achieving sustained clinical benefit and improving patient outcomes in CTCL.

For some people, compared with the comparator(s), does the test information result in:

A change in clinical management?

Not applicable

A change in health outcome?

Not applicable

Other benefits?

Not applicable

Please provide a rationale, and information on other benefits if relevant:

Not applicable

In terms of the immediate costs of the proposed technology (and immediate cost consequences, such as procedural costs, testing costs etc.), is the proposed technology claimed to be more costly, the same cost or less costly than the comparator?

☐ More costly
☒ Same cost
☐ Less costly

Provide a brief rationale for the claim:

This submission proposes no change to cost of ECP or methoxsalen. Cost-effectiveness is expected to be consistent with what was previously accepted by MSAC in 2020.

If your application is in relation to a specific radiopharmaceutical(s) or a set of radiopharmaceuticals, identify whether your clinical claim is dependent on the evidence base of the radiopharmaceutical(s) for which MBS funding is being requested. If your clinical claim is dependent on the evidence base of another radiopharmaceutical product(s), a claim of clinical noninferiority between the radiopharmaceutical products is also required.

Not applicable

Summary of Evidence

Provide one or more recent (published) high quality clinical studies that support use of the proposed health service/technology. At 'Application Form lodgement'

	Type of study design	Title of journal article or research project	Short description of research	Website link to journal article or research	Date of publication
1.	Guideline	Updated guidelines on the use of extracorporeal photopheresis 2020	European Dermatology Forum (EDF) guidelines on the use of ECP across multiple conditions. Outlines mechanisms, protocols, treatment, assessments, safety data, and expert clinical opinion.	Part 1: https://pubmed.ncbi.nlm.nih.gov/33025659/ Part 2: https://pubmed.ncbi.nlm.nih.gov/32964529/	2020 (update to 2014 version)
2.	Guideline	Guidelines on the use of extracorporeal photopheresis	Precursor to 2020 guideline (above). Recommendations and guidelines on ECP use across multiple conditions, with clinical data reviewed up to 2014.	https://pubmed.ncbi.nlm.nih.gov/24354653/	2014
3.	Guideline	Optimal care pathway for people with cutaneous T-cell lymphoma	Guideline outlining best practice for CTCL management at each stage, defining multidisciplinary roles in the care pathway. Endorsed by Cancer Australia, Cancer Council, Leukaemia Foundation, Lymphoma Australia, ANZTCT, HSANZ, and ALLG.	https://www.cancer.org.au/assets/pdf/cutaneous-t-cell-lymphoma	2023
4.	Guideline	Guidelines for phototherapy and PUVA service delivery in Australia: Minimum standards and quality assurance framework	Australian dermatology guideline establishing national framework and minimum standards for phototherapy and psoralen plus ultraviolet A radiation (PUVA) therapy. Spans management process for treatment and training for clinicians.	https://pubmed.ncbi.nlm.nih.gov/40762446/	2025

Abbreviations: ANZTCT, Australia and New Zealand Transplant & Cellular Therapies; HSANZ, Haematology Society of Australia and New Zealand; ALLG, Australasian Leukaemia & Lymphoma Group

REFERENCES

Arulogun S, HM Prince, P Gambell, S Lade, G Ryan, E Eaton and C McCormack (2008). Extracorporeal photopheresis for the treatment of Sezary syndrome using a novel treatment protocol. *J Am Acad Dermatol* 59(4): 589-595.

Bouwhuis SA, RA el-Azhary, MT McEvoy, LE Gibson, TM Habermann, TE Witzig and MR Pittelkow (2002). Treatment of late-stage Sezary syndrome with 2-Chlorodeoxyadenosine. *Int J Dermatol* 41(6): 352-356.

Campbell BA (2016). Extracorporeal Photopheresis for cutaneous T-cell lymphoma: Defining the appropriate comparators for CTCL submission. Optum**:** 1-7.

Campbell BA, PD Baade, P Dasgupta, JK Cameron, SV Porceddu, HM Prince and K Thursky (2025). Geospatial analyses demonstrate variation of cutaneous T-cell lymphomas across Australia, providing insights into possible causes. *Br J Dermatol* 192(6): 1018-1028.

Duvic M, JP Hester and NA Lemak (1996). Photopheresis therapy for cutaneous T-cell lymphoma. *J Am Acad Dermatol* 35(4): 573-579.

Edelson R (2001). Cutaneous T Cell Lymphoma. The helping hand of dendritic cells. *Annals of New York Academy of Sciences* 941: 1-11.

Edelson R, C Berger, F Gasparro, B Jegasothy, P Heald, B Wintroub, E Vonderheid, R Knobler, K Wolff, G Plewig and et al. (1987). Treatment of cutaneous T-cell lymphoma by extracorporeal photochemotherapy. Preliminary results. *N Engl J Med* 316(6): 297-303.

Gao C, C McCormack, C van der Weyden, MS Goh, BA Campbell, R Twigger, O Buelens, SJ Harrison, C Khoo, S Lade and HM Prince (2019). Prolonged survival with the early use of a novel extracorporeal photopheresis regimen in patients with Sézary syndrome. *Blood* 134(16): 1346-1350.

Heald PW, MI Perez, I Christensen, N Dobbs, G McKiernan and R Edelson (1989). Photopheresis therapy of cutaneous T-cell lymphoma: the Yale-New Haven Hospital experience. *Yale J Biol Med* 62(6): 629-638.

Hughes CF, A Khot, C McCormack, S Lade, DA Westerman, R Twigger, O Buelens, K Newland, C Tam, M Dickinson, G Ryan, D Ritchie, C Wood and HM Prince (2015). Lack of durable disease control with chemotherapy for mycosis fungoides and Sezary syndrome: a comparative study of systemic therapy. *Blood* 125(1): 71-81.

Jiang SB, SB Dietz, M Kim and HW Lim (1999). Extracorporeal photochemotherapy for cutaneous T-cell lymphoma: a 9.7-year experience. *Photodermatol Photoimmunol Photomed* 15(5): 161-165.

Knobler R, P Arenberger, A Arun, C Assaf, M Bagot, G Berlin, A Bohbot, P Calzavara-Pinton, F Child, A Cho, LE French, AR Gennery, R Gniadecki, HPM Gollnick, E Guenova, P Jaksch, C Jantschitsch, C Klemke, J Ludvigsson, E Papadavid, J Scarisbrick, T Schwarz, R Stadler, P Wolf, J Zic, C Zouboulis, A Zuckermann and H Greinix (2020). European dermatology forum - updated guidelines on the use of extracorporeal photopheresis 2020 - part 1. *J Eur Acad Dermatol Venereol* 34(12): 2693-2716.

Knobler R, G Berlin, P Calzavara-Pinton, H Greinix, P Jaksch, L Laroche, J Ludvigsson, P Quaglino, W Reinisch, J Scarisbrick, T Schwarz, P Wolf, P Arenberger, C Assaf, M Bagot, M Barr, A Bohbot, L Bruckner-Tuderman, B Dreno, A Enk, L French, R Gniadecki, H Gollnick, M Hertl, C Jantschitsch, A Jung, U Just, CD Klemke, U Lippert, T Luger, E Papadavid, H Pehamberger, A Ranki, R Stadler, W Sterry, IH Wolf, M Worm, J Zic, CC Zouboulis and U Hillen (2014). Guidelines on the use of extracorporeal photopheresis. *J Eur Acad Dermatol Venereol* 28 Suppl 1(Suppl 1): 1-37.

Knobler R, M Duvic, C Querfeld, D Straus, S Horwitz, J Zain, F Foss, T Kuzel, K Campbell and L Geskin (2012). Long-term follow-up and survival of cutaneous T-cell lymphoma patients treated with extracorporeal photopheresis. *Photodermatol Photoimmunol Photomed* 28(5): 250-257.

Leukaemia Foundation (2023). Optimal care pathway for people with cutaneous T-cell lymphoma. Leukaemia Foundation.

MSAC (2020). Public Summary Document: Application No. 1420.1 – Extracorporeal photopheresis for treatment of cutaneous T-cell lymphoma. Medical Services Advisory Committee, Australian Government.

Olsen E, E Vonderheid, N Pimpinelli, R Willemze, Y Kim, R Knobler, H Zackheim, M Duvic, T Estrach, S Lamberg, G Wood, R Dummer, A Ranki, G Burg, P Heald, M Pittelkow, MG Bernengo, W Sterry, L Laroche, F Trautinger, S Whittaker and Iscl/Eortc (2007). Revisions to the staging and classification of mycosis fungoides and Sezary syndrome: a proposal of the International Society for Cutaneous Lymphomas (ISCL) and the cutaneous lymphoma task force of the European Organization of Research and Treatment of Cancer (EORTC). *Blood* 110(6): 1713-1722.

Prince HM, S Whittaker and RT Hoppe (2009). How I treat mycosis fungoides and Sezary syndrome. *Blood* 114(20): 4337-4353.

Prinz B, W Behrens, E Holzle and G Plewig (1995). Extracorporeal photopheresis for the treatment of cutaneous T-cell lymphoma--the Dusseldorf and Munich experience. *Arch Dermatol Res* 287(7): 621-626.

Raphael BA, DB Shin, KR Suchin, KA Morrissey, CC Vittorio, EJ Kim, JM Gardner, KG Evans, CE Introcaso, SS Samimi, JM Gelfand and AH Rook (2011). High clinical response rate of Sezary syndrome to immunomodulatory therapies: prognostic markers of response. *Arch Dermatol* 147(12): 1410-1415.

Siakantaris MP, P Tsirigotis, N Stavroyianni, KV Argyropoulos, K Girkas, V Pappa, S Chondropoulos, E Papadavid, I Sakellari, A Anagnostopoulos, C Antoniou and J Dervenoulas (2012). Management of cutaneous T-Cell lymphoma patients with extracorporeal photopheresis. The Hellenic experience. *Transfus Apher Sci* 46(2): 189-193.

Stevens SR, ED Baron, S Masten and KD Cooper (2002). Circulating CD4+CD7- lymphocyte burden and rapidity of response: predictors of outcome in the treatment of Sezary syndrome and erythrodermic mycosis fungoides with extracorporeal photopheresis. *Arch Dermatol* 138(10): 1347-1350.

Tan S and K GeBauer (2025). Guidelines for Phototherapy and PUVA Service Delivery in Australia: Minimum Standards and Quality Assurance Framework. *Australas J Dermatol*.

Worel N and G Leitner (2012). Clinical Results of Extracorporeal Photopheresis. *Transfus Med Hemother* 39(4): 254-262.