



Australian Government

Medical Services Advisory Committee

Public Summary Document

Application No. 1475 – Ablative fractional laser resurfacing for burn scar treatment

Applicant: Burns Unit of Concord Repatriation General Hospital

Date of MSAC consideration: MSAC 72nd Meeting, 28-29 March 2018

Context for decision: MSAC makes its advice in accordance with its Terms of Reference, [visit the MSAC website](#)

1. Purpose of application

An application requesting Medicare Benefits Schedule (MBS) listing of carbon dioxide ablative fractional laser (CO₂ AFL) resurfacing for burn scar treatment was received from Burns Unit of Concord Repatriation General Hospital (CRGH) by the Department of Health.

Laser scar treatment works on the basis of remodelling skin by creating microscopic photo-thermal injury ('thermolysis') to specific target scarred skin areas. Skin remodelling from thermolysis following laser treatment shares the same features as wound repair and skin morphogenesis.

2. MSAC's advice to the Minister

After considering the strength of the available evidence in relation to comparative safety, clinical effectiveness and cost-effectiveness, MSAC did not support MBS funding of CO₂AFL resurfacing for burn scar treatment because the clinical benefit, safety, cost-effectiveness and financial impact for the proposed listing were highly uncertain based on the limited comparative data presented.

MSAC noted that the evidence base was exceedingly low with no direct comparisons, which limited the ability to make an objective comparison of clinical utility of the intervention and the comparator (reconstructive surgery). MSAC also considered the economic evaluation, a cost comparison between the treatment courses, was limited given the lack of clinical evidence.

MSAC advised that any resubmission should include:

- further data on co-treatments in the clinical treatment algorithm to better inform the economic model;
- higher quality comparative evidence data; and

- the amalgamation of efficacy and safety data across burn and non-burn scars if that would help interpret these results.

MSAC advised that any resubmission would need to be considered by ESC.

3. Summary of consideration and rationale for MSAC's advice

MSAC noted that laser scar treatment works on the basis of remodelling skin by creating microscopic photo-thermal injury (thermolysis) to specific target scarred skin areas. Most patients receive a series of three to six CO₂ AFL procedures, at a minimum treatment interval of one to three months between procedures. MSAC noted that CO₂ AFL procedures are currently used in Australia and are being claimed under MBS items 45506, 45512, 45515 and 45518, which are currently listed for the excision/revision of scars with or without split thickness skin graft.

MSAC noted that while the intervention specified in the PASC-rated PICO criteria was CO₂ AFL in combination with reconstructive surgery, this was changed to CO₂ AFL alone, due to lack of data. MSAC noted that data from a study in one Australian burns unit indicated that the majority of CO₂ AFL procedures were performed alone (Issler-Fischer AC et al 2017). The comparator is reconstructive surgery alone.

MSAC noted a lack of direct comparative studies of CO₂ AFL versus reconstructive surgery, limiting the conclusions that could be made with respect to relative efficacy and safety. MSAC also noted that the application had provided separate evidence for CO₂AFL and for reconstructive surgery in an attempt to conduct indirect comparisons, although the lack of a common reference arm between the two data sets precluded formal indirect comparison. MSAC considered that interpreting the results from the naïve comparison was further limited due to heterogeneity in patient populations, differences in timing of assessment post-procedure, and differences in the scoring scales used.

MSAC considered that no definitive conclusions could be drawn in terms of safety of either CO₂AFL or reconstructive surgery given the poor evidence base. MSAC noted that safety data were poorly reported across the CO₂AFL and reconstructive surgery studies, and that comparative safety data were lacking.

While it is possible that CO₂ AFL may improve symptoms, appearance and function of hypertrophic scars relative to no treatment, MSAC considered that the low level and poor quality of the evidence base made it difficult to draw conclusions about the effectiveness of CO₂ AFL. MSAC noted that in one randomised controlled trial (n = 36) comparing CO₂ AFL with no therapy in patients with hypertrophic scars, there was a trend that favoured no therapy in the Patient and Observer Scar Assessment Scale (POSAS) score (Blome-Eberwein S et al 2016). MSAC also noted limited data on CO₂ AFL in the management of keloids — a single study including four patients with keloids (El-Zawahry BM et al 2015).

Similarly, while reconstructive surgery appears to improve scars as measured by POSAS and Vancouver Scar Scale (VSS) scores, MSAC considered that the weak evidence base also made it difficult to draw conclusions about the comparative effectiveness of reconstructive surgeries. MSAC noted that the majority of reconstructive surgery trials included patients with burn scar contractures rather than hypertrophic scars or keloids.

MSAC noted that the CO₂ AFL trials provided insufficient quality of life data for burn scars to establish usable utility values for an economic evaluation. Further, given the uncertain comparative effectiveness and safety of CO₂ AFL, the economic evaluation was limited to a

comparison of the costs to deliver the respective treatment courses - CO₂ AFL and reconstructive surgery.

MSAC considered the cost comparison analysis to be highly uncertain. MSAC noted that the cost comparison was based on data (procedure information and length of stay) from a single Australian burns unit. MSAC considered this limited the applicability of results across the entire Australian healthcare setting. MSAC had several additional concerns about the calculation of costs in the economic evaluation including:

- that the cost of the CO₂ AFL therapy was based on the assumption that a single course of each treatment consists of three CO₂ AFL procedures, despite the proposed MBS item descriptor allowing for up to six CO₂ AFL procedures, which may significantly impact the total cost;
- the exclusion of adverse events;
- the lack of outcome data;
- inconsistent use of 100% and 85% MBS rebate fees; and
- the use of weighted average costs for reconstructive surgery but simple average costs for CO₂ AFL.

MSAC noted that an epidemiological approach was used to estimate the financial implications of listing CO₂ AFL on the MBS. MSAC noted that this relied upon Australian Institute of Health and Welfare data on the number of hospitalised burn injuries in Australia. MSAC noted that in the absence of epidemiological data on reconstruction of burn scars, data from a Dutch study were applied to the financial estimations (Hop MJ et al 2014). MSAC raised concerns about the applicability of this study to the local Australian setting.

MSAC noted the estimated CO₂ AFL procedures (stand-alone and combination with surgery) to be 2395 in year 1 increasing to 4265 over 5 years. The estimated cost to the MBS was approximately \$1.0 million in year 1 and approximately \$1.8 million in year 5. MSAC concluded that the net financial implications for the MBS were uncertain.

MSAC advised that any resubmission would need to include:

- further data on co-treatments in the clinical treatment algorithm to better inform the economic model;
- higher quality comparative evidence data; and
- amalgamation of efficacy and safety data across burn and non-burn scars if that would help interpret these results.

MSAC advised that any resubmission would need to be considered by ESC.

4. Background

MSAC has not previously considered this application.

CO₂ AFL procedures are currently used in Australia and claimed under MBS item numbers 45506, 45512, 45515 and 45518 for the excision/revision of scars with or without split thickness skin graft.

5. Prerequisites to implementation of any funding advice

Items listed on the Australian Register of Therapeutic Goods (ARTG) that are relevant to this application are shown in Table 1.

Table 1 Ablative fractional CO₂ laser system listed on the ARTG

ARTG no.	Product no.	Product description	Product category	Sponsor
182239	35939	Surgical/dermatological carbon dioxide laser system. Laser is used for the coagulation, ablation, vaporization and incision of soft tissue in number of dermatological and surgical procedures	Medical Device Class IIb	Lumenis Australia Pty Ltd
292015	61473	Dermatological carbon dioxide laser system. The CO ₂ Laser Therapy Systems is indicated for use in dermatological procedures requiring ablation, resurfacing and coagulation	Medical Device Class IIb	Ausmed International Pty Ltd
273755	61473	Dermatological carbon dioxide laser system. A CO ₂ Laser Device intended to incise, excise, ablate, and vaporize soft tissues	Medical Device Class IIb	Velocity 8 Pty Ltd
233364	35939	Surgical/dermatological carbon dioxide laser system. The eCO ₂ Plus laser system is indicated for a wide range of surgical and dermatological applications. In the dermatological field the device is typically used for the treatment of scars such as acne scars, surgical scars, burn scars, and striae distensae. It is also used for the treatment of pigmented lesions, nevus, warts, and skin rejuvenation	Medical Device Class IIb	Advanced Cosmeceuticals
229110	35939	Surgical/dermatological carbon dioxide laser system. Used in dermatology for acne scar removal, lightening pigmentation, chloasma, smoothing burn, surgery scars, traumatic scars etc. wrinkle removal, skin tightening and for vascular or inflammatory conditions of the skin	Medical Device Class IIb	Capricorn Skin Centres
226006	35939	Surgical/dermatological carbon dioxide laser system. Intended for incision, excision, ablation, vaporization and coagulation of body soft tissues including intraoral tissues, in medical specialties including aesthetic (dermatology and plastic surgery), otolaryngology (ENT), gynaecology and genitourinary surgery. The use with the scanning unit is indicated for ablative skin resurfacing	Medical Device Class IIb	Cynosure Pty Ltd
208045	35939	Surgical/dermatological carbon dioxide laser system. The CO ₂ laser is indicated for use in ENT, dentistry, ophthalmology, dermatology, and general surgery	Medical Device Class IIb	MD Solutions Australasia Pty Ltd

Source: Therapeutic Goods Administration, accessed 28 July 2017 <http://www.tga.gov.au/>

6. Proposal for public funding

The proposed MBS item descriptors are shown in Table 2.

Table 2 Proposed MBS item descriptors for CO₂ AFL

Category 3 – Therapeutic Procedures OPERATIONS PLASTIC & RECONSTRUCTIVE
FRACTIONAL ABLATIVE CARBON DIOXIDE LASER resurfacing of the face or neck for hypertrophic and keloid burn scars that are associated with significant functional or psychological impairment - limited to 1 aesthetic area (Anaes.) MBS Fee: \$219.95
FRACTIONAL ABLATIVE CARBON DIOXIDE LASER resurfacing of the face or neck for hypertrophic and keloid burn scars that are associated with significant functional or psychological impairment - more than 1 aesthetic area (Anaes.) MBS Fee: \$295.70
ABLATIVE FRACTIONAL CARBON DIOXIDE LASER resurfacing of the face or neck for hypertrophic and keloid burn scars that are associated with significant functional or psychological impairment – whole of face or whole of neck (Anaes.) MBS Fee: \$700
ABLATIVE FRACTIONAL CARBON DIOXIDE LASER resurfacing of areas other than the face or neck for hypertrophic and keloid burn scars that are associated with significant functional or psychological impairment - area of treatment up to 3% of total body surface (Anaes.) MBS Fee: \$198.25
ABLATIVE FRACTIONAL CARBON DIOXIDE LASER resurfacing of areas other than the face or neck hypertrophic and keloid burn scars that are associated with significant functional or psychological impairment - area of treatment between 3% and up to 6% of total body surface (Anaes.) MBS Fee: \$243.55
ABLATIVE FRACTIONAL CARBON DIOXIDE LASER resurfacing of areas other than the face or neck hypertrophic and keloid burn scars that are associated with significant functional or psychological impairment - area of treatment between 6% and up to 9% of total body surface (Anaes.) MBS Fee: \$288.25
ABLATIVE FRACTIONAL CARBON DIOXIDE LASER resurfacing of areas other than the face or neck hypertrophic and keloid burn scars that are associated with significant functional or psychological impairment - area of treatment between 9% and up to 12% of total body surface (Anaes.) MBS Fee: \$333.45
ABLATIVE FRACTIONAL CARBON DIOXIDE LASER resurfacing of areas other than the face or neck hypertrophic and keloid burn scars that are associated with significant functional or psychological impairment - area of treatment greater than 12% of total body surface (Anaes.) MBS Fee: \$423.50
<i>Up to a maximum of 6 sessions (including any sessions to which any of the above items apply) in any 12 month period.</i>

7. Summary of Public Consultation Feedback/Consumer Issues

The department received four responses to the targeted consultation survey for this application from specialists.

Key issues raised in the targeted consultation feedback were:

- The majority of the responses were in support of the proposed services being publicly funded, and identified benefits of the treatment as:
 - improvement in function and scarring,
 - minimal adverse reactions, and

- may reduce the number of surgical procedures required for rehabilitation.
- One submission suggested allowing dermatologists and plastic surgeons access to the item.
- One submission suggested that the item descriptor should specify that treatment is to be performed in-hospital, while another suggested that the location of treatment should also include inpatient private hospitals, consulting rooms, and day surgery centres.
- Another commented that the Medical Benefit Schedule (MBS) item for this service should explicitly exclude treatment by other fractional ablative lasers with shallow penetration.

8. Proposed intervention's place in clinical management

According to the clinical management pathway, immature scars (less than 2 years following the burn or last operation) can be treated with CO₂ AFL in the case of contractures over joints or if the patient is developing eyelid and lip ectropions to prevent more complex surgical interventions. Mature hypertrophic or keloid scars (more than 2 years following the burn or last operation) are candidates for treatment with CO₂ AFL therapy. CO₂ AFL may be performed with or without surgical reconstructive procedures, with or without intralesional pharmacological interventions (including intralesional injections of corticosteroids of 5-fluorouracil, or laser facilitated corticosteroid infiltration). For severe scarring and recurrent keloids, post-operative radiotherapy may also be used together with CO₂ AFL. In one Australian study, 13% of patients received CO₂ AFL in combination with reconstructive surgery and the remainder received CO₂ AFL alone (Issler-Fisher 2017).

Currently, the majority of burn scars requiring treatment are referred to burn centres to receive reconstructive procedures. Practitioners performing the CO₂ AFL and reconstructive surgery include qualified burn specialists (medical doctors/surgeons). CO₂ AFL is usually performed in an operating theatre, with approximately 60% of patients requiring general anaesthesia (Issler-Fisher 2017). The remaining patients receive local or regional anaesthesia (with or without sedation), performed by an anaesthetist. Paediatric patients are always treated under general anaesthesia. Reconstructive surgery is generally performed in an operating theatre, and general anaesthesia is received in majority of cases.

9. Comparator

The comparator for CO₂ AFL therapy is reconstructive surgical procedures for burn scars alone. Reconstructive procedures include scar excision/release with or without split-thickness skin graft, expanders (insertion and removal) and local flaps and are currently listed on the MBS.

10. Comparative safety

Limited safety data for CO₂ AFL and reconstructive surgery were available across the studies and given lack of overlap in safety events reported, naïve comparison on safety outcomes was not possible.

The adverse events reported in the CO₂ AFL studies were not serious, whereas the reconstructive surgery studies reported rare, but serious adverse events (necrosis, wound dehiscence, re-graft). This may suggest a potential safety advantage with CO₂ AFL relative to reconstructive surgery, although this could not be confirmed.

11. Comparative effectiveness

The evidence base for CO₂ AFL consisted of one, single blind randomised controlled trial (RCT) in patients with hypertrophic burn scars, one open-label cohort study in patients with hypertrophic and keloid scars. Supportive evidence consisted of six single arm studies, all of which except two were prospective. No study explicitly investigating CO₂ AFL therapy in combination with reconstructive surgery was identified.

The evidence base for reconstructive surgery consisted of two RCTs comparing treatment with flaps and full-thickness skin grafts (FTSG) (Stekelenburg 2017a) and scar excision alone (SE) versus scar excision with skin stretching (SS) (Verhaegen 2011). Two case series investigating treatment with dermal substitute and split-thickness skin graft (STSG) providing data for outcomes set out in the PICO criteria were included as supportive evidence (Moiemen 2000; Oh 2010).

Given the lack of common reference arm between the two sets of data, formal indirect comparison was not possible. An indicative, naïve comparison on overlapping outcomes of CO₂ AFL and reconstructive surgery sets of data is provided.

The naïve comparison of effectiveness indicated that both CO₂ AFL and reconstructive surgery result in improvement with respect to symptoms, appearance and function of the scar (Table 3).

Limited data exist with which to make inferences of comparative effectiveness between CO₂ AFL and reconstructive surgery. Some outcomes suggest similarity between the interventions (e.g.: Patient and Observer Scar Assessment Scale [POSAS]; Figure 1) whilst other outcomes point towards an advantage for reconstructive surgery (e.g.: Vancouver Scar Scale [VSS]; Figure 2).

As illustrated in Figure 1, both CO₂ AFL and reconstructive surgery appear to achieve minimally clinically important differences (MCID; exceeding 6 points) in the combined POSAS assessment (PSAS + OSAS, 0-120), and the difference in treatment effect between procedures is less than the MCID of 6. Caution must be exercised when interpreting the results from the naïve comparison. Data limitations meant variance around treatment effects could not be calculated.

Table 3 Balance of clinical benefits and harms of CO₂ AFL, relative to reconstructive surgery, and as measured by the critical patient relevant outcomes in the key studies

Outcomes (units) Follow-up	Participants (studies)	Quality of evidence (GRADE)	Mean change from baseline in CO ₂ AFL studies	Mean change from baseline in reconstructive surgery studies	Difference in WM change (reconstructive – CO ₂ AFL)	Comments
PSAS (6-60)	Naïve comparison: CO ₂ AFL k=4 n=114; reconstructive surgery k=1 n=28	⊕⊖⊖⊖ Very low quality (naïve comparison)	Range -4.13 to -16.90 WM=-9.25 WM (excl Issler)=-6.8 ^b	Flaps=-13.80 FTSG=-14.40 WM=-14.06	-4.80	
OSAS (6-60)	Naïve comparison: CO ₂ AFL k=3 n=68; reconstructive surgery k=1 n=28	⊕⊖⊖⊖ Very low quality (naïve comparison)	Range -6.27 to -13.00 WM=-8.42 WM (excl Issler)=-9.36 ^b	Flaps=-10.8 FTSG=-7.2 WM=-9.26	-0.84	
PSAS + OSAS (12-120)	Naïve comparison: CO ₂ AFL k=3 n=68; reconstructive surgery k=1 n=28	⊕⊖⊖⊖ Very low quality (naïve comparison)	Range -13.30 to -29.90 WM=-19.26 WM (excl Issler)=-18.01 ^b	Flaps=-24.60 FTSG=-21.60 WM=-23.31	-4.06	On average, the difference between CO ₂ AFL and reconstructive surgery does not exceed the MCID of 6.
Elasticity (Cutometer)	Naïve comparison: CO ₂ AFL k=1 n=48 reconstructive surgery k=1 n=28	⊕⊖⊖⊖ Very low quality (naïve comparison)	CO ₂ AFL=-0.05	Flaps=0.10 FTSG=0.20	Flaps – CO ₂ AFL=0.05 FTSG=0.15	Clinical relevance of difference unclear.
VSS	Naïve comparison: CO ₂ AFL k=5 n=174; reconstructive surgery k=2 n=257	⊕⊖⊖⊖ Very low quality (naïve comparison)	Range -0.96 to -4.27 WM=-1.71 WM (excl Issler)=-2.0 ^b	AlloDerm+STSG =-7.38 Integra+STSG =-4.30 WM=-5.76	Dermal sub+STSG – CO ₂ AFL=-4.05	Clinical relevance of difference unclear; Result numerically favours comparator; follow-up much longer in comparator trials.
Safety	No comparison of safety could be performed. No SAE reported with CO ₂ AFL versus 2/12 (17%) patients with FTSG and 1/16 (6.0) with FTSG experienced necrosis; wound dehiscence occurred in 20.0% of patients treated with SE and in 6.7% of those treated with SE; 6.7% of patients undergoing dermal substitution + STSG required re-grafting					

CO₂ AFL=carbon dioxide ablative fractional laser; WM=weighted mean change; FTSG=full-thickness skin graft; SE=scar excision alone; SS=scar excision with skin stretching; STSG=split-thickness skin graft; SAE=serious adverse events; sub=substitute. ^a GRADE Working Group grades of evidence (Guyatt et al., 2013)

^bIssler-Fisher 2017 was excluded as a sensitivity analysis due to: presenting medians (other studies presented means) and only assessing one treatment (other studies assessed three treatments).

⊕⊕⊕⊕ **High quality:** We are very confident that the true effect lies close to that of the estimate of effect. ⊕⊕⊕⊖ **Moderate quality:** We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. ⊕⊕⊖⊖ **Low quality:** Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect. ⊕⊖⊖⊖ **Very low quality:** We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

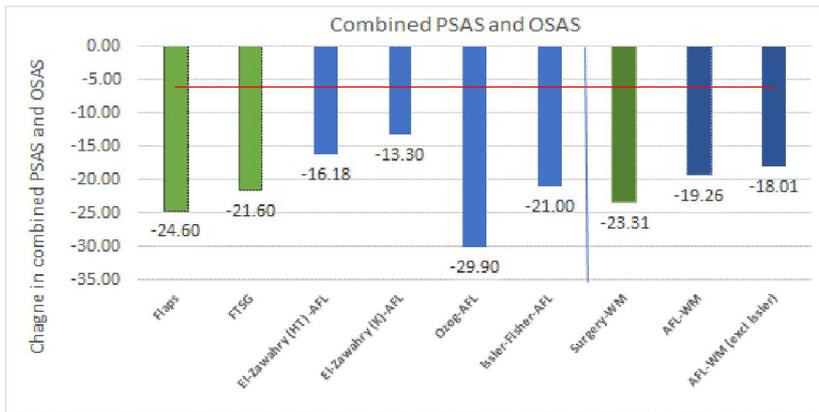


Figure 1 Comparison of mean change from baseline in combined OSAS and PSAS with CO₂ AFL and reconstructive surgery (flap and FTSG)

NB. Red line indicates the minimally clinically important difference (MCID=6) (Blijard 2013)

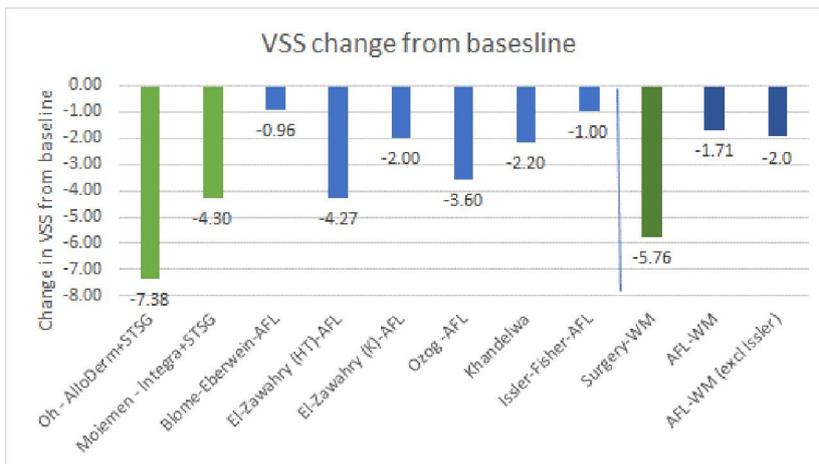


Figure 2 Comparison of mean change from baseline in VSS with CO₂ AFL and reconstructive surgery (dermal substitution + STSG)

CO₂ AFL=carbon dioxide ablative fractional laser; STSG=split-thickness skin graft; WM=weighted mean; VSS=Vancouver Scar Scale; HT=hypertrophic; K=keloid.

Clinical Claim

The PICO Confirmation provided a claim of superiority of CO₂ AFL therapy in terms of clinical effectiveness and safety outcomes in patients with severe scars resulting from burn injuries, compared to usual care. The clinical evaluation found no direct comparative evidence to support this claim. Due to limited evidence, lack of comparative evidence, lack of common reference, limited overlap in outcomes reported between CO₂ AFL and reconstructive surgery trials, a conclusion of uncertain effectiveness and uncertain safety of CO₂ AFL relative to reconstructive surgery was drawn.

12. Economic evaluation

Given the effectiveness and safety data of CO₂ AFL and reconstructive surgery, the economic evaluation presented is limited to a comparison of the costs to deliver the respective treatment courses supplemented by a review of the available quality of life literature. A summary is provided in Table 4.

Table 4 Summary of the economic evaluation

Comparator	Reconstructive surgery
Type of economic evaluation	Cost-comparison
Sources of evidence	Concord repatriation general hospital (CRGH)
Time horizon	NA
Outcomes	Average length of hospital stay, cost per course of treatment

The cost analysis is structured as a comparison of costs between a single CO₂ AFL versus surgery treatment course. The analysis assumes that a CO₂ AFL treatment course consists of three procedures and a surgery treatment course consists of one procedure. It is assumed that all procedures for both CO₂ AFL and comparator reconstructive surgeries require the administration of anaesthesia by an anaesthetist and all procedures are assumed to be performed in hospital.

Costing data was sourced from the MBS for procedure costs and costs for associated services including; specialist consultations, anaesthesia consultations, and the initiation and management of anaesthesia. Australian refined diagnosis related groups (AR-DRGs) hospitalisation costs were applied to hospital admissions data provided by the applicant. The admissions data was derived from a single centre (Concord repatriation general hospital [CRGH]) and is provided in Attachment “CRGH burn unit elective surgeries_2013-2017”. An AR-DRG hospitalisation cost was applied to all patients admitted over-night in hospital. Admissions data for stand-alone CO₂ AFL and comparator surgical procedures is provided in Table 5. Only stand-alone procedures were used in the analysis to reduce uncertainty in the comparison of burn reconstructive procedures.

Table 5 Overnight admission and subsequent length of stay for procedures conducted at the CRGH burn unit

Table redacted

The results from the cost analysis are presented in

Table 6. The total per patient cost per course of treatment with CO₂ AFL is estimated at \$2,175 compared with \$1,989 for flaps, \$1,529 for skin grafting, \$2,473 for tissue expansion and \$2,248 for scar revision. This cost comparison suggest that CO₂ AFL is comparative in terms of cost to other scar reconstruction procedures, with the increased procedure/associated services costs of CO₂ AFL, as a result of the 3:1 procedure ratio, offset by reduced length of stay.

Table 6 Cost analysis for CO₂ AFL in the reconstruction of burn scars

Parameter	CO₂ AFL	Flaps	Skin graft	Tissue expansion	Revision
Total cost of procedures	\$1,013.50	\$354.62	\$463.33	\$1,003.02	\$229.88
Total cost of hospitalisation	\$185.40	\$1,176.23	\$607.65	\$952.23	\$1,540.11
Total cost of specialist services	\$377.40	\$226.40	\$226.40	\$226.40	\$226.40
Total cost of anaesthesia services	\$598.34	\$231.52	\$231.52	\$290.92	\$251.32
Total per patient cost per course of treatment	\$2,174.63	\$1,988.77	\$1,528.90	\$2,472.58	\$2,247.71
Cost difference versus CO ₂ AFL		-\$184.57	-\$644.45	\$299.23	\$74.36

In the pre-MSAC response the applicant noted that in the Hop (2014) study, the mean number of reconstructive procedures per patient is 3.6. This means that the ratio of CO₂ AFL to

reconstructive procedures could actually be less than 3:1 if the number of elective reconstructive procedures per patient per lifetime are taken into account. Using the data from Hop et al. it is more likely that the true lifetime ratio is closer to 1:1, although the applicant acknowledged that long-term follow-up data >5-10 years are lacking for CO₂ AFL.

13. Financial/budgetary impacts

An epidemiological approach was used to estimate the financial implications of the introduction of CO₂ AFL for the treatment of burn scars on the MBS. It is projected that 2,395 CO₂ AFL services will be accessed in the first year of listing, increasing to 4,265 services annually over 5 years. These services along with associated MBS items are estimated to cost the MBS between \$1,015,860 (Year 1) and \$1,809,071 (Year 5) annually. A 75% MBS rebate was applied across all items as all services were expected to occur in a hospital setting.

Two scenarios were provided for the substitution of current MBS items. Scenario 1 assumes that current CO₂ AFL procedures are being claimed under revision MBS items (45506-45518), as such every claim of a proposed CO₂ AFL MBS item would be substituting from a current MBS item for revision. Scenario 2 assumes that CO₂ AFL procedures were not currently being claimed under revision items, instead applying a 3 to 1 substitution in which 3 proposed CO₂ AFL MBS items would substitute for the use of 1 surgical MBS item.

Scenario 1 projects an annual net cost to the MBS of between \$112,460 and \$200,272 resulting from the substitution of current revision items. Scenario 2 estimates a net cost of between \$679,680 and \$1,210,393 annually through the 3:1 substitution of surgical options. Table 7 presents the estimated use and net cost to the MBS of the introduction of CO₂ AFL for the treatment of burn scars.

Table 7 Total costs to the MBS associated with the listing of CO₂ AFL

Parameter	Year 1	Year 2	Year 3	Year 4	Year 5
Estimated use					
Number of stand-alone CO ₂ AFL procedures	2,293	3,110	3,952	4,018	4,084
Number of CO ₂ AFL procedures in combination with surgery	102	138	176	179	181
Total number of CO ₂ AFL services	2,395	3,248	4,128	4,197	4,265
Estimated cost to the MBS					
MBS costs associated with CO ₂ AFL	\$1,204,372	\$1,633,212	\$2,075,883	\$2,110,320	\$2,144,779
<u>Scenario 1</u>					
MBS costs of substituted services	\$1,091,912	\$1,480,708	\$1,882,044	\$1,913,265	\$1,944,507
Net cost of CO ₂ AFL to the MBS	\$112,460	\$152,504	\$193,839	\$197,055	\$200,272
<u>Scenario 2</u>					
MBS costs of substituted services	\$524,692	\$711,519	\$904,371	\$919,374	\$934,386
Net cost of CO ₂ AFL to the MBS	\$679,680	\$921,693	\$1,171,512	\$1,190,946	\$1,210,393

14. Key issues from ESC for MSAC

This is a new submission for MBS listing of CO₂ ablative fractional laser therapy (AFL) to treat patients with hypertrophic and keloid burns scars that are associated with significant functional or psychological impairment. CO₂ AFL therapy is a surgical procedure which removes true cores from scar tissue in order to remodel and resurface the scar. ESC noted that

the procedure is currently being used in Australia and claimed under MBS items 45506, 45512, 45515 and 45518, which were not the intentions of these items.

ESC considered that there is a clinical need for new developments in the treatment of burns scars. ESC noted that while the PASC-ratified PICO Confirmation comparator was surgical reconstruction and CO2 AFL therapy, this was changed to surgical reconstruction alone due to a lack of evidence. ESC considered that this was appropriate. ESC noted that compared to reconstructive surgery, CO2 AFL therapy is considered to be a day only procedure.

ESC noted that despite the change in comparator, there were no studies that directly compared CO2 AFL therapy to reconstructive surgery.

While a randomised trial of CO2 AFL therapy against no treatment and two randomised clinical trials (RCTs) of reconstructive surgery (one comparing flap surgery with full thickness skin graft and the other scar excision and skin-stretching with scar excision alone), the lack of a common comparator arm meant that an indirect comparison could not be carried out. Another five single arm studies and a prospective cohort study for CO2 AFL therapy were identified. These studies were considered to be low level evidence, had small sample sizes and were susceptible to bias.

ESC noted that the identified studies used a variety of scores and scales to measure patient outcomes which lead to heterogeneity in the data, making it difficult to draw any firm conclusions. These outcomes included burns specific health scale-brief (BSHS-B), patient and observer scar assessment scale (POSAS), range of motion (ROM) and Vancouver scar scale (VSS).

ESC considered that there was insufficient information to draw conclusions on the comparative safety between CO2 AFL therapy and reconstructive surgery. ESC noted that safety data on CO2 AFL therapy and reconstructive surgery was poorly reported and that comparative safety data was lacking. ESC noted that pruritus and redness were the most commonly reported adverse events for CO2 AFL, but these could also be indications of wound healing and recovery.

ESC considered that while it was possible that CO2 AFL therapy may improve symptoms, appearance and function of hypertrophic scars when compared with no treatment, this was undermined by the low quality of its evidence base. ESC noted that one RCT which compared CO2 AFL therapy with no therapy in patients with hypertrophic scars showed a trend that favoured no therapy in the POSAS score (Blome-Eberwein S et al 2016). ESC noted that there was limited available information for CO2 AFL therapy in the management of keloids.

ESC noted that reconstructive surgery seemed to improve outcomes according to POSAS and VSS, but this was undermined by a weak evidence base. ESC also noted that the studies of reconstructive surgery were mainly conducted on burns scar contractures rather than hypertrophic scars or keloids.

ESC noted that due to the lack of data on adverse events, clinical efficacy and health outcomes, the economic evaluation was restricted to a comparison of costs between CO2 AFL therapy and reconstructive surgeries. ESC noted that there were uncertainties in the composition of costs including:

- whether the cost of CO2 AFL therapy was overestimated due to the inclusion of a hospital stay of 4.2 nights for some patients, despite CO2 AFL therapy largely being a day-only procedure. ESC noted the applicant's comment that the admitted patients

seen in the Concord Repatriation General Hospital (CRGH) burn unit elective surgeries 2013–17 data were outliers in the study sample but significantly contributed to the cost of CO2 AFL therapy;

- that the cost of CO2 AFL therapy was calculated using an assumed average of three sessions of therapy procedures while the proposed item descriptors covered up to six sessions;
- the use of simple average cost for CO2 AFL but weighted average costs for reconstructive surgery;
- the use of costs for the various procedures from a single centre (CRGH) being applied to the entire of the Australian healthcare setting; and
- a lack of costing benchmark for existing interventions.

ESC noted that no information on the patient population of 0-4 years was provided despite this age group having the highest rate of hospitalisation due to burns (AIHW 2016).

ESC noted that despite CO2 AFL being intended to substitute or reduce reconstructive surgery, 13% of CO2 AFL procedures were co-administered with reconstructive surgery. ESC queried why the cost comparison did not include information on the costs of CO2 AFL in combination with other treatments. ESC suggested that a sensitivity analysis of average number of procedures and costs associated with average hospital length of stay for CO2 AFL therapy could be conducted in order to provide better clarity on cost comparisons.

ESC noted that with the exception of head and neck areas, the proposed MBS items use body surface area as a measurement of the scar instead of scar length. ESC considered this to be an appropriate method of measuring burns scar tissue.

ESC noted that most of the proposed fees reflected MBS items (45506 and 45512) for revisions of scars or MBS items 14106–14118 (laser photocoagulation of port wine stains with an additional 30% for training and capital costs added to the MBS fee) and ranged from \$198 to \$423. However, the proposed fee for treatment of the whole face and neck was \$700 and ESC queried the reasoning behind this price. ESC also considered that including costs for training and capital in the fees for CO2 AFL was not appropriate.

ESC noted that the proposed item descriptor indicated that to be eligible for treatment patients would have to have scarring that was associated with significant psychological impairment but noted that further information on this was lacking.

ESC considered that if the service was limited to people with severe burns, and considering this is a highly specialised procedure performed in specialised burns units and requiring highly specialised staff, leakage of services are unlikely.

Scars are considered immature scars until two years after injury. ESC advised that there should be no restriction that limits population eligibility by scar maturation.

ESC queried whether MBS listing of this service will result in cost shifting. ESC noted that CO2 AFL is already being performed in public hospitals as an outpatient procedure. ESC queried whether this procedure would ever be undertaken in the private setting.

ESC suggested that an Extended Medicare Safety Net (EMSN) cap should be considered for this service.

ESC noted that due to the lack of evidence for both CO2 AFL procedures and reconstructive surgery, a head-to-head clinical trial between these two interventions could be considered.

ESC noted that there is potential for such a trial to be recommended to the Medical Research Future Fund.

ESC Key ISSUES	ESC ADVICE
Evidence base	The evidence base is exceedingly low with no direct comparisons, which limits the ability to make an objective comparison of clinical utility of the intervention or the comparator.
Uncertain safety and effectiveness	On the basis of the benefits and harms reported in the evidence base relative to reconstructive surgery.
Costs include reconstructive surgery?	Confirm if administered with reconstructive surgery also (13%) – not included in cost analysis – would change costs (critique p13) [translation issue] Comparator is calculated from average weighted costs and treatment from simple average costs – confirm if this makes any difference. Also cost of treatment is average of all costs, but one outlier \$700 (not justified) Inconsistencies in cost derivation (critique – Table 70)
No adverse events included into the economic evaluation	This could impact costs but data were not available
Consider impact on admitted patients	Very low percent admitted, but they do drive the costs and applicant suggests removing these from the analysis to get average costs; (cost per admittance avoided?)
No discount rate	Evaluation assumes all procedures in one year – unclear if this is appropriate? It is not stated but assumed by critique. Also no time horizon given. Nor outcomes. It is unclear therefore what the cost sequences model would be – critique does not state explicitly, perhaps number of admittances overnight avoided?
Other MBS items	If items 45506, 45512, 45515 and 45518 are restricted (recommended), then these should be included in MBS items savings. Leakage possible with 44445, 45572, 45207 (45506, 45512 are not in PICO but are in CA – this should be clarified?)

15. Other significant factors

Nil

16. Applicant's comments on MSAC's Public Summary Document

Firstly, we would like to use this opportunity to emphasize again that the nature, clinical efficacy, and minimal invasiveness of CO2 AFL make this treatment approach very attractive for patients and surgeons alike. The morbidity associated with CO2 AFL is minimal compared to other reconstructive procedures. Most conventional reconstructive procedures

are associated with admissions to hospital, general anaesthetics, invasive, painful surgical procedures, time off work and a sometimes-prolonged rehabilitative phase. Hence, for patients, the difference between one of the traditional reconstructive procedures and CO2 AFL is substantial. Whilst the impact of the treatment on the MBS may thus not be as substantial as expected, the patient and societal benefit of such a procedure cannot be denied – albeit difficult to quantify. Secondly, because of the highly complex nature of reconstructive burn care, it is not at all surprising that the attempts to identify adequately performed and controlled studies has been met with a void of high-level medical evidence. Therefore, we feel that basing the decision solely on the currently published evidence base may negate the clear clinical benefits and thus prevent patients accessing this much needed care. Further, it should not be limited to “immature scars with contractures over joints or if the patient is developing eyelid and lip ectropions”, but to any hypertrophic immature scar as it has been outlined in several studies and reports that early intervention (immature scars) with the CO2 AFL can positively influence scar rehabilitation, accelerating scar maturation, improving early mobility and enhancing as well as accelerating the entire rehabilitative process. Further of note, radiotherapy is only very rarely used after excision of a recurrent keloid and according to our knowledge never after laser treatment. Lastly, the cited trial of Blome-Eberwein S et al. 2016 randomized one scar to the laser treatment and one scar to the control group within the same patient. There is evidence of a systemic effect on scars. Clinically, one can often observe an improvement of untreated scars, particularly if large areas are treated.

17. Further information on MSAC

MSAC Terms of Reference and other information are available on the MSAC Website: [visit the MSAC website](#)