Reasons

for the decision of the Joint Federal Committee on an amendment to the Hospital Treatment Methods Directive: Liposuction for lipedema

From July 17, 2025

Content

1. Legal basis

On the basis of Section 137c (1) of the Fifth Book of the Social Code (SGB V), the Joint Federal Committee (G-BA) reviews, upon request, examination and treatment methods that are used or are to be used at the expense of statutory health insurance funds in the context of hospital treatment, to determine whether they are necessary for the adequate, appropriate, and economical care of insured persons, taking into account the generally accepted state of medical knowledge. If the review finds that the benefits of a method are not sufficiently proven and that it does not offer the potential of a necessary alternative treatment, in particular because it is harmful or ineffective, the G-BA issues a corresponding guideline stipulating that the method may no longer be provided at the expense of the health insurance funds within the framework of hospital treatment. If the review finds that the benefits of a method have not yet been sufficiently proven but that it offers the potential of a necessary alternative treatment, the G-BA shall issue a guideline for testing in accordance with Section 137e SGB V.

In accordance with Chapter 2, Section 13, Paragraph 5, Sentence 3 of the G-BA's Rules of Procedure (VerfO), the G-BA may only decide the following based on the results of the final overall assessment of the examination or treatment method:

1. a determination that the benefit of the method is sufficiently proven and that it is necessary for the adequate, appropriate, and economical care of insured persons in hospitals,
2. the determination that the examination or treatment method offers the potential of a necessary treatment alternative, but that its benefits have not yet been sufficiently proven, and the simultaneous adoption of a guideline for testing in accordance with Section 137e (1) and (2) SGB V, suspending the assessment procedure,
3. a determination that the method does not offer the potential of a necessary alternative treatment, in particular because it is harmful or ineffective, and the exclusion of this method from hospital care at the expense of the health insurance funds.

Notwithstanding Section 7(3) sentence 3 MBVerfV, the G-BA may, in exceptional cases, suspend a method assessment procedure pursuant to Section 137c SGB V for a limited period of time if the benefits of the method have not yet been sufficiently proven but such studies are expected to be available in the near future (Section 7(3) sentence 4 MBVerfV and Section 2(1) sentence 1 VerfO). Chapter § 14(1) sentence 1 VerfO).

2. Key points of the decision

On the basis of an application for review of liposuction for lipedema pursuant to Section 135 (1) and Section 137c SGB V, the G-BA initially suspended the two method assessment procedures initiated in this regard by decisions of July 20, 2017, until September 30, 2022, and commenced deliberations on a guideline pursuant to Section 137e (1) SGB V for the testing of liposuction for lipedema.
September 30, 2022, and commenced deliberations on a guideline pursuant to Section 137e (1) SGB V for the trial use of liposuction for lipedema.

The consultations on the cross-sector, uniform assessment of the benefits of liposuction for lipedema were based on the report prepared by the G-BA on November 23, 2015 ("Lipedema"). The results of the studies identified in this evidence search did not meet the requirements for sufficient evidence of benefit within the meaning of the VerfO. However, the data showed that liposuction offers the potential of a necessary treatment alternative for lipedema. Therefore, on January 18, 2018, the guideline for testing liposuction for the treatment of lipedema was adopted. The trial is intended to answer the question of whether, in patients with lipedema, additional liposuction leads to an improvement in patient-relevant outcome measures compared to conservative, symptom-oriented treatment alone, especially when complex physical decongestive therapy is used. At the time of this decision, the trial is still ongoing, but the results of the randomized study phase for the observation period of 12 months after completion of liposuction in the intervention group compared to conservative treatment are available. According to the trial guideline, a 24-month follow-up period is required for all study participants.

In its decision of February 21, 2019, the G-BA resumed the procedures pursuant to Section 135(1) and
§ 137c SGB V for the evaluation of the method of liposuction for lipedema with regard to stage III before the expiry of the suspension period and, as a result of its evaluation, included liposuction for lipedema in stage III in Annex I (Recognized Examination or Treatment Methods) of the Directive on Methods of Contractual Medical Care (MVV-RL) and in Annex I (Methods Required for the Provision of Hospital Treatment) of the Directive on Methods of Hospital Treatment (KHMe-RL). At the same time, the quality assurance guideline for liposuction for stage III lipedema was adopted, which was also limited until December 31, 2024.

With resolutions dated September 19, 2024 – at that time, the evaluation of the results of the trial for the 12-month observation period following completion of liposuction was still ongoing – the G-BA extended the time limits until December 31, 2025, in order to ensure the provision of care for patients with stage III lipedema until a final decision by the G-BA.

On February 10, 2025, the results for the 12-month observation period following completion of liposuction were submitted to the G-BA and subsequently evaluated by the G-BA's Medical Advisory Board (FBMed) [see Chapter C-1 Summary Documentation (ZD)]. The results for the 24-month follow-up period after completion of liposuction and the final report on the trial are expected in the first quarter of 2027. Based on the results of the randomized study phase after 12 months, the G-BA has decided to include liposuction for lipedema in Appendix I (methods required for hospital treatment) of the Hospital Treatment Methods Guideline (KHMe-RL).

The previous number 14, "Liposuction for stage III lipedema," in Appendix I of the KHMe-RL is replaced by the new number 14, "Liposuction for lipedema," which applies to all three stages of lipedema.

2.1 Medical background

According to the S2k guideline, lipedema is described as a painful, disproportionate, symmetrical, and fat tissue distribution disorder of the extremities , which almost

occurs exclusively in women [1]. Men are very rarely affected, with only isolated case reports. The symptoms include painful sensations such as pressure pain, spontaneous pain, and a feeling of heaviness (ibid.).

According to current German lipedema guidelines, pain is the main symptom of lipedema and can occur both superficially and subcutaneously [1]. The pain associated with lipedema can occur around the entire circumference of the legs or arms. The pathogenesis of the pain is not yet clear (ibid.). The course of the disease is very individual [2]; some patients develop lipedema to a lesser extent, which stabilizes and does not show any progression of pain. In other patients, there is a gradual progression of lipedema or worsening after a stressful situation. In general, it is reported that lipedema develops during puberty, pregnancy, or menopause (ibid.).

Three stages of lipedema are described [3]. In stage I, the skin is smooth and the subcutaneous tissue is significantly thickened. In stage II, nodules appear in the fatty tissue and the overlying skin appears predominantly wavy and uneven. In stage III, the tissue is significantly coarser and has large nodules and deforming fat flaps. According to the S2k guideline, this staging should not be used as a measure of the severity of the disease [1].

The figures on the prevalence of lipoedema in the medical literature are very inaccurate and vary widely; therefore, no prevalence can be given. The S2k guideline emphasizes that there is little reliable evidence on the epidemiology [1].

The main goals of lipedema treatment are to reduce symptoms, improve functional limitations, and prevent the disease from getting worse [1]. Conservative treatment for diagnosed lipedema primarily involves compression therapy to reduce pain in the affected extremities. For patients with lipedema and additional edema of other origins, complex physical decongestive therapy (CPT) is recommended, which consists of a combination of compression therapy, lymphatic drainage, and exercise.

2.2 Description of the method

Liposuction is a surgical method for reducing the subcutaneous fatty tissue affected by lipedema [4], [1], [3], [5], [6]. In this surgical procedure, several liters of an anesthetic solution are first infiltrated into the subcutaneous space (known as the "wet technique"). The subcutaneous fatty tissue is then suctioned out using blunt cannulas. The procedure is performed under tumescent local anesthesia (TLA). Depending on the findings and accompanying diseases, TLA can be combined with analog sedation or general anesthesia. Supportive techniques such as vibration (power/vibration-assisted liposuction (PAL)) or water jet (water jet-assisted liposuction (WAL)) can be used. In PAL, the fat cells are suctioned out using a motor-driven, oscillating cannula. In WAL, instead of vibration, a water jet loosens the fat cells from their tissue and a mixture of fat cells, water, and tumescent solution is suctioned out (ibid.).

2.3 Cross-sector assessment of benefits

To evaluate the evidence for the procedure in question, the G-BA used the FBMed statement on the evaluation of liposuction based on the results of the LIPLEG study after 12 months dated April 14, 2025 (see Chapter C-1 ZD) as a basis for its consultation.

The G-BA assesses the benefits of liposuction compared to treatment with complex physical decongestive therapy (CPT) for lipedema.

2.3.1 Characteristics of the pilot study included in the assessment

Adult female patients with confirmed stage I to III lipedema of the legs were enrolled in a two-arm randomized controlled trial (RCT) at 11 study centers in Germany. ≥The aim of the study was to determine whether surgical treatment of lipedema (stage I, II, or III) using liposuction significantly improves leg pain compared to the use of CPT. To be included in the study, patients had to have an average leg pain score of 4 or higher on a numerical rating scale (NRS) ranging from 0 to 10 over the previous four weeks and documentation of inadequate symptom relief with conservative measures.
10 on a numerical rating scale (NRS) and there had to be documentation of insufficient symptom relief through conservative measures. Patients were not eligible to participate in the study if they had concomitant lipedema of the arms and legs, where the involvement of the arms, at the discretion of the study physician, had an impact on the average pain in the legs, and if liposuction had already been performed. These and other essential inclusion and exclusion criteria are listed in Table 1.

The RCT consisted of a run-in phase (phase 1: up to 4 weeks, phase 2: 6 months), the intervention phase (at least 12 months), and follow-up (24 months) (see Table 1). Prior to randomization, a two-part run-in phase was conducted to establish equal baseline conditions. For this purpose, complex physical decongestive therapy (CPT) was performed as a standardized conservative therapy to eliminate edema in a first step (phase 1) and then to maintain the achieved result (phase 2). Following the run-in phase, the patients were randomized in a 2:1 ratio to the liposuction arm or CPT arm, provided that all inclusion and exclusion criteria were still met.

Liposuction was performed in the liposuction arm using the "wet technique" under TLA. Depending on the findings and accompanying illnesses, this could be combined with analog sedation or general anesthesia. As part of the TLA, the subcutaneous area to be treated was infiltrated with a solution of a local anesthetic, and the resulting fat-solution mixture was then suctioned off. Due to hemodynamic risks and possible systemic pharmacological effects of the local anesthetic, different restrictions applied depending on body weight with regard to the tumescent solution infused and the maximum amount of fat tissue to be suctioned. Liposuction could be performed in up to four sessions at intervals of at least 5 and at most 7 weeks. CPT was also administered on an individual basis as required.

In the control arm, patients received CPT. The CPT was individually adjusted to the treatment developments. According to the study protocol, the frequency, duration, and type of CPT used were to be documented. After 12 months, a switch to the liposuction arm was possible if the defined inclusion and exclusion criteria were met.

This meant that the randomized design was discontinued in the follow-up phase of 12–24 months.

A detailed description of the intervention and control intervention, as well as the collected endpoints, can be found in Table 2.

Table 1: Study characteristics

Study characteristics	Description

Study design and study procedure	Randomized, controlled, investigator-blinded, multicenter, national study on the efficacy and safety of liposuction compared to complex physical decongestive therapy (CPT) alone
	Allocation was 2:1 (intervention: control). Study procedure:
	• Run-in phase (single-arm) with 2 phases
	  ○ Phase 1 (up to 4 weeks): Edema reduction
	  ○ Phase 2 (6 months): CPT to maintain the results achieved
	• Intervention phase (at least 12 months)
	• Follow-up (24 months)

Number of people included	Randomized: N= 410 Intervention: N= 278 Control: N= 132
Population	<u>Key inclusion criteria</u> • Age ≥18 years • Female • Confirmed stage I-III lipedema of the legs • Average pain in the legs in the last four weeks≥ 4 Points on a numerical rating scale • Documentation of insufficient relief of symptoms through conservative measures <u>Essential exclusion criteria</u> • Concurrent lipedema of the arms and legs, where the involvement of the arms influences the primary endpoint (i.e., average pain in the legs), at the discretion of the study physician • Previous liposuction • Diseases that may influence adequate CPT or operability, at the discretion of the medical staff • Other edema-causing diseases (such as lymphedema, phleboedema, or myxedema) • Fat distribution disorders of other origins (such as painless lipohypertrophy, benign symmetrical lipomatosis or lipomatosis dolorosa) • Weight >120.0 kg
Location and period of implementation	<u>Study centers</u> 11 study centers in Germany <u>Study period</u> • Q1/2021: Inclusion of the first patient • Q3/2022: Inclusion of the last patient • Q3/2026: End of study for last patient • Q1/2027: Final report
Endpoints	<u>Primary endpoint</u> • Pain reduction in the legs

Study characteristics	Description

	Secondary endpoints
	• Severity of pain in the legs (according to Korff)
	• Quality of life, measured using
	  ○ SF-36
	  ○ DLQI
	  ○ WHOQOL-BREF
	• Overall impairment (according to Schmeller)
	• Depression tendency (PHQ-9)
	• Tendency to develop hematomas (according to Schmeller)
	• Prevalence of edema
	• Scope of physical therapy[1)]
	• Body fat percentage
	• Leg circumference
	• Restricted movement using LEFS total score
	• Optional: Leg volume (perimetry)
	• Recurrence of surgery[2)]
	Safety
	• (S)UE
	• Discontinuation of therapy

[1)] This endpoint was specified in the study protocol. According to the SAP, the endpoint was not recorded or evaluated. According to the information in the SAP, compliance with CPT can only be verified to a limited extent, as the actual number of CPT treatments performed was not documented in many cases. If possible, the documentation on the prescription of remedies and treatment units as well as on protocol violations should be used to assess patient compliance. An evaluation of this is expected in the final report. Since this evaluation is a summary of the therapies received and compliance, the evaluation of the extent of physical therapy is not considered here as an endpoint, but as general information on the implementation of the study.

[2]The results on repeat procedures are not yet available and are expected for the final report.

Abbreviations: DLQI: Dermatology Life Quality Index; CPT: Complex Physical Decongestive Therapy; LEFS: Lower Extremity Functional Scale; PHQ-9: Patient Health Questionnaire 9; SAP: Statistical Analysis Plan; SF-36: Short Form-36; (S)UE: (serious) adverse events; WHOQOL-BREF: World Health Organization Quality of Life.

Table 2: Description of interventions

Introductory phase ("run-in phase") prior to randomization: • Use of CPT as standardized conservative therapy in accordance with the recommendations of the S1 guideline[1)] [6] as part of an introductory phase for all participants • Run-in phase to establish equal baseline conditions prior to randomization • Subsequent randomization and division into intervention and control groups	
Intervention group: liposuction	**Control group:** **Complex physical decongestive therapy**
• Liposuction using the "wet technique" under TLA, possibly in combination with analog sedation or general anesthesia depending on the findings and comorbidities • If necessary, use of supportive techniques such as vibration (PAL) or water jet (WAL) • Infiltration of the subcutaneous area to be treated with a solution of a local anesthetic and subsequent suction of the resulting fat-solution mixture as part of TLA • Restriction of the tumescent solution prior to each liposuction or WAL during liposuction to a maximum volume of 10% of the patient's body weight o Absolute maximum of 8 L of infused solution per procedure o Absolute maximum amount of fat tissue removed: 6 L for a body weight of ≤ 80 kg o Absolute maximum amount of fat tissue removed: 8 liters for a body weight of > 80 kg (especially for patients in stage III) • Liposuction performed in up to four sessions • Continuation of CPT to the extent necessary to prevent progression.	• Performance of CPT (at least) to maintain the results achieved at the end of the run-in phase • Individual adjustment of CPT to treatment developments with documentation of frequency, duration, and CPT applied • After 12 months: Option to switch to the intervention group if the inclusion and exclusion criteria are met

[1)] The S1 guideline on lipedema was valid when the study protocol was drawn up, but has now expired. According to the S1 guideline, CPT consists of the combined application of lymphatic drainage, compression therapy, skin care, and exercise therapy.

Abbreviations: CPT: complex physical decongestive therapy; PAL: power/vibration-assisted liposuction; TLA: tumescent local anesthesia; WAL: water-jet-assisted liposuction

2.3.2 Assessment of the potential for bias in the results

The risk of bias (RoB) of the study was assessed using RoB 2 – Revised Cochrane risk of bias tool for randomized trials. The study was evaluated using RoB 2 for the endpoints considered by two evaluators according to the dual-evaluator principle. Differences in the evaluation were resolved through discussion and consensus. In accordance with the RoB 2 categories, the VBP is rated as "low," "some concerns," or "high" (see Figure 1).

With regard to the randomisation process and concealed group allocation, the LIPLEG study is considered unbiased. There were no differences between the treatment groups in the patient characteristics at the time of randomisation. All efficacy endpoints were evaluated using the ITT population. The potential for bias in the efficacy endpoints is rated as "some concerns" due to the unblinded collection.
"some concerns." It cannot be ruled out that knowledge of the intervention had an influence on the endpoint assessment, especially since the endpoints reflect subjective states. Blinding of the study treatments for the clinical staff was only possible to a limited extent. Surgical scars were covered (dummy plasters in the control group) and patients were asked not to disclose the treatment they had received to the clinical staff. The statistical analysis was performed in a blinded manner. All efficacy endpoints considered were collected by the patients, who were not blinded to the treatment.

In the liposuction arm, no data were available for 41 individuals (14.7%) at V2 and in the CPE arm for 12 individuals (9.1%) due to study discontinuation or missing final examinations (see Section 2.1). For the SF-36, data were missing for an additional 5 individuals in the liposuction arm and one individual in the CPE arm. For the primary endpoint, missing data in both arms were considered treatment failure. In view of the magnitude of the effect, a statistically significant result for the primary endpoint would have been expected even with more conservative replacement strategies, so that no significant bias due to missing data is assumed for this endpoint. No data imputation was performed for the secondary endpoints. Further sensitivity analyses for secondary endpoints with single and multiple imputation are only expected in the final report. Accordingly, there remains greater uncertainty in the interpretation of the results for these endpoints, although the effect size is so clear in the secondary endpoints that no high bias is expected.

A further potential bias could be assumed due to the different observation periods (defined as the time between randomization and collection of the primary endpoint) in both arms. No information on treatment and observation durations is available. However, since the endpoints were assessed 12 months after randomization in the CPT arm and 12 months after the last liposuction treatment in the liposuction arm, it can be inferred that the treatment duration in the liposuction arm was on average approximately 5 months longer than in the CPT arm (see Section 2.1). The descriptive analysis of the continuous NRS values and the MMRM analysis show that the NRS values remained largely unchanged over the 12-month period in the CPT arm, while in the liposuction arm there was a significant improvement after 6 months that was comparable to the 12-month values. This also applies to the secondary endpoints. The descriptive values of the endpoints in the liposuction arm show that there is little difference between the endpoints V1 (6 months after the last liposuction) and V2 in the liposuction arm. Overall, particularly due to the consistent values in the CPT arm over time, it is therefore not expected that the different observation periods in both arms will cause a significant bias in the results of the efficacy parameters.

The potential for bias in the efficacy parameters is rated as "some concern" due to the unblinded collection and, in the case of the secondary endpoints, the lack of data without adequate imputation strategies for missing values. For the endpoint "movement restrictions using LEFS," it should also be noted that the validity of the questionnaire for the present indication has not been confirmed (see section 1.2.1).

The potential for bias in the safety analysis is rated as "high." As described in Chapter 1.2.3, it is unclear whether and which PTs were removed from the (S)UE. No information is available on the median observation period for the two groups. It can be assumed that patients in the liposuction group were available for observation of (S)UE for a longer period than patients in the CPE group. Consequently, the probability of observing UE is higher in the liposuction group than in the CPE group. In addition, data are only available on the number of (S)UE and not on the number of individuals with at least one UE.

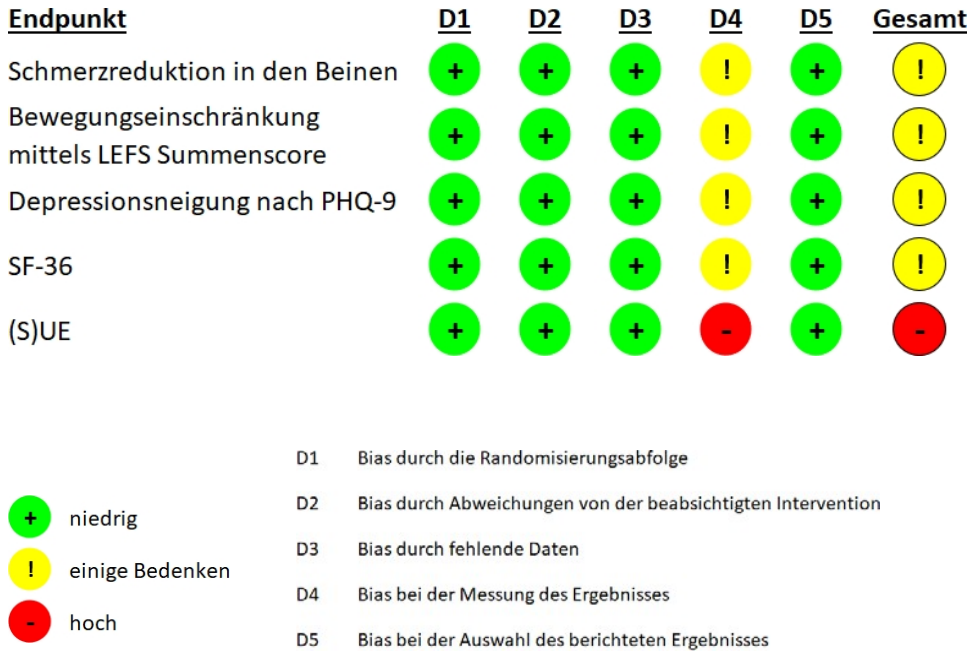

Figure 1: Potential for bias in the endpoints considered in the LIPLEG study using RoB 2

2.3.3 Results for patient-relevant endpoints

For the benefit assessment, the results after 12 months are used for all patient-relevant endpoints.

Results for the endpoint morbidity

The time frame for evaluating the efficacy endpoints was from randomization (P2) to 12 months after completion of liposuction treatment in the liposuction arm or to 12 months after randomization in the CPT arm (V2). The primary endpoint
"pain reduction in the legs" was defined as a reduction of at least 2 points on an NRS of 0 to 10 points 12 months after the last liposuction (liposuction arm) or 12 months after randomization (CPE arm). ≥The question to be answered by the patients was: "Please indicate your average pain intensity during the last 4 weeks." Missing values for the primary endpoint were replaced as "treatment failure" (failure to achieve an improvement of at least 2 points on the NRS).

In the liposuction arm, 68.3% of patients achieved the primary endpoint of pain reduction in the legs, while in the CPE arm, a relevant pain reduction was achieved in 7.6% (OR [95% CI]: 26.3 [13.2; 52.6]; p< 0.001). The analyses in the individual stages I to III also showed a clear effect in favor of liposuction (see Table 6). The results are also confirmed in the MMRM model (see Appendix, Table 13).

The LEFS is a tool for self-assessment of functional limitations in the lower extremities based on 20 questions about everyday activities. The individual items are used to calculate a total score ranging from 0 to 80 (higher scores indicate better function). A clinically relevant improvement in functional limitations was assumed to be a reduction of ≥ 9 points. In terms of movement limitation measured using the LEFS total score, a clinically relevant improvement of at least 9 points was demonstrated in 70.0% of patients in the liposuction arm compared to 10.0% in the CPE arm (OR: 21.0 [10.8; 40.7]; p < 0.001). The effect was confirmed in all stages I to III (see Table 6).

The Patient Health Questionnaire 9 (PHQ-9) is a validated screening tool for diagnosing depression. For the PHQ-9, a total score of 0-27 can be calculated (higher scores indicate more severe symptoms). A clinically relevant reduction in depressive tendencies was assumed to be a reduction of ≥ 5 points. A clinically relevant reduction in depressive tendencies, measured by a change of ≥ 5 points in the PHQ-9, was observed in 36.7% of patients in the liposuction arm compared to 5.0% in the CPE arm. The effect was significant in favor of liposuction (OR: 11.0 [4.7; 26.1]; p < 0.001) with consistent results across stages (see Table 6).

Table 3: Results for morbidity endpoints after 12 months[1)]

Endpoint *Raw values* Responder analysis	**Intervention group Liposuction N**	**Control group KPE N**	**Liposuction vs. KPE OR [95% CI]; p-value**
Pain reduction in the legs: NRS (≥ 2 points) improvement[)] [(2)]			
P2, MW (SD)	*6.2*	*6.3 (1.6)*	-
V2, MW (SD)	*2.6 (2.5)*	*6.6 (1.5)*	-
All stages, n/N (%)[3)]	190/278 (68.3)	10/132 (7.6)	26.3 (13.2; 52.6);< 0.001[4)]
			Interaction test (p-value)[5)] : 0.768
Stage I, n/N (%)	61/90 (67.8)	4/42 (9.5)	20.0 (6.5; 61.3);< 0.001[6)]
Stage II, n/N (%)	69/95 (72.6)	3/45 (6.7)	37.2 (10.6; 130.3);< 0.001[6)]
Stage III, n/N (%)	60/93 (64.5)	3/45 (6.7)	25.5 (7.3; 88.5);< 0.001[6)]
Restricted movement: LEFS total score (improvement≥ 9 points)[7)]			
P2, MW (SD)	*48.6*	*48.5 (17.3)*	-
V2, MW (SD)	*65.8 (15.5)*	*46.7 (16.0)*	-
All stages, n/N (%)	166/237 (70.0)	12/120 (10.0)	21.0 (10.8; 40.7); <0.001[3)]
			Interaction test (p-value)[4)] : 0.401
Stage I, n/N (%)	44/70 (62.9)	3/39 (7.7)	20.3 (5.7; 72.6); <0.001[6)]
Stage II, n/N (%)	56/87 (64.4)	5/43 (11.6)	13.7 (4.9; 38.5); <0.001[6)]
Stage III, n/N (%)	66/80 (82.5)	4/38 (10.5)	40.1 (12.2; 131.2); <0.001[6)]
Depression tendency: PHQ-9 (≥ 5 points) [8)]			
P2, MW (SD)	*8.9 (5.4)*	*8.3 (5.0)*	-
V2, MW (SD)	*5.7 (4.8)*	*8.7 (5.5)*	-
All stages, n/N (%)	87/237 (36.7)	6/120 (5.0)	11.0 (4.7; 26.1); p< 0.001[3)]
			Interaction test (p-value)[4)] : 0.994
Stage I, n/N (%)	25/70 (35.7)	2/39 (5.1)	<10.3 (2.3; 46.3); p-value 0.001[6)]

Endpoint *raw values* responder analysis	**Intervention group Liposuction N= 278**	**Control group KPE N**	**Liposuction vs. KPE OR [95% CI]; p-value**
Stage II, n/N (%) Stage III, n/N (%)	31/87 31/80 (38.8)	2/43 (4.7) 2/38 (5.3)	11, (2.6; 50.1);< 0.001[6)] 11.4 (2.6; 50.7); p< 0.001[6)]

[1)] 12 months after completion of liposuction treatment in the liposuction arm or up to 12 months after randomization in the CPE arm (V2) compared to the time of randomization (P2).
[2]Scale from 0 (no pain) to 10 (worst pain imaginable).
[3]In the liposuction arm, 41 (14.7%) missing values were replaced as "treatment failures" and in the CPE arm, 12 (9.1%) were replaced.
[4)] p-values of the CMH test stratified by stages.
[5]p-value of the Breslow-Day test.
[(6)] p-value of the exact Fisher test.
[7]Scale from 0-80, higher values indicate better function.
[8]Scale from 0-27, higher values indicate more severe symptoms.

Abbreviations: CI: confidence interval; CPET: complex physical decongestive therapy; LEFS: Lower Extremity Functional Scale; MW: mean value; n: number of patients with relevant improvement; N: Total number of patients per group; NRS: Numerical Rating Scale; OR: Odds Ratio; PHQ-9: Patient Health Questionnaire 9; SD: Standard deviation.

Results for the endpoint quality of life

In the mental sum scale of the SF-36, the proportion of responders (improvement of ≥ 6 points) after 12 months in the liposuction arm 44.8% and in the CPE arm 23.5%. This resulted in an overall statistically significant effect in favor of liposuction (OR: 2.6 [1.6; 4.3]; p< 0.001). In the analyses of the individual stages, significant effects in favor of liposuction were only found for stages II and III (OR: 3.5 [1.5; 8.5]; p= 0.004 and OR: 2.5 [1.1; 5.9]; p= 0.042, respectively). However, the direction and extent of the effects appear consistent overall, as indicated by the non-significant p-value of the interaction test (see Table 7).

On the SF-36 physical sum score, the proportion of responders after 12 months was 73.7% in the liposuction arm and 13.4% in the CPE arm. This resulted in an overall significant effect in favor of liposuction (OR: 18.4 [10.1; 33.8]; p< 0.001), which was also demonstrated in stages I to III (see Table 7).

Table 4: Results for the endpoint quality of life assessed using SF-36 after 12 months[1)]

Endpoint *Raw values* Responder analysis	**Intervention group Liposuction N**	**Control group CPE N**	**Liposuction vs. CPE OR [95% CI]; p-value**
SF-36 – Mental Sum Scale (improvement≥ 6 points)[2)]			
P2, MW (SD)	*40.7*	*42.6 (14.1)*	-
V2, MW (SD)	*46.1 (14.2)*	*40.8 (13.7)*	-
All stages[4)] , n/N (%)	104/232 (44.8)	28/119 (23.5)	2.6 (1.6; 4.3);< 0.001[3)] Interaction test (p-value)[5)] : 0.679
Stage I, n/N (%)	29/70 (41.4)	10/39 (25.6)	[2].1 (0.9; 4.9); 0.144[6)]
Stage II, n/N (%)	38/85 (44.7)	8/43 (18.6)	3.5 (1.5; 8.5); 0.004[6)]
Stage III, n/N (%)	37/77 (48.1)	10/37 (27.0)	2.5 (1.1; 5.9); 0.042[6)]
SF-36 – Physical Sum Scale (improvement≥ 6 points)[2)]			
P2, MW (SD)	*37.4*	*37.7*	-
V2, MW (SD)	*48.3 (8.4)*	*36.2 (8.6)*	-
All stages, n/N (%)	171/232 (73.7)	16/119 (13.4)	18.4 (10.0; 33.8); <0.001[2)] Interaction test: 0.937[4)]
Stage I, n/N (%)	51/70 (72.9)	5/39 (12.8)	18.3 (6.2; 53.6); <0.001[5)]
Stage II, n/N (%)	58/85 (68.2)	5/43 (11.6)	16.3 (5.8; 46.1); <0.001[5)]
Stage III, n/N (%)	62/77 (80.5)	6/37 (16.2)	21.36 (7.6; 60.4); <0.001[5)]

[1)] 12 months after completion of liposuction treatment in the liposuction arm or up to 12 months after randomization in the KPE arm (V2) compared to the time of randomization (P2).

[2]Discrepancy between the information in the study report and the letter requesting additional information/appendix: For both sum scales, 234 and 119 values were available for V2. However, the study report states 232 values in the liposuction arm (see Table 21).

[3]p-value of the CMH test stratified by stages.

[4]Missing values were not replaced (up to 17% (liposuction) and 10% (KPE)).

[5)] p-value of the Breslow-Day test.

[6]p-value of the exact Fisher test.

Abbreviations: CI: confidence interval; CPT: complex physical decongestive therapy, n: number of patients with relevant improvement, N: total number of patients per group; OR: odds ratio; SF-36: Short Form (SF)-36.

Results for the endpoint safety

For the assessment of the UE after 12 months, only data collected during the observation period of 12 months after randomization in the CPT arm and after 12 months after the final liposuction surgery in the liposuction arm were evaluated and presented. No precise information on the observation period is available. The data refer to the number of events (not the number of patients with at least one event). No effect estimators were calculated. The number of (S)UE is summarized in Table 8. For SUE, the individual PTs were presented separately for the liposuction arm and the CPE arm in Table 9 and Table 10.

According to the study protocol, the safety analysis was performed without taking into account events that were recorded as efficacy parameters (primary endpoint and secondary endpoints). The exact implementation of this analysis is unclear. A prespecification of certain PTs that were not included in the safety analysis

was not provided. An additional analysis taking all PT into account is also not available.

Table 5: Adverse event results – summary of (S)UE after randomization

Number of events	**Intervention group Liposuction N= 278**	**Control group CPE N**
UE	196	32
SUE	2	6
SUE that led to discontinuation of the study intervention	1	1

Abbreviations: (S)UE: (Serious) adverse event.

A total of 196 UEs were reported in the liposuction arm and 32 UEs in the CPE arm. SUE were documented in 21 individuals in the liposuction arm and in 6 individuals in the CPE arm. A possible causal relationship with the intervention was assumed for 46 AEs in the liposuction arm, including 12 cases of anemia, 11 cases of seromas, 8 cases of erysipelas, and 3 cases of thrombosis. All other AEs that had a possible causal relationship with the intervention occurred only once. A possible causal relationship with the intervention was assumed for 10 SAEs in the liposuction arm (3 cases of anemia and 1 case each of erysipelas, abscess, iron deficiency anemia, furuncle, peripheral swelling, pain, and vertigo).

Table 6: SUE after randomization in the liposuction arm

Number of SUE in the liposuction arm PT	**Total**	**Stage I**	**Stage II**	**Stage III**
Total	**21**	**11**	**4**	**6**
Anemia	3	2	1	0
Erysipelas	2	0	0	2
Abdominal discomfort	1	1	0	0
Abscess	2	1	0	1
Acinic cell carcinoma of the salivary glands	1	1	0	0
Band rupture	1	1	0	0
Diarrhea	1	0	1	0
Dysmenorrhea	1	0	0	1
Iron deficiency anemia	1	1	0	0
Boil	1	1	0	0
Benign adenoma	1	1	0	0
Colitis	1	1	0	0
Peripheral swelling	1	0	0	1
Respiratory insufficiency	1	1	0	0
Pain	1	0	1	0
Dizziness	1	0	0	1
Vertigo	1	0	1	0

Abbreviations: PT: Preferred Term; (S)UE: (Serious) Adverse Event.

Table 7: SUE after randomization in the CPE arm

Number of SUE in the KPE arm PT	**Total**	**Stage I**	**Stage II**	**Stage III**
Total	**6**	**1**	**2**	**3**
Adnexal torsion	1	0	1	0
Disc protrusion	1	0	0	1
Mammary gland abscess	1	1	0	0
Implantation of a medical device	1	0	0	1
Multiple sclerosis	1	0	1	0
Myocardial infarction	1	0	0	1

Abbreviations: CPET: Complex Physical Decongestive Therapy; PT: Preferred Term; (S)UE: (Serious) Adverse Event.

2.3.4 Conclusion of the benefit assessment

Overall, based on the results of the 12-month data from the LIPLEG study for the efficacy endpoints available for assessment and taken into account, there are significant effects in favor of liposuction, which are very clear in their severity and consistent across all stages. Taking into account the clearly pronounced and beneficial effects on pain reduction and thus on the main symptom of the disease and on other endpoints relevant to patients, such as quality of life, the certainty of the efficacy results is considered high. With regard to the safety endpoints, the results cannot yet be interpreted. Further data are expected in the final report. Findings on repeat procedures will then also be available. Table 11 summarizes the results of the LIPLEG study after a 12-month observation period.

Table 8: Summary of results from the LIPLEG study (all stages)

Presentation of results Endpoints	**Responders n/N (%)**		**OR [95% CI]; p-value[1)]**	**Effect [2)]**
	Intervention group Liposuction N= 278	**Control group CPE N= 132**		
Morbidity				
Pain reduction in the legs; NRS[3)] (≥ 2-point improvement)	190/278 (68.3)	10/132 (7.6)	26.3 (13.2; 52.6); < 0	↑
Restricted movement; LEFS total score [4)] (improvement ≥ 9 points)	166/237 (70.0)	12/120 (10.0)	21.0 (10.8; 40.7); < 0.001	↑
Depression tendency; PHQ-9[5)] (≥ 5 points)	87/237 (36.7)	6/120 (5.0)	11.0 (4.7; 26.1); < 0	↑
Quality of life				
SF-36 Mental Sum Scale[6)] (≥ mprovement 6 points)	104/232 (44.8)	28/119 (23.5)	2.6 (1.6; 4.3); < 0.001	↑
SF-36 Physical Sum Scale [6] (≥ 6-point improvement)	171/232 (73.7)	16/119 (13.4)	18.4 (10.0; 33.8); <0.001	↑

Presentation of results Endpoints	Responders n/N (%)		OR [95% CI]; p-value[1)]	Effect [2)]
	Intervention group Liposuction N= 278	Control group CPE N= 132		
Safety				
UE	196 (70.5)	32 (24.2)	Not available [7]	n/a
SUE	21 (7.6)	6 (4.5)	n/a [7]	n.a.
SUE leading to discontinuation of the study intervention	1 (0.4)	1 (0.8)	Not applicable [7]	n/a

[1]CMH test stratified by stages.

[2]It is shown whether liposuction has a statistically significant beneficial/detrimental effect in cases of high VPC or some concerns (↑/↓) or low VPC (↑↑/↓↓) or whether no statistically significant difference (↔) could be demonstrated. The certainty of the statement is thus shown in the last column.

[3)] Scale from 0 (no pain) to 10 (strongest pain imaginable).

[4]Scale from 0-80, higher values indicate better function.

[5]Scale from 0 to 27, higher values indicate more severe symptoms.

[6]Standardized scale from 0 to 100, higher values indicate a better quality of life.

[7]Not reported, will be included in the final report.

Abbreviations: n/a: not available; CI: confidence interval; CPET: complex physical decongestive therapy; LEFS: Lower Extremity Functional Scale; n: number of patients with relevant improvement; N: total number of patients per group; n.a.: not reported; NRS: Numerical Rating Scale; OR: Odds Ratio; PHQ-9: Patient Health Questionnaire 9; SF-36: Short Form (SF)-36; (S)UE: (Serious) Adverse Event; VZP: potential for bias.

2.4 Cross-sector assessment of medical necessity

The assessment of medical necessity is based on the criteria specified in the G-BA's rules of procedure. It must be examined to what extent the relevance of the disease, the spontaneous course without treatment, the benefits and risks of alternative treatment methods, the special aspects of the treatment of specific subgroups, and the effects on quality of life can further justify medical necessity.

Lipedema is a chronic condition that can progress over time, although the course of the disease cannot be predicted in individual cases, and its etiology is unknown. Spontaneous healing of lipedema is not known. There is a lack of reliable and consistent scientific data on the prevalence of lipedema.

Those affected suffer permanently from a distinct feeling of tension with spontaneous pain and sensitivity to touch and pressure. These complex symptoms lead to significant physical impairments and a significantly reduced quality of life for those affected. The pathologically altered fat cells cannot be eliminated by any form of conservative therapy, which means that the conservative treatment options currently available in standard care, such as compression therapy and CPT, can only reduce the symptoms. However, physical measures are only of limited use in reducing the volume of the extremities. The only known and available therapy with a proven benefit profile that removes fat tissue cells is currently liposuction. Although liposuction does not eliminate the cause of the disease in the true sense of the word and is therefore unlikely to lead to a complete cure, the available studies suggest that the use of

liposuction for lipedema regularly leads to patient-relevant relief of symptoms in cases where the symptoms cannot be controlled by other means.

In summary, it can be stated that the disease, which persists despite the exhaustion of conservative measures, can be considered a situation in which there are no longer any adequate therapeutic alternatives to liposuction and therefore, in the absence of alternative treatments, there is a medical emergency. Given the medical relevance of the symptoms and the lack of effective and sustainable therapeutic alternatives for lipedema to date, liposuction is therefore medically necessary.

2.5 Sector-specific assessment of the necessity of hospital treatment

Liposuction for lipedema can be performed as part of inpatient hospital treatment. The necessity of inpatient treatment depends, among other things, on the extent of the underlying disease, the planned scope of the procedure, any concomitant diseases, and the need for intensive monitoring and follow-up care in this context.

2.6 Sector-specific assessment of the cost-effectiveness of hospital treatment

For the health economic assessment of liposuction for lipedema, it is necessary to quantify the cost difference between treatment with and without this method (incremental costs) on the one hand, and the effects with and without the use of the method (incremental effects) on the other, in order to ultimately compare the two variables. Since the G-BA does not have the data required for such an assessment of the cost-effectiveness of liposuction for lipedema, a sector-specific assessment of cost-effectiveness must currently be waived. Nevertheless, the G-BA has no evidence to suggest that liposuction for lipedema is not cost-effective.

2.7 Overall assessment

The overall assessment combines the findings on the benefits and medical necessity (see sections 2.3 and 2.4) and the sector-specific assessment of necessity and cost-effectiveness (see sections 2.5 and 2.6).

After evaluating the results of the LIPLEG study for the observation period of 12 months after completion of liposuction, it was found that the benefits of liposuction for lipedema are sufficiently proven and that medical necessity can be assumed. This statement applies to all three stages of lipedema. As soon as the results of the pilot study covering the 24-month observation period are available, the G-BA will review its assessment, taking into account all data, in particular safety endpoints and the necessity of repeat procedures, and make any necessary adjustments.

As a result of the comprehensive assessment process in accordance with Chapter 2, Section 13 of the VerfO, the G-BA has therefore concluded that liposuction for lipedema is necessary for the adequate, appropriate, and economical care of insured persons, taking into account the generally accepted state of medical knowledge in accordance with
Section 137c (1) sentence 1 SGB V. Liposuction for lipedema therefore remains a service

by health insurance funds within the scope of hospital treatment, whereby the previous restriction to stage 3 no longer applies.

The validity of the benefit statement based on the results of the LIPLEG study for all three stages of lipedema justifies replacing the previous position 14, "Liposuction for stage III lipedema," in Appendix I of the KHMe-RL with the new position 14, "Liposuction for lipedema." The G-BA resumed its deliberations before the trial study was completed because the evaluation of the primary endpoint was scheduled for the end of the randomized study phase. In addition to the complete evaluation of the primary endpoint at the 12-month mark, results for other relevant endpoints are also available. All endpoints considered at this point show significant effects in favor of liposuction, which are very clear in their severity and consistent across all stages.

The study results from the second, non-randomized observation period (months 13–24) may provide additional insights. However, they do not call into question the results from the randomized study phase.

Due to the pronounced effects and high degree of certainty of the results, the G-BA has concluded that sufficient evidence is already available to assess the benefits and, taking into account the lack of effective alternative treatment options, has decided to include the method at this time. Once the further results of the pilot study are available after completion of the follow-up period, the G-BA will review the assessment and make any necessary adjustments.

3. Assessment of the comments

At its meeting on May 22, 2025, the UA MB decided to initiate a consultation procedure. Five comments were received within the set deadline (four weeks).

No changes were made to the draft resolution based on the comments received.

4. Bureaucratic cost assessment

The proposed resolution does not create any new or amended information obligations for service providers within the meaning of Annex II to Chapter 1 of the VerfO and and therefore does not entail any bureaucratic costs.

5. Procedure

Date	Committee	Subject of consultation / procedural step
July 20	Plenary	Suspension of the assessment procedure pursuant to Sections 135 and 137c of the German Social Code, Book V (SGB V) and commencement of consultations on a guideline pursuant to § 137e SGB V for trial purposes
18.01.2018	Plenary	Adoption of the guideline for testing purposes.

Date	Committee	Subject matter / procedural step
19	Plenary	• Inclusion of liposuction for stage III lipedema, limited until December 31, 2024, in Appendix I (Recognized Examination or Treatment Methods) of the MVV-RL and in Appendix I (Methods Required for the Provision of Hospital Treatment) of the KHMe-RL. • Decision of the Quality Assurance Guideline on Liposuction for Stage III Lipedema
February 8		Start of the pilot study "LIPLEG – Liposuction for lipedema in stages I, II, or III"
08	UA MB	• Resumption of consultations on liposuction for lipedema • Commissioning of expert medical advice • Initiation of the consultation process for extending the regulations regarding stage III lipedema
08/2024		End of the 12-month observation period for the last patient in the LIPLEG study.
19	Plenary	Decisions on amendments to the MVV-RL, KHMe-RL, and QS-RL (extension of the regulations for stage III until December 31, 2025)
February		Submission of the results of 12-month follow-up period of the LIPLEG study
May 22, 2025	UA MB	Initiation of the consultation procedure
26	UA MB	Hearing
July 10	UA MB	Final consultation in UA MB
July 17	Plenary	Decisions on amendments to the MVV Directive, KHMe Directive, and QS Directive

6. Conclusion

Following review by the G-BA in accordance with Section 137c (1) SGB V and positive findings regarding its benefits, medical necessity, and cost-effectiveness, liposuction for lipedema, as well as its medical necessity and cost-effectiveness, is considered necessary for the adequate, appropriate, and cost-effective care of insured persons. It therefore remains a service covered by health insurance funds within the scope of hospital treatment and will continue to be listed in Appendix I of the KHMe-RL (methods required for the provision of hospital treatment). The previous restriction to stage III no longer applies.

References

1. German Society for Phlebology and Lymphology. Lipedema; S2k guideline; long version [online]. AWMF registration number 037-012. Berlin (GER): Association of Scientific Medical Societies (AWMF); 2024. [Accessed: 08.04.2025]. URL: https://register.awmf.org/assets/guidelines/037-012l_S2k_Lipoedem_2024-01_01.pdf.
2. Child AH, Gordon KD, Sharpe P, Brice G, Ostergaard P, Jeffery S, et al. Lipedema: an inherited condition. Am J Med Genet A 2010;152A(4):970-6.
3. Meier-Vollrath I, Schmeller W. Lipedema – current status, new perspectives. J Dtsch Dermatol Ges 2004;2(3):181-6.
4. Bellini E, Grieco MP, Raposio E. A journey through liposuction and liposculpture: review. Ann Med Surg (Lond) 2017;24:53-60.
5. Rapprich S, Koller J, Sattler G, Worle B, Sommer B, Bechara FG, et al. Liposuction – a surgical procedure in dermatology. J Dtsch Dermatol Ges 2012;10(2):111-3.
6. Schmeller W, Meier-Vollrath I. Lipedema. Vascular Surgery 2009;14(6):516-522.

Berlin, July 17, 2025

Joint Federal Committee pursuant to
Section 91 of the German Social Code,
Book V
The Chairman

Prof. Hecken