1.01.05	Ultrasound Accelerated Fracture Healing Device		
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Section:	1.0 Durable Medical Equipment	**Page:**	Page 1 of 21

Policy Statement

Low-intensity pulsed ultrasound is considered **not medically necessary** as a treatment for **any** of the following:

- Fresh fractures (surgically managed or nonsurgically managed)
- Fracture nonunion and delayed union fractures
- Stress fractures, osteotomy, and distraction osteogenesis

Policy Guidelines

Fresh (Acute) Fracture

There is no standard definition for a "fresh" fracture. A fracture is most commonly defined as fresh for 7 days after the fracture occurs (Heckman et al, 1994; Kristiansen et al, 1997; Emami et al, 1999), but there is definitional variability. For example, one study defined fresh as less than 5 days after fracture (e.g., Lubbert et al, 2008), while another defined fresh as up to 10 days postfracture (Mayr et al. [Does low intensity, pulsed ultrasound speed healing of scaphoid fractures?] [German]. *Handchir Mikrochir Plast Chir*. Mar 2000;32(2):115-122). Most fresh closed fractures heal without complications using of standard fracture care (i.e., closed reduction and cast immobilization).

Nonunion

There is no consensus on the definition of nonunions. One definition is a failure of progression of fracture healing for at least 3 consecutive months (and at least 6 months postfracture) accompanied by clinical symptoms of delayed/nonunion (pain, difficulty weight bearing; Buza & Einhorn, 2016).

The definition of nonunion used in U.S. Food and Drug Administration (FDA) labeling suggests that nonunion is considered established when the fracture site shows no visibly progressive signs of healing, without providing guidance on the timeframe of observation. The following patient selection criteria are consistent with those proposed for electrical stimulation as a treatment of nonunions (see Blue Shield of California Medical Policy: Electrical Bone Growth Stimulation of the Appendicular Skeleton):

- At least 3 months have passed since the date of the fracture
- Serial radiographs have confirmed that no progressive signs of healing have occurred
- The fracture gap is 1 cm or less
- The patient can be adequately immobilized and, based on age, is likely to comply with nonweight bearing

Delayed Union

Delayed union is defined as a decelerating healing process as determined by serial radiographs, together with a lack of clinical and radiologic evidence of union, bony continuity, or bone reaction at the fracture site for no less than 3 months from the index injury or the most recent intervention.

Description

Low-intensity pulsed ultrasound (LIPUS) has been investigated as a technique to accelerate healing of fresh fractures, surgically treated closed fractures, delayed unions, nonunions, stress fractures, osteotomy sites, and distraction osteogenesis. LIPUS is administered using a transducer applied to the skin surface overlying the fracture site.

Related Policies

- Bone Morphogenetic Protein
- Electrical Bone Growth Stimulation of the Appendicular Skeleton
- Electrical Stimulation of the Spine as an Adjunct to Spinal Fusion Procedures

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates (e.g., Federal Employee Program [FEP]) prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

Regulatory Status

In 1994, the Sonic Accelerated Fracture Healing System (SAFHS®; renamed Exogen 2000® and since 2006, Exogen 4000+; Bioventus) was approved by the U.S. Food and Drug Administration through the premarket approval process for treatment of fresh, closed, posteriorly displaced distal radius (Colles) fractures and fresh, closed, or grade I open tibial diaphysis fractures in skeletally mature individuals when these fractures are orthopedically managed by closed reduction and cast immobilization. In February 2000, the labeled indication was expanded to include the treatment of established nonunions, excluding skull and vertebra. Food and Drug Administration product code: LPQ.

Rationale

Background

Bone Fractures

An estimated 7.9 million fractures occur annually in the United States. Most bone fractures heal spontaneously over several months following standard fracture care (closed reduction if necessary, followed by immobilization with casting or splinting). However, approximately 5% to 10% of all fractures have delayed healing, resulting in continued morbidity and increased utilization of health care services.[1,] Factors contributing to a nonunion include which bone is fractured, fracture site, the degree of bone loss, time since injury, the extent of soft tissue injury, and patient factors (e.g., smoking, diabetes, systemic disease).[1,]

Fracture Nonunion

There is no standard definition of a fracture nonunion.[2,] The Food and Drug Administration has defined nonunion as when "a minimum of 9 months has elapsed since injury, and the fracture site shows no visibly progressive signs of healing for a minimum of 3 months." Other definitions cite three to six months of time from the original injury, or simply when serial radiographs fail to show any further healing. These definitions do not reflect the underlying conditions in fractures that affect healing, such as the degree of soft tissue damage, alignment of the bone fragments, vascularity, and quality of the underlying bone stock.

Delayed Union

Delayed union is generally considered a failure to heal between three and nine months post fracture, after which the fracture site would be considered a nonunion. The delayed union may also be defined as a decelerating bone healing process, as identified in serial radiographs. (In contrast, nonunion serial radiographs show no evidence of healing.) It is important to include both radiographic and clinical criteria to determine fracture healing status. Clinical criteria include the lack of ability to bear weight, fracture pain, and tenderness on palpation.

Treatment

Low-intensity pulsed ultrasound (LIPUS) has been proposed to accelerate healing of fractures. LIPUS is believed to alter the molecular and cellular mechanisms involved in each stage of the healing process (inflammation, soft callus formation, hard callus formation, and bone remodeling). The mechanism of action at the cellular level is not precisely known, but it is theorized that LIPUS may stimulate the production or the activities of the following compounds that contribute to the bone healing process: cyclooxygenase-2, collagenase, integrin proteins, calcium, chondroblasts, mesenchymal cells, fibroblasts, and osteoblasts.

LIPUS treatment is self-administered, once daily for 20 minutes, until the fracture has healed, usually for 5 months.

Literature Review

Evidence reviews assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are the length of life, quality of life (QOL), and ability to function including benefits and harms. Every clinical condition has specific outcomes that are important to patients and managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of technology, two domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Low-Intensity Pulsed Ultrasound

Systematic Reviews

A systematic review by Schandelmaier et al (2017) provides the most comprehensive and rigorous overview and analysis of the existing evidence, including 26 RCTs that used LIPUS for bone healing.[3] Additional systematic reviews or meta-analyses are listed in Table 1. However, because there is a substantial degree of overlap in the studies included in these reports (see Table 2), we will primarily focus on the findings of Schandelmaier et al (2017), which include analyses that highlight the results of RCTs identified as of higher quality. The recently published meta-analysis by Seger et al (2017) analyzed healing index and average time to union following use of LIPUS in cases of scaphoid nonunion, but it did not report control group comparisons.[4] The systematic review by Lou et al (2017)[5] focused on fresh fractures and the review by Leighton et al (2017)[6] focused on nonunions. All systematic reviewers acknowledged that the evidence for the use of LIPUS has methodologic limitations (see Table 1).

Table 1. Systematic Reviews Assessing Use of LIPUS to Treat Fractures

Study	No. of Studies	Study Designs	No. of Subjects	Types of Fractures	Main Conclusions on LIPUS
Schandelmaier et al (2017)[3]	26	RCT	1593	Multiple types	Based on moderate- to high-quality evidence in fresh fracture, LIPUS does not improve outcomes important to patients and is unlikely to affect radiographic bone healing
Seger et al (2017)[4]	5	CS Registry	166	Nonunion	Encouraging results for consideration as nonoperative alternative in select cases
Lou et al (2017)[5]	12	RCT Quasi-RCT	1099	Fresh fracture	Positive results though strength of the evidence is limited
Leighton et al (2017)[6]	13	RCT CS Cohort Registry	1441	Nonunion	Potential benefit of LIPUS; however, no evidence that LIPUS can be used instead of surgery. May be useful in patients for whom surgery is high-risk.
Griffin et al (2014)[7]	12	RCT Quasi-RCT	648	Multiple types	Cannot rule out potential benefit but evidence insufficient
Busse et al (2009)[8]	13	RCT	563	Multiple types	Promising results but moderate- to low-quality evidence
TEC Assessment (1995)[9]	2	RCT	128	Fresh fracture	Meets TEC criteria for FDA-labeled indications in tibia and distal radius

CS: case series; FDA: Food and Drug Administration; LIPUS: low-intensity pulsed ultrasound; RCT: randomized controlled trial.

The study populations in RCTs included by Schandelmaier et al (2017) examined multiple types of fractures including fresh fractures surgically managed (n=7), fresh fractures not surgically managed (n=6), distraction osteogenesis (n=5), nonunion fractures (n=3), osteotomy (n=3), and stress fractures (n=2). The RCTs had a median population size of 30 patients (range, 8-501 patients).

The outcomes examined by this systematic review emphasized those reported by patients to be most important: functional recovery (e.g., time to return to work, time to full weight bearing); pain reduction; and number of subsequent operations. Additional outcomes included time to radiographic healing, because this may be used by physicians to influence clinical decision making and adverse events associated with LIPUS.

In this systematic review, two reviewers independently assessed the quality of selected RCTs, using GRADE, a modified Cochrane risk of bias tool. Generation of randomization sequence, concealment of allocation, and blinding of patients, caregivers, and outcome reporting were evaluated in each trial. Each outcome within each trial was assessed for blinding of outcome assessors, loss to follow-up, and additional limitations. Trial authors were contacted if there was uncertainty in the quality assessment. Of the 26 included trials, 6 were considered to have a low-risk of bias, with the remaining 20 trials considered to have a high-risk of bias. Reasons for high-risk of bias designation included failure to report a method for allocation concealment (15 trials), high or unclear numbers of patients excluded from the analysis (13 trials), unblinded patients (10 trials), and unblinded caregivers or outcome assessors (10 trials). Of the six trials rated to be at low-risk of bias, four were conducted in individuals with fresh fracture, three of which were operatively managed tibial fractures[10,11].

Table 2. Studies Included in Systematic Reviews

		Systematic Reviews by Fracture Type							
Studies	**N**	**Study Design**	**Schandelmaier (2017),[3] Multiple**	**Seger (2017),[4] Nonunion**	**Lou (2017),[5] Fresh**	**Leighton (2017),[6] Nonunion**	**Griffin (2014),[7] Multiple**	**Busse (2009),[8] Multiple**	**TEC Assessment (1995),[9] Fresh**
Busse et al (2016)	51	RCT	.		.				
Busse et al (2014)	501	RCT	.		.				
Dudda et al (2011)	36	RCT	.						
El-Mowafi et al (2005)	20	RCT	.					.	
Emami et al (1999)	32	RCT	.		.		.	.	
Exogen et al (1994)	85	RCT							.
Farkash (2015)	29	CS		.		.			
Gan et al (2014)	30	RCT	.						
Gebauer et al (2005)	66	CS		.		.			
Handolin et al (2005a)	22	RCT	.		.		.	.	
Handolin et al (2005b)	30	RCT	.		.		.	.	
Heckman et al (1994)	97	RCT	.		.		.	.	.
Hemery et al (2010)	14	CS				.			
Jingushi et al (2007)	72	CS				.			
Kamath et al (2015)	60	RCT	.						
Kristiansen et al (1997)	85	RCT	.		.		.	.	
Lerner et al (2004)	17	CS				.			
Leung et al (2004)	30	RCT	.		.		.	.	
Liu et al (2014)	81	RCT	.		.				
Lubbert et al (2008)	120	RCT	.		.		.	.	

		Systematic Reviews by Fracture Type							
Studies	**N**	**Study Design**	**Schandelmaier (2017),[3] Multiple**	**Seger (2017),[4] Nonunion**	**Lou (2017),[5] Fresh**	**Leighton (2017),[6] Nonunion**	**Griffin (2014),[7] Multiple**	**Busse (2009),[8] Multiple**	**TEC Assessment (1995),[9] Fresh**
Mayr et al (2002)	100	CS				.		.	
Mayr et al (2000)	30	RCT	.		.		.		
Nolte et al (2001)	28	CS		.		.			
Patel et al (2014)	28	RCT	.						
Pigozzi et al (2004)	15	CS		.		.			
Ricardo (2006)	21	RCT	.					.	
Roussignol et al (2012)	60	CS				.			
Rubin et al (2001)	118	Review a		.					
Rue et al (2004)	40	RCT	.				.	.	
Rutten et al (2007)	20	RCT	.			.			
Salem et al (2014)	21	RCT	.						
Schofer et al (2010)	101	RCT	.			.			
Schortinghuis et al (2008)	9	RCT	.						
Schortinghuis et al (2005)	8	RCT	.					.	
Strauss et al (1999)	20	RCT			.		.		
Tsumaki et al (2004)	42	RCT	.					.	
Urita et al (2013)	27	RCT	.						
Wang et al (2007)	59	RCT					.		
Watanabe et al (2013)	151	Cohort				.			
Yadav et al (2008)	67	RCT					.		
Zacherl et al (2009)	52	RCT	.						
Zura et al (2015)	767	Registry				.			
No. of studies			26	5	12	13	12	13	2

CS: case series; RCT: randomized controlled trial.a This review contained data from a registry analysis.

Meta-analysis results are summarized in Tables 3 and 4. Variation in results was observed for days to full weight bearing, pain, and radiographic healing. When only trials with low-risk of bias were included, there was no difference between treatment and control groups (see Table 3).

Table 3. Summary of LIPUS Results From the Schandelmaier Meta-Analysis

Outcomes	No. of Trials and Results (95% Confidence Intervals)						Heterogeneity	
	High Risk of Bias		Low Risk of Bias		Total		p	I^2
	n	Results	n	Results	n	Results		
Percent difference in days to return to work	Not reported separately		Not reported separately		3	2.7 (-7.7 to 14.3)	0.76	0%
Percent difference in days to full weight bearing	1	-40.0 (-48.4 to -30.3)	2	4.8 (-4.0 to 14.4)	3	-16.6 (-44.9 to 26.1)	<0.001	95%
Mean difference in pain reduction on 1-100 VAS (follow-up, 4-6 wk)	1	-28.1 (-37.1 to -19.2)	3	-0.9 (-2.5 to 0.6)	4	-6.9 (-15.4 to 1.6)	<0.001	91%
RR of subsequent operations (follow-up, 8 wk to 44 mo)	Not reported separately		Not reported separately		7	0.8 (0.6 to 1.2)	0.67	0%
Percent difference in days to radiographic healing	12	-32.8 (-39.5 to -25.3)	3	-1.7 (-11.2 to 8.8)	15	-27.3 (-34.7 to -19.0)	<0.001	85%
Risk difference in adverse events	Not reported separately		Not reported separately		9	0.0 (-0.0 to 0.03)	0.40	4%

RR: relative risk; VAS: visual analog scale; LIPUS: low-intensity pulsed ultrasound.
Adapted from Schandelmaier et al (2017).[3,]

Table 4. Summary of Findings and Quality of Evidence

	Outcomes	QOE	LIPUS Effect on Outcome
1	Percent difference in days to return to work	Moderate[a]	Probably little or no impact
2	Percent difference in days to full weight bearing	High	No impact
3	Mean difference in pain reduction on 1-100 VAS (follow-up, 4-6 wk)	High	No impact
4	Relative risk of subsequent operations (follow-up, 8 wk to 44 mo)	Moderate[a]	Probably little or no impact
5	Percent difference in days to radiographic healing	Moderate[a]	Probably little or no impact
6	Risk difference in adverse events	High	No impact

Adapted from Schandelmaier et al (2017).[3,]
LIPUS: low-intensity pulsed ultrasound: QOE: quality of evidence: VAS: visual analog scale.
[a] Due to serious imprecision.

Fresh Fractures

Clinical Context and Therapy Purpose

The purpose of LIPUS in patients who have fresh fractures (either surgically managed or non-surgically managed) is to provide an adjunctive treatment option to standard of care.

The question addressed in this evidence review is: Does the use of LIPUS improve net health outcomes in patients with fresh fractures (either surgically or non-surgically managed) compared with standard care without the adjunctive use of LIPUS?

The following PICOTS were used to select literature to inform this review.

Patients
The relevant population of interest are patients with fresh fractures (either surgically or non-surgically managed). A fracture is most commonly defined as fresh for seven days after the fracture occurs.

Interventions
The therapy being considered is LIPUS. LIPUS is believed to alter the molecular and cellular mechanisms involved in each stage of the healing process (inflammation, soft callus formation, hard callus formation, and bone remodeling). The mechanism of action at the cellular level is not precisely known, but it is theorized that LIPUS may stimulate the production or the activities of the following compounds that contribute to the bone healing process: cyclooxygenase-2, collagenase, integrin proteins, calcium, chondroblasts, mesenchymal cells, fibroblasts, and osteoblasts. LIPUS would be an adjunctive therapy following setting and immobilizing the bone. LIPUS is a 20 minute/day self-administered treatment.

Comparators
The comparator is standard fresh fracture management without LIPUS as an adjunctive therapy.

Outcomes
The general outcome of interest is time to healing, which may be measured radiologically and assessed by an orthopedic surgeon. Clinically meaningful measures for healing would involve functional outcomes such as assessment of pain, use of analgesics, the need for secondary procedures, and ability to return to activities of daily living.

Timing
Follow-up should extend for months, the duration of time required for fracture healing.

Setting
The patient takes the LIPUS device home and self-administers the treatment. Recommended time of treatment administration is 20 minutes/day.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies
- Studies with duplicative or overlapping populations were excluded

Systematic Reviews
Lou et al (2017) conducted a meta-analysis focusing on fresh fractures.[5,] The literature search, conducted through November 2016, included 12 studies, all of which were included in the Schandelmaier et al (2017) meta-analysis, except for a small study (n=20) by Strauss et al (1999), which only appeared in a conference abstract.[12,] Studies included patients that had been surgically managed and conservatively managed. Results from the Lou et al(2017) meta-analysis showed that time to fracture union was significantly lower in patients receiving LIPUS than in patients not receiving LIPUS (standard mean difference, -0.65; 95% 95% confidence interval [CI], -1.13 to -0.17). However, subgroup analysis showed that this significant reduction in healing time with LIPUS was seen only among patients conservatively managed, while there was no difference in healing time among patients surgically managed. Reviewers concluded that patients with fresh fractures might benefit from the use of LIPUS but warned that there were methodologic limitations in the trials. Separate analyses using only low-risk of bias trials was not conducted in the Lou et al (2017) meta-analyses.

Surgically Managed

Randomized Controlled Trials

Busse et al (2016) reported on results from a concealed, blinded, sham-controlled, randomized trial (TRUST) evaluating LIPUS for the treatment of patients who underwent intramedullary nailing for fresh tibial fractures.[13] This is the largest RCT to date, enrolling 501 patients; 250 received a LIPUS device, and 251 received a sham device. Treatment was self-administered for 20 minutes a day until there was radiographic evidence of healing. Coprimary endpoints were radiographic healing and return to function (as measured by the 36-Item Short-Form Health Survey Physical Component Summary score). Both radiographic and functional assessments had to show a clinically important effect for the results to be considered positive. All patients, clinicians, investigators, data analysts, and the industry sponsor were blinded to allocation until data analysis was complete. Patient compliance was considered moderate, with 73% of patients administering over half of all recommended treatments. There was no difference in time to radiographic healing between the treatment groups (hazard ratio, 1.07; 95% CI, 0.86 to 1.34; p=0.55). Additionally, there was no difference in the 36-Item Short-Form Health Survey Physical Component Summary scores (mean difference, 0.55; 95% CI, -0.75 to 1.84; p=0.41). A previously conducted pilot double-blind RCT by Busse et al (2014), including 51 subjects not assessed in the 2016 study, also did not find any statistically significant differences in pain reduction, number of subsequent operations, or radiographic healing time.[14]

Tarride et al (2017) provided additional analyses using data from the TRUST trial, comparing health care resource use among patients using LIPUS with patients using the sham device.[15] There were no significant differences between groups (11% in patients receiving LIPUS vs 10% in patients receiving sham) in need for secondary procedures (e.g., removal of lock screw, implant exchange or removal. There were also no statistically significant differences in use of physical therapy (44% vs 46%), use of anticoagulants (42% vs 36%), or use of nonsteroidal anti-inflammatory drugs (28% vs 35%) among patients receiving LIPUS compared with patients receiving sham, respectively.

Emami et al (1999) conducted a double-blind, sham-controlled trial that randomized 32 patients who had a fresh tibial fracture fixed with an intramedullary rod to additional treatment with an active (n=15) or inactive (n=17) LIPUS device.[16] LIPUS treatment began within 3 days of surgery (1 patient began treatment within 7 days of injury) and was self-administered for 20 minutes a day for 75 days. Radiographs were taken every third week until healing. Results showed that LIPUS did not shorten healing time based on any of the following measures: time to first visible callus (mean, 40 days for LIPUS vs 37 days for sham; p=0.44); time to radiographic healing assessed by radiologist (mean, 155 days [median, 113 days] for LIPUS vs mean, 125 days [median, 112 days] for sham; p=0.76); and time to radiographic healing assessed by orthopedic surgeon (mean, 128 days, for LIPUS vs mean, 114 days for sham; p=0.40).

Nonsurgically Managed

Randomized Controlled Trial

Lubbert et al (2008) performed a multicenter, double-blind RCT (n=101) of LIPUS treatment of fresh (<5 days) clavicle shaft fractures.[17] Patients used the LIPUS devices for 20 minutes once daily for 28 days and recorded their subjective feeling as to whether the fracture healed (the primary outcome measure), pain on a visual analog scale, level of daily activities (hours of work, household work, sport), and analgesic use. Patient perception of the day the fracture healed was determined in 92 patients (47 active, 45 placebo); mean time to healing was 26.77 days in the active group and 27.09 days in the placebo group (p=0.91). Between-group differences regarding analgesic use and mean visual analog scale scores for pain also did not differ significantly.

Section Summary: Fresh Fractures

Evidence for the use of LIPUS following fresh fracture includes three RCTs that evaluated patients that were surgically managed and one RCT that evaluated patients that were nonsurgically managed. The RCTs reported no statistically significant differences in radiographic healing,

physical component score of the 36-Item Short-form Health Survey, use of physical therapy, need for secondary procedures, use of nonsteroidal anti-inflammatory drugs, and time to first visible callus.

Fracture Nonunion or Delayed Union Fracture
Clinical Context and Therapy Purpose
The purpose of LIPUS in patients who have fracture nonunion or delayed union fracture is to provide an adjunctive treatment option to standard of care.

The question addressed in this evidence review is: Does the use of LIPUS improve net health outcomes in patients with fracture nonunion or delayed union fracture compared with standard care without the adjunctive use of LIPUS?

The following PICOTS were used to select literature to inform this review.

Patients
The relevant population(s) of interest are patients with fracture nonunion or delayed union fracture. There is not a consensus definition of nonunion or delayed union. In general, these conditions are considered if serial radiographs either do not show progressive healing, or show a decelerating healing process after three months since the fracture occurrence.

Interventions
The therapy being considered is LIPUS. LIPUS is believed to alter the molecular and cellular mechanisms involved in each stage of the healing process (inflammation, soft callus formation, hard callus formation, and bone remodeling). The mechanism of action at the cellular level is not precisely known, but it is theorized that LIPUS may stimulate the production or the activities of the following compounds that contribute to the bone healing process: cyclooxygenase-2, collagenase, integrin proteins, calcium, chondroblasts, mesenchymal cells, fibroblasts, and osteoblasts. LIPUS would be an adjunctive therapy following setting and immobilizing the bone. LIPUS is a 20 minute/day self-administered treatment.

Comparators
The comparator is standard nonunion or delayed union fracture management without LIPUS as an adjunctive therapy.

Outcomes
The general outcome of interest is time to healing, which may be measured radiologically and assessed by an orthopedic surgeon. Clinically meaningful measures for healing would involve functional outcomes such as assessment of pain, use of analgesics, the need for secondary procedures, and ability to return to activities of daily living.

Timing
Follow-up should extend for months, the duration of time required for fracture healing.

Setting
The patient takes the LIPUS device home and self-administers the treatment. Recommended time of treatment administration is 20 minutes/day.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies
- Studies with duplicative or overlapping populations were excluded

Systematic Reviews

The meta-analysis by Seger et al (2017) included 5 studies focused on scaphoid nonunions and analyzed healing index and average time to union following LIPUS.[4] Among 166 cases in the analysis, 78.6% (range, 33%-100%) were reported to show healing following LIPUS, with an average time to union of 4.2 months (range, 2.3-5.6 months). Comparative results were not conducted.

The meta-analysis by Leighton et al (2017) included 13 studies, one of which was an RCT.[6] The date of the literature search was not provided. Quality of the studies was assessed using the Methodological Index for Non-Randomized Studies. Quality scores ranged from 5 to 12 (an "ideal" is 16 for nonrandomized trials). While the pooled estimate of effect size for the healing rate was 82% (95% CI, 77% to 87%), significant heterogeneity was detected (I^2=62). A separate analysis, excluding studies with quality scores of 6 or lower, resulted in a comparable heal rate of 80% (95% CI, 74% to 85%). Because some patients in the analysis were treated conservatively and some underwent surgical interventions, the authors could not recommend LIPUS as a replacement for surgery or as an adjunct to surgery. Reviewers contended that LIPUS might be useful in patients for whom surgery is high-risk.

The systematic review by Schandelmaier et al (2017) included 3 RCTs of nonunion fractures operatively managed. Because all the RCTs were rated at high-risk of bias, the authors could not adequately assess the efficacy of LIPUS for nonunion fractures.[3] Two of the RCTs are discussed below; One is not discussed below because it was published only as a thesis.

Randomized Controlled Trials

Schofer et al (2010), reported on a multicenter, randomized, double-blinded, sham-controlled trial of LIPUS in 101 patients with delayed union of the tibia (Table 5).[18] Delayed union was defined as a lack of clinical and radiologic evidence of union, bony continuity, or bone reaction at the fracture site for no less than 16 weeks from the index injury or the most recent intervention. Roughly one-third of patients had an open fracture. Patients were randomized to LIPUS (n=51) or to an inactive sham device (n=50), to be administered 20 minutes a day for 16 weeks. The primary outcome was change in bone mineral density assessed by computed tomography attenuation coefficients. Gap area was a secondary outcome. Intention-to-treat analysis showed that LIPUS improved mean bone mineral density by 34% (90% CI, 14% to 57%) compared with sham treatment. The mean reduction in bone gap area was -0.13 mm^2 in the LIPUS group and -0.10 mm^2 in the sham group (effect size, -0.47; 95% CI, -0.91 to -0.03 mm^2). At the end of 16 weeks, physicians judged 65% of patients in the LIPUS group healed and 46% of the patients in the sham group healed (p=0.07) (Table 6). This trial did not report functional outcomes or pain assessment, limiting the utility of results.

Ricardo (2006) published a blinded RCT evaluating 21 subjects with scaphoid nonunion who were treated with LIPUS or a sham device following a pedicled vascularized bone graft (Table 5).[19] Time to healing was defined as the number of days from the operation to healing both clinically (solid and not causing tenderness or pain) and radiographically (bridging cortices). Additional outcomes included pain, wrist range of motion, radiographic evidence of union, carpal height index, and scapholunate-capito lunate angles; however, the authors did not report these outcome by treatment arm. The authors reported a statistically significant reduction in time to radiographic healing (-40.4%; 95% CI, -48.7% to -30.8%) with LIPUS (Table 6).

Table 5. Summary of Key RCT Characteristics

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
Schofer (2010)[18]	Germany	6	2002 to 2005	Patients with tibial delayed unions	LIPUS (n=51)	sham device (n=50)
Ricardo (2006)[19]	Cuba	1	1999 to 2004	Patients with scaphoid nonunion fractures treated with pedicled vascularized bone grafts from the distal radius	LIPUS (n=10)	sham device (n=11)

LIPUS: low-intensity pulsed ultrasound; RCT: randomized controlled trial.

Table 6. Summary of Key RCT Results

Study	Healing		p value
	LIPUS	Sham device	
Schofer (2010)[18,]	physician assessed 65% healed	physician assessed 46% healed	0.07
Ricardo (2006)[19,]	56± 3 days	94± 5 days	<0.0001

; RCT: randomized controlled trial; .

The purpose of the gaps tables (see Tables 7 and 8) is to display notable gaps identified in each study. This information is synthesized as a summary of the body of evidence following each table and provides the conclusions on the sufficiency of evidence supporting the position statement.

Table 7. Relevance Gaps

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Schofer (2010)[18,]				2. Primary outcome was bone mineral density and secondary outcome was gap area. Physicians judged patients as healed/not healed, but no description of criteria used by physician	
Ricardo (2006)[19,]					

The evidence gaps stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a]Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
[b]Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest.
[c] Comparator key:1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 8. Study Design and Conduct Gaps

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Schofer (2010)[18,]				1. Dropout rate for LIPUS group was 10% and dropout rate for sham device was 24%		
Ricardo (2006)[19,]	No description of randomization procedure				1. Power calculations not reported and sample size is small (N=21)	4. Only time to healing was compared statistically; additional outcomes (pain, return to activities) were not reported by treatment group

The evidence gaps stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

[a]Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b]Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
[c] Selective Reporting key:1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4.Comparative treatment effects not calculated.

Observational Study
Nolte et al (2016) conducted a retrospective comparison of patients with metatarsal fractures treated by LIPUS and by surgical techniques[20]. For the comparative analysis, patients from a Food and Drug Administration-required LIPUS registry (n=594) were propensity-matched 1:1 with patients treated surgically from a health claims database. The overall heal rates for all types of fractures combined was comparable for LIPUS (97%) and surgery (95%) (p=0.07). A subgroup analysis of patients with delayed or nonunion metatarsal fractures (n=226) also showed comparable rates of healing among the LIPUS group (96%) and the surgery group (96%).

Section Summary: Fracture Nonunion or Delayed Union Fracture
The evidence for LIPUS treatment of fracture nonunion consists only of lower quality and uncontrolled studies. There are 2 meta-analyses (2017) without controlled comparative results. A third meta-analysis, which included all types of fractures, identified three RCTs of patients with nonunion; however, all three trials were considered at high-risk of bias (one published as a thesis).Of the two RCTs, the larger one had primary and secondary outcomes that were physiological assessments, rather than functional measures. It is unclear how healing status was determined in this study, as the outcome was described as "physician-assessed". Limitations of the second published RCT include no description of the randomization process and a small sample size.

Stress Fractures, Osteotomy Sites, or Distraction Osteogenesis
Clinical Context and Therapy Purpose
The purpose of LIPUS in patients who have stress fractures, osteotomy sites or distraction osteogenesis, is to provide an adjunctive treatment option to standard of care.

The question addressed in this evidence review is: Does the use of LIPUS improve net health outcomes in patients with stress fractures, osteotomy sites, or distraction osteogenesis compared with standard care without the adjunctive use of LIPUS?

The following PICOTS were used to select literature to inform this review.

Patients
The population of interest consists of patients with stress fractures, osteotomy sites, or distraction osteogenesis.

Interventions
The therapy being considered is LIPUS. LIPUS is believed to alter the molecular and cellular mechanisms involved in each stage of the healing process (inflammation, soft callus formation, hard callus formation, and bone remodeling). The mechanism of action at the cellular level is not precisely known, but it is theorized that LIPUS may stimulate the production or the activities of the following compounds that contribute to the bone healing process: cyclooxygenase-2, collagenase, integrin proteins, calcium, chondroblasts, mesenchymal cells, fibroblasts, and

osteoblasts. LIPUS would be an adjunctive therapy following setting and immobilizing the bone. LIPUS is a 20 minute/day self-administered treatment.

Comparators
The comparator is standard stress fracture, osteotomy sites, or distraction osteogenesis management without LIPUS as an adjunctive therapy.

Outcomes
The general outcome of interest is time to healing, which may be measured radiologically and assessed by an orthopedic surgeon. Clinically meaningful measures for healing would involve functional outcomes such as assessment of pain, use of analgesics, the need for secondary procedures, and ability to return to activities of daily living.

Timing
Follow-up should extend for months, the duration of time required for fracture healing.

Setting
The patient takes the LIPUS device home and self-administers the treatment. Recommended time of treatment administration is 20 minutes/day.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies
- Studies with duplicative or overlapping populations were excluded

Stress Fractures
Rue et al (2004) reported on a double-blind RCT that examined the effects of 20 minutes of daily LIPUS on tibial stress fracture healing outcomes such as pain, function, and resumption of professional and personal activities in 26 military recruits.[21] The delay from onset of symptoms to diagnosis was 32 days in the LIPUS group and 28 days in the placebo group. This trial found no significant difference in healing times between LIPUS treatment and sham, with a mean time of return to duty of 56 days for both groups. The trial was rated with a high-risk of bias in the Schandelmaier (2017) meta-analysis.[3]

Osteotomy Sites
Urita et al (2013) published a small (n=27) quasi-randomized study (alternating assignment) of LIPUS after ulnar-shortening osteotomy for ulnar impaction syndrome or radial-shortening osteotomy for Kienböck disease.[22] Patients in the LIPUS group received a daily 20-minute treatment for at least 12 weeks postoperatively. Blinded evaluation of radiographic healing showed that LIPUS reduced the mean time to the cortical union by 27% (57 days vs 76 days) and endosteal union by 18% (121 days vs 148 days) compared with sham treatment. At the time of endosteal healing, the osteotomy plus LIPUS group and the osteotomy-only group had similar results, as measured using the Modified Mayo Wrist Score and no pain at the osteotomy site. The study was rated at high-risk of bias in the meta-analysis by Schandelmaier.[3]

Distraction Osteogenesis
The Schandelmaier systematic review also included six trials of LIPUS for distraction osteogenesis following surgery. Four of six studies were rated at high-risk of bias.[3] Four studies were in the tibia,[10,11] No clinically meaningful results were reported for the mandible studies in the meta-analysis.[3] The remaining studies in the tibia were all unblinded. No statistically significant difference was noted in subsequent operations (relative risk, 0.63; 95% CI 0.13 to 2.99) in the meta-analysis.[3] Four of the studies[23,24,25,26] were included in the meta-analysis[3] for time to radiographic healing with mixed results, three not reporting statistically significant results.

Lou et al (2018) conducted a systematic review and meta-analysis on the use of LIPUS for the treatment of patients with distraction osteogenesis.[27,] The literature search, conducted in May 2018, identified 7 RCTs (172 patients) for inclusion. The Cochrane risk of bias tool was used to assess trial quality. Three of the trials were considered low-risk of bias and four were considered to have high-risk of bias. Main limitations in the trials were related to the lack of treatment allocation details and outcome assessors knowledge of treatment. Pooled results did not find statistically significant differences in: treatment time, radiological gap fill area, histological gap fill length, or bone density.

Section Summary: Stress Fractures, Osteotomy Sites, or Distraction Osteogenesis
The evidence for LIPUS treatment of stress fractures, osteotomy sites, or distraction osteogenesis consists only of lower quality RCTs and were all rated to have a high-risk of bias. Results do not generally include functional outcomes and results across various outcomes, primarily including time to radiographic healing, are inconsistent. A meta-analysis of three trials on the use of LIPUS for patients with distraction osteogenesis reported no statistically significant differences in treatment time, gap fill, or bone density.

Summary of Evidence
For individuals who have fresh fractures (surgically or nonsurgically managed) who receive LIPUS as an adjunct to routine care, the evidence includes RCTs and several meta-analyses. The relevant outcomes are symptoms, morbid events, functional outcomes, and QOL. The evidence base has recently evolved with the publication of a large RCT and meta-analysis significantly shifting the weight of the evidence. Conclusions based on several earlier and small RCTs, rated at high-risk of bias, showed a potential benefit of LIPUS; however, the large RCT published in 2016, rated at low-risk of bias, showed no benefit. A 2017 meta-analysis including only trials with low-risk of bias found no difference in days to full weight bearing, pain reduction, or days to radiographic healing. Similarly, the overall results of the meta-analysis found no significant difference in return to work, subsequent operations, or adverse events. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have fracture nonunion or delayed union fracture who receive LIPUS as an adjunct to routine care including surgery, if appropriate, the evidence includes only lower quality studies consisting of a small systematic review in scaphoid nonunions, a meta-analysis of nonunion in various locations, two low-quality RCTs, and one observational comparative study. The relevant outcomes are symptoms, morbid events, functional outcomes, and QOL. Of the two RCTs, one did not include functional outcomes. The second RCT had a small sample size and did not describe the randomization procedure. The observational study reported similar healing rates with LIPUS and surgery, though the retrospective nature of the study, limits meaningful interpretation of these results. Additionally, the evidence base on the use of LIPUS in the management of fresh fractures has evolved as described above, and there is no demonstrated physiologic mechanism suggesting differential results of LIPUS in fracture nonunion or delayed union. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have stress fractures, osteotomy sites, or distraction osteogenesis who receive LIPUS as an adjunct to routine care, the evidence includes only lower quality studies consisting of small RCTs and one meta-analysis for distraction osteogenesis. The relevant outcomes are symptoms, morbid events, functional outcomes, and QOL. Results do not generally include functional outcomes and results across various outcomes, primarily time to radiographic healing, are inconsistent. The meta-analysis of three trials using LIPUS for distraction osteogenesis reported no statistically significant differences in physiological or functional outcomes. Additionally, the evidence base on the use of LIPUS in the management of fresh fractures has evolved as described above and there is no demonstrated physiologic mechanism suggesting differential results of LIPUS in stress fractures, osteotomy sites, or distraction osteogenesis. The evidence is insufficient to determine the effects of the technology on health outcomes.

Supplemental Information

Clinical Input from Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

2012 Input

In response to requests from Blue Cross Blue Shield Association, input was received from 4 academic medical centers in 2012. Input supported the use of low-intensity pulsed ultrasound for delayed unions and nonunions of bones excluding the skull and vertebra, and in fresh closed fractures at high-risk for delayed fracture healing or nonunion. Commentators agreed that other applications of low-intensity pulsed ultrasound treatment are investigational, including, but not limited to, treatment of congenital pseudoarthrosis, open fractures, stress fractures, arthrodesis, or failed arthrodesis. Additional risk factors were noted, including use of anticoagulants, immunosuppressive drugs or chemotherapy, infection at the fracture site, severe anemia, obesity, and fracture locations more prone to nonunion such as tibial and distal radial fractures.

2011 Input

In response to requests from Blue Cross Blue Shield Association, input was received from 2 physician specialty societies and 1 academic medical center in 2011. Input supported the use of ultrasound for nonunion and for fresh closed fractures at high-risk for delayed fracture healing or nonunion as described in the policy. One reviewer supported including chemotherapy, immunosuppressive agents, history of infection, Charcot neuroarthropathy, and fractures of the tibial shaft or clavicle as additional risk factors, and another supported including fractures of the talus and sesamoids as additional risk factors.

2008 Input

In response to requests from Blue Cross Blue Shield Association, input was received from 1 physician specialty society in 2008. Input obtained through the American Academy of Orthopaedic Surgeons supported the positions on the criteria for medical necessity and the conditions considered investigational (e.g., delayed union and open/unstable grade II or III fractures).

Practice Guidelines and Position Statements

British Medical Journal Rapid Recommendation

The BMJ Rapid Recommendations are a series of articles, produced by BMJ in collaboration with the MAGIC group,[28] to provide clinicians with practice guidelines. BMJ Rapid Recommendations (2017) published guidelines on the use of low-intensity pulsed ultrasound (LIPUS) for bone healing.[29] The guidelines were based on a 2017 systematic review, which included 26 randomized controlled trials evaluating patients with fresh fractures not surgically managed, fresh fractures surgically managed, nonunion fractures, osteotomy, and distraction osteogenesis.[3] The committee concluded that there is "moderate to high certainty evidence to support a strong recommendation against the use of LIPUS for bone healing." Furthermore, the guideline expert panel discussed whether the results of higher quality studies in patients with fresh fractures reported in Schandelmaier et al (2017) would apply to other types of fractures including nonunions and osteotomies.[3] "After extensive deliberations, the panel found no compelling anatomical or physiological reasons why LIPUS would probably be beneficial in these other patient populations."[29]

National Institute for Health and Care Excellence

The NICE (2018) published a guidance on the use of LIPUS to promote healing of fresh fractures at low-risk of non-healing.[30] The guidance states that the "current evidence does not show efficacy. Therefore, this procedure should not be used for this indication."

The NICE (2018) published a guidance on the use of LIPUS to promote healing of fresh fractures at high-risk of non-healing.[31] The guidance states that the "current evidence on efficacy is very limited in quantity and quality. Therefore, this procedure should only be used in the context of research.

The NICE (2018) published a guidance on the use of LIPUS to promote healing of delayed and nonunion fractures.[32] The guidance states that the "current evidence on efficacy is inadequate in quality. Therefore, this procedure should only be used with special arrangements for clinical governances, consent and audit or research."

The NICE (2013) published guidance on Exogen for the treatment of long-bone fractures with nonunion and delayed fracture healing.[33] The NICE concluded that use of the Exogen bone healing system to treat long-bone fractures with nonunion is supported by "clinical evidence" and "cost savings … through avoiding surgery." For long-bone fractures with delayed healing, defined as no radiologic evidence of healing after three months, there was "some radiologic evidence of improved healing." However, due to "substantial uncertainties about the rate at which bone healing progresses without adjunctive treatment between 3 and 9 months after fracture" and need for surgery, "cost consequences" were uncertain. The next review of this guidance is in 2018.

American Academy of Orthopaedic Surgeons

The American Academy of Orthopaedic Surgeons (2009) published guidelines on the treatment of distal radius fractures.[34] The Academy issued a limited recommendation for the use of LIPUS for adjuvant treatment of distal radius fractures. While evidence from one study demonstrated an increased rate of healing (measured by the absence of pain and radiographic union), the additional cost of LIPUS resulted in a "limited" recommendation.

U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

Effective 2001, ultrasonic osteogenic stimulators were covered as medically reasonable and necessary for the treatment of nonunion fractures.[35] Nonunion fractures of the skull, vertebrae, and those that are tumor-related are excluded from coverage. Ultrasonic osteogenic stimulators may not be used concurrently with other noninvasive osteogenic devices. Ultrasonic osteogenic stimulators for fresh fractures and delayed unions are not covered.

Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this review are listed in Table 9.

Table 9. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT02383160[a]	A Randomized Controlled Trial Comparing Low-Intensity, Pulsed Ultrasound to Placebo in the Treatment of Operatively Managed Scaphoid Non-unions	154	Dec 2018 unknown status
NCT03382483[a]	Observational, Non-Interventional use of LIPUS to Mitigate Fracture Non-Union in Patients at Risk (BONES)	3000	Dec 2019

NCT: national clinical trial. [a] denotes an industry-sponsored trial

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Documentation for Clinical Review

Please provide the following documentation (if/when requested):

- History and physical and/or consultation notes including:
  - Date of original injury
  - Initial and serial radiologic findings
  - Past medical/surgical treatment and response
  - Reason for request
  - Treatment plan

Post Service

- Operative report(s) if applicable

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms of the Policy. Inclusion or exclusion of codes does not constitute or imply member coverage or provider reimbursement.

NMN
The following services may be considered not medically necessary.

Type	Code	Description
CPT®	20979	Low intensity ultrasound stimulation to aid bone healing, noninvasive (nonoperative)
HCPCS	E0760	Osteogenesis stimulator, low intensity ultrasound, noninvasive
ICD-10 Procedure	None	

Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

Effective Date	Action	Reason
06/05/1996	New Policy Adoption	Medical Policy Committee
02/23/2000	Policy Revision	Medical Policy Committee
11/15/2001	Policy Revision Modification based on external reviews	Administrative Review
12/07/2006	Policy Revision - BCBSA MPP	Medical Policy Committee
01/11/2008	Policy Revision Defined criteria for medical necessity treatment of fresh, closed fractures, fusions, delayed unions, and nonunions of the appendicular skeleton based on peer reviewed literature research	Medical Policy Committee
03/17/2008	Policy Revision Added the following: nonunions to the policy statement (as intended to be included), axial to skeleton regarding not medically necessary, axial to skeleton for investigational section, definition of axial skeleton to the definitions section, nonunions to the Policy history statement of revision	Medical Policy Committee
04/01/2011	Policy title change from Ultrasound Accelerated Fracture Healing Device and alignment with BCBSA policy	Medical Policy Committee
01/11/2013	Policy revision with position change	Medical Policy Committee
07/31/2015	Policy title change from Ultrasound Bone Growth Stimulation Policy revision without position change	Medical Policy Committee
11/01/2016	Policy revision without position change	Medical Policy Committee
11/01/2017	Policy revision with position change	Medical Policy Committee
05/01/2018	Policy revision without position change	Medical Policy Committee

Effective Date	Action	Reason
05/01/2019	Policy revision without position change	Medical Policy Committee

Definitions of Decision Determinations

Medically Necessary: A treatment, procedure, or drug is medically necessary only when it has been established as safe and effective for the particular symptoms or diagnosis, is not investigational or experimental, is not being provided primarily for the convenience of the patient or the provider, and is provided at the most appropriate level to treat the condition.

Investigational/Experimental: A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

Split Evaluation: Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

Prior Authorization Requirements (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department. Please call (800) 541-6652 or visit the provider portal at www.blueshieldca.com/provider.

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.