Medical Policy

Blue Cross Blue Shield Blue Care Network of Michigan

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***Current Policy Effective Date: 5/1/22**
(See policy history boxes for previous effective dates)

Title: Bone Growth Stimulation: Ultrasound Accelerated Fracture Healing Device

Description/Background

Low-intensity pulsed ultrasound has been investigated as a technique to accelerate healing of fresh fractures, delayed unions, and nonunions. Ultrasound is delivered with the use of a transducer applied to the skin surface overlying the fracture site.

Most bone fractures heal spontaneously over the course of several months following injury. However, approximately 5% to 10% of all fractures have delayed healing, resulting in continued morbidity and increased utilization of health care services. Ultrasound (US) may accelerate healing of fractures by stimulating new bone growth, and therefore, has been proposed as a treatment for fractures with delayed healing or at high risk for nonhealing.

The current policy does not limit the use of the device to specific fracture sites. Depending on their function, bones are composed of a varying combination of cortical and trabecular bone. However, at the cellular level, the type of bone cannot be distinguished histologically. The inclusion of all bones regardless of the anatomic site is based on this histologic similarity of all bones; it is not anticipated that the efficacy of US-accelerated healing would vary according to the anatomic site and function of the bone.

The definition of a fracture nonunion has remained controversial. For electrical bone growth stimulators (see Policy *Bone Growth Stimulation: Electrical Bone Growth Stimulation of the Appendicular Skeleton*), the U.S. Food and Drug Administration (FDA) labeling defined nonunion as follows: “A nonunion is considered to be established when a minimum of 9 months has elapsed since injury and the fracture site shows no visibly progressive signs of healing for minimum of 3 months.” Others have contended that 9 months represents an arbitrary cutoff point that does not reflect the complicated variables that are present in fractures, i.e., degree of soft tissue damage, alignment of the bone fragments, vascularity, and quality of the underlying bone stock. Other proposed definitions of nonunion involve 3 to 6

months' time from original healing, or simply when serial x-rays fail to show any further healing. According to the FDA labeling for a low-intensity pulsed ultrasound device, "a nonunion is considered to be established when the fracture site shows no visibly progressive signs of healing."

Delayed union is generally considered a failure to heal between 3 and 9 months after fracture, after which the fracture site would be considered a nonunion. 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.) Together, delayed union and nonunion are sometimes referred to as "ununited fractures." To determine the status of fracture healing, it is important to include both radiographic and clinical criteria. Clinical criteria include the lack of ability to bear weight, fracture pain, and tenderness on palpation.

Ultrasound treatment can be self-administered with 1 daily 20-minute treatment, continuing until the fracture has healed. The mechanism of action at the cellular level is not precisely known but is thought to be related to a mechanical effect on cell micromotion/deformation, causing an increase in stimulation of transmembrane cell adhesion molecules and upregulation of cyclooxygenase-2.

Regulatory Status

The Sonic Accelerated Fracture Healing System, SAFHS® (also referred to as Exogen 2000®) was initially cleared for marketing by the U.S. Food and Drug Administration (FDA) in October 1994 as a 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. FDA product code: LPQ.

Medical Policy Statement

The safety and effectiveness of low-intensity ultrasound treatment for the treatment of specified fractures have been established. It is useful therapeutic option for patients at high risk for delayed fracture healing or nonunion.

Inclusionary and Exclusionary Guidelines (Clinically based guidelines that may support individual consideration and pre-authorization decisions)

Inclusions:

- Low-intensity ultrasound treatment may be considered established when used as an adjunct to conventional management (i.e., closed reduction and cast immobilization) for the treatment of fresh, closed fractures in skeletally mature individuals. A fracture is most commonly defined as "fresh" for 7 days after the fracture occurs. Candidates for ultrasound treatment are those at high risk for delayed fracture healing or nonunion. These risk factors may include either locations of fractures or patient comorbidities and include the following:

Patient comorbidities:
- Diabetes
- Steroid therapy
- Osteoporosis
- Autoimmune disease
- Chemotherapy
- History of alcoholism
- History of smoking

Fracture locations:
- Jones fracture (fracture in the meta-diaphyseal junction of the fifth metatarsal of the foot)
- Fracture of navicular bone in the wrist (also called the scaphoid)
- Closed fractures of the distal radius (Colles fracture)
- Closed or grade I open, tibial diaphyseal fractures
- Fracture of metatarsal
- Fractures associated with extensive soft tissue or vascular damage

- Low-intensity ultrasound treatment may be considered established when used as a treatment of delayed union of bones, excluding the skull and vertebra. Delayed union is defined as a decelerating healing process as determined by serial x-rays, 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.
- Low intensity ultrasound treatment may be considered established for nonunions of the appendicular skeleton (non-skull or vertebrae) if there has been no x-ray evidence of progression of healing for 3 or more months despite appropriate fracture care, and the following criteria are met:
  - Bone is noninfected; and
  - Bone is stable on both ends by means of cast or fixation; and
  - The two portions of the involved bone are separated by less than 1cm
  - Nonunion is not related/secondary to malignancy

Exclusions:
Other applications of low-intensity ultrasound treatment are experimental/investigational, including, but not limited to, treatment of
- Congenital pseudarthroses
- Open fractures
- Fresh surgically treated closed fractures in patients who are not at high risk for delayed fracture healing or nonunion stress fractures
- Stress fractures
- Arthrodesis
- Failed arthrodesis.

CPT/HCPCS Level II Codes *(Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure.)*

Established codes:

20979 E0760

Other codes (investigational, not medically necessary, etc.):

N/A

Rationale

Fresh Fractures

The policy regarding fresh fractures is based in part on a 1995 TEC Assessment that concluded that ultrasound fracture healing met the TEC criteria for the indications labeled by the U.S. Food and Drug Administration (FDA) as a treatment of closed, fresh fractures of the tibial or distal radius (i.e., Colles) fractures.[7] Since the TEC Assessment, there have been numerous randomized controlled trials (RCTs) and systematic reviews of clinical trials on the use of ultrasound to improve healing in fresh fractures.

Systematic Reviews

A 2002 meta-analysis conducted by Busse and colleagues[8] supported the use of low-intensity ultrasound as a technique for fractures treated nonoperatively. This systematic review was updated in 2009 and included RCTs of low-intensity pulsed ultrasonography for any type of fracture.[9] Thirteen trials were included; in 5 of them, patients were managed conservatively, and in 8 studies, patients had ultrasound therapy after operative management (distraction osteogenesis in 3 studies, bone graft for nonunion in 1, and operative treatment of fresh fractures in 4). US therapy significantly accelerated radiographic healing of fractures in all 3 RCTs of conservatively managed fresh fractures that assessed this outcome. (These trials are described in more detail next.)

The trials of operatively managed (open) fresh fractures outcomes were inconsistent; 4 trials provided low-quality evidence for acceleration of healing by US therapy. Pooled results of 2 trials showed a nonsignificant mean reduction in radiographic healing time of 16.6%.

A 2014 update of a Cochrane review on US and shockwave therapy included 12 studies on US; 8 of the studies were RCTs with placebo controls, 2 were RCTs without placebo controls, and 2 were quasi-randomized.[10,11] The included studies were limited in methodologic quality, with all having some evidence of bias. There was very limited evidence on functional outcomes. Pooling results from 8 studies (446 fractures) showed no significant reduction in time to union of complete fractures. This systematic review included studies of conservatively managed fractures along with surgically treated fractures and stress fractures. Subgroup analysis comparing conservatively and operatively treated fractures raised the possibility that pulsed US may be effective in reducing healing time in conservatively managed fractures, but a test for subgroup differences did not confirm a significant difference between the subgroups. The review concluded that while a potential benefit of US for acute fractures could not be ruled out, the currently available evidence was insufficient to support its routine use.

In a 2017 systematic review, Schandelmaier et al tried to determine the efficacy of LIPUS for healing of fracture or osteotomy.[14] RCTs of LIPUS compared with sham devices or no device in patients with any kind of fracture or osteotomy were reviewed. The authors included 26 randomized controlled trials with a median sample size of 30 (range 8-501). The most trustworthy evidence came from four trials at low risk of bias that included patients with tibia or clavicle fractures. Compared with control, LIPUS did not reduce time to return to work (percentage difference: 2.7% later with LIPUS, 95% confidence interval 7.7% earlier to 14.3% later; moderate certainty) or the number of subsequent operations (risk ratio 0.80, 95%

confidence interval 0.55 to 1.16; moderate certainty). For pain, days to weight bearing, and radiographic healing, effects varied substantially among studies. For all three outcomes, trials at low risk of bias failed to show a benefit with LIPUS, while trials at high risk of bias suggested a benefit (interaction P<0.001). When only trials at low risk of bias trials were considered, LIPUS did not reduce days to weight bearing (4.8% later, 4.0% earlier to 14.4% later; high certainty), pain at four to six weeks (mean difference on 0-100 visual analogue scale: 0.93 lower, 2.51 lower to 0.64 higher; high certainty), and days to radiographic healing (1.7% earlier, 11.2% earlier to 8.8% later; moderate certainty). Based on moderate to high quality evidence from studies in patients with fresh fracture, LIPUS may not improve outcomes important to patients. The applicability to other types of fracture or osteotomy is uncertain.

Seger et al (2017) performed a meta-analysis of relevant literature to determine success of the use of LIPUS for treatment of scaphoid nonunion.[15] A total of 686 studies met initial search criteria. Studies reporting fewer than 5 cases, those not published in English, those not related to LIPUS nonoperative scaphoid nonunion treatment, and those without sufficient data were excluded. Five studies met these criteria, and statistical analysis was performed to determine overall union rates. The use of LIPUS on 166 nonunions reported a mean healing index of 78.6%. The average time to union following LIPUS treatment was 4.2 months. The authors concluded that while surgical intervention is still the standard, the results show that LIPUS may serve as a nonoperative alternative to scaphoid nonunion in certain cases. The results are encouraging in which these challenging fracture and nonunions can heal without further surgical intervention in the majority of patients.

Lou et al (2017) conducted a meta-analysis to assess the effect of LIPUS for fresh fractures in adults.[16] A total of 12 trials with 1099 patients were included. The pooled results showed that LIPUS significantly reduced the time to fracture union (SMD: 0.65, 95% CI: 1.13 to 0.17), improved the quality of life (SMD: 0.20, 95% CI: 0.03-0.37) without affecting the time to full weight bearing (SMD: 0.76, 95% CI: 1.92 to 0.4), the time to return to work (SMD: 0.06, 95% CI: 0.14 to 0.27), or the incidence rate of delayed union and nonunion (RR: 1.02, 95% CI: 0.60-1.74). The authors found moderate-to-high quality evidence showing that LIPUS treatment reduces the time to fracture union and improves the quality of life without affecting functional recovery and incident rate of delayed union and nonunion, suggesting that LIPUS treatment may be a good treatment modality for adults with fresh fractures. However, there are some methodological limitations in the eligible trials, further studies are needed to determine the clinical circumstances under which LIPUS is truly valid and to examine the optimal approach for the use of this adjunctive therapy.

Leighton et al (2017) presented a systematic review and meta-analysis of published papers describing nonunions treated with LIPUS.[17] Thirteen eligible papers reporting LIPUS treatment of 1441 nonunions were evaluated. The pooled estimate of effect size for heal rate was 82% (95% CI: 77-87%), for any anatomical site and fracture age of at least 3 months, with statistical heterogeneity detected across all primary studies (Q=41.2 (df=12), p<0.001, Tau =0.006, I =71). With a stricter definition of nonunion as fracture age of at least 8 months duration, the pooled estimate of effect size was 84% (95% CI: 77%-91.6%; heterogeneity present: Q=21 (df=8), p<0.001, Tau =0.007, I =62). Hypertrophic nonunions benefitted more than biologically inactive atrophic nonunions. An interval without surgery of <6months prior to LIPUS was associated with a more favorable result. Stratification of nonunions by anatomical site revealed no statistically significant differences between upper and lower extremity long

bone nonunions. The authors concluded that LIPUS treatment can be an alternative to surgery for established nonunions. Given that no spontaneous healing of established nonunions is expected, and that it is challenging to test the efficacy of LIPUS for nonunion by randomized clinical trial, findings are compelling. LIPUS may be most useful in patients for whom surgery is high risk, including elderly patients at risk of delirium, or patients with dementia, extreme hypertension, extensive soft-tissue trauma, mechanical ventilation, metabolic acidosis, multiple organ failure, or coma. With an overall average success rate for LIPUS >80% this is comparable to the success of surgical treatment of non-infected nonunions.

RCTs of Closed Fractures

In a 1997 multicenter RCT by Kristiansen et al., 60 patients with dorsally angulated fractures of the distal radius treated with manipulation and cast were randomly assigned to 10 weeks of daily treatment with a pulsed US device or an inactive device.[2] All patients started US within 7 days after having sustained the fracture. Blinded radiographic and clinical examinations showed faster healing in the US group (61 days) than in the control group (98 days) ($p<0.001$). Each radiographic stage of healing also was significantly accelerated in the treatment group.

Heckman et al (1994) performed a double-blind RCT comparing US treatment (n=33) with a placebo-control device (n=34) in closed or grade-I open fractures of the tibial shaft.[1] Treatment was started within 7 days after the fracture and consisted of one 20-minute period each day. Time-to-healing was 86 days in the treatment group versus 114 days in the control group ($p=0.01$), and time to overall (clinical and radiographic) healing was 96 days in the active-treatment group compared to 154 days in the control group ($p=0.0001$). Scaphoid fractures were treated with ultrasound in a study done in Germany.[5] (5) Fifteen patients were randomly assigned to treatment and 15 to placebo device groups. Healing was assessed by computed tomography (CT) scans every 2 weeks. Fractures treated with US healed in 43.2 days versus 62 days in the control group ($p<0.01$). Pooled data from these studies demonstrated a mean reduction in radiographic healing time of 36.9% (95% CI: 25.6% to 46.0%).

Lubbert et al (2008) performed a multicenter double-blind RCT of US treatment of fresh (<5 days) clavicle shaft fractures.[4] Patients were taught to use US devices for 20 minutes each day for 28 days and to record daily their subjective feeling as to whether the fracture healed (the primary outcome measure), pain on visual analog scale (VAS), level of daily activities once a day expressed as hours of activity (work, household work, sport), and analgesic use. A total of 120 patients (61 active, 59 placebo) started study treatment. Nine patients in the active group and 10 in the placebo group were excluded from analysis because of incomplete follow-up or early withdrawal from the study. The day that the fracture clinically healed according to patient perception was determined in 92 patients (47 active, 45 placebo); mean duration of time to clinical healing was 26.77 days in the active group versus 27.09 days in the placebo group. Between-group differences in analgesic use and mean VAS were not significant.

RCTs of Open Fractures and Surgically Treated Closed Fractures

For the treatment of open fractures, the data are conflicting regarding the efficacy of ultrasonic accelerated fracture healing system (UAFHS), specifically those treated surgically with placement of an intramedullary nail. For example, Emami et al (1999) randomly assigned 32 patients with a fresh tibial fracture that was fixed with an intramedullary rod to undergo additional treatment with an active or inactive US device.[3] US treatment began within 3 days of surgery, and with 1 exception, within 7 days of injury. Time-to-healing was not significantly different in the two groups, and the authors concluded that there was no benefit in operatively treated fractures. In contrast, Leung et al (2004) randomly assigned 30 fractures in 28 patients

with complex tibial fractures treated with internal or external fixation to receive or not receive additional treatment with low-intensity US.[12] US treatment was begun when the patient's condition had stabilized, and the open wound was covered with simple closure or skin grafts. The duration of tenderness, time to weight bearing, and time to callus formation were significantly less in those in the US group. Due to the inconsistent results in the two small randomized trials, and the negative results of the meta-analysis, low-intensity US is considered investigational for open fractures.

In 2011 Dijkman et al reported data from a substudy of 51 patients of a larger RCTs that enrolled patients with open or closed tibial shaft fractures that were treated surgically with an intramedullary nail.[13]

Section Summary
There is some RCT evidence that US treatment improves radiographic healing for closed fresh fractures, but this finding is not consistent for studies of open fresh fractures. A 2009 systematic review and meta-analysis of RCTs found moderate- to very low-quality evidence for low-intensity pulsed ultrasonography in accelerating functional recovery among patients with fracture. The systematic review concluded that large trials of high methodologic quality focusing on patient important outcomes such as quality of life and return to function are needed to determine whether ultrasound fracture healing devices provide important benefits to patients. A 2014 Cochrane review that did not distinguish between closed and open fractures reported that there is a possibility that pulsed US may be effective in reducing healing time in conservatively managed fractures, but that currently available evidence was insufficient to support its routine use.

Nonunions
The policy regarding nonunion of fractures is based on data presented to the FDA as part of the approval process for Sonic Accelerated Fracture Healing System (SAFHS®) as a treatment of fracture nonunions. The following data were reported and are included in the package insert for the device[18] :

- Data were collected on 74 cases of established nonunion with a mean fracture age of nearly 3 years. The principal outcome measure was the percentage of patients with healed nonunions, as determined clinically and by radiographic analysis. Each case served as its own control, based on the definition of nonunion that suggests that nonunions have a 0% probability of achieving a healed state without an intervention.
- A total of 64 of 74 cases (86%) were healed with use of low-intensity ultrasound. The time-to-healing was 173 days. The healed rate of scaphoid bones was lower, at 33% (2 of 6 cases), which was partially responsible for a significant difference between the healing rates of long bones (92%) versus other bones (67%).
- Fracture age also affected healing rates, with fractures over 5 years-old having a healing rate of 50% compared to a healing rate of 95% in those present for no more than 1 year.

A 2007 study by Rutten et al used prospectively defined criteria for analysis of all Dutch patients (96 participating clinics) who had been treated with ultrasound for established nonunion of the tibia (characterized by a total stop of all fracture repair processes).[19] Included in the analysis were 71 patients who were at least 3 months from the last surgical intervention and did not show any healing improvements in the 3 months before ultrasound treatment (average fracture age: 257 days; range: 180–781 days). All patients were followed up (average 2.7 years) by questionnaire, or by phone, if needed. There was an overall healing rate of 73%,

at an average 184 days to healing (range: 52–739 days). No difference in healing rate for open or closed fractures was observed.

Majeed et al (2019) prospectively reviewed the clinical and patient-reported outcomes of patients treated with LIPUS following post-traumatic and post-surgical nonunions in the foot and ankle.[31] Forty-seven consecutive patients underwent Exogen treatment. Patient-reported outcome scores included MOXFQ, EQ-5D and VAS. Patients were divided in to 3 groups: fractures (A), hindfoot procedures (B) and midfoot/forefoot procedures (C). Thirty-seven patients (78.7%) clinically united, 4 patients (8.5%) noticed no significant improvement but did not want further intervention and 6 patients (12.8%) underwent revision surgery. The mean duration of Exogen treatment was 6 months. Union rates of 93%, 67% and 78% were noted in the three groups. Significant improvement in functional outcomes and potential cost savings were observed.

Delayed Union

In 2010, Schofer et al reported an industry-sponsored, multicenter, randomized, double-blinded, sham-controlled trial of low-intensity pulsed US in 101 patients with delayed union of the tibia.[20] Delayed union was defined as 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 the patients had an open fracture. Fifty-one patients were randomized to daily treatment with ultrasound, and 50 were assigned to an inactive sham device (20 minutes daily for 16 weeks). The primary outcome measure was the change in bone mineral density (BMD) over the 16 weeks, assessed by computed tomography (CT) attenuation coefficients, or Hounsfield units (Hus). Gap area at the fracture site was a secondary endpoint. The primary analysis was intention-to-treat with imputation of missing values (24% of sham-treated subjects and 9.8% of active-treated subjects were missing post-treatment values). The mean improvement in BMD was 1.34 (90% CI: 1.14 to 1.57) times greater for ultrasound-treated subjects compared to sham. Analysis of ‘completers’ showed a medium effect size (0.53) of the treatment. A mean reduction in bone gap area also favored ultrasound treatment, with a mean change of log gap area of -0.131 mm2 for the active treatment and -0.097 mm^2 for sham (effect size of -0.47, 95% CI: -0.91 to -0.03). Untransformed data showed a difference between groups of -0.457 mm2 (90% CI: -0.864 to -0.049), which was statistically significant by a 1-sided test. The clinical significance of this difference is unclear. There was a trend (p=0.07) for more subjects receiving low-intensity pulsed ultrasound to be judged to be healed by the participating physicians by the end of the 16-week study period, 65% (33 of 51) of ultrasound versus 46% (23 of 50) sham subjects. While there was not a statistically significant improvement in the rate of healing, the improvements in intermediate outcomes and the corroborating evidence from trials of patients with similar indications, e.g., fracture nonunion, make it very likely that this treatment is efficacious for delayed union.

Stress Fractures

Rue et al (2004) examined the effect of 20-minute daily low-intensity pulsed US on tibial stress fracture healing issues 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 US group and 28 days in the placebo group. Pulsed US did not significantly reduce the healing time for the tibial stress fractures; the time to return to duty was 56 days in each group.

Osteotomy Sites

In 2013, Urita et al published a small (N=27) quasi-randomized study (alternating assignment) of low-intensity pulsed US after ulnar shortening osteotomy for ulnar impaction syndrome or radial shortening osteotomy for Kienbock disease.[22] Patients in the US group received once-daily 20-minute US treatments for at least 12 weeks postoperatively. Blinded evaluation of radiographic healing showed that US reduced the mean time to cortical union by 27% (57 vs. 76 days) and endosteal union by 18% (121 vs. 148 days). At the time of endosteal healing (mean, 121 or 148 days), the two groups had similar results on the Modified Mayo Wrist Score and no pain at the osteotomy site. Limitations of this study include the lack of a sham control and the long interval between the 16 and 24-week assessments, which may have increased group differences. In addition, clinical outcomes appear to have been assessed only at the time of radiographic healing and did not show any differences at this time point. Additional study is needed to determine with greater certainty the effect of low-intensity pulsed US on healing of osteotomy sites.

Distraction Osteogenesis

The 2009 systematic review by Busse et al found 3 trials of distraction osteogenesis that used a variety of surrogate outcome measures with inconsistent results and provided very low-quality evidence of accelerated functional improvement.[9] In 2011, a small (N=36) non-blinded RCT of low-intensity pulsed ultrasound found no significant differences between the active and control groups in efficacy measures, although the treatment period (fixator gestation period) was decreased by more than a month.[23] A 2014 study randomized 21 patients undergoing callus distraction for posttraumatic tibial defects to pulsed US or no treatment (controls).[24] In this non-blinded study, US shortened healing by 12 d/cm and the total fixator time by 95 days. Double-blind trials with a larger number of subjects are needed to evaluate the health benefits of this procedure.

Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this review are listed below.

Table1. Clinical 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 nonunions.	154	Dec 2022
Unpublished			
NCT03382483[a]	Observational, non-interventional use of LIPUS to mitigate fracture nonunion in patients at risk (BONES)	3000	Dec 2019

Clinical Input Received Through 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.

2008 Input
In response to requests by BCBSM for input from physician specialty societies and academic medical centers for the 2008 policy update, input was received from one physician specialty society while this policy was under review. Physician input obtained through the American Academy of Orthopedic Surgeons agreed with the positions regarding the criteria for medical necessity and the conditions that are considered investigational (e.g., delayed union and open/unstable grade II or III fractures).

2011 Input
In response to requests from BCBSM, input was received through two physician specialty societies and one academic medical center for the policy review in January 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 a different reviewer supported including fractures of the talus and sesamoids as additional risk factors.

2012 Input
In response to BCBSM requests, input was received through four academic medical centers for the policy review in December 2012. Input supported the use of low-intensity ultrasound in delayed union and nonunion of bones excluding the skull and vertebra and in fresh closed fractures at high risk for delayed fracture healing or nonunion. Input agreed that other applications of low-intensity ultrasound treatment are investigational, including, but not limited to, treatment of congenital pseudoarthroses, 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.

Summary of Evidence
There is evidence from published studies that ultrasound (US) improves healing rates in closed fresh fractures, delayed union, and fracture nonunion. As a result, US may be considered medically necessary for BCBSM. For treatment of open, fresh fractures, the evidence is less consistent across RCTs, and systematic reviews do not report strong conclusions on efficacy of ultrasound for improving healing when data on closed and open fresh fractures are combined. Most fresh closed fractures heal without complications with the use of standard fracture care, i.e., closed reduction and cast immobilization. Therefore, the most appropriate candidates for ultrasound treatment may be those with closed fractures at high risk for delayed fracture healing or nonunion. Based on the available evidence and support from clinical input, low intensity ultrasound treatment may be considered established for fresh fractures (closed), delayed union of fractures, and nonunion of fractures.

Evidence is insufficient to evaluate health outcomes with use of low-intensity ultrasound as a treatment of congenital pseudarthroses, arthrodesis of the appendicular skeleton, stress fractures or spinal fusions. Use of ultrasound for these conditions is considered experimental/investigational. Based on one small trial with results showing no benefit to use of ultrasound treatment in the treatment of stress fractures, this is considered experimental/investigational.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

National Institute for Health and Clinical Excellence (NICE)
The NICE (2018) published a guidance on the use of LIPUS to promote healing of fresh fractures at low-risk of non-healing.[25] 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. 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. 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. 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.

American Academy of Orthopedic Surgeons (AAOS)
The American Academy of Orthopaedical Surgeons (AAOS) published 2009 guidelines on the treatment of distal radius fractures.[26] The AAOS provided a weak recommendation for use of ultrasound for adjuvant treatment of distal radius fractures. This recommendation was based results from 2 studies that used non-validated patient outcome measures.

Government Regulations
National:
National Coverage Determination (BCBSM) for OSTEOGENIC STIMULATORS (150.2)

Ultrasonic Osteogenic Stimulators
Nationally Covered Indications
Effective January 1, 2001, ultrasonic osteogenic stimulators are covered as medically reasonable and necessary for the treatment of *nonunion* fractures. In demonstrating non-union fractures, CMS expects:

- A minimum of 2 sets of radiographs, obtained prior to starting treatment with the osteogenic stimulator, separated by a minimum of 90 days. Each radiograph set must include multiple views of the fracture site accompanied with a written interpretation by a physician stating

that there has been no clinically significant evidence of fracture healing between the 2 sets of radiographs; and,
- Indications that the patient failed at least one surgical intervention for the treatment of the fracture.
- Effective April 27, 2005, upon reconsideration of ultrasound stimulation for nonunion fracture healing, CMS determines that the evidence is adequate to conclude that noninvasive ultrasound stimulation for the treatment of nonunion bone fractures prior to surgical intervention is reasonable and necessary. In demonstrating non-union fractures, BCBSM expects:
- A minimum of two sets of radiographs, obtained prior to starting treatment with the osteogenic stimulator, separated by a minimum of 90 days. Each radiograph set must include multiple views of the fracture site accompanied with a written interpretation by a physician stating that there has been no clinically significant evidence of fracture healing between the two sets of radiographs.

Nationally Non-Covered Indications
- Ultrasonic osteogenic stimulators may not be used concurrently with other non-invasive osteogenic devices.
- Ultrasonic osteogenic stimulators for fresh fractures and delayed unions remains non-covered.[27]

Local:
Osteogenesis Stimulators (L33796); effective on or after 01/01/2020
- An ultrasonic osteogenesis stimulator (E0760) is covered only if all of the following criteria are met:
  - Nonunion of a fracture documented by a minimum of two sets of radiographs obtained prior to starting treatment with the osteogenic stimulator, separated by a minimum of 90 days. Each radiograph set must include multiple views of the fracture site accompanied by a written interpretation by a physician stating that there has been no clinically significant evidence of fracture healing between the two sets of radiographs; and
  - The fracture is not of the skull or vertebrae; and
  - The fracture is not tumor related.
- An ultrasonic osteogenesis stimulator will be denied as not medically necessary if any of the criteria above are not met.
- Use of an ultrasonic osteogenic stimulator for the treatment of a fresh fracture or delayed union will be denied as not medically necessary.
- Ultrasound conductive coupling gel is covered and separately payable if an ultrasonic osteogenesis stimulator is covered.
- An ultrasonic osteogenesis stimulator will be denied as not medically necessary if it is used with other noninvasive osteogenesis stimulators.[28]

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

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

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The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through January 2022, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
5/1/13	2/19/13	3/4/13	Joint policy established. This policy speaks to ultrasonic bone growth stimulation only. This topic split out from the combined policy on bone stimulation, which included electrical stimulation of the appendicular skeleton, electrical stimulation of the spine, and ultrasound stimulation.
9/1/14	6/20/14	6/23/14	Routine maintenance
11/1/15	8/18/15	9/14/15	Routine maintenance. Added the treatment of fresh surgically treated closed fracture to exclusions section.
11/1/16	8/16/16	8/16/16	Routine policy maintenance. No change in policy status
11/1/17	8/15/17	8/15/17	Policy retired. No change in policy status.
9/1/19	6/18/19		Policy unretired, updated rationale, NICE guidelines and clinical trials sections with references 14-17 added.
5/1/20	2/18/20		Updated rationale, added reference 31. Added stress fractures to exclusion section for clarification. No change in policy status.
5/1/21	2/16/21		Routine policy maintenance. Added autoimmune disease and chemotherapy under comorbidities. No change in policy status.
5/1/22	2/15/22		Routine policy maintenance, no change in policy status.

Next Review Date: 1st Qtr. 2023

Pre-Consolidation Medical Policy History

Original Policy Date	Comments
BCN: N/A	Revised: N/A
BCBSM: N/A	Revised: N/A

BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: BONE GROWTH STIMULATION: ULTRASOUND ACCELERATED FRACTURE HEALING DEVICE

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Covered; criteria apply.
BCNA (Medicare Advantage)	See government section.
BCN65 (Medicare Complementary)	Coinsurance covered if primary Medicare covers the service.

II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- Coverage is based on each member's certificate and is not guaranteed. Please consult the individual member's certificate for details. Additional information regarding coverage or benefits may also be obtained through customer or provider inquiry services at BCN.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.