Low Intensity Ultrasound Accelerated Fracture Healing Device

**Number:** DME101.030

**Effective Date:** 01-01-2015

**Coverage:**

Low-intensity ultrasound treatment may be considered medically necessary when used as an adjunct to conventional management (i.e., closed reduction and cast immobilization) for the treatment of fresh (<14 days) closed fractures in skeletally mature individuals.

Low-intensity ultrasound treatment may be considered medically necessary as a treatment of delayed union of bones, excluding the skull and vertebra.

**NOTE:** 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 medically necessary as a treatment of fracture nonunions of bones, excluding the skull and vertebra.

**NOTE:** A nonunion is normally defined as a fracture that shows no progressive visible signs of healing after three months.

Other applications of low-intensity ultrasound treatment are considered experimental, investigational and/or unproven including, but not limited to, treatment of congenital pseudarthroses, open fractures, stress fractures, arthrodesis or failed arthrodesis.

**Description:**
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.

Ultrasound treatment can be self-administered with one 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.

The most appropriate candidates for ultrasound treatment may be those at high risk for delayed fracture healing or nonunion. These risk factors may include both of the following:

**Patient comorbidities**

- Diabetes,
- Steroid therapy,
- Osteoporosis,
- History of alcoholism,
- History of smoking.

**Fracture Locations**

- Jones fracture,
- Fracture of navicular bone in the wrist (also called the scaphoid),
- Fracture of metatarsal,
- Fractures associated with extensive soft tissue or vascular damage.

**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. According to the FDA labeling, a nonunion is considered to be established when the fracture site shows no visibly progressive signs of healing.

**Rationale:**

**Fresh Fractures**

The policy regarding fresh fractures is based in part on a 1995 BCBSA 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.

(2) 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 (3) supported the use of low-intensity ultrasound as a technique for fractures treated nonoperatively. This systematic review was updated in 2009 which included RCTs of low-intensity pulsed ultrasonography for any type of fracture. (4) 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). Ultrasound 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 below.)

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

A 2012 Cochrane review on ultrasound and shockwave therapy included 11 studies on ultrasound; 8 of the studies were randomized controlled trials. (5) The included studies were limited in methodologic quality, with all having some evidence of bias. There was very limited evidence on functional outcomes, and the available data showed no significant difference between ultrasound and placebo control on functional outcomes. There was a significant effect of ultrasound on time to healing when all types of fractures were pooled (standardized mean difference
This effect on time to healing was not present when upper or lower limb fractures were examined separately and was not robust in sensitivity analyses performed as a "worst case analysis". There was also no significant treatment effect found in pooled analyses for treatment of nonunion or delayed union. This review did not distinguish between closed and open fractures.

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 ultrasound device or an inactive device. (6) All patients started ultrasound within 7 days after having sustained the fracture. Blinded radiographic and clinical examinations showed faster healing in the ultrasound 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 and colleagues performed a double-blind RCT comparing ultrasound treatment (n=33) with a placebo-control device (n=34) in closed or grade-I open fractures of the tibial shaft. (7) 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. (8) 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 ultrasound 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%).

Authors of another study included in the 2009 systematic review observed that the clinical relevance of accelerated radiologic healing has not described and examined the effect of low-intensity pulsed ultrasound on fracture healing issues such as pain, function, and resumption of professional and personal activities. (9) They performed a multicenter double-blind RCT of ultrasound treatment of fresh clavicle fractures. Patients were taught to use the ultrasound devices for 20 minutes each day for 28 days and to
record daily their subjective feeling as to whether the fracture healed or not (the primary outcome measure), pain on visual analogue 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 and 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 and 45 placebo), and 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

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 and colleagues conducted a study that 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 ultrasound device. (10) The time-to-healing was not significantly different in the 2 groups, and the authors concluded that there was no benefit in operatively treated fractures. In contrast, Leung and colleagues reported on the results of a study that 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 ultrasound. (11) Based on radiologic assessment, the time to callus formation was significantly less in those in the ultrasound group. Due to the inconsistent results in the 2 small randomized studies, and the negative results of the meta-analysis, low-intensity ultrasound is considered experimental, investigational and unproven for open fractures.

Conclusions

There is some RCT evidence that ultrasound 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 2012 Cochrane review that did not distinguish between closed and open fractures reported that there was an improvement in time to healing when all studies were pooled but that this finding was not robust on further analyses. The Cochrane review did not find any evidence that ultrasound improves functional outcomes.

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 expansion of the policy to include all bones regardless of the anatomic site is based on this histologic similarity of all bones; it is not anticipated that the efficacy of ultrasound-accelerated healing would vary according to the anatomic site and function of the bone.

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 (12):

• 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 study 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). 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.

**Delayed Union**

In 2010, Schofer et al. reported an industry-sponsored multicenter randomized double-blinded sham-controlled trial of low-intensity pulsed ultrasound in 101 patients with delayed union of the tibia. 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 mm² 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.

**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. (4) 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. (15) Double-blind trials with a larger number of subjects are needed to evaluate the health benefits of this procedure.

**Ongoing trials**

The Trial to Evaluate Ultrasound in the Treatment of Tibial Fractures (TRUST) (NCT00667849) is an ongoing trial of low-intensity ultrasound for tibial fractures. This is a double-blind trial with sham ultrasound control, and is scheduled to enroll 500 patients. The primary outcome measure is radiographic healing at up to one year, and a secondary outcome is the rate of fracture non-union. The trial is scheduled for completion in December 2012.

**Summary**

There is evidence from published studies that ultrasound improves healing rates in closed fresh fractures, delayed union, and fracture nonunion. As a result, ultrasound may be considered medically necessary for these indications. 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 medically necessary 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, or spinal fusions. Use of ultrasound for these conditions is considered experimental, investigational and unproven. 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 and unproven.

Practice Guidelines and Position Statements

In 2010, the United Kingdom’s National Institute for Health and Clinical Excellence (NICE) concluded that current evidence on the efficacy of low-intensity pulsed ultrasound to promote fracture healing is adequate to show that this procedure can reduce fracture healing time and gives clinical benefit, particularly in circumstances of delayed healing and fracture non-union. (16)

The American Academy of Orthopaedic Surgeons (AAOS) has published 2009 guidelines on the treatment of distal radius fractures. (17) 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.

Contract:

Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.

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Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member’s benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

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**Medicare Coverage:**

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does have a national Medicare coverage position.

A national coverage position for Medicare may have been changed since this medical policy document was written. See Medicare’s National Coverage at <http://www.cms.hhs.gov>.
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Policy History:

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3/15/2013  Document updated with literature review. The following was added: 1) Low-intensity ultrasound treatment may be considered medically necessary as a treatment of delayed union of bones, excluding the skull and vertebra. NOTE: 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. 2) Arthrodesis or failed arthrodesis added as examples of experimental, investigational and unproven indications.

7/1/2011  Document updated with literature review. No change in coverage. Stress fracture added as example of experimental, investigational and unproven indications. Rationale completely revised. Title changed to Low Intensity Ultrasound Accelerated Fracture Healing Device.

6/1/2009  Coverage revised

4/15/2008  Revised/updated entire document

11/1/2000  Revised/updated entire document

3/1/2000  Revised/updated entire document

4/1/1999  Revised/updated entire document

2/1/1997  Revised/updated entire document

4/1/1996  New medical document

Archived Document(s):

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