APPENDIX to Ultrasound Bone Growth Stimulation Policy

Prior Authorization Requirements

This service (or procedure) is considered **medically necessary** in certain instances and **investigational** in others (refer to policy for details).

For instances when the indication is **medically necessary**, clinical evidence is required to determine **medical necessity**.

For instances when the indication is **investigational**, you may submit additional information to the Prior Authorization Department.

Within five days before the actual date of service, the Provider MUST confirm with Blue Shield of California / Blue Shield of California Life & Health Insurance Company (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 also be directed to the Prior Authorization Department. Please call 1-800-541-6652 or visit the Provider Portal www.blueshieldca.com/provider.

Evidence Basis for the Policy

Rationale

. The Sonic Accelerated Fracture Healing System, SAFHS® (now referred to as Exogen 2000®) (Smith & Nephew, Inc., Nashville, TN) was initially cleared for marketing by the U.S. Food and Drug Administration (FDA) in October 1994 as a treatment for fresh, closed, posteriorly displaced distal radius (Colles') fractures and fresh, closed, or grade I open tibial diaphysis fractures. Candidates need to be 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 non-unions, excluding skull and vertebra. According to the FDA labeling in 2000, a non-union is considered to be established when the fracture site shows no visibly progressive signs of healing. Healing of fractures depends on the vascularity at the fracture site. Common sites which are prone to show impaired blood flow following fracture include the humeral head, distal radius, tibial shaft, scaphoid and fifth metatarsal.

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. 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.

A 2002 meta-analysis conducted by Busse and colleagues supported the use of low-intensity ultrasound as a technique for fractures treated nonoperatively. This systematic review was updated in 2009 and included randomized controlled trials (RCTs) of low-intensity pulsed ultrasonography for any type of fracture. Thirteen trials were included: in 5 of the trials, patients were managed conservatively, and in 8 trials, 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 outcomes of trials of operatively managed (open) fresh fractures were inconsistent. Four 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 RCTs (Griffin et al., 2012). The included studies were limited in methodologic quality, with all having some evidence of bias. There was very limited evidence on functional outcomes. 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 -0.69, [95% confidence interval (CI): -1.31 to -0.07]). 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.

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 in 1999 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. 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 in 2004 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. 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 investigational for open fractures.

Closed Fractures

In a 1997 multicenter RCT by Kristiansen and colleagues, 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. 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 in 1994 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. 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 (Lubbert et al., 2008). 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 the clinical relevance of accelerated radiologic healing has not been described (Rue et al., 2004). They examined the effect of low-intensity pulsed ultrasound on fracture healing issues such as pain, function, and resumption of professional and personal activities. 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 placebos) 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.

Conclusion

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 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 by the manufacturer Exogen as part of the approval process for SAFHS as a treatment of fracture nonunions. The following data were included in their inset for the device:

- 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 by Rutten and colleagues in 2007 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 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 mm for the active treatment and -0.097 mm for sham (effect size of -0.47, 95% CI: -0.91 to -0.03). Untransformed data showed a difference between groups of -0.457 mm (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. In 2011, a small ($n = 36$) nonblinded 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 (Dudda et al., 2011). Double-blind trials with a larger number of subjects are needed to evaluate the health benefits of this procedure.

Summary

There is evidence from published studies that ultrasound improves healing rates in closed fresh fractures, delayed union, and fracture nonunion. This finding is less consistent across RCTs of open fresh fractures, 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 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 investigational.

Practice Guidelines

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.

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

Clinical Input Received Through Physician Specialty Societies and Academic Medical Centers

In response to requests, Blue Cross Blue Shield Association (BCBSA) obtained clinical input from 2 physician specialty societies and 1 academic medical center 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.

In December 2012, in response to requests, BCBSA received input through 4 academic centers which supported the use of 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 fracture, stress fractures, arthrodesis or failed arthrodesis.

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)) prohibit 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.

This Policy relates only to the services or supplies described herein. Benefits may vary according to benefit design; therefore, contract language should be reviewed before applying the terms of the Policy. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement.

Type	Number	Description
CPT	None	
HCPC	E0760	Osteogenesis stimulator, low intensity ultrasound, noninvasive
ICD9 Procedure	99.86	Non-invasive placement of bone growth stimulator
ICD9 Diagnosis	All Diagnoses	
Place of Service	All Places of Service	

Tables

N/A

Definitions

Axial skeleton - These are bones that form the axis of the body and support and protect the organs of the head, neck, and trunk. They include the ribs, skull, sternum, and vertebral column, including the coccyx and sacrum.

Appendicular skeleton - These are bones that anchor the upper and lower limbs to the axial skeleton, including the shoulder or pectoral girdle and the hip or pelvic girdle.

Congenital pseudarthrosis - Refers to a spontaneous fracture which progresses to non-union, this is rarely present at birth but commonly develops during the first 18 months of life; the tibia is the most frequent site, but may also occur in the fibula, radius, ulna, femur, and clavicle.

Delayed union - Occurs when fracture healing has not progressed within the expected timeframe for the site and type of fracture in a given patient despite ongoing bone growth activity; demonstrated by slow radiographic progress and confirmed mobility and pain.

Fracture non-union - A fracture in which all evidence of bone growth activity at the fracture site has ceased, leaving a persistent unhealed fracture of the bone.

Fresh fracture - There is currently no definition of a fresh fracture in the literature. For the purpose of these criteria a fresh fracture is considered a fracture that has not yet met the definition of non-union (e.g., less than four weeks through 12 weeks).

Skeletal maturity - Refers to a system of fused skeletal bones, which occurs when bone growth ceases after puberty. For females, this occurs at approximately 16 years and for males, at approximately 18 years of age.

Index / Cross Reference of Related BSC Medical Policies

The following Medical Policies share diagnoses and/or are equivalent BSC Medical Policies:

- Electrical Bone Growth Stimulation

Key / Related Searchable Words

N/A

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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
6/5/1996	New Policy Adoption	Medical Policy Committee
2/23/2000	Policy Revision	Medical Policy Committee

Effective Date	Action	Reason
11/15/2001	Policy Revision Modification based on external reviews	Administrative Review
12/7/2006	Policy Revision - BCBSA MPP	Medical Policy Committee
1/11/2008	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
3/17/2008	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
4/1/2011	Policy title change from Ultrasound Accelerated Fracture Healing Device and alignment with BCBSA policy	Medical Policy Committee
1/11/2013	Policy revision with position change	Medical Policy Committee

The materials provided to you are guidelines used by this plan to authorize, modify, or deny care for persons with similar illness or conditions. Specific care and treatment may vary depending on individual need and the benefits covered under your contract. These Policies are subject to change as new information becomes available.

Click here to view the policy statement for this policy

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