Clinical Policy Title: Bone growth stimulators for non-healing fractures

Clinical Policy Number: 14.02.03

Effective Date: January 1, 2015
Initial Review Date: July 16, 2014
Most Recent Review Date: March 15, 2017
Next Review Date: March 2018

Related policies:
CP# 00.02.06 Infusible pharmaceuticals for bone pain management
CP# 17.01.01 Bone mineral density measurement

About this policy: Keystone First has developed clinical policies to assist with making coverage determinations. Keystone First’s clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of “medically necessary,” and the specific facts of the particular situation are considered by Keystone First when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. Keystone First’s clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. Keystone First’s clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Keystone First will update its clinical policies as necessary. Keystone First’s clinical policies are not guarantees of payment.

Coverage policy

Keystone First considers the use of bone growth stimulators to be clinically proven and, therefore, medically necessary when all of the following criteria are met:

Electrical noninvasive (transdermal) device:
- Congenital pseudoarthroses.
- A multiple-level fusion entailing three or more vertebrae (e.g., L3 to L5 or L4 to S1).
- Adjunct for spinal fusion in skeletally mature patients with a previously failed fusion at the same site.
- Nonunion of long bone fractures after six or more months without healing and when serial radiographs (minimum of two sets, separated by 90 days, and each with multiple views of the fracture site) confirm that healing ceased after three months.
Electrical implantable device:
- Adjunct for spinal fusion in skeletally mature patients with a previously failed fusion at the same site.
- A multiple-level fusion entailing three or more vertebrae (e.g., L3 to L5 or L4 to S1).
- Nonunion of long bone fractures after six or more months without healing and when serial radiographs (minimum two sets, separated by 90 days, and each with multiple views of the fracture site) confirming that healing ceased after three months.

Ultrasonic stimulators (covered for nonunion fractures) demonstrated by:
- Two sets of radiographs obtained prior to stimulator treatment and separated by at least 90 days.
- Each set to include multiple views of fracture site.
- Written interpretation by physician confirming no clinically significant evidence of healing.

Limitations:
Coverage does not apply to:
- Fractures of skull or vertebrae and tumor-related fractures.
- Ultrasonic devices concurrently with other noninvasive devices, or for fresh fractures or nonunions.

Note: The following CPT/HCPCS codes are not listed in the Medicaid fee schedule:

E0747 — Osteogenesis stimulator, electrical, noninvasive, other than spinal application.
E0748 — Osteogenesis stimulator, electrical, noninvasive, other than spinal application.
E0749 — Osteogenesis stimulator, electrical, surgically implanted.

Alternative covered services:
Surgical or closed reduction with casting.

Background

Bone fractures are a common event experienced by approximately 6 million North Americans of all ages each year, of whom 5 percent – 10 percent show delayed healing or nonunion. Approaches to delayed or non-healing include bone stimulation devices using ultrasound or electrical stimulation, which were approved by the U.S. Food and Drug Administration (FDA) in 1994 for accelerating conservatively managed fresh fractures, and in 2000 for established nonunion.
However, the devices remain controversial, and definitive evidence of improved outcomes, such as a return to bearing weight or other function, is lacking despite supporting arguments from pathophysiology provided by laboratory research. One of the more common applications for stimulators is in operatively managed tibial fractures. The electrical or ultrasound pulses may be applied through skin over the fracture site or implanted directly into the site.

A spinal cord stimulator is a device that sends electrical pulses to the spinal cord to control chronic pain or motor disorders. Pain applications (most commonly failed back syndrome, complex regional pain, and refractory pain due to ischemia) involve electrodes implanted in the epidural space, a pulse generator (in abdominal or gluteal areas), and a remote control.

**Searches**

Keystone First searched PubMed and the databases of:

- UK National Health Services Center for Reviews and Dissemination.
- Agency for Healthcare Research and Quality’s National Guideline Clearinghouse and other evidence-based practice centers.
- The Centers for Medicare & Medicaid Services (CMS).

We conducted searches on January 30, 2017. Search terms were: "non-healing fractures (MeSH)," "osteogenic stimulator (MeSH)," and "bone growth stimulator device."

We included:

- **Systematic reviews**, which pool results from multiple studies to achieve larger sample sizes and greater precision of effect estimation than in smaller primary studies. Systematic reviews use predetermined transparent methods to minimize bias, effectively treating the review as a scientific endeavor, and are thus rated highest in evidence-grading hierarchies.
- **Guidelines based on systematic reviews.**
- **Economic analyses**, such as cost-effectiveness, and benefit or utility studies (but not simple cost studies), reporting both costs and outcomes — sometimes referred to as efficiency studies — which also rank near the top of evidence hierarchies.

**Findings**

There is not a great deal of solidly convincing evidence regarding bone growth stimulation for nonhealing fractures. Observational studies of electrical stimulation are frequent in the study of nonunion fractures, but overall these are poor-quality studies, with a lack of long-term follow up, and insufficient attention to the functional outcomes important to patients. A pilot study of ultrasound for similar indication conducted by Busse (2014) suggests significant progress in the ultrasound treatment of tibial fractures, but recruitment rates in participating centers, investigator ability to adhere to protocol/data collection requirements, and patient noncompliance continue to hamstring efforts to report significant effectiveness.
Ebrahim (2014) conducted a systematic review of 27 eligible trials inclusive of patients with a fresh fracture, and suggested benefit of low-intensity pulsed ultrasound (LIPUS) at six months (risk ratio [RR] 1.17, 95 percent confidence interval [CI] 0.97 – 1.41). In patients with an existing nonunion or delayed union, electrical stimulation had a suggested benefit over standard care on union rates at three months (RR 2.05, 95 percent CI 0.99 – 4.24). The study concluded that there is only very low-quality evidence suggesting a potential benefit of LIPUS versus electrical stimulation in improving union rates at six months (RR 0.76, 95 percent CI 0.58 – 1.01) in fresh-fracture populations. The authors opined that further study, with safeguards against bias and assessing outcomes important to patients, such as functional recovery, are required to make bolder statements of efficacy.

A narrative review of electrical stimulation (ES) to enhance bone healing by Griffin (2011) identified 105 clinical studies and 35 in vitro studies of the technology. Direct current was found to be effective in enhancing bone healing in spinal fusion and the authors supported its use for nonunions. Eleven studies were retrieved for capacitive coupling demonstrating its effectiveness for treating nonunions. The majority of studies used inductive coupling, supporting its application for healing osteotomies and nonunions. Overall, the studies, although in favor of ES application in bone repair, displayed variability in treatment regime, primary outcome measures, follow-up times, and study design, making critical evaluation and assessment difficult. They implied that electrical stimulation shows promise in enhancement of bone healing; however, better-designed clinical studies are necessary to enable its optimization for clinical practice.

Policy updates:

A randomized, double-blind trial of eight patients with a fifth metatarsal delayed or nonunion, with no progressive signs of healing for a minimum of three months underwent an open biopsy of the fracture site and were fitted with an ES device. All fractures healed, with an average time to complete radiographic union of 14.7 weeks and 8.9 weeks for the inactive and active ES groups, respectively. A significant increase in placental growth factor (PIGF) level was found after active ES treatment (P = .043). Other factors trended higher, including brain-derived neurotrophic factor (BDNF), bone morphogenetic protein (BMP)-7, and BMP-5. The authors concluded that the adjunctive use of ES for fifth metatarsal fracture nonunions produced a significant increase in local placental growth factor, higher levels of multiple other factors, and faster average time to radiographic union compared to unstimulated controls.

Summary of clinical evidence:

<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streit (2016)</td>
<td>Key points:</td>
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<tr>
<td></td>
<td>• A randomized, double-blind trial of eight patients with a fifth metatarsal delayed or nonunion fracture.</td>
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| **adjunctive use of pulsed electromagnetic fields for fifth metatarsal nonunion fracture** | weeks for the inactive and active ES groups, respectively.  
- A significant increase in PIGF level was found after active ES treatment (P = .043).  
- Other factors trended higher, including BDNF, BMP-7, and BMP-5. |
| **Busse (2014)** | **Key points:**  
- Randomized controlled trial pilot study of ultrasound in the treatment of tibial fractures.  
- Limitations noted included recruitment rates in participating centers, investigator ability to adhere to protocol and data collection requirements, and patient compliance issues.  
- Methodology shortcomings identified in pilot may render definitive trial unfeasible. |
| **Ebrahim (2014)** | **Key points:**  
- Ultrasound versus electrical stimulation.  
- 15 trials suggested benefit for ultrasound in fresh fractures at three months.  
- Overall, very low-quality evidence for ultrasound over electrical in fresh fractures.  
- Additional trials reporting outcomes important to patients (e.g., functional recovery) are needed. |
| **Hayes (2013)** | **Key points:**  
- Non-invasive electrical stimulation was reviewed from 2009 – 2013.  
- Long-term results up to 52 weeks were generally beneficial, and no significant safety concerns. |
| **WLDI (2013)** | **Key points:**  
- Study limited to forearm, wrist, and hand.  
- Stimulators considered, but not addressed in recommendations. |
| **Griffin (2011)** | **Key points:**  
- A narrative review of ES to enhance bone healing.  
- Direct current was found to be effective in enhancing bone healing in spinal fusion and nonunions.  
- Capacitive coupling was effective for treating nonunions.  
- Inductive coupling was supported for healing osteotomies and nonunions.  
- Better-designed clinical studies are necessary. |
| **WLDI (2011)** | **Key points:**  
- Acute and chronic knee and leg injuries were evaluated.  
- Stimulators were considered, but not addressed in recommendations. |
| **Busse (2009)** | **Key points:**  
- Systematic review of patients with any fracture treated with LIPUS was studied.  
- 13 trials (five assessing outcomes important to patients).  
- Moderate-quality evidence for no effects on functional recovery from conservatively managed fresh clavicle fractures.  
- Low-quality evidence for faster radiographic healing in non-operatively managed fresh fractures.  
- Overall — moderate- to low-quality evidence and conflicting results.  
- Large blinded trials are needed. |
| **Hayes (2009)** | **Key points:**  
- Invasive electrical bone growth stimulation.  
- Some evidence for radiographically assessed healing, but sparse and of low quality for other outcomes.  
- Hayes C rating:  
  - Adjunct to spinal fusion for patients at high risk of pseudoarthrosis due to previously failed |
<table>
<thead>
<tr>
<th>Citation</th>
<th>Key points:</th>
</tr>
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</table>
| Hayes (2009a) | **Ultrasound stimulation.**  
**Hayes B rating:**  
- Fresh, closed, grade 1 open tibial fractures treated with closed reduction and cast immobilization.  
- Nonunions other than skull or vertebrae in skeletally mature patients, excluding malignancy-related fractures.  
**Hayes C:**  
- Fresh closed fractures of distal radius (Colles fracture) treated with closed reduction and cast immobilization.  
- Adjunct to surgical treatment — fresh fractures of fibula, tibial diaphysis, or distal radius.  
- Delayed healing (clinical) and radiographic evidence of delay.  
- Insufficient evidence for use in skeletal immaturity/pediatric patients; pregnancy or lactation; patients receiving medications that interfere with bone metabolism (nonsteroidal anti-inflammatory drugs [NSAIDs], bisphosphonates, calcium channel blockers); or those with alcoholism or nutritional deficiencies. |
| CMS (2005): NCD for osteogenic stimulators (150.2) | **Electrical noninvasive device:**  
- Congenital pseudoarthroses.  
- Adjunct for spinal fusion in patients with a previously failed fusion at the same site.  
- Nonunion of long bone fractures after six or more months without healing and when serial radiographs (minimum two sets, separated by 90 days, and each with multiple views of the fracture site) confirm that healing ceased after three months.  
**Electrical implantable device:**  
- Adjunct for spinal fusion in patients with a previously failed fusion at the same site.  
- Nonunion of long bone fractures after six or more months without healing.  
- Nonunion of long bone fractures after six or more months without healing and when serial radiographs (minimum of two sets, separated by 90 days, and each with multiple views of the fracture site) confirm that healing ceased after three months.  
**Ultrasonic stimulators:**  
- Covered for nonunion fractures demonstrated by:  
  - Two sets of radiographs obtained prior to stimulator treatment and separated by at least 90 days.  
  - Each set including multiple views of the fracture site.  
  - Written interpretation by the physician confirming no clinically significant evidence of healing.  
**Noncovered indications:**  
- Fractures of the skull or vertebrae and tumor-related fractures.  
- Ultrasonic devices concurrently with other noninvasive devices, or for fresh fractures or nonunions. |
**Professional society guidelines/other:**


**Peer-reviewed references:**


CMS National Coverage Determinations (NCDs):

CMS covers electrical and ultrasound devices, transdermal and implanted, for fresh fractures, excluding skull, vertebral, and tumor-associated fractures.

NCD for osteogenic stimulators (150.2).


Local Coverage Determinations (LCDs):

No LCDs identified as of the writing of this policy.

Commonly submitted codes

Below are the most commonly submitted codes for the service(s)/item(s) subject to this policy. This is not an exhaustive list of codes. Providers are expected to consult the appropriate coding manuals and bill accordingly.

<table>
<thead>
<tr>
<th>CPT Codes</th>
<th>Description</th>
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<tbody>
<tr>
<td>20974</td>
<td>Electrical stimulation to aid in bone healing, noninvasive.</td>
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<tr>
<td>20975</td>
<td>Electrical stimulation to aid in bone healing, invasive (operative).</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>ICD-10 Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>M80.011K-M80.079K</td>
<td>Age-related osteoporosis with current pathological fracture, subsequent encounter for fracture with nonunion</td>
</tr>
<tr>
<td>M80.811K-M80.879K</td>
<td>Other osteoporosis with current pathological fracture, subsequent encounter for fracture with nonunion</td>
</tr>
<tr>
<td>M84.411K-M84.4173K</td>
<td>Pathological fracture, subsequent encounter for fracture with nonunion</td>
</tr>
<tr>
<td>M84.619K-M84.673K</td>
<td>Pathological fracture in other disease, unspecified shoulder, subsequent encounter for fracture with nonunion</td>
</tr>
<tr>
<td>M96.0</td>
<td>Pseudoarthrosis after arthrodesis or fusion</td>
</tr>
<tr>
<td>S42.413K-S42.96XK</td>
<td>Fracture with subsequent encounter for fracture with nonunion</td>
</tr>
<tr>
<td>S49.001K-S49.199K</td>
<td>Fracture of humerus with subsequent encounter for fracture with nonunion</td>
</tr>
<tr>
<td>S52.201M-S52.92XX</td>
<td>Fracture of radius with subsequent encounter for nonunion</td>
</tr>
<tr>
<td>S52.019K-S56.92XX</td>
<td>Fracture of ulna, wrist or hand with subsequent encounter for nonunion</td>
</tr>
<tr>
<td>S72.001K-S79.199K</td>
<td>Fracture femur with subsequent encounter for nonunion</td>
</tr>
<tr>
<td>S82.101K-S89.399K</td>
<td>Fracture lower leg with subsequent encounter for nonunion</td>
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<tr>
<td>HCPCS Codes</td>
<td>Description</td>
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<tr>
<td>E0747</td>
<td>Osteogenesis stimulator, electrical, noninvasive, other than spinal application.</td>
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<tr>
<td>E0748</td>
<td>Osteogenesis stimulator, electrical, noninvasive, spinal application.</td>
</tr>
<tr>
<td>E0749</td>
<td>Osteogenesis stimulator, electrical, surgically implanted.</td>
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</tbody>
</table>