



Mechanism of Action

Activating bone healing at every stage



exogen[®]
ultrasound bone healing system

 **bioventus**

EXOGEN[®] Ultrasound Bone Healing System

The EXOGEN Ultrasound Bone Healing System is an FDA-approved bone healing device that uses low-intensity pulsed ultrasound (LIPUS) technology to stimulate the body's natural bone healing process.¹

EXOGEN is osteoinductive, stimulating cells to differentiate into osteoblasts that begin the formation of new bone. EXOGEN is safe and effective for non-union† fractures with metal fixation or implants² (see EXOGEN User Guide).



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EXOGEN Mechanism of Action

1. Stimulation

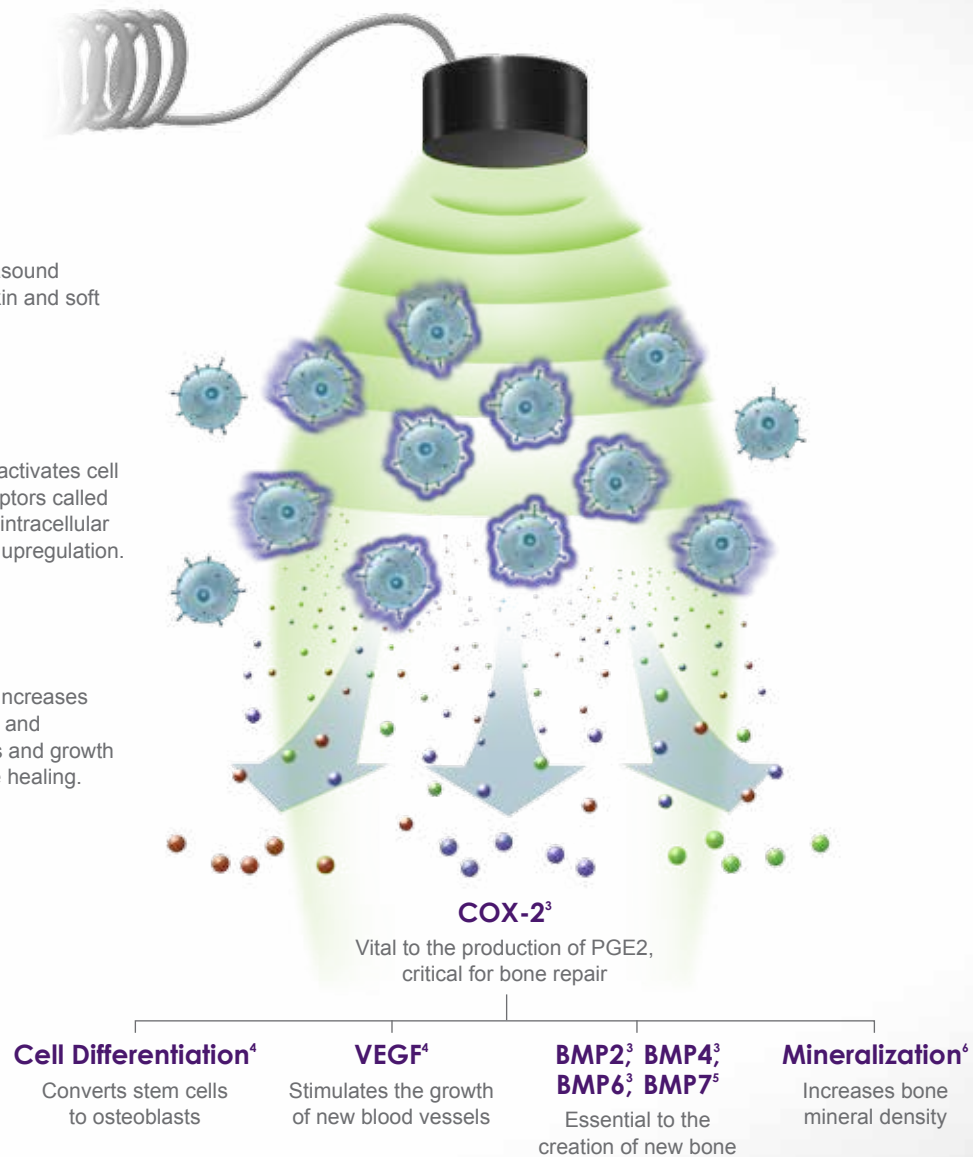
EXOGEN sends ultrasound waves through the skin and soft tissue to the fracture.

2. Activation

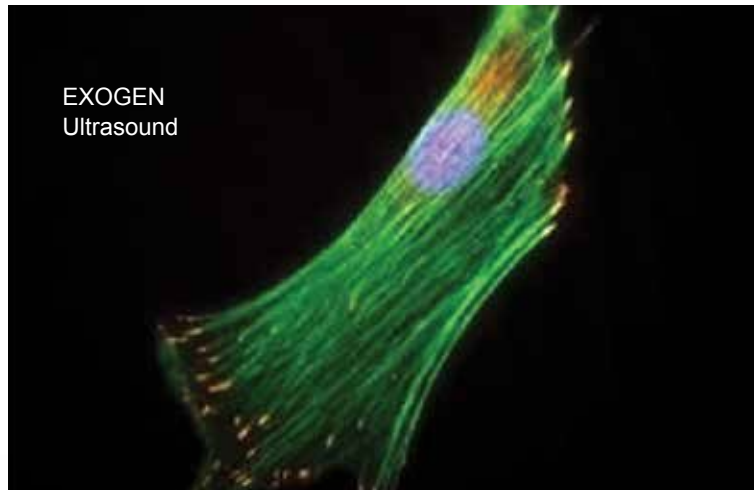
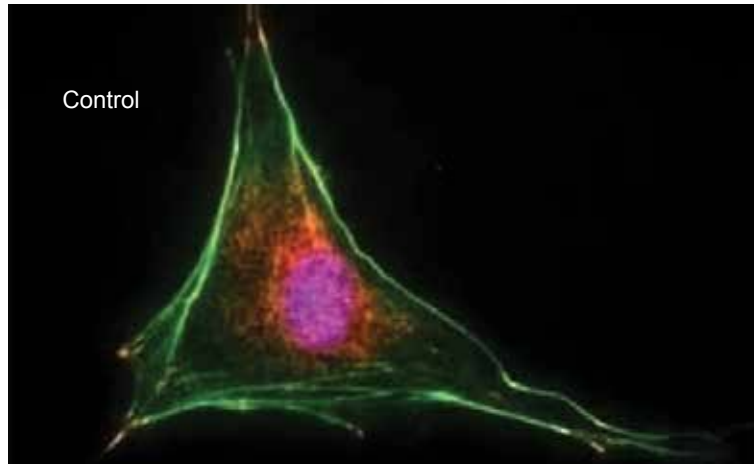
EXOGEN ultrasound activates cell surface mechanoreceptors called integrins, initiating an intracellular cascade that leads to upregulation.

3. Upregulation

EXOGEN ultrasound increases upregulation of genes and expression of proteins and growth factors critical to bone healing.

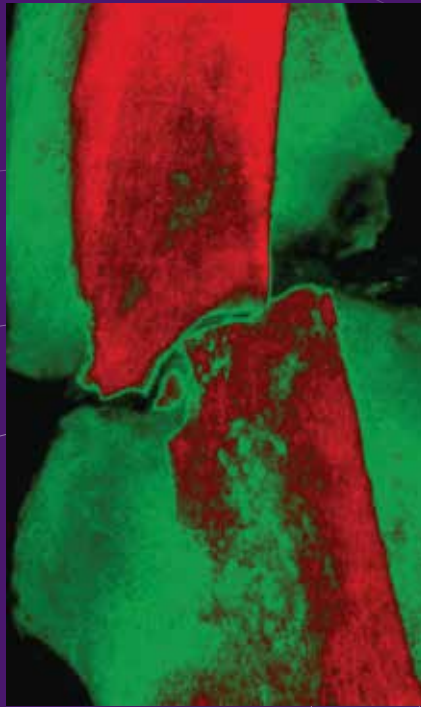


A clear biological response

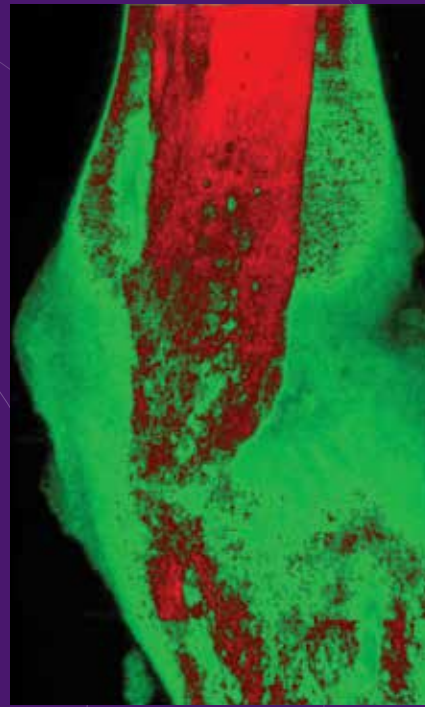


The lower image shows EXOGEN's impact on the formation of the cytoskeleton (in green) and focal adhesions (orange dots) in osteoblasts in vitro, caused by the clustering of integrins.⁷

Bridging the fracture gap



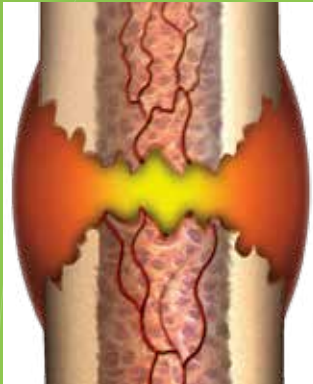
Control



EXOGEN Ultrasound

Micro-computed tomography shows that EXOGEN treatment increases the removal of original cortical bone and enhances endochondral ossification. The image on the right shows the growth of new, less-dense bone (in green) bridging the fracture gap of older, denser bone (in red).⁸

EXOGEN at every stage of the fracture healing process



Inflammation

EXOGEN's ultrasound signal increases cell division among periosteal cells in culture and upregulates growth factors that trigger the formation of new blood vessels.⁴



Soft Callus

The ultrasonic treatment enhances the TGF β -triggered differentiation of chondrocytes in culture and accelerates the formation of extracellular matrix.^{9,10}



Hard Callus

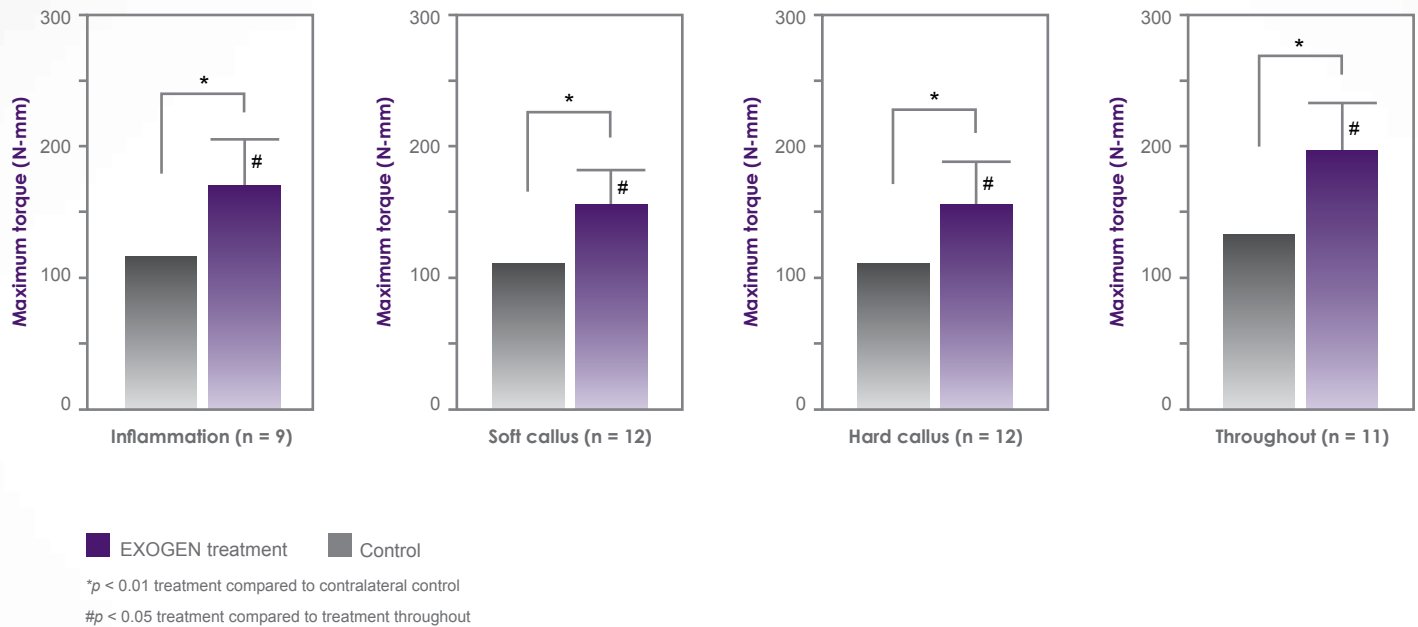
EXOGEN upregulates endochondral ossification^{11,12} and enhances osteoblast differentiation¹³ and mineralization.⁴



Bone Remodeling

Accelerating both the formation and resorption of bone, EXOGEN ultrasound treatment yields faster remodeling of the mineralized callus.⁸

EXOGEN accelerates healing throughout the fracture healing process¹



Maximum torsional torque of the EXOGEN-treated femurs was significantly greater than the placebo controls at each phase of fracture healing in an animal model.¹

EXOGEN can easily penetrate soft tissue to reach both deep and superficial fractures

The depth and breadth of the EXOGEN signal enable it to treat superficial and deep indicated fractures, as well as non-union[†] fractures with metal fixation or implants.^{2,14} Because the ultrasound waves travel easily through adipose tissue, it is suggested that EXOGEN therapy is effective for normally weighted and obese patients.¹⁵

Depth and breadth of penetration:¹⁵

- Beam reaches a depth of more than 260 mm
- Effective diameter of the ultrasound beam is more than 5 cm
- Therapeutic span is 3.4 cm, even after passing through 20 cm of soft tissue

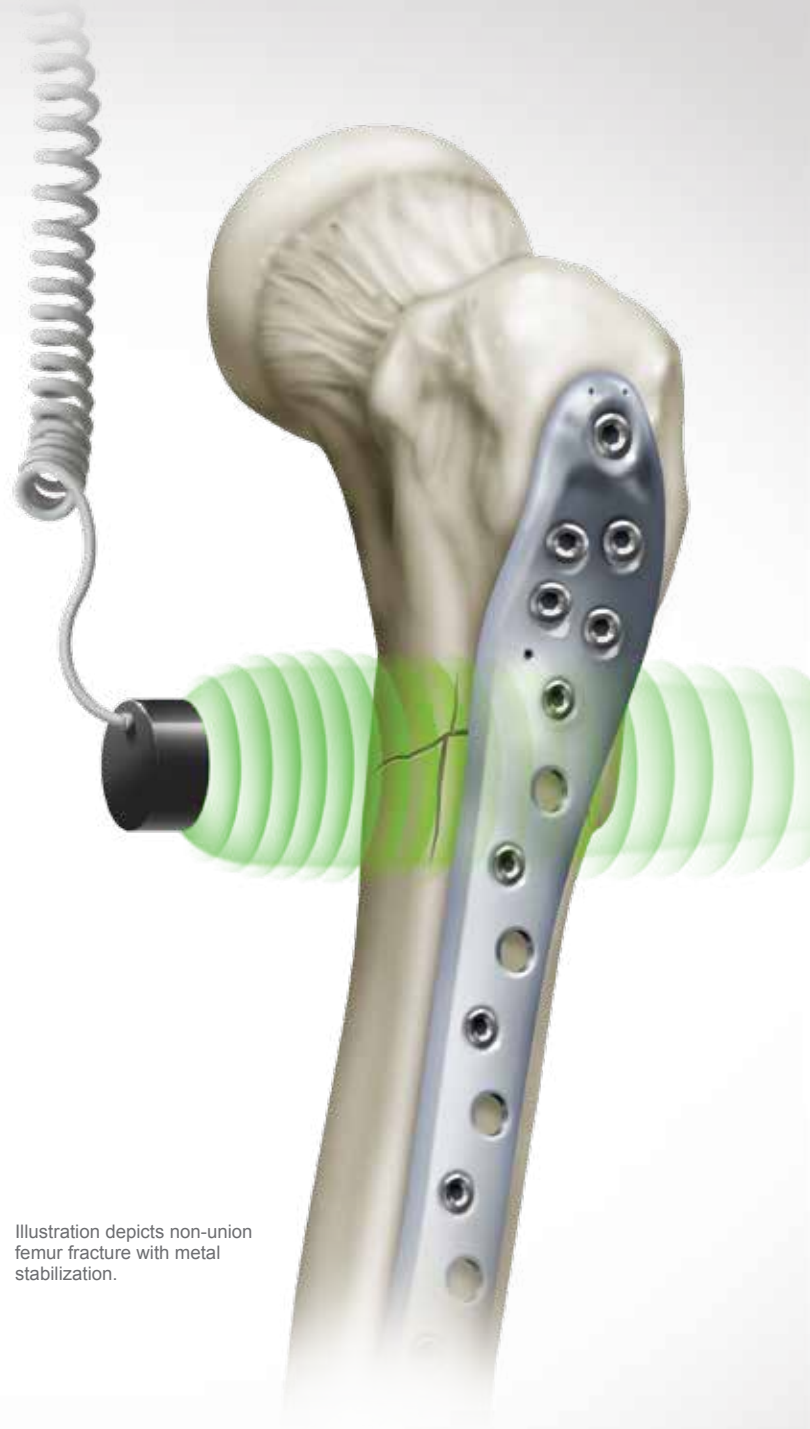


Illustration depicts non-union femur fracture with metal stabilization.

Effective in a wide range of patients and fractures

EXOGEN shows results in special patient populations:

- Smokers¹⁶
- Infected non-union¹⁷
- Deep or superficial fractures¹⁴
- Atrophic non-union¹⁴
- Hypertrophic non-union¹⁴

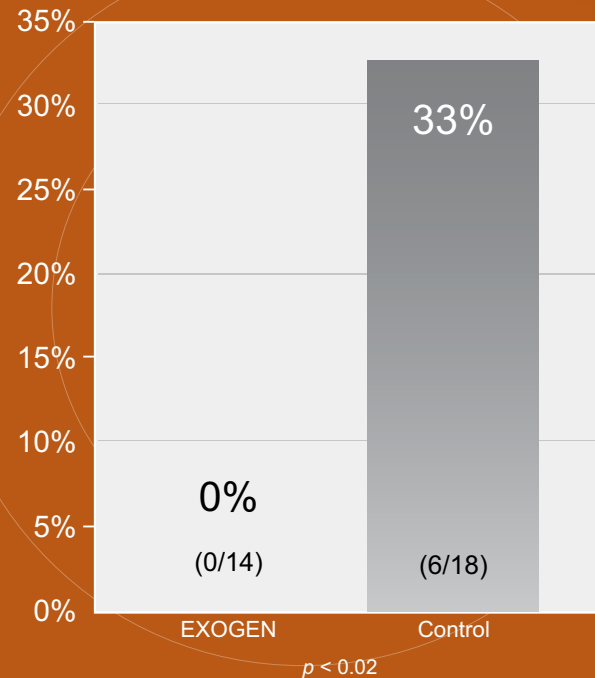
EXOGEN is effective on non-unions with metal implants:¹⁴

- Cells respond even if the fracture is fixed with metal implants

EXOGEN used on animal models with metal fixation has been shown to be:

- Safe²
- Non-cavitating¹⁸
- Non-thermal¹⁹

0% of EXOGEN-treated smokers developed a delayed union¹⁶

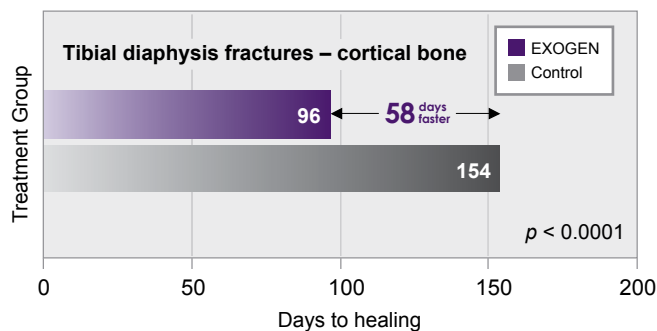


38% faster healing of indicated* fresh fractures^{20,21}

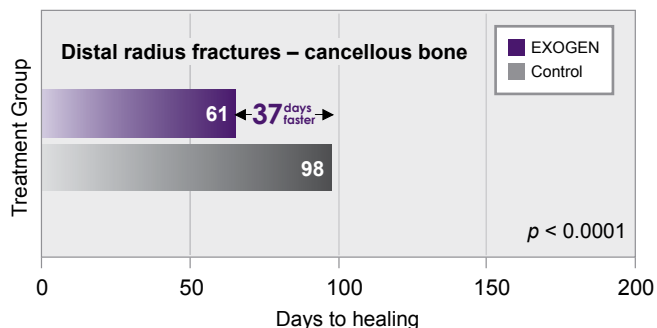
EXOGEN treatment accelerates healing in both cortical and cancellous bone

Analysis of these studies showed an 83% reduction in delayed unions.¹⁶

EXOGEN is a unique fracture healing device that has demonstrated the ability to accelerate fresh fracture healing.



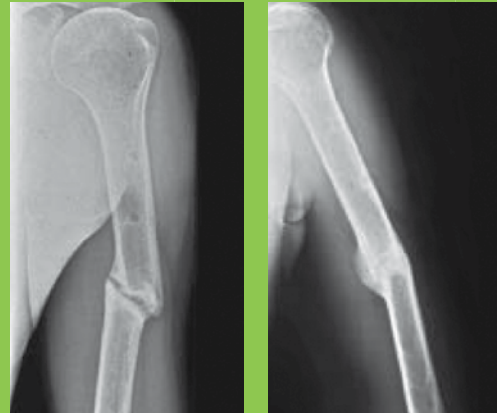
In a prospective, randomized, double-blind, placebo-controlled (Level I) study of 67 tibial fractures, EXOGEN treatment accelerated healing by 38%²⁰ – a difference of more than 8 weeks.



A separate Level I trial of 61 distal radius fractures also reported a 38% acceleration of healing, as well as significantly greater fracture alignment.²¹

86% non-union[†] heal rate²²

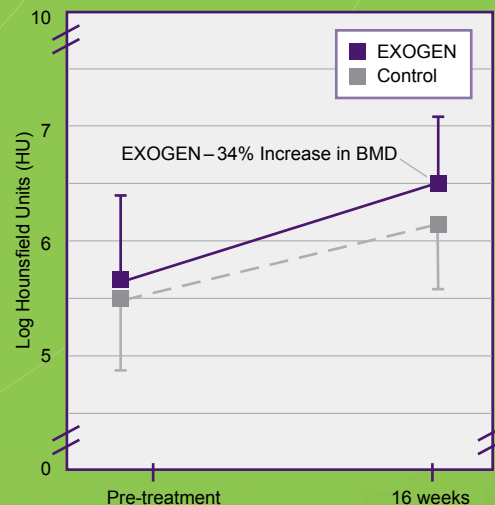
EXOGEN has been shown to successfully resolve 86% of non-union fractures.²² The EXOGEN ultrasound signal is safe and effective as an adjunct to conservative treatment or surgical management, including metal fixation and implants.^{2,14}



Radiograph depicting humeral non-union fracture healing.

In a study on non-union fracture healing, bone mineral density showed an estimated 34% increase in subjects treated with EXOGEN for 20 minutes a day. EXOGEN also demonstrated a significant benefit in fracture gap reduction compared to the control group.⁶

Line graph illustrating improvement in bone mineral density for each treatment group separately through 16 weeks of follow-up.



High treatment compliance.⁶ Proven clinical effectiveness.²⁰⁻²² Successful fracture healing outcomes.

Backed by a full suite of patient support tools, EXOGEN is the only bone healing device with documented 91% treatment compliance.⁶

EXOGEN Performance Program

The EXOGEN Performance Program guarantees progression of non-union[†] fracture healing. If program requirements are met and no healing progression is shown, Bioventus will refund all out-of-pocket costs.

20-Minute Treatment

With treatments lasting just 20 minutes, EXOGEN can fit easily into the patient's daily routine.

Customer Support

EXOGEN Customer Support is available to answer questions and help maintain continuity of treatment.

Smartphone App with Treatment Reminder

EXOGEN CONNECTS is a free smartphone app that sends automated treatment reminders and provides helpful healing information.

exogen[®]
connects



1. Download

The EXOGEN CONNECTS app, available on the App Store, is easy to download and activate.

2. Receive

Patients receive daily treatment reminders on their smartphone.

3. Treat

Automated reminders encourage patients to complete their daily 20-minute treatment.

4. Heal

Using EXOGEN as prescribed can help put patients on the road to faster healing.



Treatment Tracking Calendar

EXOGEN's built-in treatment tracking calendar tracks device usage, making treatment compliance tracking convenient for patients and verifiable for physicians.

*Summary of Indications for Use:

The EXOGEN Ultrasound Bone Healing System is indicated for the non-invasive treatment of established non-unions[†] excluding skull and vertebra. In addition, EXOGEN is indicated for accelerating the time to a healed fracture for fresh, closed, posteriorly displaced distal radius fractures and fresh, closed or Grade I open tibial diaphysis fractures in skeletally mature individuals when these fractures are orthopaedically managed by closed reduction and cast immobilization.

There are no known contraindications for the EXOGEN device. Safety and effectiveness have not been established for individuals lacking skeletal maturity, pregnant or nursing women, patients with cardiac pacemakers, on fractures due to bone cancer, or on patients with poor blood circulation or clotting problems. Some patients may be sensitive to the ultrasound gel. Full prescribing information can be found in product labeling, at www.exogen.com, or by calling customer service at 1-800-836-4080.

[†]A non-union is considered to be established when the fracture site shows no visibly progressive signs of healing.

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Count on EXOGEN.



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graph TD; A((Count on EXOGEN.)) --- B((High treatment compliance6)); A --- C((Proven clinical effectiveness20-22))); A --- D((Successful fracture healing outcomes))
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High treatment
compliance⁶

Proven clinical
effectiveness²⁰⁻²²

Successful
fracture healing
outcomes

Bioventus LLC
4721 Emperor Blvd., Suite 100
Durham, NC 27703
USA

Customer Service: 1-800-836-4080
1-919-474-6700

www.BioventusGlobal.com
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