The Science of Ultrasound Technology
You treat the injury. EXOGEN treats the biology.
EXOGEN uses low-intensity pulsed ultrasound to stimulate a cellular reaction.

EXOGEN uses an ultrasound mechanical pressure wave composed of 1,000 pulses per second to stimulate a response at the cellular level. The ultrasound wave has an intensity of 30 mW/cm² which is lower than with fetal sonography. The ultrasound wave penetrates up to 26 cm (10.5 inches) into the body, and is safe to use with metal fixation. After contacting the bone, the mechanical pressure wave creates a nanomotion at the fracture site, producing a reaction at the cellular level.
**EXOGEN** jump starts bone healing by stimulating biological processes.

When the ultrasound signal reaches the fracture site, it causes movement in the extracellular matrix, and is simultaneously detected by cells through mechanical surface receptors called integrins. When stimulated by a mechanical force such as the low-intensity pulsed ultrasound signal from EXOGEN, intracellular proteins such as paxillin and vinculin cause the integrins to cluster, together forming a complex known as a focal adhesion. There are many activities that are initiated by the formation of focal adhesions, such as cytoskeleton reorganization and intracellular signaling events. These activities create an intra-cellular cascade that ultimately enhances gene expression and protein production.\(^3\text{5}\)

**Mechanism of Action**

1. **Stimulation**
   EXOGEN sends ultrasound waves through the skin and soft tissue, creating nanomotions that stimulate the cells at the fracture site.

2. **Activation**
   EXOGEN ultrasound activates cell surface mechanoreceptors called integrins,\(^3\) initiating an intracellular cascade that leads to gene upregulation.

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

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**COX-2**
Vital to the production of PGE2, critical for bone repair

**Cell Differentiation**\(^7,8\)
Converts stem cells to osteoblasts

**VEGF**\(^8,9\)
Stimulates the growth of new blood vessels

**BMP-2, BMP-4, BMP-6, BMP-7**\(^4,10\)
Essential to the creation of new bone

**Mineralization**\(^6,11\)
Increases bone mineral density

*Summary of Indications for Use:* The EXOGEN Ultrasound Bone Healing System is indicated for the non-invasive treatment of established nonunions excluding skull and vertebra.

The EXOGEN device has also been reported as effective as an adjunctive non-invasive treatment of established nonunions in patients:

- With internal or external fracture fixation hardware present. EXOGEN cannot penetrate metal and therefore should not be applied directly over hardware.
- Undergoing treatment for infection at the fracture site. EXOGEN is not intended to treat the infection.
- Believed to have diminished bone quality. EXOGEN is not intended to treat diminished bone quality.

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; or fractures due to bone cancer; or on patients with poor blood circulation or clotting problems. Some patients may be sensitive to the ultrasound gel.

*A nonunion is considered to be established when the fracture site shows no visibly progressive signs of healing.*

Full prescribing information can be found in product labeling, at [www.exogen.com](http://www.exogen.com) or by contacting customer service at 1-800-836-4080.

Visit EXOGEN.com to learn more.