U.S. Food and Drug Administration
Protecting and Promoting *Your* Health

Use of Bone Graft Substitutes Containing Recombinant Proteins or Synthetic Peptides in Patients under Age 18 – FDA Safety Communication

Date Issued: January 21, 2015

Audiences:

- Healthcare providers
- Patients under age 18 with bone grown defects
- Parents/Guardians of patients under age 18 with bone growth defects

Specialties: Pediatrics, Plastic Surgery, Dentistry, Orthopedic Surgery, Neurosurgery

Product:

Certain recombinant proteins and synthetic peptides mimic bone growth substances normally found in the body and may be added to a carrier or scaffold to be used as bone graft substitutes. Once combined, these products are surgically implanted in a patient with a bone defect to promote new bone growth or to replace or heal existing bone.

The FDA has approved these products for orthopedic and dental use only in patients over the age of 18 who are done growing (skeletal mature). The labeling for each product provides the specific indications for use.

These products are not approved for any use in patients under the age of 18 who are still growing (skeletally immature).

Purpose:

The FDA is informing healthcare providers, patients, and parents/guardians that bone graft substitutes containing recombinant proteins or synthetic peptides should not be the first treatment considered for patients under age 18 with significant bone defects or rare bone disorders. The FDA has not approved these products for use in patients under age 18 because their bones may still be growing and using this product may cause serious injuries. The agency recommends that health providers consider other treatment options first.

Summary of Problem and Scope:

Through scientific literature and medical device reports (MDRs), the FDA is aware of healthcare providers using bone graft substitutes containing recombinant proteins or synthetic peptides in patients under age 18. Reports of serious injuries, such as excess bone growth, fluid accumulation, inhibited bone healing, and swelling, have increased the FDA's concern. While these types of events are similar to those seen in patients over age 18, they are of more concern in patients under age 18 because of their overall smaller size and because their bones are still growing.

In a body that is still growing, vital organs and tissues are closer together than in a body that is done growing. This could potentially allow small changes from one organ/tissue to have serious effects on another. For example, there is less space between the spinal cord and the bones surrounding it. If one of these products is used in the spine of a patient under age 18, who then experiences the same amount of excess bone growth or fluid accumulation as a patient over age 18, it may more easily lead to spinal nerve injury, pain, or weakness.

Any product that affects bone growth could have the potential to negatively impact skeletal development by altering normal bone formation and growth, especially if implanted near open growth plates.

The FDA considers bone graft substitutes containing recombinant proteins or synthetic peptides high-risk (Class III) medical devices. Before marketing the products, manufacturers are required to submit a premarket approval application (PMA) that includes clinical data supporting safety and effectiveness. The FDA has not evaluated their safety and effectiveness in patients under age 18.

The FDA understands that patients under age 18 with significant bone defects or rare bone disorders may have limited treatment options and that their healthcare providers may determine these products to be the best or only option. However, healthcare providers should consider other options before using bone graft substitutes containing recombinant proteins or synthetic peptides. These options, whose use is better understood in patients under age 18, include autograft bone (bone that comes from another part of the patient's body), allograft bone ("banked bone" which is transplanted bone from another person), and FDA cleared bone graft substitutes that do not contain recombinant proteins or synthetic peptides.

Recommendations:

For Health Care Providers:

- The FDA recommends against routine use of these products in patients under age 18 because their safety and effectiveness has not been reviewed or approved for use in this population.
- Consider alternatives such as autograft bone, allograft bone, and bone graft substitutes that do not contain recombinant proteins or synthetic peptides before using bone graft substitutes containing recombinant proteins and synthetic peptides in patients under age 18.
- Carefully consider the benefits and risks before using these products in any patient. If considered the best or only option, inform parents/guardians and patients about the risks and benefits of using the product when discussing surgical options.
- Closely monitor patients under age 18 for adverse events and if necessary, refer them to the appropriate healthcare provider for corrective treatment. Adverse events may include problems with skeletal development, excess growth of other tissues, and tissue swelling or fluid accumulation that could put pressure on adjacent organs or tissues.
- **Report to the FDA (/Safety/MedWatch/HowToReport/ucm2007306.htm)** if you become aware of a patient experiencing an adverse event associated with the use of recombinant proteins or synthetic peptides.

For Parents/Guardians/Patients:

- Ask your healthcare provider about the benefits and risks of treatments for bone defects and discuss his/her experience with performing these procedures.
- Ask your healthcare provider if the treatment option recommended is FDA-approved or cleared and appropriate for the procedure you or your child is undergoing.
- If you or your underage child was treated with these products, discuss with your healthcare provider how often bone healing should be monitored.
- Contact your healthcare provider if you or your underage child was treated with these products and is experiencing adverse events, such as fever, swelling, rash, pain, or physical changes near the implantation site.

Reporting Problems to the FDA:

Prompt reporting of adverse events can help the FDA identify and better understand the risks associated with these products.

If you suspect or experience a problem with recombinant proteins and synthetic peptides or other bone graft products, we encourage you to file a voluntary report through **MedWatch, the FDA Safety Information and Adverse Event Reporting program (/Safety/MedWatch/HowToReport/ucm2007306.htm)**. Healthcare personnel employed by facilities that are subject to **FDA's user facility reporting**