VHA Office of Integrated Veteran Care
Clinical Determination and Indication
Osseoanchored Prostheses for the Rehabilitation of Amputees (OPRA) Implant System for Transfemoral Amputations

CDI Number: 00008

Original Effective Date: June 1, 2024

Last Review Date: June 1, 2024

I. Disclaimer

This document is currently in draft and is intended to be used as a reference for non-VA providers and not intended to replace clinical judgment when determining care pathways. These guidelines do not guarantee benefits or constitute medical advice.

II. Clinical Determinations and Indications

a. Indications for the OPRA Implant System for Transfemoral Amputations

The OPRA Implant System for transfemoral amputations is the only FDA approved osseointegration implant system and is considered **medically necessary** when **ALL** the following criteria are met:

- History of unilateral or bilateral transfemoral amputation due to trauma or cancer
- Current or anticipated rehabilitation problems secondary to challenges with wearing a conventional socket prosthesis such as:
  - Recurrent skin infections and/or ulcerations in the socket contact area
  - Pain in the socket contact area
  - A short stump preventing the use of socket prosthesis
  - Volume fluctuation in the stump
  - Soft tissue scarring
  - Extensive (large) area of skin grafting
  - Socket retention problems due to excessive perspiration
  - Restricted joint mobility

b. Limitations/Exclusions

For all other conditions and amputation types and levels not listed in section II.a. of this document, the OPRA Implant System is considered **not medically necessary** due to insufficient evidence of efficacy and safety.

c. Description of Treatment

The OPRA Implant System is currently the only fully FDA approved osseointegration implant system for direct skeletal attachment of prosthetic limbs in patients with amputations at the transfemoral level. Osseointegration at all other amputation levels has not yet received full FDA approval.

The OPRA Implant System is an alternative treatment option to traditional socket prosthesis, where the external prosthesis is anchored directly to the patient's remaining bone through a permanently implanted titanium screw that comes through the skin. Therefore, the prosthesis always attaches correctly, remains firmly in place, and is free from pressure sores, pain, heat, chafing and general discomfort found with traditional solutions.

Two surgeries are needed to install the OPRA Implant System:

- The goal of the first surgery is to implant the threaded intramedullary bone anchor, a cylindrical-shaped fixture, into the center canal of the remaining thigh bone or residual limb
- In the second surgery, approximately three to six months later to allow the implant to integrate with the host bone and anchor to one another, an abutment is attached to the implanted fixture, creating a stoma at the skin-implant interface, which will complete the prosthesis connection

The OPRA Implant System extends through the skin at the bottom of the patient's remaining limb to connect to the prosthesis. The leg prosthesis is attached to the abutment screw through a quick connection Axor II device. During the first stage of rehabilitation, a specially designed training prosthesis is used before moving on to the full-length prosthesis.

III. Background and Supporting Information

The following information is for reference purposes only in accordance with the medical benefits package outlined in 38 C.F.R. § 17.38 (b). Each subsection supports VA's determinations for medical necessity and alignment with generally accepted standards of medical practice.

a. Background of Osseointegration

Osseointegration & Osseointegration for Skeletal Attachment of Prosthetic Limbs

The term osseointegration refers to a technique where an artificial implant is permanently and surgically anchored and integrated into bone. In this process, bone will eventually grow into the artificial implant to secure the implant in place. This technique is used with both dental implants and joint replacement surgery.

In the use of osseointegration for skeletal attachment of a prosthetic limb, a percutaneous implant system is directly connected to the residual bone following an amputation. The portion of the implant system that extends through the soft tissues and skin is used to connect the implant to the prosthetic limb.

Potential Advantages of Osseointegration

There are many potential advantages of osseointegration, which include improved mobility and proprioception (a sensory function that allows one to determine position of their body part), reduced nerve pain, and elimination of the common problems associated with the traditional socket prosthesis, like pinching, sweating, poor fit, poor control, skin irritations and sores. Because the artificial implant is directly connected to the skeletal bone, this technique provides great stability, strength, and energy transfer. Touch vibrations (usually felt during impact with the ground while walking) may be transferred to the natural bone, resulting in the ability to walk more smoothly, feel more stable, and transfer strength from the limb to the prosthesis.

Risks/Complications

Osseointegration presents the risk of serious complications such as infection, failure of the implant, and bone fracture. Additionally, the osseointegration surgical procedure requires not using a prosthesis for a period of time, along with an extensive rehabilitation period.

Improper use such as failure to follow and complete the required training, excessive physical activity creating an overload on the device, or injuries such as falls, will increase the risks.

b. Research, Clinical Trials, and Evidence Summaries

The modern research literature related to osseointegration spans a period of over 20 years from 2000 to present. The literature in this field has been summarized in 7 systematic reviews published between 2015 and 2020. Most studies evaluating the safety and efficacy of osseointegrated implants have been classified as Level III or IV observational studies because they used retrospective or prospective observational cohort designs. Only a few studies have been classified as Level II evidence. Most investigations have utilized a pre-post design with subjects serving as their own controls while a few have utilized a separate control group using socket-based prosthetic limbs. Due to the inability to blind either subjects or investigators from the intervention, no formal randomized controlled trials have been performed.

Despite methodologic limitations in previously reported studies, summaries of the literature support favorable and statistically significant positive outcomes in prosthesis use, general physical health, and walking ability. While some

outcomes following osseointegration relate to changes that occur at the tissue level (residual limb bone changes at the implant interface), the most widely reported and significant outcomes relate to either functional performance or quality of life. Functional performance has been assessed through both self-report and physical performance measures. Less frequently reported outcomes include vibratory stimulation, biomechanics and energy consumption, pain, and economic implications.

Complications associated with osseointegration implants used for the direct skeletal attachment of prosthetic limbs include infection (superficial and deep), other soft tissue complications, implant bending and breakage, implant loosening, peri-implant fracture, and implant failure. These complications may require additional complication-related procedures to be performed including long-term antibiotic use, soft tissue surgical debridement or revision, implant revision surgery, and implant removal.

In the systematic review by Al Muderis et al. (2018), seven studies were identified reporting on complications associated with osseointegration. Studies reporting complications were rated as low quality and used different types of OI prostheses and protocols which resulted in inconsistent findings across the studies. The review by Hebert et al. (2017) identified that infection or other complications were reported in 13 of the 14 articles reviewed. This descriptive review noted that superficial infection was the most commonly reported complication across studies. Other complications such as fractures, implant loosening, implant breakage and need for surgical revision surgery were reported less frequently. The systematic review conducted by Kunutsor et al. (2018) identified 14 studies that specifically reported infection rates. The majority of infections were reported as low-grade soft tissue or superficial infections, which were treated effectively with oral antibiotics. Across these studies, the infection rate ranged from 1% (95% C.I. 0 to 5) to 77% (95% C.I. 59 to 88%) over a mean follow-up of five months to five years.

The review conducted by Atallah et al. (2018), which included 12 studies, provided a more detailed review of both complications and complication-related interventions. Removal of the implant was the only complication that was reported in all articles included in the systematic review. This review is also unique in that subgroup analyses were performed by implant type (screw, press-fit and other types of implants) and level of amputation (transfemoral, transtibial and upper extremity amputation). Soft tissue infections and complications were commonly noted in the reviewed studies. Implant infection rates in transfemoral implants were (screw: 2±11%, press-fit: 0±3%, Compress: 0%) and implant loosening rates were (screw: 6%, press-fit: 0±3%, Compress: 0%).

Matthews et al. (2019) reported osseointegration outcomes with the Osseointegrated Prostheses for the Rehabilitation of Amputees (OPRA) implant in the United Kingdom between 1995 and 2018. Twenty eight percent of the implants failed and had to be removed during the mean follow-up period between 11.4 and 12.3 years with most failures related to deep infection. The study highlights that infection and implant failure can occur even 10 years or later after implant placement and that distal bone resorption is also common in the long-term.

An article by Tillander et al. (2017) is a retrospective review of 96 individuals treated at the investigators center in Sweden between 1990 and 2010. Implant associated osteomyelitis was diagnosed in 16 subjects (10-year cumulative risk of 20%). Ten implants were removed for infection resulting in a 10-year cumulative risk of 9%.

Brånemark et al. (2019) published a study of 5-year outcomes and reported a revision-free survival rate of 45%. Complications included thirty-four patients with seventy superficial infection episodes including fourteen deep infections. Fifteen patients had mechanical complications and four required implant removal.

Hagberg et al. (2020) conducted a cohort study to assess a 15-year follow-up of transfemoral amputees with the OPRA bone-anchored transcutaneous prostheses, the survival rate of the osseointegrated implant part (the fixture) was 89% and 72% after seven and 15 years, respectively. However, a total of 61 patients (55%) had mechanical complications (mean 3.3 (SD 5.76)), resulting in exchange of the percutaneous implant parts and a positive relationship between a higher activity grade and the number of mechanical complications was noted. These findings emphasize that activity restrictions and improvements to the mechanical properties of the implant system are required. The study showed that the OPRA Implant System improved prosthetic use, led to better mobility, caused less problems, improved overall situation, and improved general physical health-related quality of life at 24 months compared to the subjects' scores preoperatively. Early loosening was the most common complication requiring surgical removal of the OPRA Implant System. Eight percent (4/51) of patients had their implants removed due to loosening or persistent pain. The most frequently reported adverse events were superficial infections.

Nebergall et al. (2012) conducted a study to address radiostereometric analysis (RSA) and periprosthetic bone remodeling, to assess long-term fixation of the OPRA Implant System. The RSA analysis for the OPRA Implant System indicated stable fixation of the implant (no substantial motion) up to 7 years after the second surgical procedure. Although some implants showed slight initial motion, the implants had stabilized at the 5-year follow-

up. The majority of radiographs showed only minimal amounts of bone remodeling around the implant, and ultimately this remodeling did not compromise implant fixation of performance. The team concluded that the OPRA Implant System provides a solution for patients who are unsuitable candidates for a conventional socket prosthesis.

c. U.S. Food & Drug Administration (FDA) Information

VA generally only approves use of medical devices that have received at least FDA clearance for 510(k) Premarket Notification. The following device has received Premarket Approval from the FDA and is indicated for use in patients with above knee amputations.

To search for devices that have received FDA 510(k) clearance or Premarket Approval (PMA), please visit the FDA Devices database.

Information	Description
Product Name	Osseoanchored Prostheses for Rehabilitation of Amputees (OPRA) Implant System
PMA Applicant	Integrum AB
Address	Krokslätts Fabriker 50, SE-431 37 Mölndal, Sweden
Approval Date	December 18, 2020
Approval Letter	Premarket Approval Letter

d. Medicare Coverage Determinations

There are currently no available Medicare coverage determinations for Osseoanchored Prostheses. VA and Medicare are governed by separate laws and regulations; thus, VA coverage determinations may be different.

e. TRICARE Policy Manual

Available TRICARE coverage determinations are listed below as a resource. VA and TRICARE are governed by separate laws and regulations; thus, VA coverage determinations may be different.

TRICARE Policy Manual 6010.63-M, Chapter 8, Section 5.1

- A medical device with FDA Premarket approval may be a TRICARE covered benefit
- Medical devices may be covered when medically necessary, appropriate, the standard of care, and not otherwise excluded.

- Medical devices must be FDA approved or of a type not requiring pre-market approval by the FDA. Coverage of any such device is subject to all other requirements of the law, rules, and policy governing TRICARE

IV. Definitions

Term	Definition
Amputation	Removal of a limb by trauma, medical illness, or surgery
Abutment	A skin-penetrating device that is connected to the fixture part of the implant system for connection to the external prosthesis
Metastasis	The spread of cancer cells from the place where they first formed to another part of the body. In metastasis, cancer cells break away from the original (primary) tumor, travel through the blood or lymph system, and form a new tumor in other organs or tissues of the body. The new, metastatic tumor is the same type of cancer as the primary tumor. For example, if breast cancer spreads to the lung, the cancer cells in the lung are breast cancer cells, not lung cancer cells
Neuropathy	Sometimes referred to as peripheral neuropathy and associated with symptoms such as tingling, numbness, pain, or increased sensitivity to touch. Poorly controlled diabetes accounts for about 60 percent of cases. Other causes include chemotherapy, HIV, shingles, kidney disease, autoimmune diseases, infectious diseases, alcoholism, nutrient deficiencies, hereditary disorders, and physical trauma
Osseointegration	The scientific term for bone ingrowth into a metal implant. Osseointegration can be applied in persons with amputations as a method for anchoring an external prosthesis directly to the bone
Prosthesis	An artificial device that replaces a missing body part, intended to restore the normal functions of the missing body part
Transfemoral amputation	An above knee amputation that is a surgical procedure performed to remove the lower limb at or above the knee joint
Ulceration	The formation of a break on the skin or on the surface of an organ

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VI. CDI History/Revision Information

- Explanation of changes to the CDI

Revision Type	Date of Revision	Update(s) Made to CDI
	MM/DD/YYYY	
	MM/DD/YYYY	