Summary of Safety and Clinical Performance (SSCP)

DocNo:012 933

Revision 2

02-10-2024

This summary of Safety and Clinical Performance (SSCP) is intended to provide public access to an updated summary of the main aspects of the safety and clinical performance of the device.

The SSCP is not intended to replace the Instructions for Use as the main document to ensure the safe use of the device, nor is it intended to provide diagnostic or therapeutic suggestions to intended users or patients.

The following information is intended for users/healthcare professionals.

Device Identification and general information

Device trade name(s)	OPRA™ Implant System
Manufacturer's name and address	Integrum AB Gemenskapens gata 9 SE-431 53 Mölndal, Sweden
Manufacturer's single registration number (SRN)	SE-MF-000026900
Basic UDI-DI	73401521oprasystemRW
Medical device nomenclature description/text	OPRA Implant EMDN code: P9099
Class of device	IIb (MDR 2017/745 Annex VII – Rule 8)
Year (CE) certificate covering device first issued	Year 1999
Authorized representative if applicable; name and SRN	Inapplicable
Validating notified body name (notified body validating SSCP) and notified body's single identification number	BSI Group the Netherlands B.V. NB 2797

Device intended purpose

Intended purpose	OPRA™ Implant System provides direct skeletal anchorage of external amputation prostheses for individuals with amputations who have had an amputation due to trauma or cancer and who have or are anticipated to have rehabilitation problems with, or cannot use, a conventional socket prosthesis. The OPRA™ Implant System is intended for skeletally mature patients.
Indication(s)	OPRA™ Implant System is indicated for patients who have had an amputation due to trauma or cancer. OPRA™ Implant System is intended for patients whose bone growth is complete. The patient currently has or is expected to have rehabilitation problems with a socket prosthesis. Examples of rehabilitation problems: • Recurrent skin infections and ulcerations in the socket contact area • Pain • A short stump preventing the use of socket prosthesis • Volume fluctuation in the stump • Soft tissue scarring • Extensive area of skin grafting • Socket retention problems due to excessive perspiration

	• Restricted mobility
Specific medical conditions	Medical condition is individuals with amputations who have had an amputation due to trauma or cancer and who have or are anticipated to have rehabilitation problems with, or cannot use, a conventional socket prosthesis
Specific anatomical locations	OPRA™ Implant System depends on amputation level
Target population(s)	OPRA™ Implant System for long bones is indicated for patients who have an amputation due to trauma or cancer and who have or are anticipated to have rehabilitation problems with, or cannot use, a conventional socket prosthesis. The OPRA™ Implant System is intended for skeletally mature patients. The OPRA™ Implant System for digit amputations is a skeletal attachment of external amputation prostheses provided as an alternative to conventional finger/thumb prostheses. Each patient is assessed for suitability prior to treatment with OPRA™ Implant System. A medical team assessment is performed to reach consensus in relation to the benefits and risks of the treatment. The team consists of at least one orthopedic surgeon, one prosthetist and one physiotherapist. A thorough analysis and clinical examination of the patient is performed.
Contraindications and / or limitations	The patient's skeletal growth is not complete. Completed skeletal growth is deemed as the finding of generally closed epiphyseal zones on X-ray. The patient has atypical skeletal anatomy which may affect treatment with OPRA™. Examples of atypical skeletal anatomy: • Bone measurements outside defined interval • Congenital anomalies that might affect treatment with OPRA™ • Conditions which are not favourable for the device to be installed such as deformities, fractures, infections The patient should have the following amount of remaining cortex bone around the implant, depending on implantation level: • Femur: at least 2 mm • Humerus: at least 1.5 mm • Digits: at least 1 mm The patient has pronounced osteoporosis.

	The patient suffers from concurrent diseases that might affect treatment with OPRA™. Examples of concurrent diseases are: • Severe peripheral vascular disease • Diabetes mellitus with complications • Skin disorder involving the residual extremity • Neuropathy or neuropathic disease and severe phantom pain • Active infection or dormant bacteria • Metabolic bone disease and/or metastatic lesions in the residual bone The patient is not expected to be able to comply with the treatment and the follow-up requirements. For transfemoral amputations, patient's body weight is higher than 100 kg/ 220 lbs. including the prosthesis.

Device description

The OPRA™ device is an implant system for direct skeletal anchorage of amputation protheses. The OPRA™ Implant System constitutes a rehabilitation alternative for amputees when treatment with socket prostheses is or anticipated to be insufficient.

OPRA™ is indicated for patients who have had an amputation due to trauma or cancer and who have or are anticipated to have rehabilitation problems with, or cannot use, a conventional socket prothesis. The OPRA Implant System is intended for skeletally mature patients.

The OPRA™ Implant System consists of an anchorage element (Fixture) and a skin-penetrating device (Abutment) secured with a screw (Abutment Screw). These implants are inserted surgically into the bone of the residual limb in two separate surgical sessions Stage 1 (S1) and Stage 2 (S2).

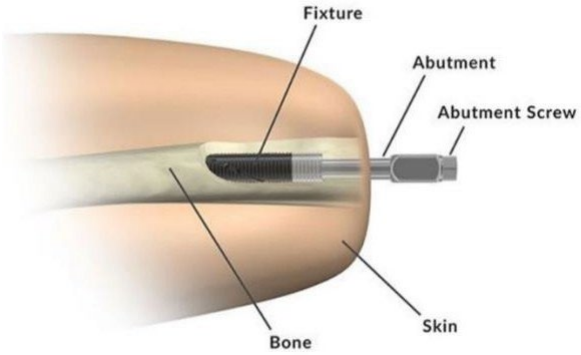

Figure 1. Illustration of the OPRA™ Implant System placed in the bone of the residual limb after Stage 1 and Stage 2 surgical sessions.

The Abutment is connected to an artificial limb such as a prosthetic leg, arm, or digit through various prosthetic components, depending on the amputation level. The prosthetic components could include attachment, alignment, and load-control functions which protect the implant from accidental loads.


Figure 2. Left: Transfemoral OPRA™ Implant System depicting prosthetic components, Axor II.
Right: Transhumeral OPRA™ Implant System depicting prosthetic components, Attachment Device and Puck.

3.1 OPRA™ Platform Structure

The OPRA™ implantable components are divided into *Platforms based on the internal geometry of the Fixture/Abutment connection*.

The OPRA™ Implant System platforms are divided in Implantable Components, Prosthetic Components and Accessories. Implantable Components are further divided into Implants (Fixtures, Abutments, Abutment Screws, and Central Screws) and Healing components (Healing Screws, Graft Screws, Healing Cylinders, and Healing Washers).

The term pre-OPRA refers to the implant system variants which were used before standardization of the OPRA™ Implant System components manufactured by Integrum AB. Pre-OPRA implants should be interpreted as precursor models of the standardized OPRA™ Implant System and are considered custom-made devices with characteristics specific to individual patient conditions and needs. The precursor models were designed according to the same design concept as the standardized OPRA™ Implant System with common features such as a threaded Fixture, a percutaneous Abutment and an Abutment Screw.

From a biological point of view, regarding osseointegration and fixture survival, there is little differences between the pre-OPRA implants and the standardized OPRA™ Implant System. The same is true for the percutaneous part. The mechanical performance of the abutment and abutment screw has however been improved over time (increased strength while the Young's Modulus remains similar).

Differences between Platform F and G include further improvements made to the components to enhance mechanical strength and performance, increase resistance to fatigue, improve sealing properties, improve bone-to-implant contact area (thus improving initial stability of the implant), and simplify design.

The overall design concept of the OPRA™ Implant System, for all platforms, regarding attachment features to the user, between components and to external prosthetic devices,

remains the same or very similar and the pre-OPRA implants and the F/G platforms of the standardized OPRA™ Implant System were/are used in the same patient groups and with similar intended use. Clinical evidence available for pre-OPRA, Platforms F and G can be utilised as parallel data where dedicated platform information is unavailable.

Prosthetic Components used to connect OPRA™ Implant System to the external prosthesis to each platform are summarized in table below.

PLATFORM	**Prosthetic components**
A / B	Digit Prosthetic Component angulated
	Digit Prosthetic Component straight
E / F	Attachment Device
	Puck
	Alignment Device
	Rotation Safety Device
F / G	Axor II

<table>
<tr><td>Key functional elements</td><td colspan="4">OPRA™ Implant System incorporates the following components:
• Fixture
• Abutment
• Abutment screw
• Central screw*
• Healing components
• Prosthetic components
* Central screw is only applicable for transhumeral and transfemoral amputation levels</td></tr>
<tr><td rowspan="9">Any materials and substances in contact with the patients' tissues</td><td>Component</td><td>Materials</td><td>Surface treatment</td><td>Mode of contact with human body</td></tr>
<tr><td>Fixture</td><td>Titanium alloy TiAl6V4 ELI - Gr 23</td><td>BioHelix ™ surface treatment</td><td>Direct Long- term implant principally contacting bone/tissue</td></tr>
<tr><td>Abutment</td><td>Titanium alloy TiAl6V4 ELI - Gr 23</td><td>N/A</td><td>Direct Long- term implant principally contacting bone/tissue</td></tr>
<tr><td>Abutment Screw</td><td>Titanium alloy TiAl6V4 ELI - Gr 23</td><td>DLC coating**
** DLC is only available in Abutment Screw variants for transfemoral level</td><td>Direct Long- term implant principally contacting bone/tissue</td></tr>
<tr><td>Central screw</td><td>c.p Gr 2 Titanium</td><td>N/A</td><td>Direct Long- term implant principally contacting bone/tissue</td></tr>
<tr><td colspan="4">Healing components</td></tr>
<tr><td>Healing Screw</td><td rowspan="2">Titanium alloy TiAl6V4-Gr 5</td><td rowspan="2">N/A</td><td rowspan="2">Direct Long- term implant principally</td></tr>
<tr><td>Healing cylinder</td></tr>
</table>

	Graft screw			contacting bone/tissue
	Healing washer			
	Prosthetic components			
	Axor™ II	Aluminum Stainless steel Polymeric materials	N/A	Certain components have direct transient contact with skin
	Puck	POM F25	N/A	Direct transient contact with intact skin
	Humerus Attachment Device	Aluminum EN-AW 6026 Natural anodized, Stainless steel EN 1.4404 Acetal	N/A	Certain components have direct transient contact with intact skin
	Humerus Alignment Device	Aluminum EN- AW6026 Natural anodized, Stainless steel, washer	N/A	Certain components have direct transient contact with intact skin
	Humerus Rotation Safety Device	Aluminum EN-AW 6026 Natural anodized, Stainless steel EN 1.4404 Polymeric materials	N/A	Certain components have direct transient contact with intact skin
	Digit prosthetics angulated	Stainless Steel 1.4404 Brass	N/A	Direct transient contact with intact skin
	Digits prosthetics straight			
Device single use	OPRA™ Implant System is single use			
Method of sterilization	Ionising (gamma (γ))-radiation sterilisation			
Absorbable implants	N/A			
Device incorporates:				
• medicinal substance (including human blood or plasma derivative), or				N/A
• tissue(s) or cells of human or animal origin, or their derivatives, or				N/A
• substances or combinations of substances absorbed by or locally dispersed in the human body, or				N/A
• materials incorporated into device containing or consisting of CMR (carcinogenic, mutagenic or toxic to reproduction) substances or endocrine-disrupting substances, or				N/A
• materials that could result in sensitisation or allergic reaction by patient or user.				N/A
Basic UDI-DI:				
OPRA™ Implant System	73401521oprasystemRW			

Reference to previous generation(s) or variants of such exist, and description of differences	Since initial CE-marking of the product, OPRA™ Implant System has only undergone one significant change, as defined by Council Directive 93/42/EEC “wherever the changes could affect conformity with the essential requirements” was implemented in 2014 and was notified to BSI [BSI Assessment Report Extended Applications SMO 8184427].

	All changes specified below were made under Council Directive 93/42/EEC. No design changes were made under Regulation (EU) 2017/or in the transition period. Implementation of platform G is not considered a significant change as defined by Council Directive 93/42/EEC and therefore not included in the table.		
	Year	**Devices**	**Nature of change**
	1999	OPRA Implantable components for transfemoral applications	No change initial launch to the market
	2001	Rotasafe, prosthetic component for transfemoral applications	No change initial launch to the market
	2013	Axor, prosthetic component for transfemoral applications – successor of Rotasafe	No change initial launch to the market
	2014	OPRA Implantable components for transhumeral and digits applications OPRA Prosthetic components for humerus and digits	Extended application

Description of any accessories intended to be used in combination with device	OPRA™ Implant System is not supplied with any accessories.	
	Accessory	**Description**
	OPRA Connector	The Connector is used for adaption of short training prostheses to the implantable products. During the initial phase of rehabilitation after Stage 2 surgery, a short training prosthesis is used for gradually increasing the load on the implant, and for mobilization training.
	OPRA Humerus Training kit	The Humerus training kit is used during the initial phase of rehabilitation after Stage 2 surgery. The training kit is used for gradually increasing the load on the implant before final protheses fitting
	OPRA Abutment Support E	The Abutment Support encloses the Abutment in the postoperative period after S2. It assists the dressing to keep a slight pressure on the soft tissues during healing.
	OPRA Abutment Support F/G	The Abutment Support encloses the Abutment in the postoperative period after S2. It assists the dressing to keep a slight pressure on the soft tissues during healing.
	OPRA Soft Tissue Support Pylon II	Placed surrounding the exterior part of the Abutment shaft. Together with the Plate it provides support for the soft tissue of the residual limb. To be used with Axor™ II or with OPRA™ Connector. Pylon II is compatible with Abutment, Axor™ II and Soft Tissue Support Plate large and small.
	OPRA Soft Tissue Support Plate Small	The Soft Tissue Support Plate is placed on top of the Pylon. Together with the silicone casting it provides support for soft tissue of time residual limb.

	OPRA Soft Tissue Support Plate Large	The Soft Tissue Support Plate is placed on top of the Pylon. Together with the silicone casting it provides support for soft tissue of time residual limb.
Description of any other devices and products intended to be used in combination with device	OPRA™ Implant System is used with external prosthesis Femur: the OPRA™ System is recommended for use with commercially available non-microprocessor- controlled prosthetic knees and microprocessor controlled prosthetic knees that do not include powered activation of flexion and extension of the prosthetic knee. Digits: used with custom made cosmetic cover made from OPRA™ Straight or Angulated external prosthetic component. Humerus: used with generally available external prosthetic components for upper limb.	

Risks and warnings

Residual risks and undesirable side effects

The following device related complications were observed during OPRA™ study and recorded from clinical literature:

Product platform	Observed and possible complications

Platform F/G
Femur
	• Infection
	  • Superficial infection
	  • Deep infection
	• Mechanical implant complications such as
	  • Loose Abutment Screw
	  • Bending or fracture of Abutment and/or Abutment Screw
	  • Wear
	• Soft tissue problems
	• Fixture removal due to Fixture fracture or Fixture loosening, including distal bone resorption
	• Skeletal fracture
	• Severe or persistent pain
	• Pain when loading
	• Fall
	• Injury

Platform E/F Humerus	
Platform A/B Digits	

Author(s)	Amputation level	Platform	No. of patients	Study period	Complication type								
					Infection		Abutment and abutment screws	Soft tissue problems	Implant loosening	Pain	Fracture	Implant removal	Incomplete fracture	Death
					Deep infection	Superficial infection								
Hagberg et al. (2020)	Femur	OPRA F	111	1999- 2017	Not reported	Not reported	61 (55%)	Not reported	2 (1.8%)	Not reported	Not reported	Not reported	Not reported	3 (2.7%)
Hagberg et al. (2008)	Femur	OPRA F	18	1999	Not reported	6 (33%)	Not reported	Not reported	1 (5.5%)	1 (6%)	Not reported	Not reported	Not reported	Not reported
Hagberg et al. (2009)	Femur	Pre-OPRA OPRA F	100	1990–2008	16/96 (16%)	Not reported	Not reported	Not reported	11/100 (11%)	Not reported	Not reported	11/100 (11%)	Not reported	Not reported
Hagberg et al. (2014)	Femur	OPRA F	39	1999-2007	Not reported	Not reported	Not reported	Not reported	Not reported	1 (2.5%)	Not reported	Not reported	Not reported	Not reported
Hagberg et al (2018)	Femur	Pre-OPRA OPRA F	12	1990 -2015	1 (8,3%)	3 (25%)	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported
Brånemark et al (2014)	Femur	OPRA F	48	1999-2007	4 (8.33%)	Not reported	Not reported	Not reported	1 (2%)	Not reported	Not reported	Not reported	Not reported	Not reported
Brånemark et al (2018)	Femur	OPRA F	51		11 (21%)	34 (66%)	8 (15%)	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported
Tillander et al. (2017) and Tillander et al. (2010)	Femur Humerus Other (tibia, radialis, ulna)	Pre-OPRA OPRA E and F	96	Patients were selected during a 6-month period in 2005 and re-evaluated after 3 years	16 (16.6%)	19.5%	Not reported	Not reported	Not reported	Not reported	Not reported	10 (10.4%)	Not reported	Not reported
Tsikandylakis et al. (2014)	Humerus	Pre-OPRA OPRA E and F	18	1995-2010	Not reported	15 (83.3%)	Not reported	Not reported	2 (11.1%)	Not reported	Not reported	Not reported	8 (44.4%)	Not reported
Li et al. (2019)	Thumb	Pre-OPRA OPRA A and B	13	1990-2014 (retrospective)	1 (5.5%)	5 (7 times in 5 patients)	8 (in 3 patients)	Not reported	3 (16.6%)	Not reported	0	3 (16.6%)	Not reported	2 (unrelated cause)

Warnings and precautions

Warnings OPRA™ Implant System Instructions for Use contains the following warnings:	The OPRA™ components are for single use only. Do not use OPRA™ components if the package is opened or damaged. Do not use OPRA™ past its expiration date. Smoking negatively impacts bone osseointegration. Healing problems can occur in obese patients. For transfemoral and transhumeral amputations, patients with the OPRA™ Implant System who undergo elective surgery for any reason are recommended to be given antibiotic prophylaxis (e.g. cephalosporins intravenously). Patients with a medical history of previous infection on the amputated side should be carefully evaluated with laboratory analysis including sedimentation rate CRP, RBC and WBC to verify that there is no on-going infection. Further, dormant bacteria should be excluded, especially in the skeleton. We recommend intramedullary culturing. For transfemoral and transhumeral amputations, joint problems that might affect ambulation (i.e. joints of the contra lateral limb, the sacroiliac joint, the ipsilateral hip joint, i.e., inflammatory, noninflammatory disease or rheumatoid arthritis) may negatively affect the outcome of the treatment. The following drugs may negatively affect osseointegration and cause loosening of the Fixture: - Steroids for systemic use, - Chemotherapy agents, The following drugs should not be used during the first year of treatment: - NSAIDs (Non-Steroidal Anti-Inflammatory Drugs) and ASA (Acetylic Salicylic Acid) two weeks preoperatively or for continued use postoperatively, - Bisphosphonates, Other drugs that might affect bone remodeling.
Precautions OPRA™ Implant System is supplied with Instructions for Use containing the following	OPRA™ Implant System is supplied with Instructions for Use containing the following precautions: If bone quality is not the best, full weight bearing on the prosthesis should begin more gradually and at a reduced pace as determined by the treating physician. The healthcare professional should inform the patient of the following special care to be exercised: • The patient should always check carefully that the prosthesis is adequately attached to the Abutment. • The patient should never try to fix any problems with the device or use any tools on the device as that may damage the Abutment and the Fixture.

precautions:	• The patient should always protect the Abutment when he or she is in hot or cold places. • In the sauna, wrap a wet towel around the Abutment to protect it from heat. • Protect the amputated limb when in a cold environment. • The patient should always avoid damaging themselves or others with the Abutment. If the patient's bone quality is judged to be suboptimal, the mobilization should be carried out at a reduced pace. Prosthesis components should be chosen so as to minimize the risk of overloading the implant system. The components should be inspected for crack formation and signs of wear in the connection to external prosthesis components. Signs of wear in the connection between Fixture and Abutment include the dark colouring of secretion or tissue. A change of Abutment must be considered if: • There is movement in the connection between Fixture and Abutment. • Dark-coloured secretion continues • The Abutment is deformed, or mechanical complication is suspected. For transfemoral amputations, the following additional precautions shall apply: The Abutment Screw should be tightened with a counter torque device clockwise to 12 Nm torque. Tightening must be carried out in accordance with the protocol (see Surgical Technique Stage 2). Retightening of the Abutment Screw shall only be performed by professionals. If the Abutment or Abutment Screw is replaced, the screw must be retightened by treating physician. Additional appointments may be necessary to ensure that the system is working correctly. The device is designed for releasing at the Abutment/ prosthetic interface, through the security coupling, Axor™ II, if overloaded. For more detailed information, see the OPRA™ Axor™ II instructions for use. OPRA™ is intended for use with activities of daily living such as: sitting, standing, and walking. Excessive physical activities that can lead to high torque, such as climbing, running, and jumping, are not recommended. This can lead to fatigue and damage to system components. It is recommended that special care is taken to protect the Abutment during sleep by patients. The protection will be provided by the prosthetist. The patient should always use a cane or crutches for longer walks, never lift, or carry heavy items and never subject the OPRA™ Implant System to high torques. While riding a bike, the patient's knee joint might lock in the fully stretched position which can seriously damage the Fixture. The patient should always position the bike seat low enough that the artificial knee cannot fully stretch out while cycling. The patient should never stand up while cycling. Extension defects in hip joints should be avoided. Extension defects exceeding 10 °result in adverse biomechanical stress on the implant system, which could lead to an impaired gait pattern and increase the risk of complications.

<table>
<tr><td></td><td>Depending on patient skeletal anatomy, the Fixture must not be subjected to direct load for three to six months. A full load with a definitive prosthesis is normally permitted approximately 6 months postoperatively Stage 2 (52) following a check- up by the physician responsible for the treatment.
For transhumeral and digit amputations, the following additional precautions shall apply:
• Rehabilitation must be carried out according to individualized training programs.
• Rehabilitation must be carried out at a pace adapted to the healing conditions of the individual patient.
• Bone quality is an important parameter for judging healing conditions.
• In the event of pain or other discomfort, loading on the OPRA™ Implant System should be discontinued until the cause of the symptoms has been established by the responsible physician.</td></tr>
<tr><td>Other relevant aspects of safety including summary of any Field Safety Corrective Action (FSCA including FSN) if applicable</td><td>
<table>
<tr><th>Date</th><th>Device</th><th>FSCA/FSN</th><th>Reason</th></tr>
<tr><td>2021</td><td>Axor II</td><td>FSCA (FSN)</td><td>Alert users regarding Axor II service intervals and other parameters</td></tr>
</table>
</td></tr>
</table>

Clinical evaluation and post-market clinical follow-up (PMCF) Summary

<table>
<tr><td>Equivalent device clinical data summary, if applicable</td><td colspan="2">Integrum does not declare equivalence to any reference devices within the meaning of Appendix A1, MEDDEV 2.7/1 Revision 4 and MDCG 2020-5 Guidance on clinical evaluation – Equivalence.

Socket prostheses and Bone-anchored limb prostheses are considered benchmark devices, i.e., products currently available on the market with a similar principle of operation and similar intended use as the OPRA™ Implant System.</td></tr>
<tr><td rowspan="3">Conducted Investigation clinical data summary of device before CE-marking, if applicable</td><td colspan="2">Clinical data from clinical investigation on OPRA™ Implant System the OPRA study – Prospective study of 51 patients with two years follow-up (1999-2007):</td></tr>
<tr><td>Study title</td><td>Osseointegrated Prostheses for the Rehabilitation of Amputees</td></tr>
<tr><td>Device name including any model</td><td>OPRA Implant System/OPRA Platform F
OPRA Implant System shows the study design fulfills ICH/GCP
Guidelines and Article 62 | Annex XV, Regulation (EU) 2017/745.</td></tr>
</table>

	Study sponsor	Integrum AB Medicinaregatan 3 A SE – 413 46 Gothenburg Sweden Tel +46 (0) 31 / 741 1760 Fax +46 (0) 31 / 741 1761 Email: info@integrum.se
	Principal Investigator	Björn Gunterberg Department of Orthopaedics, Sahlgrenska University Hospital SE – 413 45 Gothenburg Sweden
	Clinical investigation site	Department of Orthopaedics, Sahlgrenska University Hospital, Gothenburg, Sweden SE – 413 45 Gothenburg Department of Prosthetics and Orthotics, Sahlgrenska University Hospital SE – 413 45 Gothenburg Sweden
	Ethics committee review	Clinical Investigation approved by the Ethics Committee, Gothenburg University (R-402-98 with amendments T-42701 and T-21603)
	Competent Authority notification	Clinical Investigation notified to Competent Authority in Sweden (34:1861/99)
	Intended use of the device in the investigation	The implant prosthetic system OPRA (Osseointegrated Prostheses for the Rehabilitation of Amputees) Implant System is considered a rehabilitation alternative when treatment with socket prostheses is unsatisfactory
	Study objectives	Verify benefits and safety of OPRA when used for intended purpose, under normal conditions and according to instructions
	Primary objectives	To evaluate the improvement of prostheses attachment, comparing OPRA to socket prostheses. To evaluate possible severe complications related to the use of OPRA.
	Secondary objectives	To evaluate improvements in functional ability when using OPRA. To evaluate improvements in quality of life when using OPRA. To evaluate the frequency of possible medical complications when using OPRA. To evaluate the type and frequency of mechanical complications when using OPRA.
	Primary and secondary endpoint(s)	
	Inclusion criteria	• Patient must be a transfemoral amputee or must be undergoing uni- or bilateral transfemoral

		amputation. • Patient must have present problems or must be expected to have problems with conventional socket prosthesis. • Patient must have undergone pre-operative Radiographic assessment including Computer Tomography imaging. • Patient's skeletal maturation must be completed • Patient must have normal skeletal anatomy. • Patient must not be over 70 years of age. • Patient's body weight must be less than 100 kg (225 lb.). • Patient must be suitable for surgery based upon medical history and physical examination. • Patient must not have severe peripheral vascular disease, diabetes mellitus with complications, skin diseases involving the amputated limb or other diseases that could affect the suggested treatment negatively. • Patient must not be or must not have been treated with systemically administrated • corticosteroids, chemotherapy drugs or other drugs in a way that could affect the suggested treatment negatively. • Patient must not be pregnant. • Patient must be likely to comply with treatment and follow- up requirements. • Patient must have given written Informed Consent to participate in the Clinical Investigation.
	Exclusion criteria	Patients experiencing or expect significant problems with conventional prostheses or not being able to use a prosthesis Patients who: 1) have inadequate skeletal anatomy 2) have severe overweight 3) suffer from certain diseases 4) use certain medications and/or 5) are unable to comply with the treatment plan
	Sample Size	50 patients
	Recruitment	Patients recruited among transfemoral amputated patients seen at the Department of Orthopaedics, Sahlgrenska University Hospital
	Sample size determination	Sample size determination based on primary efficacy variable, the problem score, and the secondary efficacy variable and he function score.

	Summary of study methods	A total of 51 patients with TFA were included and followed up for 5 years. 45 patients had unilateral and 6 bilateral transfemoral amputations. 4 of the 6 patients with bilateral TFAs were treated bilaterally, whereas 2 with bilateral TFAs were treated on one side only. A total of 55 limbs were evaluated. The main reasons for amputation were trauma and tumour. At inclusion, 42/51 (82.35%) patients were using socket-suspended prostheses, but 9 did not use any prostheses because of difficulty obtaining adequate socket fit. Among those, 8 had tried to use a prosthesis, and one did not. Treatment involved two surgeries S1 (bone of the femur is prepared to receive the Fixture and it is precisely threaded into the medullary canal of the bone and once in place the soft tissues and skin are closed) and S2 (Abutment is attached to the Fixture and protrudes through the skin) separated by 6 months, followed by rehabilitation. Clinical examination and safety assessment were conducted at 3, 6, 12, and 24 months following S2 follow-up visits and adverse events, and complications recorded. At 5-year follow-up, a clinical assessment was made, radiographs were performed, and patient reported outcomes were recorded. Adverse events were also recorded. Transfemoral Amputation (Q-TFA) and Short Form 36 (SF-36) Health Survey were completed before S1 and 1, 2, and 5 years after S2.
	Summary of results of clinical benefits;	The following Q-TFA scores were applied: Prosthetic Use Score (0 - 100) Prosthetic Mobility Score (0 - 100) Problem Score (100 - 0, reversed) Global Score (0 - 100) A Prosthetic Use Score of 0 means that the prosthesis is not used at all, whereas 100 means that the prosthesis is used 7 days per week for more than 15 hours per day. Fixture survival was calculated using cumulative success rate. Analyses of differences between baseline and 5-year follow-up revealed statistically significant improvements in all four Q-TFA scores ($p < 0.0001$) and in the Physical Function ($p < 0.0001$), Role Physical ($p = 0.020$) and Physical Component scores ($p < 0.0001$) on the SF-36. All other differences were non-significant. Prosthetic use at baseline showed that 29/42 (69%) used their prostheses daily for at least 13 hours *per* day. At 5-year follow-up, this was reported by 28/40 (70%) patients. No statistically significant differences between the 2- and 5-year follow-up periods were found.

		The following benefits include: Increased prosthesis use Improved mobility with the prosthesis Reduced problems related to the amputation and the prosthesis Improved function Improved quality of life
	Any undesirable side-effects or adverse events, and their frequency in relation to time	The commonest adverse event was superficial infection typically treated with oral antibiotics for 10 days (34 patients). The following serious adverse events (n=85) were reported in 26 patients: • Fixture removal (4 patients) • Stump revision (3 patients) • Deep infection (11 patients) • Exchange of the abutment and/or abutment screw (15 patients) A total of 14 deep infections were diagnosed in 11 patients during the 5-year period. One of these infections caused early loosening/failure of the fixture. 9 patients with deep infections were successfully treated with oral antibiotics, with a mean time of 5 months. One deep infection was not resolved at 5-year follow-up. 43 mechanical complications occurred in 15 patients, resulting in replacement of damaged abutment and/or the abutment screw. Accidental overload was reported in 16 bent abutments in 9 patients. 1 patient had the abutment temporarily removed (fixture in *situ*) four months before the 5-year follow-up appointment because of mechanical issues with the abutment and abutment screw. The relationship between activity level (mobility) and mechanical complications (i.e., abutment and abutment screw changes) was investigated and there is a positive correlation between higher activity level and mechanical complication frequency.
	Percentage completeness of follow-up should be provided.	45 of 51 (88,23%) patients completed 2-year follow-up; 3 patients were withdrawn for reasons unrelated to the implant.
	Any limitations of the study, such as high loss to follow-up, or potential confounding factors that	A total of 40 patients were followed up at 5 years. Contemporaneously, 1 other patient was withdrawn from the study (unrelated to implant), and three patients failed to present for 5-year follow-up. 5-year fixture cumulative survival rate was 92%, and revision-free rate was 45%.

	may question the results.	
	Any device deficiency and any device replacements related to safety and/or performance during the study.	43 mechanical complications occurred in 15 patients, resulting in replacement of damaged abutment and/or the abutment screw.

Summary of other clinical data and main findings pertaining to device

Data sources have been considered during clinical evaluation:

- Clinical investigations
- Clinical in-house knowledge and experience
- Post-marketing data
- Retrieved publications

Published Review Articles

Author (s)	Study design Study duration / period	Article objective	Conclusions by the author(s)	Device used
Hoyt *et al,* (2020)	Review	The article presents a review of OPRA™ Implant System focused on indications, surgical procedure, complications, and results of clinical studies. The article is not a systematic review, but it includes all relevant references up regarding the clinical studies of the OPRA™ Implant System up to the time of publication in 2020	The OPRA™ Implant System has been successfully employed as an alternative in patients who cannot tolerate their socket prostheses. Recent applications in the upper extremity have similarly increased the utility of prostheses and may lead to substantial improvements in function, quality of life, and return to activity. Currently, few centers are performing the procedure, but they are achieving marked success, excellent patient outcomes, and educating other surgeons in its use, including surgical residents. Improvements in design, cutaneous interface, and surgical technique have improved the safety of this device to decrease the potential for infection, risk of	OPRA Implant System, all platforms

				periprosthetic fracture or catastrophic failure, and reduce time to safe weightbearing.	
	Zaid *et al,* (2019)	Review	The article reviews history and biology of osseointegration, indications and contraindications for use of currently available implant systems and reported outcomes. The article is not a systematic review, but it includes all relevant references up regarding the clinical studies of the OPRA™ Implant System and other systems for bone-anchored attachment of limb prostheses up to the time of publication in 2019.	Few systems besides the OPRA™ Implant System have a proven track record beyond 10 years. Because of this, it is critical that each system be evaluated rigorously, within the context of observational clinical trials. Osseointegration is an appropriate surgical alternative for a select group of amputees who are unable to tolerate a conventional socket prosthesis. It represents a promising treatment option for carefully selected patients, which may become the standard of care in the relatively near future. The benefits of osseointegration from improved functional outcomes, quality of life, and increased prosthesis utilization have been outlined by several studies. However, several unique designs are being used, and the technique of transdermal implantation remains in its early stages, warranting post marketing surveillance within a centralized registry. Superficial infection remains the most common complication across all prosthesis types; nonetheless, most instances can be successfully managed with conservative treatment.	OPRA Implant System, all platforms Other Bone-anchored systems for the attachment of limb prostheses
	Thesleff *et al,* (2018)	Review	This review provides an overview of the biomechanical characteristics of current percutaneous implant systems for direct skeletal	It is difficult to compare the available systems as they have undergone several changes over time, and clinical trials continue to be limited. Current systems for bone anchoring of limb prostheses use intramedullary implants. Primary stability between bone and implant is achieved	OPRA Implant System, Integral Leg Prosthesis (ILP; Orthodynamics GmbH, Lübeck, Germany),

			attachment of amputation limb prostheses.	by one of three strategies: a threaded connection, a press-fit connection, or axial compression. Secondary stability is achieved by bone ingrowth into porous surfaces of the implant. Although there are large differences between current implant systems, all systems (OPRA, ILP, and OPL) have shown functional improvements for patients with socket-related issues. Recent developments of implant systems, surgical protocols, and safety devices have reduced the rate of mechanical failure and infectious complications	Osseointegrated Prosthetic Limb (OPL; Permedica s.p.a, Milan, Italy)
	Li *et al,* (2017)	Review	The article reviews the development of the OPRA Implant System, surgical techniques, rehabilitation protocols for each level of amputation. The article includes brief reports of long-term follow-up for transhumeral and thumb amputee operations. The article reports the results from the clinical trial of the OPRA Implant System for transfemoral amputees. The article was published in 2017, before the 5-year results from the clinical trial of the OPRATM Implant System for transfemoral amputees was published, and before the publication of long-term results of OPRATM Implant System for thumb amputation. More recent information regarding	The direct attachment of osseointegrated prostheses avoids the inherent problems of socket suspension. Physiological weight bearing, improved range of motion in the proximal joint, as well as osseoperceptive sensory feedback enable better control of the artificial limbs by amputees. Pioneering efforts on extremity osseointegrated surgeries in Sweden and the development of the Osseointegrated Prostheses for the Rehabilitation of Amputees (OPRA) program allows for structured rehabilitation with standard surgical techniques to achieve adequate bone–fixture integration	Pre-OPRA and OPRA Implant System, all platforms

			these amputation levels is available in other publications described under original research articles section		
	Published Original Research Articles				
	Author (s)	**Study design Study duration / period**	**Study objective**	**Main results**	**Device used** **Amputation level**
	Brånemark *et al*, (2018)	Prospective	The purpose of this article was to report the prospective 5-year follow-up results of PRO measures compared with the patients' status at treatment start, complications, and success rate in 51 patients	The cumulative fixture survival rate at 5 years was 92%, and the revision-free survival rate was 45%. 34 patients had 70 superficial infections. 11 patients had 14 deep infections. 15 patients had mechanical complications. 4 fixtures were removed (i.e., one deep infection and three loosening). PRO measures showed significant improvements including more use of the prosthesis, better mobility, fewer issues, and improved physical health-related quality of life (all $P < 0.0001$) compared with baseline.	OPRA™ Implant System Platform F Femur
	Brånemark *et al,* (2014)	Prospective, single-centre, non-randomised study 1999-2007	Report on the results of a two-year follow-up of 51 consecutive patients.	Cumulative implant survival at two years was 92%. Q-TFA showed improved prosthetic use, mobility, global situation, and fewer problems (all $p < 0.001$). SF-36 physical scores were also improved ($p < 0.001$). Superficial infection occurred 41 times in 28 patients (rate of infection 54.9%). Most were treated effectively with oral antibiotics. Implant removal in four patients because of loosening (three aseptic, one infection)	OPRA™ Implant System Platform F
	Hagberg *et al,* (2020)	Cohort, retrospective 1999-2017	Describe implant and patient- reported outcome in patients with a unilateral transfemoral amputation (TFA) treated with a bone-	The Q-TFA scores at 2, 5, 7, and 10 years showed significantly more prosthetic use, better mobility, fewer problems, and an improved global situation, compared with baseline. The survival rate of the osseointegrated implant part (the	OPRA™ Implant System Platform F

			anchored, transcutaneous prosthesis.	fixture) was 89% and 72% after 7 and 15 years, respectively. 61 patients (55%) had mechanical complications (mean 3.3 (SD 5.76)), resulting in exchange of the percutaneous implant parts. There was a positive relationship between a higher activity grade and the number of mechanical complications	
	Hagberg *et al,* (2018)	Retrospective study 1990-2015	Describe the rehabilitation experience and outcome of treatment with bone-anchored prostheses in individuals with bilateral transfemoral amputations (TFAs) treated in Sweden over a period of 25 years	At baseline, 9/12 used prostheses and 3/12 did not. The main means of locomotion was in a wheelchair (n = 8) or wheelchair + prosthetic walking (n = 4). All prosthetic users had problems with sitting comfort. At follow-up the main means of locomotion was in a wheelchair (n = 5) or wheelchair + prosthetic walking (n = 4). Prosthetic walking (n= 4), of which three patients walked unsupported by walking aids. Seven patients had no problem with prosthetic sitting comfort, 3 had small problems.	OPRA™ Implant System Pre-OPRA and Platform F
	Hagberg *et al,* (2014)	Prospective 2-year case- control study. 1999-2007	Report on the prospective outcome, including details not yet reported, regarding prosthetic function, problems, and physical HRQOL in the subset of individuals with a unilateral TFA included in the OPRA study and followed for 2 years	6 of 7 Q-TFA scores improved (P<.0001) compared with baseline (prosthetic use, mobility, problem, global, capability, walking habits). Increased prosthesis use was reported by 26 (of 39) (P<.05). Unchanged items included problems regarding phantom limb pain and pain from the back, shoulders, and contralateral limb. The PF, PCS, and SF-6D improved a mean of 24.1± 21.4 (P<.0001), 8.5 ± 9.7 (P<.0001), and 0 .039 ± 11 (P<.007) points, respectively. Walking energy cost decreased (mean PCI at baseline, 0.749; mean PCI at follow-up, 0.61; P<.0001).	OPRA™ Implant System Platform F
	Hagberg *et al*, (2008)	Prospective 1999	Analyze general and condition-specific health related quality of life (HRQL) at 2-year follow-up	17/18 patients used the OI-prosthesis; one did not due to pain and loosening of the implant. Four of the scales of the SF-36 (Physical	OPRA™ Implant System Platform F

			as compared to the preoperative situation	Functioning, Role Functioning Physical, Bodily Pain and Physical Component Score) and all four scores of Q-TFA (Prosthetic Use, Prosthetic Mobility, Problems and Global Health) were statistically significantly improved at follow-up showing superior general physical HRQL, increased prosthetic use, better prosthetic mobility, fewer problems and a better global amputation situation.	Femur
	Hagberg *et al*, (2005)	Prospective	Study aim: (1) to study hip joint motion, when wearing and not wearing a trans-femoral socket prosthesis; (2) to study the phenomena of uncomfortable sitting when using the prosthetic limb; and (3) to compare the results with individuals provided with a bone-anchored trans-femoral prosthesis.	The hip motion decreased in all directions when wearing the socket prosthesis compared to without it (P<0.001 for all directions), and 37% of the subjects had less than 90% of hip flexion when wearing their prosthesis. Discomfort when sitting was reported among 44% (n= 19) in the socket group and was more common among individuals with less than 90% of hip flexion motion (P= 0.025). In the OI group, no restriction in hip motion was measured with the prosthesis, and no subject had less than 90% of flexion and 5% (n=1) reported discomfort when sitting.	Not described Femur
	Jacobs *et al,* (2000)	Prospective	Gain more insight into the osseoperception phenomenon and to obtain more info on the somatosensory feedback mechanisms with prosthetic limbs.	32 patients 16 upper limb amputees and 16 lower limb amputees. 9 of the upper limb amputees and 8 of the lower limb amputees had osseointegrated prostheses, the remaining used socket prostheses. Bone-anchored prostheses yielded significantly lower threshold levels for vibratory stimulation than socket prostheses, there was no significant difference between groups for pressure stimulation.	Not described Femur Humerus
	Jönsson *et al,* (2011)	1990-2010	Describe the osseointegration procedure for surgery, prosthetics, and rehabilitation.	37 patients were treated with osseointegrated implants on the upper extremities. 16 transhumeral, 10 transradial, 10 thumbs and	pre-OPRA OPRA™ Implant System Platform

				1 partial hand. Patients indicated that function and quality of life had improved since osseointegration.	A/B, E/F Humerus Radius Partial hand Thumb
	Li *et al*, (2019)	A retrospective single center case series study of 13 patients 1990-2013	Summarize the long-term follow-up of 13 thumb amputees with osseo-integrated prostheses between 1990and 2014. We present data on cumulative success rate, radiologic analysis, functional outcomes, and adverse events	Compared to unaffected hand: 70 % grip strength, pinch strength 66 %, lateral grip strength 71%. 94 % of normal hand function in SHFT test. Opposition of thumb to index finger normal in 6 of 7 patients All patients were able to feel tactile sensation in osseointegrated prosthesis. Implants removed: 3 (failed osseointegration n=2 and infection n=1). 7 superficial infections/inflammations in 5 patients. The success rates for the custom-designed implants (pre-OPRA) were 57%, for the standardized implants 100%.	pre-OPRA OPRA™ Implant System Platform A/B Thumb
	Li *et al,* (2018)	Prospective, single-center non- randomized study with 2 years follow- up. 1999-2007	This article describes the Swedish experience with bone-anchored prosthesis surgery for transfemoral amputees based on the application of the OPRA implant system	51 patients with 55 transfemoral amputations, were enrolled. Cumulative implant survival rate was 92% after 2 years (95% confidence interval, 80% to 97%). The mean prosthetic use score improved from 47 (range, 0 to 100) to 79 (range, 0 to 100) The overall situation as an amputee was reported to be improved among 31 (69%) of the patients.SF-36 also improved (P<.0001). Superficial infection occurred 41 times in 28 patients (infection rate, 54.9%). 9 mechanical complications with the abutment	OPRA™ Implant System Platform F Femur

				and/or the abutment screw, were reported in 4 patients. Six of these occurred in the same patient.	
	Lundberg *et al,* (2011)	A qualitative phenomenological research method. 1992-2005	The aim of this study was to improve our understanding about the experience of living with an osseointegrated prosthesis (OI-prosthesis) compared to one suspended with a socket, using qualitative research methodology.	13 patients participated. All participants described living with an OI-prosthesis as a revolutionary change. These experiences were described in terms of three typologies, 'Practical prosthesis', 'Pretend limb' and 'A part of me'. The most important finding was that the change went beyond the functional improvements, integrating the existential implications in the concept of quality of life.	pre-OPRA OPRA™ Implant System Platform E/F Femur Humerus
	Matthews *et al,* (2019)	Study design not reported 1997-2008	To report outcome data for the UK trial of the Osseointegrated Prosthesis for the Rehabilitation of Amputees Implant System with a minimum of 9-year follow-up.	Five implants (28%) removed, three (17%) for deep infection, one (5.6%) for chronic pain, later proven to be infected and one (5.6%) due to implant fracture secondary to loosening due to infection. Two patients (11%) have deep infections suppressed with oral antibiotics. Eleven cases (61%) of superficial infection, successfully treated with antibiotics. Significant improvements in quality of life up to 5 years after implantation.	OPRA™ Implant System Platform F Femur
	Stenlund *et al,* (2019)		The aim of the present study was to investigate, in a population of eleven transhumeral amputees with osseointegrated implants, the load levels reached during specific prosthetic movements at maximum voluntary effort and during daily activities	11 patients included. The data showed a wide range of maximum load levels throughout the different activities. Furthermore, the data indicate that some test subjects felt apprehensive about loading the prosthesis, resulting in relatively low loads compared with the group. Within the limits of the present study, it was concluded that loading the implant system was subject specific, which resulted in large subject-to-subject variability. The study	OPRA™ Implant System Platform E/F

				illustrates the diversity and uncertainty that exist in a population of transhumeral amputees treated with bone anchored prostheses in terms of loading in daily life.	
	Tranberg *et al,* (2011)	Prospective study	The objective of the present prospective study was to assess the first 19 patients, in the OPRA study. The gait patterns pre-operatively and with the use of a socket prosthesis were compared with the those at 2 years following OI-prosthetic treatment. Changes in hip- and pelvic motion in the sagittal plane were recorded	At follow-up, the patients had increased hip extension from on the prosthetic side. Despite this improvement there was still less hip extension compared with the control side. In the patient group the maximum anterior pelvic tilt decreased which was still less compared to the control.	OPRA™ Implant System Platform F
	Tsikandylakis *et al,* (2014)	Retrospective study 1995-2010	This study reports on 2- and 5-year implant survival, adverse events, and radiologic signs of osseointegration and bone remodeling in transhumeral amputees treated with osseointegrated prostheses.	The 2- and 5-year implant survival rates were 83% and 80%, respectively. 3 implants were removed due to loosening. The most common adverse event was superficial infection of the skin penetration site (15 infections in 5 patients) followed by skin reactions of the skin penetration site (8) incomplete fracture at the first surgery (8), defective bony canal at the second surgery (3), avascular skin flap necrosis (3), and one deep implant infection. The most common radiologic finding was proximal trabecular buttressing (10 of 20 implants) followed by endosteal bone resorption and cancellization (7 of 20), cortical thinning (5 of 20), and distal bone resorption (3 of 20).	Pre-OPRA OPRA™ Implant System Platform E/ F Humerus

Clinical data obtained from implementation of manufacturer's PMCF and PMS plans	Data from literature review, and clinical data from post-market phase concluded OPRA™ Implant System demonstrates benefits such as improved quality of life, increased prosthesis use, improved ability to perform activities of daily living, improved function, improved range of movement, compared to the benchmark device. Superficial infection is the most common minor complication across all prosthesis types but can be successfully managed with conservative treatment (antibiotics). Major complications such as deep infections, re-operations, and periprosthetic fractures, are rare. Post-Marketing Surveillance activities and vigilance system ensure any unforeseen risks or increased occurrence of risks for OPRA™ Implant System will be identified without delay.
Analysis of clinical data from medical device registries	Inapplicable
Overall summary of clinical performance and safety	The OPRA™ Implant System has been found to be an alternative for patients who cannot tolerate their socket prostheses. Clinical evidence indicates substantial improvements in function, quality of life, and return to activity. Superficial infection is the most common minor complication across all prosthesis types but can be successfully managed with conservative treatment (antibiotics). Major complications such as deep infections, re-operations, and periprosthetic fractures, are rare. Safety data from ongoing US clinical investigations, conducted on Platform G and captured through Integrum's vigilance system support the above. No new risks have been identified. The term pre-OPRA refers to the implant system variants which were used before standardization of the OPRA™ Implant System components. Pre-OPRA implants should be interpreted as precursor models of the standardized OPRA™ Implant System. The precursor models were designed according to the same design concept as the standardized OPRA™ Implant System with common features such as a threaded Fixture, a percutaneous Abutment and an Abutment Screw. From a biological point of view, regarding osseointegration and fixture survival, there is little differences between the pre-OPRA implants and the standardized OPRA™ Implant System. The same is true for the percutaneous part. The mechanical performance of the abutment and abutment screw has however been improved over time (increased strength while the Young's Modulus remains similar). Differences between Platform F and G include further improvements made to the components to enhance mechanical strength and performance, increase resistance to fatigue, improve sealing properties, improve bone-to-implant contact area (thus improving initial stability of the implant), and simplify design. The overall design concept of the OPRA™ Implant System, for all platforms, regarding attachment features to the user, between components and to external prosthetic devices, remains the same or very similar and the pre-OPRA implants and the F/G platforms of the standardized OPRA™ Implant System were/are used in the same patient groups and with similar intended use. Clinical

	evidence available for pre-OPRA, Platforms F and G can be utilised as parallel data where dedicated platform information is unavailable. Clinical data adequacy was assessed according to A10. MEDDEV 2.7/1 revision 4 and MDCG 2020-6 guidance.

	Description of Activity	**Objective**	**Rationale**	**Timeline/ Completion date**
Planned and ongoing Post Market Clinical Follow Up activities	Review of scientific literature and other sources of clinical data	Collect any new information on device safety and performance	Establish safety and performance of OPRA™ Implant System Review of state-of-the-art and advances in medical practice, surgical options and prosthetic limb technology	Annual
	Collect data from on-going transfemoral level registry studies in USA, etc.	Determine safety and performance	Confirm safety and performance of OPRA™ Implant System	On-going until study completion
	Non-interventional retrospective registry based clinical investigation	Long-term Post-Market Clinical Follow-up (PMCF) of transhumeral patients Follow-up time of from 6 months to >20 years	Collect and evaluate clinical data on safety and performance. Transhumeral amputation level, within the scope of normal use.	Completion estimated in 2025

	Survey to 10 prosthetists (N.B. previous experience with Axor is required) who provide patients with the new Axor II Guide.	Collect information on how the patients and prosthetists perceive the addition of the Guide in terms of ease of donning, ability to achieve correct alignment, and if they find the new version better or worse than the old one.	New Guide added to the Axor II component of the OPRA Implant System to help with positioning during donning. Does not affect safety or performance	Completion estimated in 2025
	Preparation of PMCF report	Analysis and presentation of data.	Conclusion from post-market activities Analyse findings and update technical documentation including hazard analysis Determine any preventive and/or corrective measures	Yearly

Clinical benefits for patients	**Benefits and Claims**	**Evidence**	**Verification route**
	Increased prosthesis use	Demonstrated by significant increases in Q-TFA prosthesis use score at follow-up times up to 10 years	Brånemark *et al.,* 2014 Brånemark *et al.,* 2018 Hagberg *et al.,* 2014 Hagberg *et al.,* 2020 Hagberg *et al.,* 2018
	Improved mobility with prosthesis	Demonstrated by significant increases in Q-TFA prosthesis mobility score at follow-up times up to 10 years	Brånemark *et al.,* 2014 Brånemark *et al.,* 2018 Hagberg *et al.,* 2014 Hagberg *et al.,* 2020

	Reduced problems related to amputation and prosthesis	Demonstrated by significant reductions in Q-TFA problem score at follow-up times up to 10 years	Brånemark *et al.,* 2014 Brånemark *et al.,* 2018 Hagberg *et al.,* 2014 Hagberg *et al.,* 2020
	Ability to perform activities of daily living	Demonstrated by users ability to perform activities of daily living	Thesleff *et al.,* 2020 Stenlund *et al.,* 2019 Li *et al.,* 2019
	Improved function	Demonstrated by significant increases SF-36 physical functioning component. Improved ability to perform activities of daily living with prosthesis (ambulation for femur and, manipulate objects with prosthetic hand for upper limb)	Hagberg *et al.,* 2014 Lundberg et al., 2011 Jönsson *et al.,* 2011 Li *et al.,* 2019 Brånemark *et al.,* 2014 Brånemark *et al.,* 2018 Hagberg *et al.,* 2014
	Improved quality of life	Demonstrated by significant improvement in health-related quality of life in SF-36 at 5-years follow up	Brånemark *et al.,* 2014 Brånemark *et al.,* 2018 Hagberg *et al.,* 2014 Lundberg *et al., 2011*
	Reduced problems related to attachment of external prosthesis to the body	Demonstrated by significant reduced problems related to prosthesis at 5- years follow up (Q-TFA problem score)	Brånemark *et al.,* 2018
	Improved range of movement of proximal joint	Demonstrated by user's ability to move proximal joint uninhibited by a socket	Tranberg *et al.,* 2011 Hagberg *et al.,* 2005
	Improved sitting comfort	Demonstrated by user's ability to sit with prosthesis without discomfort. Shown by reduced discomfort during for users with the OPRATM Implant System at the lower limb compared with users of conventional socket prostheses	Hagberg *et al.,* 2005 Hagberg *et al.,* 2014
	Reduced physiological cost during walking	Demonstrated by reduced physiological cost associated with walking at self-selected speed for individuals with OPRA Implant	Hagberg *et al.,* 2014

		System at the lower limb	
	Easier to attach and detach prosthesis	Demonstrated by users self-reported responses in Q-TFA	Hagberg *et al.,* 2014
	Improved osseoperception	Demonstrated by reduced detection threshold for vibratory, and pressure stimuli and ability to perceive stimuli of external prosthesis transmitted via skeletal connection	Hagberg *et al.,* 2014 Jacobs *et al.,* 2000 Häggström et al., 2013 Li et al., 2019
	Suitable attachment method for short amputation stumps	Demonstrated by ability of users with short residual limbs to perform activities of daily living with their prosthesis despite having short residual limbs of length which would not provide adequate attachment with a socket prosthesis	Clinical Investigation report OPRA™ Implant System
Benefit-risk assessment	Identified risks have been mitigated as far as possible. Residual risks are reduced to an acceptable level. The benefit-risk ratio is assessed positive. Post-market clinical follow-up activities shall continue to assess continued acceptability of OPRA™ Implant System benefit-risk ratio.		
Ongoing or planned post- market clinical follow-up	Post-market clinical follow-up is gathered continuously in accordance with the Regulation (EU) 2017/745. Clinical data about the OPRA™ Implant System and information relevant for the clinical evaluation is also obtained from published scientific literature by systematic searches of relevant scientific database according to defined search protocol.		

Possible diagnostic or therapeutic alternatives

Alternative treatments	• Socket prostheses • Bone-anchored limb prostheses
General description of therapeutic alternatives	A socket prosthesis is the standard treatment for an individual with a major limb amputation. The suspension of the prosthesis to the limb can be achieved with the socket in direct contact with the residual limb or with a liner (flexible soft cover) between the socket and the residual limb. Specific combination of socket shape and materials together with a specific suspension system determines the distribution of pressure, shear stress, temperature, and perspiration of the residual limb. Three other systems for bone-anchored attachment of limb prostheses are commercially available in specific countries. Most of the systems are implanted using a 2-stage surgical approach where the bone- anchoring element is implanted in the first surgery and the percutaneous element is implanted in a second surgery. However, certain systems are routinely implanted in a single surgical procedure.
State-of-the art	Medical background and state-of-the-art and clinical evidence on selected reference devices confirm recognized un-desirable side- effects associated with such product and predicted by the company's formal risk analysis are not inconsistent with present medical practice, therefore, Integrum AB product may be considered well-established in the area of medicine. Clinical evaluation did not reveal medium- or long-term concerns that would be peculiar to OPRA™ Implant system. Additionally, no revolutionary advancements are evident in fundamental properties and characteristics influencing clinical safety and performance.

Suggested profile and training for users

Intended users	Medical professional and prosthetists (end users are amputated patients)
Experience	Certified clinical professionals
Education	Clinical professionals
Specific mandatory training	Training provided to clinical professionals by means of certification courses

Reference to any harmonized standards and CS applied

Applied common specification (CS)	No common specification applied	
Harmonized standards applied under Regulation (EU) 2017/745	**Standards**	**Title**
	EN ISO 10993-9:2021	Biological evaluation of medical devices - Part 9: Framework for identification and quantification of potential degradation products (ISO 10993-9:2019)
	EN ISO 10993-12:2021	Biological evaluation of medical devices - Part 12: Sample preparation and reference materials (ISO 10993-12:2021)
	EN ISO 11137-1:2015, EN ISO 11137-1:2015/ A2:2019	Sterilization of health care products - Radiation - Part 1: Requirements for development, validation and

		routine control of a sterilization process for medical devices (ISO 11137-1:2006, including Amd 1:2013)
	EN ISO 11737-1:2018, EN ISO 11737-1:2018/ A1:2021	Sterilization of health care products - Microbiological methods - Part 1: Determination of a population of microorganisms on products (ISO 11737-1:2018)
	EN ISO 11737-2:2020	Sterilization of health care products - Microbiological methods - Part 2: Tests of sterility performed in the definition, validation and maintenance of a sterilization process (ISO 11737-2:2019)
	EN ISO 13485:2016, EN ISO 13485:2016/ A11:2021 EN ISO 13485:2016/ AC:2018	Medical devices - Quality management systems - Requirements for regulatory purposes (ISO 13485:2016)
	EN ISO 14971:2019, EN ISO 14971:2019/ A11:2021	Medical devices - Application of risk management to medical devices (ISO 14971:2019)
	EN ISO 15223-1:2021	Medical devices - Symbols to be used with information to be supplied by the manufacturer - Part 1: General requirements (ISO 15223-1:2021)
	EN ISO 17664-1:2021	Processing of health care products - Information to be provided by the medical device manufacturer for the processing of medical devices - Part 1: Critical and semi-critical medical devices (ISO 17664-1:2021)

Revision History

Rev	Change Description	Issuer	Date	Revision validated by the Notified body
00	Initial version including BSI's comments on drafts	JK	04-01-2024	× Yes Validation language: English □ No (only applicable to class IIa or some IIb implantable devices (MDR, Article 52 (4) 2nd paragraph) for which SSCP not yet validated by notified body)
01	Update of the company address (page 1 and 42)	JK	16-01-2023	× Yes Validation language: English □ No (only applicable to class IIa or some IIb implantable devices (MDR, Article 52 (4) 2nd paragraph) for which SSCP not yet validated by notified body)
02	Clarification to the description of accessories. Feedback from BSI regarding PMCF activities incorporated, date format and page numbering added.	KG	02-10-2024	× Yes Validation language: English □ No (only applicable to class IIa or some IIb implantable devices (MDR, Article 52 (4) 2nd paragraph) for which SSCP not yet validated by notified body)