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URGENT FIELD SAFETY NOTICE – Precice IMLL

Date: October 14, 2021

Commercial Name: Precice Intramedullary limb lengthening (IMLL) device system, including the Precice IMLL and Precice Short trade names

Type of Action: Advisory Notice

NuVasive Specialized Orthopedics, Inc. (NSO) voluntarily issues this Field Safety Notice (FSN) to inform healthcare providers of the following, in follow-up from the prior February 2021 Precice FSN and April 2021 - NSO Statement communications:

1. In February 2021, NSO informed healthcare providers of gaps in the biological assessments and ongoing additional testing leading to a voluntary removal of Precice Systems devices and recommended user actions.
2. In April 2021, NSO alerted healthcare providers to the temporary suspension of the Precice IMLL System Devices CE certificate pending audit of files by DQS Medizinprodukte GmbH (DQS), its notified body, and local regulatory bodies.
3. As of 05 October 2021, the CE certificate has been reinstated by DQS. This notice informs users of the immediate availability of the implant along with the following additional information.
4. The Precice Intramedullary Limb Lengthening (IMLL) System Instructions for Use (IFU) has been updated and is located at www.nuvasive.com/eIFU .

The following are the changes from the prior to the current Precice IMLL system IFU:

IFU Section	Prior IFU Language	Updated IFU Language
Intended Use	The PRECICE Intramedullary Limb Lengthening System is intended for limb lengthening, open and closed fracture fixation, pseudoarthrosis, mal-unions, non-unions, or bone transport of long bones.	The PRECICE Intramedullary Limb Lengthening System is intended for limb lengthening, open and closed fracture fixation, pseudoarthrosis, mal-unions, non-unions, or bone transport of long bones in adults.
Warnings	The PRECICE Intramedullary Limb Lengthening System has not been evaluated for biological safety in patients in relation to reproductive	Patients of the PRECICE Intramedullary Limb Lengthening System should not be implanted with more than two devices at a time, and the patient's weight should be a minimum of 50 lbs. Failure to follow these criteria may result

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IFU Section	Prior IFU Language	Updated IFU Language
	health or in patients under the age of 18 years of age.	in the potential adverse events and complications described above.
Potential Adverse Events	Did not contain a *Potential Adverse Events and Complications* section.	Potential Adverse Events and Complications: As this is a major surgical procedure, there are known complications associated with orthopedic surgery such as bone fractures, nonunion, delayed union, malunion, premature healing (consolidation), decrease in bone density due to stress shielding, inadequate screw fixation, difficulty with nail or screw removal, early or late infection that may result in the need for additional surgeries, damage to blood vessels or nerves, deep venous thrombosis or pulmonary embolism, acute local inflammatory response, loss of sensory and/or motor function or paralysis, pain, and/or permanent deformity. The following list of failures and adverse events are possible with the Precice IMLL system. Failure to follow the contraindications, warnings, cautions and precautions listed in this IFU constitute off-label use and may increase the likelihood of these events. • Soft tissue contractures, loss of joint motion, subluxation and/or dislocation • Local tissue discoloration (i.e., metallosis), osteolysis, local acute inflammatory response, pain or other harms associated

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IFU Section	Prior IFU Language	Updated IFU Language
Potential Adverse Events		with exposure to wear debris, metal nanoparticles, and elevated titanium serum ion levels (including neurological issues and the risks associated with reproductive and developmental toxicity). • Exposure to biohazards or non-biocompatible materials potentially leading to immunological response, pain, skin irritation/rash/sensitization, developmental toxicity related harms and/or infection and which may require medical intervention such as revision surgery. • Loss of distraction or uncontrolled lengthening which may lead to pain, loss of correction, extension of treatment, progression of deformity, increased limb length discrepancy, over-lengthening, poor regenerate and/or necessitate revision surgery. • Implant bending, fracture, loosening, disassociation and/or loss of fixation resulting in medical intervention such as revision surgery. • Failure to lengthen which may lead to delays in surgery (leading to additional blood loss and extended exposure to anesthesia), extension of treatment, suboptimal correction, and/or necessitate revision or reoperation. • Treatment complications from anatomical compatibility issues due to implant configuration selection, implant removals and/or implant sterility which may lead to delays in surgery (leading to additional blood loss and extended exposure to anesthesia), inability to complete the procedure and/or cancellation of the procedure, or may result in pain, abnormal sensations and/or suboptimal correction.

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Reasons for IFU Updates:

- These changes are a follow up to the prior communications here:
  - Feb 2021 Precice FSN and April 2021 - NSO Statement
- The update clarifies instructions regarding the target patient population based on the latest scientific evidence.
- Further clarify to healthcare providers and patients the potential adverse events that can occur when using the device.

Clinical Impact:

NuVasive continues to monitor all post-market surveillance reports of adverse events as required by the regulations and laws in markets which it operates. To date, there have been no reports of toxicological harms identified. Additional biological assessments are ongoing to determine whether there are potential toxicological risks to patients under 50lbs or for patients with more than two implanted devices. Until that testing is completed, the use of Precice IMLL is not recommended for patients under 50lbs or greater than 2 implanted devices.

Recommended User Action:

This FSN details updates to the IFU document that physicians should consult prior to and during patient care of those being treated with Precice IMLL System devices. This should be consulted for currently implanted and future potential Precice IMLL system patients.

- The IFU should be consulted on an ongoing basis before and throughout patient treatment.
- An NSO representative will be contacting your office or you to help with any questions or concerns.
- Acknowledgement of these changes is critical. Please review, complete, sign and return the attached Consignee Confirmation Form in accordance with the directions on the form (accompanying this notification).
- Precice IMLL System Devices, for patients currently weighing less than 50 pounds and/or with more than two devices implanted should consult their healthcare team for assessment of their treatment progression and consider removal of nails promptly at the end of treatment in order to minimize the potential for implantation risks while also minimizing the risks associated with repetitive surgical interventions and sub-optimal conversion to alternative therapies mid-treatment.

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Additionally, this is a reminder to reference the existing language within the IFU, including but not limited to:

- The PRECICE Intramedullary Limb Lengthening nail remains implanted until bone consolidation has been completed. Once the physician determines that the nail has achieved its intended use and is no longer required, it is removed using standard surgical techniques
- Device should be removed after implantation time of no more than one year.
- The PRECICE Intramedullary Limb Lengthening device is contraindicated in patients in which the Precice IMLL nail would cross joint spaces or open epiphyseal growth plates.
- The PRECICE Intramedullary Limb Lengthening device is contraindicated in patients unwilling or incapable of following postoperative care instructions.
- The PRECICE Intramedullary Limb Lengthening nail cannot withstand the stresses of full weight bearing for tibia and femur applications.
- The PRECICE Intramedullary Limb Lengthening device is contraindicated for use in patients with metal allergies and sensitivities.
- Metallic implants can loosen, fracture, corrode, migrate, or cause pain.
- Smoking, chronic steroid/drug use and the use of other anti-inflammatory drugs have been determined to affect bone healing and could potentially have an adverse effect of the bone regenerate during the lengthening process. Additionally, patients should be evaluated for narcotic dependencies associated with pain management.

Transmission of this Field Safety Notice:

This notice needs to be passed on to all those who need to be aware of it within your organization.

This notice has been reported to all applicable regulatory authorities.

Matthew Collins
Vice President, Global Quality Assurance
101 Enterprise #100
Aliso Viejo, CA 92656

October 14, 2021
Date

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Consignee Confirmation Form

It is important that your organization takes the actions detailed in this FSN and confirms that you have received this FSN. Please complete and return this form to NSO per the instructions below.

Your organization's reply is the evidence we need to monitor the dissemination of this notice.

Customer Name: _____

Address: _____

_____

_____

_____

Phone: _____

(Information required for regulatory effectiveness check)

I acknowledge receiving and reading the October 14, 2021, Precice IMLL FSN

_____	_____	_____
Name/Title	**Signature**	**Date**
_____	_____	_____
NSO representative, if applicable	**Signature**	**Date**

This form is to be returned to NSO – Scan and email this form to FSNprecice@nuvasive.com