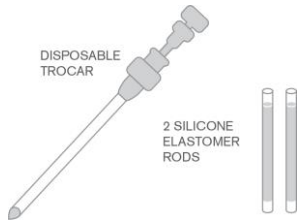
Sino-implant (II)/Levoplant Overview

HEALTH

Questions and answers



Sino-implant (II) has been sold under various trade names, including Femplant, Trust and Zarin.

WHAT IS SINO-IMPLANT (II)?

Sino-implant (II) is a safe, highly effective, long-acting, reversible hormonal contraceptive implant made up of 2 rods that are inserted into a woman's upper arm. The rods contain a hormone called levonorgestrel, which is slowly and continuously released over time. Shanghai Dahua Pharmaceutical Co., Ltd., (Dahua) has been manufacturing Sino-implant (II) since 1996. The product has been registered by more than 20 drug regulatory authorities, and more than 11 million units have been distributed worldwide.

WHAT IS LEVOPLANT?

Dahua augmented the Sino-implant (II) product specifications and test methods and changed the levonorgestrel supplier in pursuit of World Health Organization (WHO) prequalification. **This product is now sold under the global brand Levoplant.**

WHAT IS THE STATUS OF WHO PREQUALIFICATION FOR LEVOPLANT?

WHO prequalified Sino-implant (II)/Levoplant on June 30, 2017, after reviewing the product dossier, including new clinical trial data, and inspecting Dahua's manufacturing facility to ensure it complies with WHO Good Manufacturing Practices. Levoplant is prequalified for 3 years of use, with the pivotal trial on-going for a 4th year; national registrations are being updated. (See https://extranet.who.int/prequal/sites/default/files/RH028part4v1.pdf.)

WHAT DOES WHO PREQUALIFICATION MEAN?

WHO prequalification recognizes that Levoplant meets international quality standards for manufacturing and clinical performance. WHO evaluated data from a rigorously conducted clinical trial that compared Levoplant to Jadelle and found the product to be safe and highly effective during 3 years of use. The United Nations Population Fund had approved Levoplant for purchase by its country programs through the WHO Expert Review Panel process in November 2016. WHO prequalification will now allow additional donors and procurers to purchase the product for country programs.

HOW LONG IS LEVOPLANT EFFECTIVE?

Levoplant is labeled for 3 years of use. Should the ongoing clinical trial support 4 years of use of Levoplant, the data will be submitted to WHO in late 2017 for consideration of a change in the label.* The product has a shelf life of 4 years.

HOW EFFECTIVE IS LEVOPLANT?

Levoplant is one of the most effective family planning methods available. Each year, fewer than 1 pregnancy per 100 users is expected.

* Sino-implant II/Levoplant contains the same active ingredient as the 5-year Jadelle implant and has similar dimensions, but it is not a generic version of Jadelle. There are no plans to label Levoplant for a 5-year duration of use.

Questions and answers

WHERE IS LEVOPLANT AVAILABLE?

Building on existing national approvals for Sino-implant (II), registration of Levoplant at the country level is ongoing. For information about the regulatory status in a particular country, please contact: sino_implant@fhi360.org.

WHAT IS THE PRICE OF LEVOPLANT?

In FP2020 countries, the product is available for US$8.00 per unit for orders under 300,000 and for US$7.50 for orders over 300,000; this pricing structure applies to approved procurers, donors and governments.

WHO CAN USE LEVOPLANT?

Almost all women of childbearing age can use Levoplant: women of any age (with or without children), women in the immediate postpartum period, breastfeeding mothers, HIV-positive women, women who smoke and women who have had a miscarriage or an abortion. Levoplant is ideal for women with limited access to health services because it does not require regular resupply from a provider.

HOW DOES LEVOPLANT WORK?

Levoplant works by inhibiting or altering ovulation and thickening the cervical mucus, making it difficult for sperm to unite with an egg. Fertility returns immediately after removal of the implants.

HOW IS LEVOPLANT INSERTED AND REMOVED?

Both insertion and removal are minor surgical procedures that take a few minutes and can be done in a health provider's office. The implants are inserted into the inner side of either upper arm and are removed by making a small incision and using forceps to gently pull out the rods. To minimize the risk of breakage, Dahua's recommendations for removal of Sino-implant (II)/Levoplant differ slightly from the recommendations for removing another 2-rod implant, Jadelle (see Key messages, p. 3).

WHAT ADDITIONAL EVIDENCE EXISTS ABOUT THE QUALITY OF THE PRODUCT?

Quality assurance: Dahua is designated by the National Health and Family Planning Commission of the People's Republic of China (NHFPC) and the China Food and Drug Administration (CFDA) as an approved manufacturer of contraceptive products. Dahua continually evaluates the quality of the final product by testing each lot prior to distribution. Since 2008, an independent quality evaluation has been conducted annually by FHI 360. The findings show Dahua demonstrates the ability to produce a contraceptive implant that meets international quality standards.[1]

Earlier clinical trials: Chinese clinical data from the early 1990s from 4 randomized trials among over 15,000 women support 4-year duration of use of Sino-implant (II), with annual pregnancy rates below 1 percent.[2] With funding from the Bill & Melinda Gates Foundation and the U.S. Agency for International Development, FHI 360 and partners have since completed prospective cohort studies in Bangladesh, Kenya, Madagascar and Pakistan, following over 2,000 Sino-implant (II) users for 12 months. The results show Sino-implant (II) is a safe, highly effective method. In Bangladesh and Madagascar, no post-insertion pregnancies were reported; in Kenya and Pakistan, the combined annual pregnancy rate was below 1 percent.[3-5]

REFERENCES

1 FHI 360. Sino-implant (II) Quality Evaluation Reports, 2008-2016. Available at: https://www.k4health.org/toolkits/implants/sino-implant-ii-quality-evaluation-report.

2 Steiner MJ, Lopez LM, Grimes DA, et al. Sino-implant (II) — a levonorgestrel-releasing 2-rod implant: systematic review of the randomized controlled trials. Contraception. 2010;81(3):197-201.

3 Hossain S, Alam M, Searing H. Acceptability of Sino-implant (II) in Bangladesh: Final report on a prospective study. New York: EngenderHealth RESPOND Project; 2012.

4 Feldblum PJ, Hanitiniaina O, Lendvay A, et al. Performance of Sino-implant (II) in routine service delivery in Madagascar. Contraception. 2013;88(1):103-8.

5 Lendvay A, Otieno-Masaba R, Azmat SK, et al. Effectiveness, safety and acceptability of Sino-implant (II) during the first year of use: results from Kenya and Pakistan. Contraception. 2014;89 (3):197-202.

What to consider: Levoplant scale-up

The following steps are recommended when introducing or scaling up Levoplant:

Informing stakeholders and coordinating introduction

- ✓ Key stakeholders should be identified in each country, including those who will decide whether and how to introduce Levoplant and those who will be involved in guiding and supporting its implementation.
- ✓ Typically, key stakeholders are engaged through meetings convened by the country's Family Planning Technical Working Group (FP TWG) or a similar coordinating body that includes policy makers, program managers, procurement agents, donors and distributors.
- ✓ An integrated communication plan should be developed to ensure that clinicians, supervisors and patients all have the information needed for successful introduction of Levoplant.

Updating national guidelines

- ✓ The FP TWG or other coordinating committee should incorporate up-to-date information about Levoplant in the national reproductive health guidelines, including the labeled duration of effectiveness.
- ✓ Involving a range of key stakeholders in updating the guidelines can help ensure a broad base of support for Levoplant introduction and scale-up.

Key messages

Duration of use: Levoplant is currently registered for 3 years of use. The labeled duration of use must be effectively communicated to providers. In turn, women must be informed about the type of product they receive and counseled on its duration of use. A woman may return at any time to have the Levoplant rods removed, if pregnancy is desired or for any other reason. If the implants are not removed early, they must be removed after 3 years of use. A new set of rods can be inserted at that time if continued protection from pregnancy is desired.

Removal: In the training materials for the 2-rod implant Jadelle, Bayer HealthCare recommends using Mosquito forceps to stabilize Jadelle rods at the site of the incision during removal and using Crile forceps to remove the rods. Dahua's recommendation for Sino-implant (II)/Levoplant removal differs slightly. The company advises that Mosquito forceps can be used if Crile/Kelly forceps are not available; however, the use of Crile/Kelly forceps to stabilize and remove the rods has been shown to reduce the risk of breakage during removal. More information is available at: https://www.k4health.org/toolkits/implants/levoplantsino-implant-ii-reference-guide-healthcare-providers.

What to consider: Levoplant scale-up

Procuring sufficient commodities

- ✓ Procurement efforts should be guided by a plan that describes the quantification process, indicates who will be responsible for quantification and procurement and specifies lead times to ensure that supplies are in place before the launch.
- ✓ Quantification efforts should include estimates of the number of implants needed for training as well as roll-out.
- ✓ A system for tracking supply needs should be part of the procurement plan, to help programs avoid stock-outs.

Training providers

- ✓ A communication plan should identify the channels and the materials that will be used to inform program managers and providers of essential information about Levoplant, including how many years of contraceptive protection it provides (see Key messages, p. 3).
- ✓ Implementation of the communication plan may involve revisions to pre-service and in-service implant training curricula and/or dissemination of an official clinical guidance addendum by the FP TWG and/or Ministry of Health.
- ✓ Providers already skilled in insertion and removal of other 2-rod implants will not need retraining, but must be oriented on Levoplant's duration of use and should be advised about Dahua's recommendation regarding the use of forceps for removal (see Key messages, p. 3).
- ✓ Providers should review information included as part of the Levoplant packaging before offering the product to patients. Levoplant is also distributed with a client reminder card to give to the woman at the time of insertion; the provider should write the removal date on the card.
- ✓ Additional implant service delivery resources can be found in the online Knowledge for Health Implants Toolkit, which is available at: https://www.k4health.org/toolkits.implants. Professional organizations and networks can also help disseminate information to their members.

Guaranteeing reliable access to insertion and removal services

- ✓ Women must be able to have Levoplant removed whenever they want.
- ✓ High-quality service delivery — including ensuring that providers are trained and have adequate supplies for removal as well as insertion — is critical for safe, effective implant provision.
- ✓ A comprehensive plan for ensuring that providers are skilled in insertion and removal of 2-rod implants is essential.
- ✓ Monitoring Levoplant introduction should be incorporated into routine supportive supervision visits to health facilities.

Including Levoplant in pharmacovigilance efforts.

- ✓ It is important to report any adverse events that occur with Levoplant.
- ✓ Healthcare professionals and facility managers can download and submit pharmacovigilance forms at the manufacturer's website: http://www.dahua-sh.com.

For more information, please contact Dahua at inquiry@dahua-sh.com or FHI 360 at sino_implant@fhi360.org.

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October 2017