Depo-subQ Provera 104® in the Uniject™ Injection System

Technology Opportunity Assessment

Prepared for the Merck for Mothers Program
Depo-subQ Provera 104® in the Uniject™ Injection System

Summary

The Uniject™ injection system* (hereafter referred to as Uniject) is a prefilled syringe that makes it easier to administer the injectable contraceptive Depo-subQ provera 104®. One injection every three months provides a safe, effective, reversible, and discreet method to prevent pregnancy. This user-friendly product is well suited for use by less-skilled health workers in non-clinical settings, including convenient community locations and clients' homes.

Statement of Need

Improving access to effective family planning methods offers numerous health and development benefits to women and families. Research suggests that between 1990 and 2005 an estimated 1.2 million maternal deaths were averted because of declining fertility, largely due to increases in contraceptive use. Family planning improves maternal health by reducing births among women who are too young or too old, births that are too closely spaced, and high parity births (four or more births). Use of family planning also contributes to broader health and development goals; educational and employment opportunities for women improve, and social and economic development goals are easier to achieve. Use of family planning methods also has an impact on other health outcomes. For example, increased use of condoms for contraception reduces transmission of HIV and other sexually transmitted diseases.

Globally, more than 215 million women have an unmet need for contraception. An estimated 31 million women in India and 35 million women in sub-Saharan Africa have an unmet need to space their pregnancies (spacing) or to stop having children altogether (limiting). Based on women’s preferences, unmet need for spacing is higher than unmet need for limiting in sub-Saharan Africa, while in India unmet need for limiting is slightly higher than unmet need for spacing.

Many factors influence the use of family planning methods including cultural norms that favor large families, religion, poverty, lack of access to information, provider bias, and spousal disapproval. Some contraceptive users find available contraceptive methods to be unacceptable, while others confront challenges using a method consistently because of limited availability of supplies and services. In many developing countries donors pay for a significant proportion of the cost of contraceptives, which means that funding constraints further limit contraceptive supply levels. At a minimum, any contraceptive method should be both safe for the user and effective at preventing pregnancy. Ideally, each user should also be able to select a method that suits his or her personal preferences and lifestyle.

* Uniject is a trademark of BD.
† MEASURE DHS Demographic and Health Surveys uses the following definitions of unmet need, spacing, and limiting in all country reports. Currently married women who are not using any method of contraception but who do not want any more children are defined as having an unmet need for limiting; those who are not using contraception but want to wait two or more years before having another child are defined as having an unmet need for spacing.
Technology Solutions Landscape and Gap Analysis

Over 35 million women worldwide use injectable contraceptives. In sub-Saharan Africa, more than one-third of contraceptive users choose injectables, making it the leading modern method in that region. In contrast, injectable contraceptive use in India represents only 0.10% of contraceptive use.7

The progestin-only depo-medroxyprogesterone acetate (DMPA) 150-mg formula delivered via deep intramuscular (IM) injection is the most widely used injectable contraceptive formula and presentation. One brand of DMPA-IM that is widely used in developing countries is Pfizer’s Depo-Provera® (Figure 1). Depo-Provera was approved by the US Food and Drug Administration (USFDA) for contraceptive use in 1992.8

Unmet demand for injectables remains high in many sub-Saharan African and South Asian countries. In 2010, PATH analyzed available secondary data on current use of injectable contraceptives and women’s stated intentions with respect to future use of contraceptives for 21 countries.‡,9 The analysis showed that there were approximately 14 million current users of injectable contraceptives in these 21 countries. Potential future use of injectables in these same countries was almost double current use—there were approximately 24 million potential new users of injectables among women who currently do not use any contraceptive method but who state that they intend to use contraception and that injectables are their preferred method.10 Note that these figures do not include India.

Despite this high level of unmet demand, several factors inhibit greater access to and use of injectables. Some women do not tolerate DMPA-IM’s side effects and the time required for fertility to return after the method is discontinued. Side effects include intermittent bleeding and spotting in the first several months of use, nausea, headache, and weight gain. After one year of use, approximately 55% of women using DMPA will experience amenorrhea,11 a side effect that is unacceptable to some users. The average return to fertility is nine to ten months after the last injection.12,13 Analysis of 12-month discontinuation shows similar rates for oral contraceptives and injectables; 47.6% of women using oral contraceptives and 49.2% of women using injectables will discontinue their method after one year of use for a variety of reasons.14

Technology opportunities likely to improve access to and more consistent use of injectables would be longer-acting formulations (for example, six rather than three-month duration per injection); formulations with fewer side effects, including shorter times for return to fertility; and presentations that increase user convenience and control. Early-stage candidate formulations for longer-acting injectable contraceptives are also under study; Family Health International 360 (FHI360), a global development health and family planning research organization, recently received funding from the Bill & Melinda Gates Foundation to identify and evaluate candidate formulations.15

With respect to injectable contraceptive access and convenience, a Cochrane review of injectable contraceptives noted that a key to improving injectable contraceptive acceptability and use is developing approaches that support “providing injections in settings more convenient than clinical sites [and] methods for women to administer their own injections.”16 Currently available injectables are effective for one to three months (depending on the formulation), requiring women to return to their provider between 4 and 12 times per year.

Injectable contraceptives are most often delivered by a medical provider such as a physician, nurse, nursing aid, or medical assistant working from a static facility, requiring users to return to a provider or facility for reinjection. In some countries, small but growing cadres of community health workers, community-based distributors, and other lower-level, non-clinic providers are trained to deliver injectable contraceptives, thereby expanding coverage and increasing convenience for women. Other recent reports indicate that retail sellers such as pharmacies and drug shops sometimes sell injectable contraceptives over the counter directly to users, who are then injected on site or elsewhere.17

Global policy guidelines support the deployment of lower-level providers to expand access to injectable contraceptives. A June 2009 technical consultation held at the World Health Organization concluded that evidence supports the introduction, continuation, and scale-up of community-based provision of progestin-only injectable contraceptives.18 However, with some exceptions,§ formal nonclinical distribution and delivery systems for injectable contraceptives are not widely or consistently established, even where they are supported by local service-delivery policies.

A new formulation and presentation of Pfizer’s Depo-Provera® offers the potential to improve access to injectable contraceptives. Based on information provided by Pfizer, depo-subQ provera 104® in the UnijectTM injection system (hereafter referred to as depo-subQ in Uniject) contains 104 mg of DMPA with safety and efficacy equivalent to the widely accepted DMPA-IM 150-mg benchmark product in the single-use, prefilled Uniject.19 Uniject is a small, autodisable injection system prefilled with the precise dosage of depo-subQ provera 104 required for three months of contraceptive protection (Figure 2).

§ Examples include Bangladesh, Ethiopia, and Pakistan.
Pfizer’s labeling on the product indicates that the contraceptive efficacy of depo-subQ provera 104 is equivalent to that of DMPA-IM 150 mg with 30% less active ingredient. Clinical studies on depo-subQ provera 104 indicate that the product’s side effects and return to fertility profiles are similar to those of the benchmark product.

Depo-subQ in Uniject is administered via subcutaneous (SC) injection rather than the traditional IM injection. SC injections offer benefits over IM injections especially for training lower-level providers and for self-injection including:

- Greater area for target injection sites.
- Fewer landmarks required for targeting injection sites.
- Shorter needles can be used (3/8 to 5/8 inch for SC versus 1 inch for IM).
- Readily self-administered.
- Muscle mass not an issue.

Depo-subQ provera 104 was approved by the USFDA in 2004 and by the Medicines and Healthcare Regulatory Agency (UK) in 2006, with mutual recognition in 2007 by other European Union regulatory authorities. The approved presentations are in a glass prefilled syringe, not in Uniject. The Uniject presentation received provisional approval by the Medicines and Healthcare Regulatory Agency in June 2010.

The objective of introducing depo-subQ in Uniject is to reach new users of injectable contraceptives and improve women’s ability to obtain repeat injections by accelerating access through nonclinical channels. Because depo-subQ in Uniject is uniquely suited to self-injection, it is possible that the product may offer future opportunities for well-regulated use through home- and self-administration of injectable contraceptives.

DMPA-IM 150 mg is widely accepted and used in many developing countries; ensuring sufficient supplies is a constraint in locations with high demand. To maximize impact on contraceptive prevalence and maternal morbidity and mortality, depo-subQ in Uniject should, ideally, be targeted to channels that extend service delivery beyond the clinic, complementing injectable contraceptive delivery in systems already utilizing DMPA-IM effectively.

** DMPA-IM cannot readily be self-administered because of the skill required to draw up the drug into a needle and syringe from a vial, and the injection sites (gluteals, deltoid muscle) cannot be easily reached.
Investment Opportunity

Depo-subQ in Uniject is a potentially game-changing technology uniquely suited to outreach settings and home- and self-injection. Its use is expected to increase access to injectable contraceptives among women in the most difficult-to-reach delivery settings, building on already strong existing and future demand for progestin-only injectable contraceptives. The product is developed, clinically tested, and in the final 12 to 18 months of regulatory approvals.

Depo-subQ in Uniject faces obstacles to advancement toward impact, specifically:

- At current production volumes, the product’s manufacturing cost, and thus its price, is estimated to be higher than that of the benchmark DMPA-IM 150 mg. This cost and price situation may present an obstacle to international procurement commitments by the major donors.

- There is not yet experience with the product in developing-country delivery settings to validate and measure the product’s potential to generate new users, increase continuation, and save on delivery costs.

Several interventions are needed to gain experience that may help the global health community understand the potential value of this product. Initial market introductions at sufficient scale to validate and measure the product’s value proposition will contribute important information to procurement bodies concerning purchase of this product. Creative financing mechanisms that include partial support to introductory pricing and/or volume purchase guarantees during the initial years of production would move the product past the initial higher-cost, lower-volume stage.
References


10. Tifft S. Increasing access to injectable contraceptives. Presented at: PATH, February 16, 2011; Seattle, WA.


