



One in a series discussing PATH's activities, research findings, experiences, and recommendations to support decision-making and product introduction planning for the injectable contraceptive depo-subQ provera 104™ in the Uniject™ injection system.

BRIEFING SUMMARY JULY 2011

Home-based administration of depo-subQ in the Uniject injection system

A summary of key findings on acceptability and feasibility

Injectable contraceptives are among the world's most popular modern methods for preventing pregnancy. Many women choose injectables because of their effectiveness, long-acting contraceptive effects, discreet administration, and reversibility. Injectables are most popular in the less developed regions of the world—particularly sub-Saharan Africa—and their popularity continues to grow. Estimates suggest that the number of women using injectables globally will increase by 31 percent to almost 40 million women by 2015, a jump that will require improved access to injectable services and supplies.

PATH is implementing a four-year project to facilitate decision-making and introduction strategies for depo-subQ provera 104™ in the Uniject™ injection system, a new subcutaneous presentation of the popular injectable contraceptive depot medroxyprogesterone acetate (DMPA). This brief summarizes key findings on the feasibility and acceptability of home delivery of depo-subQ in Uniject from a literature review conducted by PATH. This review focused on self-injection and looked specifically at subcutaneous DMPA* compared to intramuscular formulations, home administration of injectable

contraception particularly in low-resource settings, and identifying research needs regarding home administration and self-injection of depo-subQ in Uniject.

INTRAMUSCULAR VS. SUBCUTANEOUS DMPA

Historically, DMPA has been administered via an intramuscular injection into a woman's upper arm or buttocks using a vial and syringe. In 2004, the US



Rafael Avila/CCP

* For the purposes of the literature review, "DMPA" references all formulations of depot medroxyprogesterone acetate, including DMPA SC. "DMPA IM" refers to depot medroxyprogesterone acetate administered intramuscularly, while "DMPA SC" refers to depot medroxyprogesterone acetate administered subcutaneously. "Depo-subQ" references Pfizer's brand name DMPA SC product.

Research suggests that depo-subQ in Uniject increases the possibility for a woman to easily inject herself at home.

Food and Drug Administration approved Pfizer Inc.'s new subcutaneous form of DMPA, depo-subQ provera 104™ (DMPA SC). DMPA SC is administered through a subcutaneous injection in a woman's thigh or abdomen using a prefilled, single-use syringe. Because DMPA SC is administered subcutaneously, the progestin is absorbed more slowly in the body, allowing for a lower dose of the hormone than in the intramuscular form of DMPA (DMPA IM). DMPA SC contains only 70 percent of the progestin dose in DMPA IM (104 mg compared to 150 mg), but is equally effective in preventing pregnancy. Assessments of the contraceptive efficacy of DMPA SC demonstrate a zero percent pregnancy rate after one and two years of use. Studies also suggest that the efficacy of DMPA SC is not affected by race, ethnicity, or body mass. Overall, the existing research points to the subcutaneous formulation as an effective, reliable, and safe contraceptive method that offers the same benefits as DMPA IM.

The side effects of DMPA SC are consistent with the common side effects of DMPA IM and other progestin-only injectables, and include headache, weight gain, intermittent bleeding and spotting, and amenorrhea. In a two-year comparison study between DMPA SC and DMPA IM among 225 women in the Brazil, Canada, and the United States, Kaunitz and colleagues found that side effects were similar in both study groups.

While the clinical profiles of intramuscular and subcutaneous DMPA are roughly equivalent, many authors suggest that DMPA SC may offer advantages over the intramuscular formulation. These include ease of administration, potential for self-injection, and increased tolerability. One researcher notes injections delivered subcutaneously offer more surface area for the provider, do not require the provider to be familiar with “anatomical landmarks,” and are less likely than intramuscular injections to pierce blood vessels, hit nerve endings, or make contact with bone due to the shorter needle length required.

DEPO-SUBQ IN THE UNIJECT INJECTION SYSTEM

Currently, DMPA SC is manufactured solely by Pfizer Inc. and packaged in a glass, prefilled syringe under the brand name of depo-subQ provera 104 (depo-subQ) in the United States and Sayana® outside of the United States. Pfizer has packaged depo-subQ in the Uniject injection system and is currently seeking stringent regulatory approval from the European Medicines Agency for this change in delivery system.

Packaging the contraceptive in the easy-to-use Uniject supports lower-level health workers administering

contraceptive injections and also offers the potential for home and self-injection. Providing DMPA SC in the prefilled Uniject will minimize waste, ensure the correct dose every time, simplify procurement and logistics, and eliminate the need for separate vials and syringes. Uniject's compact size eases transport, storage, and disposal; facilitates outreach to patients; and its auto-disable feature minimizes the transmission of blood-borne pathogens through needle reuse.

Uniject has been used by nurses, midwives, community health workers (CHWs), and self-injectors to deliver other injectable contraceptives, medicines, and vaccines. Proponents of depo-subQ in Uniject hope that by making the product available for home use by lay caregivers and women interested in self-injection, women's access to family planning services will improve, especially in areas where access to traditional health facilities is limited. Moreover, increasing non-clinic access to injectables may also lead to an increase in new users of family planning, thereby helping to reduce unmet need and improve contraceptive prevalence rates.

NON-CLINIC ACCESS TO INJECTABLES

The possibility for home use of depo-subQ in Uniject is one of the more innovative potential advantages of this injectable contraceptive delivery system. For the purposes of this literature review, the term “home use” refers to administration of depo-subQ in Uniject either by a third party (e.g., a family member) delivering the injection in a woman's home, or by the woman herself through self-injection. Our literature review looked at the acceptability and feasibility of administration by lay caregivers and self-injectors, with a focus on self-injectors.

Administration by lay caregivers

Although there is no literature available on the provision of injectable contraception in a woman's home by lay caregivers, such as friends or relatives, research on provision of other medicines suggests this is a feasible option for contraceptives. It is quite common for children with diabetes, for example, to receive insulin injections from their parents or other caregivers. Studies assessing the home-based provision of subcutaneous injections for pain management found that caregivers preferred prefilled syringes and that careful screening criteria and thorough training were essential to ensuring caregivers were appropriate, confident, and skilled in providing injections. Additionally, follow-up mechanisms were important to answer caregivers' questions and provide further training reinforcement as needed.



Community-based distribution programs are increasingly providing services in rural areas, oftentimes through home visits.

Administration by self-injection

As noted by many researchers, depo-subQ in Uniject increases the possibility for a woman to easily inject herself with her chosen contraceptive method in her own home. While depo-subQ in Uniject is currently labeled only for administration by a trained clinical provider, the World Health Organization acknowledges the potential for self-injection associated with the subcutaneous formulation of DMPA.

As depo-subQ in Uniject is not yet available for use, there is no published research on the feasibility and acceptability of self-injection using this particular contraceptive method and delivery system. There is, in fact, no quantitative data on self-injection using any formulation of DMPA. However, there is data on self-injection using other formulations of injectable contraception, including administration using Uniject.

Data from two studies evaluating the acceptance of contraceptive self-administration indicate that

self-administration of injectable contraception is both feasible and acceptable. A study in Brazil that assessed self-administration of once-a-month injections of the contraceptive Cyclofem® using Uniject found that participants were not only able to administer the intramuscular injection safely and easily, but that more than half of them would prefer to self-administer using Uniject in the future. In a study in the United States comparing home-based, intramuscular self-injection of the monthly injectable Lunelle™, using a standard vial and syringe, to clinic-based injections by a trained clinician, researchers found that 80 percent of women preferred self-injection at home to clinic administration. While the sample sizes in both studies were small—56 women in Brazil and 10 women in the United States—the results indicate that, with comprehensive training, women are capable of self-administering contraceptive injections. Moreover, the women in these studies were self-administering intramuscular injections which, as previously noted, are more challenging to administer than subcutaneous injections.

A qualitative survey conducted in the United Kingdom assessed interest among current DMPA IM users in switching from DMPA IM to self-injection of DMPA SC. The researchers found that 67 percent of respondents would prefer to self-administer their contraception. The evidence suggests that there is both precedent and preference for self-administration of injectable contraception, and indicates that self-injection of DMPA SC using Uniject may be both acceptable and feasible.

CONSIDERATIONS FOR HOME DELIVERY OF DEPO-SUBQ IN UNIJECT IN LOW-RESOURCE SETTINGS

As stated previously, a large body of evidence suggests that administration of injectable medicines is both feasible and acceptable when delivered by lay caregivers or through



The number of women using injectables globally will likely increase by 31 percent to almost 40 million women by 2015.

self-administration. There is also sufficient evidence to suggest that administering contraceptives via Uniject is feasible and acceptable. After taking the existing evidence into account, a number of considerations emerged that may need to be addressed for successful home delivery of depo-subQ in Uniject, particularly for self-administration.

Training

Experience and evidence indicate that the training curriculum for a depo-subQ in Uniject home-delivery program would need to contain follow-up and supervision components. While skilled personnel may only need limited training on administration of the Uniject injection system, the literature suggests that individual home users may require more instruction to acquire confidence in the technique, as well as sufficient knowledge on proper storage, waste disposal, and side-effects management. Developing robust selection criteria for enrolling potential self-injectors in a training program can help mitigate potential challenges, increase the effectiveness of the training program, and preclude unnecessary discontinuation of the method.

In the available literature on contraceptive self-injection, the majority of training practices include an initial training led by a skilled clinician, at least one follow-up session in a facility where the trainee self-administers her injection under the supervision of a skilled provider, and a follow-up system for the trainee to ask questions or receive support and counseling. Because DMPA SC requires injections only every three months, there is a risk that self-injectors will not retain their learning in the time between injections. A successful depo-subQ in Uniject self-injection program will likely require a long-term implementation period—possibly as long as one year, or four injection cycles—for a woman to become confident and proficient in administering her own injections. It will need to incorporate clear reminders to help keep women on schedule with their injections.

Storage

A key component of a training curriculum for home delivery of depo-subQ in Uniject will be ensuring participants are knowledgeable and comfortable with the storage protocols for the drug. Pfizer recommends that DMPA SC packaged in a prefilled glass syringe be stored between 20°C and 25°C, which are the same storage recommendations as DMPA IM; it does not require refrigeration or maintenance of cold-chain procedures. Depo-subQ in Uniject is expected to have a shelf life of five years.

Studies conducted in Indonesia demonstrated that midwives were capable of safely storing medications in Uniject in their homes without compromising viability, and many CHWs in developing countries currently store DMPA IM in their homes. The evidence suggests that CHWs will be able to safely store depo-subQ in Uniject in their homes. However, more research is needed of the storage practicalities for women living in low-resource settings who are interested in self-injection.

Safe injection and waste management

Another consideration for home delivery of depo-subQ in Uniject is safe-injection practices, including proper disposal of the used Uniject after injection. Experience with the use of Uniject has demonstrated improved safe-injection practices by providers. Proper disposal techniques for Uniject follow standard practices for autodisable syringes and call for placing it in a sturdy, leak- and puncture-proof sharps container and, when it is three-quarters full, incinerating the container in a medical facility incinerator. If incineration is not possible, as in many developing countries, the sharps container could be burned in a controlled setting and the remains buried in a pit designated for medical waste. Women injecting themselves at home may have difficulty disposing of their used Unijects as they will generate a very low volume of waste—approximately three or four Unijects per year—and will likely not have access to incineration facilities.

Evidence suggests CHWs delivering injectable contraceptives are, in many cases, able to safely and effectively dispose of their used needles, syringes, and medical supplies. However, there are no established waste management guidelines for community-based distribution programs. Additionally, there is little literature on waste disposal practices and guidelines for self-injectors of medicines in developing countries. Storage of used Unijects at home may be hazardous to children or other family members in the household, as well as animals, and may negatively impact a woman's desire for discretion.

Infrastructure and political support

Proper infrastructure that can facilitate home delivery of depo-subQ in Uniject will be critical to a successful home-delivery program. Home users will need access to facilities to acquire the contraception and safely dispose of the used Unijects. National governments, nongovernmental organizations, and private-sector providers who procure depo-subQ in Uniject will need to have accurate forecasting, procurement, storage, and distribution

structures in place to ensure the consistent availability of the contraceptive.

The necessary infrastructure will require significant support from local and national stakeholders. Successful introduction and long-term use of depo-subQ in Uniject will likely rely on country-specific research and advocacy to influence new laws, guidelines, and policies.

CONCLUSION AND NEXT STEPS

DMPA SC is a safe, reliable, and effective alternative to DMPA IM, according to the available literature. As the popularity of injectable contraception grows, research indicates that depo-subQ in Uniject will offer new opportunities for expanding access to family planning services through home delivery, potentially including self-injection. The availability of depo-subQ in Uniject may present an opportunity to determine how and under what conditions non-clinical family planning access can be further expanded through home and self-injection, potentially offering many women in remote areas more control over the use of their chosen family planning method.

Specific research needs identified through the literature review include the following:

- Assess the acceptability of self-injection using depo-subQ in Uniject.
- Assess the training, systems, policies, and infrastructure necessary to sustainably implement a home-based delivery program for depo-subQ in Uniject, including self-injection.
- Assess storage and waste disposal requirements and options for depo-subQ in Uniject in a home setting in developing countries.

To provide critical information to decision-makers, PATH plans to carry out research to fill some of the gaps noted above. PATH plans to undertake qualitative research in a selected country with the aim of assessing the acceptability of depo-subQ in Uniject provided in a home setting, focusing on self-injection. Also of interest will be determining best practices and assessing the needs for training, storage, waste disposal, and other practical considerations.

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About depo-subQ in the Uniject injection system

A new formulation and presentation of the contraceptive depot medroxyprogesterone acetate (DMPA) for subcutaneous administration in a prefilled injection system, known as depo-subQ provera 104™ in the Uniject™ injection system (depo-subQ in Uniject), will soon be available to women in developing countries. The contraceptive will be prepackaged with a single dose inside Uniject, an autodisable syringe developed by PATH. Due to its ease of administration and likely high acceptability among women seeking contraception options, introduction of depo-subQ in Uniject provides opportunities to both strengthen clinic injection services and extend injectable contraceptive delivery safely and effectively beyond the clinic, such as through home delivery. The product is also expected to have advantages for supply chain management. The product will be marketed by Pfizer, and PATH is leading global planning for its introduction.

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