CLINICAL PRACTICE

ALERT

July 2011

INJECTABLE CONTRACEPTION:

The advantages of DMPA include high efficacy, a 12-week interval between injections, and the absence of interactions with other drugs. Some women prefer to use it because it is highly private, and once injected, is not "discoverable" by others. DMPA is an important contraceptive option for women who cannot use estrogen. This *Clinical Practice Alert* (CPA) updates the August 2005 "Depo-Provera® and Bone Density" CPA.

KEY RECOMMENDATIONS

- The "grace period" for a late DMPA injection is four weeks (up to 16 weeks between injections).
- Counseling women about menstrual cycle changes associated with DMPA can substantially lower discontinuation rates.
- Bone mineral density (BMD) screening should not be recommended to a client for the sole purpose of evaluating appropriateness of DMPA usage. BMD screening tests are not a benefit of the Family PACT Program.

QUESTIONS AND ANSWERS

How often should DMPA be injected and how long is the grace period for late injections?

- The standard interval between injections of DMPA is 12 weeks. The World Health Organization (WHO) recommends that repeat injection of DMPA can be given up to four weeks late without requiring additional contraceptive protection.[1] However, this does not mean that the regular DMPA injection interval can be extended by four weeks, since there will be no "grace period" for late injections.
- If the client is more than four weeks late for a DMPA injection, she may receive it if it is reasonably certain that she is not pregnant. Additional contraception for the next seven days and emergency contraceptive pills should be offered.

When should women initiate DMPA injections?

- *If having menstrual cycles*, give the first DMPA injection within seven days after the start of her menses. No additional contraceptive protection is needed.
- *Quick Start*: The first injection can be done at other times if it is reasonably certain that she is not pregnant and a back-up method is used for the next seven days.
- *Amenorrhoeic* women can have the first injection at any time, if it is reasonably certain that she is not pregnant. She will need to abstain from sex or use additional contraceptive protection for the next seven days.
- *Postabortion* clients can have the first injection immediately postabortion. No additional contraceptive protection is needed.
- *Women switching from a hormonal method* can have the first injection immediately if she has been using her hormonal method consistently and correctly or if it is reasonably certain that she is not pregnant.
- *Women switching from intrauterine contraception (IUC)* can start at any time. The IUC can be removed at the time of the first injection. A back-up method then should be used for seven days after the injection.

In which circumstances will DMPA used as a contraceptive improve or treat other medical conditions?

Women with seizure disorders may experience fewer grand mal seizures, and those with sickle cell anemia may have a reduction in the frequency of painful sickle cell crises. DMPA also is effective for the treatment of chronic pelvic pain and dyspareunia resulting from endometriosis.

Are there clinical circumstances where DMPA should not be used?

The only medical condition considered to be United States Medical Eligibility Criteria (US-MEC) Category 4* is a history of breast cancer treated within the past five years.

Why is DMPA considered to be category US-MEC Category 3* in women with risk factors for heart attack and stroke?

Among users of DMPA, concern exists that low estrogen levels may reduce high-density lipoprotein levels, which is a cardiovascular disease risk factor. In addition, DMPA may increase the risk for heart attack, although the magnitude of increase is substantially less than with combined oral contraceptives. The effects of DMPA might persist for some time after discontinuation.

How should irregular bleeding episodes be managed in women who use DMPA?

40-50 percent of women have amenorrhea after the fourth injection of DMPA and 80 percent after five years of use. This is a benefit of DMPA for many women and clients should be counseled that less bleeding reduces the risk of anemia. However, until amenorrhea occurs, bleeding may be unpredictable with many women experiencing infrequent but prolonged episodes of bleeding or spotting. Short courses of combined oral contraceptives, estrogen, or nonsterioidal anti-inflammatory drugs may help, but when discontinued, irregular bleeding patterns usually return.

How long does it take for fertility to return after the last injection of DMPA?

While some women have return of fertility by 16 weeks after the last injection, others may take as long as 18 months. The average woman will experience return of ovulation by 9-10 months after the last injection.

Do any drugs interfere with DMPA and reduce its efficacy?

Concomitant use of drugs that induce hepatic enzymes, such as rifampin and some anti-epileptic drugs (e.g., carbamazepine) do not affect the risk of method failure, as is the case with estrogen-containing contraceptive methods. Two anti-retrovirals used to treat human immunodeficiency virus, nevirapine, and efavirenz, may reduce the efficacy of DMPA.

* Please refer to CDC. **U.S. Medical Eligibility Criteria for Contraceptive Use, 2010** MMWR 2010;59 RR-4.

INJECTABLE CONTRACEPTION (CONTINUED) JULY 2011

What is the relationship between DMPA use and obesity?

Overweight or obese adolescent DMPA users may gain more weight than normal weight DMPA users, although this effect was not seen in adults. DMPA users who experience a five percent or greater increase in body weight increase within six months of DMPA initiation are most likely to gain excessive weight.[2] Such women should be counseled regarding weight control or offered another method.

DMPA has a "black box" warning listed in the patient package insert regarding loss of BMD. Do all women who use DMPA lose bone density?

Studies show that about one quarter of DMPA users have estrogen levels in the menopausal range. In addition, most but not all studies show that groups of DMPA users lose about seven percent of bone density while using DMPA. However, most women will regain lost vertebral bone within two years and hip bone within three years of discontinuing DMPA.

Do prior users of DMPA have increased fracture rates?

A 2006 Cochrane review[3] concluded that the influence of steroidal contraceptives on fracture risk cannot be determined from existing information. A recent United Kingdom case-control study[4] of females aged 20-44 with an incident fracture suggests that use of DMPA is associated with a slightly increased risk of fractures. A study of prior DMPA users[5] shows that they have slightly lower bone density levels than never users, but the difference was so small that it was felt to be unlikely that this would affect fracture risk.

Are there unique concerns regarding bone loss and fracture in adolescents who use DMPA?

A 2006 position paper of the Society for Adolescent Medicine[6] recommended that clinicians should:

- Continue prescribing DMPA to adolescent girls needing contraception with adequate explanation of benefits and potential risks.
- Determine an individual risk profile for osteopenia. The strongest risk factor for osteopenia in an adolescent on DMPA is low body weight, especially a body mass index $\leq$16. Physical immobility, renal disease, cystic fibrosis, anorexia nervosa, previous estrogen deficiency, hyperthyroidism, malabsorption, chronic corticosteroids and other immunosuppressive drugs, and family history of osteoporosis also adversely affect bone density.
- Recommend sufficient calcium intake (including supplemental calcium) and daily exercise to all adolescents receiving DMPA.

Why not perform a BMD test (e.g., DEXA scan) in prospective or current DMPA users?

BMD tests are intended to evaluate the degree of bone loss in women who already have achieved peak bone density in order to predict future fracture risk or to evaluate whether a medial condition, or drug such as an oral steroid, is causing "secondary" osteoporosis. There is no standard for interpretation of BMD test scores that is clinically useful in the evaluation of prospective or current DMPA users.

Should DMPA users take "breaks" from DMPA use in order to regain bone or at least slow its loss?

Insufficient data exist regarding the effect of intermittent DMPA on bone density, so this strategy cannot be recommended. In addition, there is no limitation on the number of years that a woman can use DMPA or an upper age limit.

Does DMPA cause depression? Can women with depression use DMPA?

While studies of post-partum women[7] and adolescents[8] using DMPA show no greater likelihood of depression, individual women may experience an increase in depression during DMPA use. DMPA use in women with a history of depression is US-MEC Category 1.*

APPLICATION OF FAMILY PACT POLICIES

Can I prescribe DMPA and have my client pick-up it up in a pharmacy, then inject it in my office?

No. DMPA prescriptions dispensed by pharmacies are not reimbursed by Family PACT. DMPA vials must be ordered and stocked at the provider's office or clinic, and then once injected, a claim submitted for the office visit (with an evaluation and management code) and the drug itself (J1055). Providers can have an agreement with a pharmacy for the delivery of DMPA vial(s) to the provider's office or clinic, but in this case, the provider must purchase the drug from the pharmacy and then bill Family PACT for the drug once it is injected.

Which laboratory tests are available to DMPA users?

While certain screening tests are available as primary benefits to all Family PACT clients, other specified laboratory tests are covered as medically necessary to evaluate whether a client is a candidate for a particular contraceptive method. In the case of current or potential DMPA users, covered lab tests include:

- Liver function tests, to evaluate women with chronic liver disease for severe cirrhosis (US-MEC Category 3*).
- Blood glucose level (and if abnormally elevated, a two-hour glucose tolerance test) for Type 2 diabetes screening and diagnosis.

Which DMPA complications are covered by Family PACT?

- Heavy vaginal bleeding. Estradiol tablets are a Family PACT benefit, but claims by those eligible to dispense medication on-site require a secondary diagnosis code of 626.6 (irregular vaginal bleeding).
- A vaso-vagal episode resulting from the injection of DMPA.
- Allergic reaction to treatment for a secondary diagnosis (e.g., an antibiotic used for a sexually transmitted infection treatment).

Is there special counseling that is necessary for women who choose to use DMPA?

The information contained in the patient package insert shall be provided to clients as part of the informed consent process.

Providers should refer to the Family PACT Policies, Procedures, and Billing Instructions manual for the complete text of the Family PACT standards, official administrative practices, and billing information.

RESOURCES FOR INFORMATION ON DMPA

1. WHO Selected Practice Recommendations For Contraceptive Use 2008 Update. Accessed at http://whqlibdoc.who.int/hq/2008/WHO_RHR_08.17_eng.pdf.
2. Bonny AE, Secic M, Cromer B. Early weight gain related to later weight gain in adolescents on depot medroxyprogesterone acetate.Obstet Gynecol. 2011 Apr;117(4):793-7.
3. Lopez LM, Grimes DA, Schulz KF, Curtis KM. Steroidal contraceptives: effect on bone fractures in women. Cochrane Database Syst Rev. 2009 Apr 15;(2):CD006033.
4. Meier C, Brauchli YB, Jick SS, et.al. Use of DMPA and fracture risk. J Clin Endocrinol Metab. 2 010 Nov; 95(11):4909-16.
5. Orr-Walker BJ et al. The effect of past use of the injectable contraceptive depot medroxyprogesterone acetate on bone mineral density in normal post-menopausal women. Clin Endocrinol (Oxf). 1998 Nov; 49(5):615-8.
6. SAM. Depot Medroxyprogesterone Acetate and Bone Mineral Density in Adolescents-The Black Box Warning: A Position Paper of the Society for Adolescent Medicine Journal of Adolescent Health 39 (2006) 296-301.
7. Tsai R, Schaffir J. Effect of depot medroxyprogesterone acetate on postpartum depression. Contraception. 2010 Aug; 82(2):174-7.
8. Gupta N, et. al. Mood changes in adolescents using DMPA: a prospective study. J Pediatr Adolesc Gynecol. 001 May; 14(2):71-6.