

PRETERM BIRTH PREVENTION



**Tarrant County
Public Health**

17P
Initiative

A program for prematurity prevention

**17P PRACTICE BULLETIN,
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ACOG Committee Opinion on Use of 17P to Reduce Preterm Birth

Tarrant County's protocol for the use of 17 alpha hydroxyprogesterone caproate (17P) is based on the Committee Opinion set forth by the American College of Obstetricians and Gynecologists (ACOG). In October 2008, the ACOG issued its second statement in support of 17P to reduce recurring preterm birth. The committee opinion stated: "progesterone supplementation for the prevention of recurrent preterm birth should be offered to women with a singleton pregnancy and a prior spontaneous preterm birth due to spontaneous preterm

labor or premature rupture of membranes. "They also call for further research to determine if there are other indications for progesterone therapy in the prevention of preterm delivery." Clinical leaders in Texas continue to review and discuss emerging research on preterm birth prevention in order to provide the highest quality care possible to the state's women and infants.

Use of progesterone to reduce preterm birth. ACOG Committee, Opinion No. 419. American College of Obstetricians and Gynecologists. *Obstet Gynecol.* 2008; 112:963-5.

Vaginal Progesterone Suppository Use in Preventing Preterm Birth Among Women with Short Cervix

An new area of interest in preterm birth prevention is the potential use of progesterone in otherwise normal risk women who have asymptomatic cervical shortening in the mid trimester. Cervical length of $< 25\text{mm}$ noted by vaginal ultrasound between 18-24 weeks estimated gestational age (EGA) is associated with an increased risk of preterm birth. To date, there are five randomized controlled trials that have investigated the use of vaginal progesterone in these women. A meta-analysis by Romero, et al, indicated that vaginal progesterone started prior to 24 weeks gestation and continued to 36 6/7 weeks was associated with a 42% reduction in preterm birth < 33 weeks gestation. This analysis also demonstrated improvements in neonatal outcomes, such as reduced admission to the NICU and respiratory distress, in the treated groups. The effect was most consistent with cervical lengths between 10-20mm. The use in twin pregnancies with midtrimester cervical shortening demonstrated a non-significant 30% Reduction in PTB < 33 weeks.

Progesterone formulations used in these trials included vaginal progesterone gel (marketed as CrinoneTM or Prochieve, 90-100mg daily) and compounded micronized progesterone (200mg daily). Both the 90-100mg and 200mg preparations demonstrated reductions in preterm birth < 33 weeks EGA in this analysis (47% and 37% reduction in PTB < 33 weeks respectively. Cost-benefit analyses have demonstrated the potential benefit of universal screening of cervical length in all pregnancies between 18-24 weeks EGA with subsequent use of

vaginal progesterone when the cervical length $< 25\text{ mm}$ is noted, although universal cervical length screening has not been advocated by any national organization at this time.

Thus, in asymptomatic women, with a singleton pregnancy, with transvaginal US cervical length $< 25\text{mm}$ between 19-24 weeks EGA, vaginal progesterone appears to have benefit in prevention of preterm birth and improvement in neonatal outcome. Consultation with Maternal Fetal Medicine in these cases may be of benefit in determining if vaginal progesterone may be indicated on an individual basis.

Note: For information about Medicaid reimbursement for this treatment, please refer to the Texas Medicaid Provider Procedures Manual 8.2.39.4 *17-Alpha Hydroxyprogesterone Caproate*.

Hassan SS, Romero R, Vidyadhari D, Fusey S. Baxter JK, Khandelwal M, et al. Vaginal progesterone reduces the rate of preterm birth in women with a sonographic short cervix: a multicenter, randomized, double-blind, placebo-controlled trial. *Ultrasound Obstet Gynecol.* 2011; 38(1):18-31.

Romero R, Nicolaides K, Conde-Agudelo A., Tabor A, O'Brien JM, Centigöz E, et al. Vaginal progesterone in women with an Asymptomatic sonographic short cervix in the midtrimester decreases Preterm delivery and neonatal morbidity: a systematic review And meta-analysis of individual patient data. *Am J of Obstet Gynecol.* 2011. doi:10.1016/j.ajog.2011.12.003

Werner EF, Han CS, Pettker CM, Buhimschi CS, Copel JA, Funai EF, et al. Universal cervical-length screening to prevent preterm birth: a cost effectiveness analysis. *Ultrasound Obstet Gynecol.* 2011;38(1):32-7.



Frequently Asked Questions about 17P

Does a patient need to sign a written consent form prior to receiving 17P?

While written consent for 17P is not required, the prescribing provider should review all risks and benefits with the patient, as with any medical treatment. Some facilities have asked patients to sign a consent form or a patient contract to emphasize the importance of adhering to the weekly dosing regimen. Examples are available on www.mombaby.org.

What is the appropriate dosing interval for 17P?

17P should be given on a weekly basis; the recommended interval is every 5-9 days. Some facilities try to schedule all 17P injections early in the week, allowing for time to make up a missed appointment while remaining on the treatment schedule.

What do we do if a patient misses one or several doses of 17P?

While the treatment is likely to be less effective due to missed doses, patients should continue to receive 17P injections even if they miss some doses.

How do we get a patient back on schedule if she misses a dose?

The first step is to talk with the patient and find out why she missed previous dose(s). Then work with her to find a time and day that will work for her schedule and yours to receive her injection. If she has Medicaid, it is important to connect her with a pregnancy care manager who could help her address other issues such as transportation. Begin her treatment regimen again as soon as possible.

If I am keeping a vial in the clinic for a specific patient and she miscarries, can I use the remaining doses as my stock vial?

If this vial never leaves the control of your practice site, it may be used for multiple patients. Some practice sites choose to use one vial at a time for multiple patients, so that only one vial is unsealed at a time. Be sure to check the expiration date regularly; the shelf life for 17P is six months.

How can we insure patients continue to receive 17P during a hospital stay?

Hospital pharmacies may purchase a vial of 17P directly from a local compounding pharmacy. They will be billed for the vial of 17P and can bill private insurers or Medicaid for doses given to Medicaid patients. Local 17P compounding pharmacies include Randol Mill Pharmacy, Arlington, TX 817-274-1883 (www.randolmillpharmacy.com). Online compounding pharmacy is Wedgewood Pharmacy, 1-800-331-8272 (www.wedgewoodrx.com).

Can I use vaginal progesterone for a patient with a prior preterm birth who refuses to take injections?

Randomized trials of vaginal progesterone for prevention of recurrent PTB in women with prior PTB have mixed results: at this time, IM injection is the only ACOG-endorsed progesterone treatment of 17P for the prevention of recurrent PTB.

Does TX Medicaid pay for the commercial form of 17P – Makena™?

Yes, there is a mechanism for providers to be reimbursed for Makena™. Detailed instructions are available online in the TX Medicaid Procedures manual. Call TMHP Contact Center at 1-800-925-9126, or go to www.tmhp.com, click on “providers” and search “Makena.”

Protocol for 17P Use:

For a woman to be eligible for 17P she must meet the following criteria:

- ✓ Have a history of a previous singleton spontaneous preterm birth between 20⁰ and 36⁶ weeks gestation
- ✓ Have a current singleton pregnancy
- ✓ Initiate treatment between 16⁰ and 21⁶ weeks gestation. If she presents to prenatal care late, 17P may be initiated as late as 23⁶ weeks.

- ✓ Receive 17P injections weekly until 36⁶ weeks gestation or until she delivers – whichever comes first.

17P has been proven to be ineffective in reducing the risk of recurring preterm birth in multi-fetal pregnancies. It is also not effective when used for a woman with a previous medically indicated preterm birth.

Does 17P increase the risk of Gestational Diabetes?

From the MFMU randomized trials of 17P in both twins and singleton pregnancies, the rates of gestational diabetes were similar between those who received 17P vs placebo (5.8% vs 4.7% for singletons, 7.4% vs 7.6% for twins). Women taking 17P should receive the usual recommended screening for gestational diabetes in pregnancy as the general population. Gyamfi C, Horton AL, Momirova V, Rouse DJ, Caritis SN, Peaceman AM, et al. The effect of 17-alpha hydroxyprogesterone caproate on the risk of gestational diabetes in singleton or twin pregnancies. Am J Obstet Gynecol. 2009 Oct;201(4):392.

What is the status of the FDA's Approval for the Use of 17P to Prevent Preterm Labor?

The FDA approved the use of IM 17P injections to prevent preterm labor for women with a prior singleton spontaneous preterm birth on February 4, 2011. While their initial statement only approved the use of the manufactured product Makena™, public outcry over the high cost of this medication prompted the release of a second statement that the FDA did not intend to take enforcement action against pharmacies that compound hydroxyprogesterone caproate unless the compounded products are unsafe, of substandard quality, or are not being compounded in accordance with appropriate standards for compounding sterile products.

How can patients who are uninsured or underinsured access 17P?

Please refer to this website: www.tmhp.com (under Providers Manual 8.2.39.4). The Makena™ Care Connection program also has a program to provide reduced cost and free 17P to women.

To learn more about their program go to www.makena.com.

They also have a program for women with private insurance who may not be able to afford their co-payment.

For more Frequently Asked Questions

Go to www.mombaby.org or <http://health.tarrantcounty.com> and search “17P.”





Medicaid Billing Tips for 17P for Prevention of Recurrent Preterm Birth

- To obtain Medicaid reimbursement for 17P, a health care professional must administer each dose of 17P.
- To expedite reimbursement, providers should file electronic claims for 17P.
- The ICD-9-CM diagnosis code to be used for billing is V23.41 (history of preterm labor). Providers must verify that the recipient's history includes a previous spontaneous singleton preterm delivery that occurred before 37 weeks. Providers bill for the 17P medication using the HCPCs procedure code J1725 for compounded form; for Makena™ J1725 with modifier U1. Providers should bill their usual and customary charges, including either CPT code 96372 for 17P administration or CPT code 99211 if administered as part of a nurse visit.
- Patients should NOT be given a prescription for compounded 17P to take to a pharmacy as few compounding pharmacies will bill Medicaid directly for 17P, so the patient will be asked to pay out of pocket. Patients cannot be reimbursed by Medicaid for out-of-pocket expenses.
- To remain up-to-date on Medicaid billing changes visit the website www.tmhp.com.
- See Texas Medicaid Reimbursement handouts provided.

Tarrant County Public Health 17P Initiative

Tarrant County is a leader among regions in its implementation of 17P to prevent recurring preterm birth. Since 2012 the Tarrant County Public Health Department and UNT's Health Sciences Center and Ob/Gyn Division have been collaborating with clinical leaders throughout the County to bring awareness and to increase availability to all eligible women in Tarrant County. This initiative has been successful thanks to strong support from the Tarrant County Fetal/Infant Mortality Review Council. This initiative has helped educate health care providers, patients, and other members of the care team about the importance of consistent and appropriate use of 17P.

Selecting a Quality Compounding Pharmacy for 17P

Compounding refers to a method of preparing a specialized product from separate ingredients to meet the needs of a patient or group of patients. Because it is paramount that Tarrant County women receive safe and effective 17 alpha hydroxyprogesterone (17P), choosing a reliable compounding pharmacy is critical. The Pharmacy Compounding Accreditation Board (PCAB) was established to enforce compounding standards. This agency ensures that providers can be confident in their pharmacy selection, and that medicines compounded in accredited pharmacies are safe.

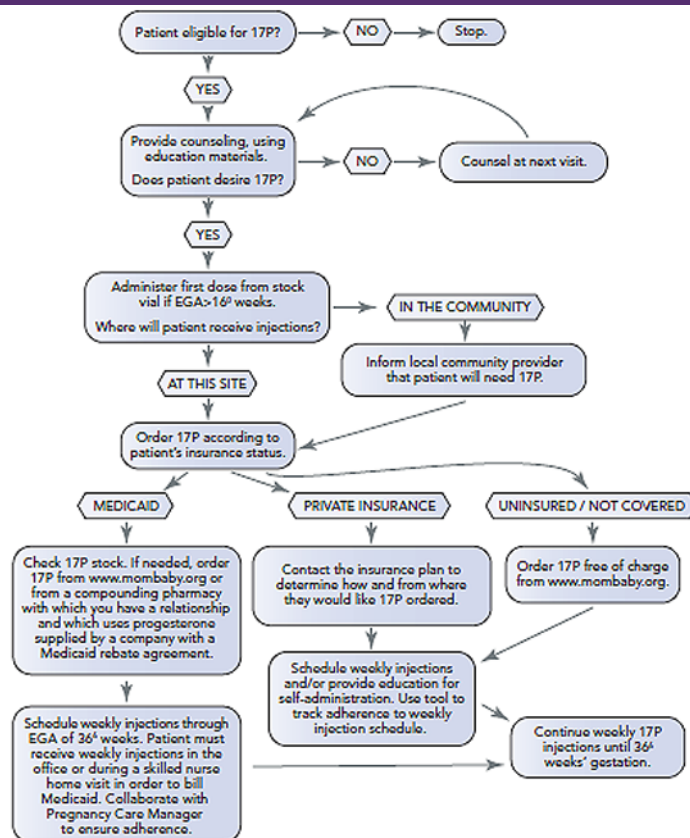
PCAB is a non-profit organization created by the American Pharmacists Association, the United States Pharmacopeial Convention (USP), and the International Academy of Compounding Pharmacists along with five other national pharmacy organizations. PCAB has rigorous requirements that must be met for a pharmacy to receive accreditation. Their review process guarantees that PCAB-accredited pharmacies meet strict national compounding standards, have appropriate on-site chemicals and equipment, and that staff has been trained and is competent in compounding. As compounding preparations become more complicated, the additional training required by PCAB ensures that pharmacists and technicians receive regular and current training specific to this field.

PCAB offers the public and physicians a way to identify pharmacies that satisfy strict compounding criteria for medications such as 17P. Visit www.pcab.org to view a list of accredited compounding pharmacies, and to download a copy of a pharmacy's accreditation report. When selecting a pharmacy to provide 17P or another compounded medication, look for the PCAB accreditation seal.

Once a PCAB accredited compounding pharmacy has been selected, providers should ensure they are licensed to provide medications in Texas by the Texas State Board of Pharmacy (verify here at www.tsbp.state.tx.us). The pharmacy should use only chemicals that meet USP criteria purchased from an FDA registered and inspected cGMP chemical supplier to prepare 17P. 17P should only be compounded in an isolator or clean room that has been certified to meet USP 797 criteria for sterile compounding. The 17P formulation should be terminally sterilized by dry heat instead of filtration to ensure the highest level of sterilization. The pharmacy should be able to provide you with a Certificate of Analysis (COA) from an independent laboratory that proves each lot they prepare is tested for sterility, potency, and endotoxins.

Randol Mill Pharmacy, Arlington, TX; 817-274-1883
www.randolmillpharmacy.com

Incorporating 17P into Practice



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- 17P: North Carolina's 17P articles, updates and tools are available at www.mombaby.org; click on 17P. Easy-to-read 17P patient booklets are available in English and Spanish online and in print. A DVD created by the Forsyth Infant Mortality Reduction Coalition called *Footprints of Hope: Preventing Preterm Birth* may be viewed from the www.mombaby.org website. This 15-minute video was filmed in English and in Spanish. It focuses on the stories of three different mothers who used 17P.
- Clinical algorithms for managing high risk pregnancies and conditions are available free of charge on www.mombaby.org – click on algorithms to access.
- The March of Dimes website is another valuable resource for clinicians and patients. Go to www.marchofdimes.com for complete information about preterm birth, including patient materials, blogs and the latest perinatal statistics and news.
- Pregnancy spacing of at least 9 months between delivery and conception is a key health message for new mothers. A good online resource for women about family planning is www.bedsider.org.
- Smoking during pregnancy is associated with preterm birth and low birth weight. Resources for patients and providers are available at www.YouQuitTwoQuit.com. This site has practice bulletins, multiple resources for health care providers and patients as well as a link to a free 3 credit CME online tutorial from ACOG on *Smoking Cessation During Pregnancy: A Clinician's Guide to Help Pregnant Women Quit Smoking*. Another great resource is www.MinutetoAsk.com. Tarrant County's smoking cessation program can be accessed by emailing smokefree@tarrantcounty.com or by calling **817-321-4976, ext. 103**. This program helps smokers learn to quit smoking in a supportive group, uses face to face and telephone counselors to help smokers quit, save money, and experience immediate health benefits and improved quality of life.
- Pregnant women and new mothers can receive free text messages with helpful information, tips and reminders. They just text the word BABY to 511411 and get FREE messages on their cell phone. The messages are tailored to gestational age and continue through baby's first birthday. Messages can be sent in English or in Spanish. For more information go to www.text4baby.org. This program is available through the National Healthy Mothers Healthy Babies Coalition.
- Free outreach materials are available from **Stephani Adams** (saadams@tarrantcounty.com), Prematurity Prevention Coordinator, Tarrant County Public Health.

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