

17 Alpha-hydroxyprogesterone caproate (17P)

Making the Case for 17P

Nearly 500,000 babies are born preterm in the United States each year.¹ Preterm birth (PTB), or birth less than 37 weeks gestation, increases infants' risk of death and is the leading cause of long-term neurological disability in children. Additionally, PTB-related health expenses cost the United States healthcare system more than \$26 billion each year.² Preventing PTB is critical to fostering the long-term health and development of infants across the country.

What Is 17P?

17 alpha-hydroxyprogesterone caproate (17P) is a synthetic form of progesterone that has been shown to reduce the recurrence of PTB for women with singleton gestations that have a history of previous PTB.^{3,4} Women with a previous history of PTB are more likely to have another preterm infant compared to women without this history. Available only by prescription, 17P is administered through weekly injections beginning at 16-20 weeks, 6 days (according to FDA guidelines) until delivery. Studies show that administering 17P to an eligible woman reduces the chance of having another PTB by 33 percent.⁵ Each year, approximately 30,000 pregnant women are considered eligible for 17P.⁶

The 2013 United States PTB rate was 11.4 percent, equal to the Healthy People 2020 goal of 11.4 percent.⁷ However, there are marked racial disparities in preterm births, contributing to large disparities in infant health outcomes. While other methods like the use of vaginal progesterone are being studied for use in preventing PTB, 17P provides a strong solution to halting premature birth in eligible women. Increasing the availability of and access to 17P is a critical step in improving PTB rates and reducing disparities.

The State and Territorial Health Agency Role in Promoting Access to 17P

Coordinated efforts to promote the appropriate use of 17P will provide state and territorial health agencies with the unique opportunity to reduce the incidence of PTB among eligible women. State agencies can partner with Medicaid, healthcare providers, professional organizations, and other key stakeholders to improve identification of eligible women, increase availability of and access to 17P, and educate providers and patients on the appropriate use of 17P. Eliminating barriers to access and increasing affordable availability of 17P are the biggest challenges to increasing 17P's uptake. Health agencies and their partners can take the lead in promoting efficient, cost-appropriate, and safe dissemination of 17P.

State Examples of 17P Interventions

Louisiana

The Louisiana Department of Health and Hospitals' Birth Outcomes Initiative has partnered with the Louisiana Hospital Association to improve access to 17P and streamline the ordering process through the [17P Louisiana Resource Center](#) website. In September 2014, Louisiana linked vital records data with statewide Medicaid data. A weekly report of women who have had a previous preterm birth, those potentially eligible for 17P, is generated from the linked vital records and Medicaid data. This list is shared with Medicaid managed care plans and helps ensure that women who are eligible for 17P are easily identified upon registering with their plan, which allows plans to conduct immediate outreach. Additionally, Louisiana is the first state to create a progesterone pay for performance measure for

Medicaid managed care plans. Its goal is to increase the percent of eligible women receiving 17P from the current 5 percent to 20 percent. Hoping to incentivize providers to order and administer 17P, Louisiana is also working to increase the price paid for compounded 17P. Louisiana Medicaid covers both Makena, the brand name version of the drug, and compounded 17P, and is conducting ongoing provider education on 17P.

North Carolina

Stagnant statewide PTB rates and widening health disparities galvanized the University of North Carolina Center for Maternal and Infant Health, the North Carolina Division of Public Health and the North Carolina Perinatal Health Committee of the Child Fatality Task Force to make 17P accessibility a priority. In 2006, the North Carolina General Assembly began appropriating funds to improve access to 17P for uninsured women and an advisory council guided implementation activities. The Division of Medical Assistance joined the partnership in 2007 and remains an essential stakeholder. In March 2011, the [Pregnancy Medical Home](#) program through Community Care of North Carolina was launched to enhance the quality of maternal care, including increasing screening for 17P eligibility and case management for women receiving 17P treatment. As a result, 17P use has become a standard of care for eligible women in North Carolina.

Policy changes regarding the use of compounded and commercial products have created challenges for stakeholders, but the partnerships developed over the past nine years remain strong through the shared goal that all eligible women receive treatment. Currently, the North Carolina team is conducting focus groups, key informant interviews and data analysis to assess the “state of the state” in terms of 17P penetration and treatment completion, and aims to launch a quality improvement initiative in August 2015.

Ohio

The Ohio Collaborative to Prevent Infant Mortality, the Ohio Department of Health, and the Ohio Department of Medicaid secured state general revenue and Medicaid funds to support a request for proposals to make supplemental progesterone available as the standard of care for all Ohio women at risk of PTB. In 2013, the Ohio Perinatal Quality Collaborative (OPQC) initiated its statewide Progesterone Project to help identify and provide progesterone treatment for both women with a history of PTB and those identified as having a short cervix on ultrasound in the current pregnancy. In January 2014, OPQC convened participants from 23 outpatient clinics associated with the original 20 OPQC Charter hospitals that conducted the 39 week and Antenatal Corticosteroid improvement projects. Participating providers were asked to educate pregnant women and their caregivers about PTB, to promote wide access to sonographers skilled in ultrasound measurement of the cervix, and to record the number of at-risk women identified and the treatments offered each month. OPQC is currently tracking the percentage of patients who accept progesterone treatment, when providers initiate progesterone treatment, and rates of preterm birth before 37 weeks and 32 weeks of gestation in at-risk women.

OPQC has worked closely with Ohio Medicaid to improve access to both injectable 17P and vaginal progesterone preparations. However, plans to promote use of compounded 17P, an economical alternative to the more expensive manufactured 17P, were severely affected in July 2014 by an FDA announcement that led most Ohio compounding pharmacies to cease offering the drug. Although manufactured 17P is still available, the drug’s cost has limited its use in both Medicaid- and privately-insured women. OPQC is working with Ohio Medicaid, Medicaid managed care companies, and

pharmacies and manufacturers to offer alternate vaginal forms of progesterone and to reduce financial barriers to manufactured 17P.

Preliminary data from the participating sites indicates a growing number of 17P-eligible women are being identified, but their receipt of progesterone prophylaxis has not achieved targeted levels. The project continues to receive strong support from the Ohio Department of Health, the Department of Medicaid, and from local providers and participants.

South Carolina

In July 2011, the South Carolina Department of Health and Human Services led a statewide effort with partners including the March of Dimes, South Carolina Hospital Association, and Blue Cross Blue Shield of South Carolina to form the South Carolina Birth Outcomes Initiative (SCBOI), a collaborative that aims to improve health outcomes for all babies and moms. One of SCBOI's original six core objectives for improving birth outcomes was to make 17P "available to all at-risk pregnant women with no 'hassle factor.'" SCBOI developed the [Universal 17P Authorization Form](#), which has been updated since its inception with the following items:

- The yes or no question "Delivery was due to preterm labor or PPROM even if it resulted in C-section" was added.
- The yes or no question "Delivery was not due to medical indication, e.g. preeclampsia, abruption, etc." was added.
- Fields were added for practice name, practice NPI, contact person, phone number, and fax number.
- The option to prescribe Makena was added.

Though both Makena and compounded 17P are now available, SCBOI's Universal Authorization form clearly indicates that a physician must make the decision to prescribe either of these products. If the compounded product is not available when prescribed, Medicaid managed care plans must pay for Makena. Through a grant funded by the March of Dimes, the Medical University of South Carolina has also made great efforts to educate providers on appropriate use of and access to 17P through the Progesterone Outreach Program. This project was funded from 2009 to 2011, during which time its activities reached more than 1,150 perinatal professionals.

Availability and Access Challenges

Makena's cost poses a budgetary challenge for many states, and its manufacturer is working directly with states on pricing. To reduce costs, providers have used (and some continue to use) compounding pharmacies where 17P could be purchased at a lower cost. Traditional compounding pharmacies are commonly used to customize drugs for individuals with specific needs. However, the safety, quality, and level of regulatory oversight of compounded drugs produced by facilities that exceed the bounds of traditional pharmacy compounding operations remain a concern, especially for sterile injectable drugs.

If 17P is being used in compounded form, it is strongly recommended that the state board of pharmacy with jurisdiction over the compounding pharmacy of interest is consulted to ascertain the current level of regulatory oversight being provided and the compounder's compliance track record before making a decision. On Nov. 27, 2013 President Obama signed into law the Drug Quality and Security Act,

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legislation that contains important provisions relating to the increased regulatory oversight of compounding of human drugs. The FDA has initiated a number of key actions to implement this new law.⁸

The company that produces Makena (initially Ther-Rx, and now Lumara, a division of AMAG Pharmaceuticals) negotiates with state Medicaid agencies individually to determine the price. Two factors that complicate the challenges for state health agencies are the variation in prices across states, and the concerns about legal issues in using only the FDA-approved drug versus continuing to use the compounded medication at a lower cost.

In addition to cost and quality, accessing 17P can pose a challenge to providers. Because 17P must be injected weekly, physicians must have prompt access to the medication in order to meet the needs of their patients. Ordering 17P can be complicated, costly, and time-consuming for providers, although Lumara has offered its assistance to work through this issue with states. Regardless of how 17P is obtained, it is vital to support quality case management and patient-centered care so that eligible women are able to complete the full course of treatment and receive the full benefit.

¹ CDC. "Preterm Birth." Available at

<http://www.cdc.gov/reproductivehealth/maternalinfanthealth/pretermbirth.htm>. Accessed 1-21-2014.

² *Ibid.*

³ Meis PJ, Klebanoff M, Thom E, *et al.* "Prevention of recurrent preterm delivery by 17 alpha-hydroxyprogesterone caproate." *N Engl J Med.* 2003. 348:2379-2385. Available at

<http://www.nejm.org/doi/full/10.1056/NEJMoa035140>. Accessed 1-30-2014.

⁴ da Fonseca EB, Bittar RE, Carvalho MH, *et al.* "Prophylactic administration of progesterone by vaginal suppository to reduce the incidence of spontaneous preterm birth in women at increased risk: a randomized placebo-controlled double-blind study." *Am J Obstet Gynecol.* 2003. 188:419-424. Available at

<http://www.ncbi.nlm.nih.gov/pubmed/12592250>. Accessed 1-30-2014.

⁵ UNC Center for Maternal & Infant Health. "Preventing preterm birth: Progesterone treatment (17P) important information you need to know." Available at <http://mombaby.org/PDF/17P%20Factsheet.pdf>. Accessed 1-21-2014.

⁶ Petrini JR, Callaghan WM, Klebanoff M, *et al.* "Estimated effect on 17 alpha-hydroxyprogesterone caproate on preterm birth in the United States." 2005. 105(2): 267-272. Available at

<http://www.ncbi.nlm.nih.gov/pubmed/15684150>. Accessed 1-30-2014.

⁷ Preterm Births and Infant Deaths. HealthyPeople.gov. Available at <http://www.healthypeople.gov/2020/leading-health-indicators/infographic/maternal-infant-and-child-health-0>. Accessed March 30, 2015.

⁸ FDA. "Compounding." Available at

<http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/default.htm>.

Accessed 1-21-2014.