

## 17 Alpha-hydroxyprogesterone caproate (17P)

### **Making the Case for 17P**

Nearly 500,000 babies are born preterm in the United States each year.<sup>1</sup> Preterm birth (PTB), or birth less than 37 weeks gestation, puts infants at a higher risk of death and is the leading cause of long-term neurological disability in children. Additionally, PTB-related health expenses cost the U.S. healthcare system more than \$26 billion each year.<sup>2</sup> 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.<sup>3,4</sup> Women with a previous history of PTB are more likely to have another preterm infant compared to women who have not. Commonly prescribed by doctors, 17P is administered through weekly injections beginning at 16-24 weeks until delivery. Studies show that administering 17P to an eligible woman reduces the chance of having another PTB by 33 percent.<sup>5</sup> Each year, approximately, 30,000 pregnant women meet the qualification and are considered eligible for 17P.<sup>6</sup>

The U.S. PTB rate is 11.5 percent (2012), well above the Healthy People 2020 goal of 11.4 percent.<sup>7</sup> Furthermore, there is marked racial disparity in preterm births, contributing to large disparities in infant health outcomes. With no other safe and tested technologies available to effectively prevent PTB, 17P provides the strongest solution to halting premature birth in eligible women. Increasing the availability and access to 17P is a critical step in improving PTB rates and reducing disparities.

### **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 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 appropriate use of 17P. Eliminating barriers to access and increasing affordable availability of 17P is the biggest challenge 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 and the Louisiana Hospital Association have partnered to improve access to 17P and streamline the ordering process through the [17P Louisiana Resource Center](#) website. A statewide survey identified that difficulty ordering 17P posed the greatest barrier to care; the website, therefore, facilitates the ordering process so that every eligible woman in the state of Louisiana has access to 17P. Louisiana has also bolstered education efforts by partnering with Medicaid-Bayou Health Coordinated Care to provide information on premature birth recurrence prevention and the use of 17P. Louisiana is going to cover Makena, the only brand of 17P available, for providers' offices, so that if prenatal care providers want to stock the medication, they can use Makena or pharmacy compounded 17P. Finally, three of the five managed care companies in

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Louisiana pay for home administration of 17P, and this program has more than quadrupled the use of 17P in patients enrolled in Medicaid.

## *North Carolina*

A steady increase in statewide PTB rates and widening health disparities galvanized the UNC Center for Maternal and Infant 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 nonrecurring funds to improve access to 17P and an advisory council guided implementation activities. In March 2011, the [Pregnancy Medical Home](#) program was launched to enhance the quality of maternal care including increased screening for 17P eligibility. As a result, the use of 17P has become a standard of care for all at-risk women in North Carolina. While continued funding by the General Assembly for the program for FY14 is not certain, the partnerships developed over time remain strong and will ensure ongoing collaborative efforts to realize their goal that all women eligible receive treatment.

## *Ohio*

Spurred by the Ohio Collaborative to Prevent Infant Mortality (OCPIM), the Ohio Department of Health (ODH) and the Ohio Department of Medicaid secured state general revenue and Medicaid funds to support a request for proposals to make 17P available as the standard of care for all Ohio women at risk of PTB. The [Ohio Perinatal Quality Collaborative](#) (OPQC) was selected to develop a statewide Progesterone Project to promote identification and 17P treatment for women with a history of PTB and those identified as having a short cervix on ultrasound in the current pregnancy. OPQC will apply Institute for Healthcare Improvement quality improvement techniques to enable clinics and providers to find and treat all eligible women, educating pregnant women and their caregivers about PTB, and assuring wide access to sonographers skilled in ultrasound measurement of the cervix. OPQC, OCPIM, Ohio Medicaid, the Ohio Hospital Association and Ohio March of Dimes are collaborating to improve access and to assure that compounded 17P is obtained only from credentialed pharmacies that are fully compliant with state regulations for compounders. The project began in November 2013 and will continue for at least two years. It is being introduced in the six major metropolitan areas of Ohio and will then spread throughout the state.

## *South Carolina*

In July 2011, the South Carolina Department of Health and Human Services led a statewide effort with partners the March of Dimes, South Carolina Hospital Association, Blue Cross Blue Shield of South Carolina, and other key stakeholders to form the South Carolina Birth Outcomes Initiative (SCBOI) – a collaborative to improve health outcomes for all babies. Included in SCBOI’s [six core objectives](#) for improving birth outcomes is a goal to make 17P “available to all at-risk pregnant women with no ‘hassle factor.’” To simplify the process, SCBOI developed the [Universal 17P Authorization Form](#). 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 and access to 17P through the [Progesterone Outreach Program \(POP\)](#).

## **Availability and Access Challenges**

Makena is the only FDA-approved 17P drug currently on the market and was initially marketed at \$1,500 per injection.<sup>8</sup> To reduce costs, many providers use compounding pharmacies where they can purchase 17P at a fraction of the price. Traditional compounding pharmacies are commonly used to customize

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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 the use of compounded medications is being considered for 17P, it is strongly recommended that the state board of pharmacy having jurisdiction over the compounding pharmacy of interest be consulted to ascertain the current level of regulatory oversight being provided and the compounder's compliance track record before making a decision. On November 27, 2013 President Obama signed into law the Drug Quality and Security Act, legislation that contains important provisions relating to the increased regulatory oversight of compounding of human drugs. The U.S. Food and Drug Administration has initiated a number of key actions to implement this new law.<sup>9</sup>

The company that produces Makena (initially Ther-Rx, and now K-V Pharmaceutical Co.) 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 poses a challenge to providers. Because 17P is a weekly injection, 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.

<sup>1</sup> CDC. "Preterm Birth." Available at

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

<sup>2</sup> *Ibid.*

<sup>3</sup> 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.

<sup>4</sup> 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.

<sup>5</sup> 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.

<sup>6</sup> 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.

<sup>7</sup> <http://www.healthypeople.gov/2020/topicsobjectives2020/objectiveslist.aspx?topicId=26>

<sup>8</sup> Patel Y, Rumore M. "Hydroxyprogesterone caproate injection (Makena) one year later: to compound or not to compound that is the question." *Pharmacy and Therapeutics.* 2012.37(7):405-411. Available at

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3411212/pdf/ptj3707405.pdf>. Accessed 1-21-2014.

<sup>9</sup> FDA. "Compounding." Available at

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

Accessed 1-21-2014.