# February 2021 E-Newsletter: The FDA Proposed withdrawing 17OHPC from the Market: Now What?



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In light of the recent results of the PROLONG trial (1) an international randomized clinical trial (RCT), ACOG released a practice Advisory in October of 2019 suggesting it is reasonable to continue to offer 17 Hydroxyprogesterone Caproate (17-OHPC) after discussing risks and benefits and incorporating shared decision making.  Recommendations did not change from the previously published Practice Bulletin No. 130 in 2012. (2)

The PROLONG trial did not demonstrate a difference in outcome between17-OHPC and placebo.

The Practice Advisory (available at ACOG.org) stated:

“This study demonstrated no statistical difference in the co-primary outcome of preterm birth less than 35 0/7 weeks of gestation (17-OHPC 11.0% versus 11.5%; Relative Risk [RR] 0.95 [95% CI 0.71-1.26]; *P* = 0.72) and neonatal composite index (17-OHPC 5.6% versus 5.0%; RR 1.12 [95% CI 0.70-

1.66]; *P* = 0.73). Similarly, the rate of preterm birth less than 37 weeks and less than 32 weeks were not different. No other differences in perinatal or maternal outcomes were detected. However, despite having the same eligibility criteria and study protocol as the trial by Meis et al in 2003 (3) that provided randomized trial evidence for 17-0HPC for the prevention of recurrent preterm birth."

The practice advisory pointed out that the risk of spontaneous preterm birth was much lower in the PROLONG Trial (11% and 11.5% in treatment vs control groups for delivery less than 35 weeks, P=0.72) vs the Meis trial (36.3% treatment group vs 54.9% control group, delivery before 37 weeks). Also US participants may have been biased toward those at lower risk for preterm delivery as those with higher risk would not want to take the chance of receiving placebo.

In response to the FDA proposal to withdraw 17-OHPC from the market, the Society for Maternal Fetal Medicine (SMFM) released a statement on October 5, 2020 (available at SMFM.org) reiterating the recommendation to continue offering 17-OHPC while discussing risks and benefits and incorporating a shared decision making approach.

"Today the U.S. Food and Drug Administration's Center for Drug Evaluation and Research (CDER) proposed that Makena (hydroxyprogesterone caproate injection) and generic equivalents of Makena be withdrawn from the market. The FDA announcement states that Makena and its approved genetic equivalents will remain on the market until the manufacturers decide to remove the drugs or the FDA Commissioner mandates removal. In the interim, the FDA is recommending that health care professionals discuss Makena's benefits, risks, and uncertainties with their patients to decide whether to use Makena while a final decision is being made."

Both ACOG and SMFM have not changed their guidance and continue to recommend offering progesterone supplementation, including 17-OHPC to patients after fully informing them of the state of the current data, which

remains incomplete.  Further reviews of the data are likely to be forthcoming.

Until more data are available, it is reasonable to continue offering progesterone supplementation in patients with a history of previous spontaneous preterm delivery, particularly those in the highest risk groups.


1. Blackwell SC, Gyamfi-Bannerman C, Biggio JR Jr, Chauhan SP, Hughes BL, Louis JM, et al. 17-OHPC to prevent recurrent preterm birth in singleton gestations (PROLONG study): a multicenter, international, randomized double-blind trial [published ahead of print]. Am J Perinatol 2019;DOI: 10.1055/,3400227.
2. Prediction and prevention of preterm birth. Practice Bulletin No. 130. American College of Obstetricians and Gynecologists. Obstet Gynecol 2012;120:964-73.
3. Meis PJ, Klebanoff M, Thom E, Dombrowski MP, Sibai B, Moawad AH, et al. Prevention of recurrent preterm delivery by 17 alpha-hydroxyprogesterone caproate [published erratum appears in N Engl J Med 2003;349:1299]. N Engl J Med 2003;348:2379-85.