Progestosterone for the Prevention of Preterm Birth

I. Women with a history of spontaneous preterm birth less than 37 weeks gestation secondary to preterm labor or premature preterm rupture of membranes

   a. Currently pregnant, singleton gestation: offer weekly progesterone intramuscular 17α-hydroxyprogesterone caproate 250mg (17-OHPC, Makena™) supplementation starting at 16-24 weeks of gestation

* Treatment with 17-OHPC has been shown to significantly reduce the risk of delivery at less than 37 weeks of gestation (relative risk, 0.66, 95% CI 0.54 to 0.81), delivery at less than 35 weeks of gestation (relative risk, 0.67, 95% CI 0.48 to 0.93), and delivery at less than 32 weeks of gestation (relative risk, 0.58, 95% CI 0.37 to 0.91). Infants of women treated with 17-OHPC had significantly lower rates of adverse neonatal outcomes1.

II. Women with a short cervical length less than or equal to 25mm at or before 24 weeks of gestation

   a. Currently pregnant, singleton gestation: offer daily vaginal progesterone 200 mg (Prometrium™)

   b. There is insufficient evidence regarding whether adding vaginal progesterone or switching to vaginal progesterone for a woman with a short cervix who is already receiving IM progesterone is additionally beneficial.

* Randomized studies indicate that in women with singleton gestations, no prior PTB, and short cervix vaginal progesterone is associated with reduction in PTB and perinatal morbidity and mortality, and can be offered in these cases.2-4,14

III. Multiple gestation

   a. Multiples with a short cervix less than 25mm may benefit from vaginal progesterone.5,6

   b. 17-OHPC does not reduce the incidence of preterm birth in women with twin or triplet gestations without a prior preterm birth, and is not recommended for current multiple gestation alone.

   c. For special circumstances see reference #13 or refer to maternal fetal medicine for individualized consultation.

* Data from meta-analysis of vaginal progesterone for short cervix in twin pregnancies showed >50% reduction in composite adverse neonatal outcome (RR 0.52; 95% CI, 0.29 – 0.93)5.

* Review of 13 RCTs (3768 twin pregnancies): 17-OHPC or vaginal progesterone compared with placebo/no treatment. Neither reduced the overall incidence of adverse perinatal outcome, however in
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women with short cervix, vaginal progesterone led to a reduction in the rate of adverse perinatal outcomes (RR 0.57, 95% CI 0.47-0.70)⁶.

* RCT: 247 women received vaginal progesterone gel or placebo. Rate of adverse events did not differ between two groups (OR 1.36, 95% CI 0.89-2.09; p=0.16)⁷.

* RCTs of 17-OHPC in twin and triplet pregnancies shows no benefit in reducing the rate of preterm birth⁸-¹².

**17-OHPC (Makena™) Prescribing Instructions**

1. Patient identified as candidate for 17-OHPC
2. Notify RN or clinic staff that patient is 17-OHPC candidate
3. Determine whether injection is in home or in office (Caresource only allows in home and requires buy and bill for in office method. We are not set up for the buy and bill method for entire pregnancy. All other MCPs will do in office or in home)
   a. If patient has Medicaid insurance and is starting 17-OHPC: RN or clinic staff will have clinician fill out and sign prescription section of PIP form
      i. RN or clinic staff will fax “Progesterone PIP Streamlined Skinny Communication Form” (PIP form) to:
         1. Managed Care Plan (eg Caresource, Molina, etc)
         2. Contracted specialty pharmacy
         3. Home Health Care Company
      ii. For those patients who need to start injections immediately due to urgent issues such as presenting late to care, the clinic has a limited number of one-time in office doses available
      iii. If ordering Makena in Epic please do not route the prescription to the patients pharmacy
   b. Non-Medicaid patients: RN or clinic staff will fill out Makena Care Connection form
4. For hospitalized patients, 17-OHPC should be ordered from the inpatient pharmacy
References


