Progesterone for the Prevention of Preterm Birth

History of spontaneous preterm birth less than 37 weeks gestation secondary to preterm labor or premature preterm rupture of membranes

Currently pregnant, singleton gestation: offer progesterone supplementation in the context of shared decision-making process incorporating available evidence and patient's preferences.(1)
Options:

- **Intramuscular 17α-hydroxyprogesterone caproate 250mg** (17-OHPC, Makena™) weekly from 16-24 weeks through 36 6/7 weeks of gestation.
- **Progesterone 200 mg capsules** (Prometrium™ or generic equivalent) administered vaginally daily from 16-24 weeks through 36 6/7 weeks of gestation.

Conflicting evidence exists regarding the efficacy of 17-OHPC to reduce recurrent preterm birth.(2) However, there are no significant reported safety concerns. Subcutaneous preparation is available, and FDA approved at the same dose as IM for the same indication.

There is recent data reporting equivalent or superior efficacy of vaginal progesterone compared to 17-OHPC for prevention of recurrent spontaneous preterm birth. (2, 3)

Considering ease of self-administration and fewer issues related to cost and payor coverage, vaginal administration may be favored for most patients.

Asymptomatic short cervical length ≤25mm at or before 24 weeks of gestation

a. Currently pregnant, singleton gestation: offer daily vaginal progesterone 200 mg (Prometrium™ or generic equivalent)(2, 4-6)
b. There is insufficient evidence to support efficacy of IM 17-OHPC for the indication of short cervix in women with no prior preterm birth.(2, 7, 8) Therefore, vaginal progesterone is the route of administration recommended for this indication. (1)
c. Women with prior spontaneous preterm birth and short cervix ≤25mm may also be offered cerclage

Multiple gestation

a. There is conflicting evidence regarding the efficacy of vaginal progesterone in multiple gestations with asymptomatic short cervix ≤ 25mm. Although ACOG states that no recommendation for or against this treatment can be made at this time(1, 9, 10), considering the favorable risk profile and some evidence of benefit in this population, we feel that use of vaginal progesterone for short cervix in multiples is advisable. (10)
b. Progesterone may be beneficial in twin gestations with a prior spontaneous preterm birth and may be considered in twins for this indication. (1, 13)
c. 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 the sole indication of multiple gestation with no other risk factor (such as prior preterm birth or short cervix).(1, 11, 12)

d. For special circumstances regarding use of progesterone to prevent preterm birth not covered in this document, consider maternal-fetal medicine referral for individualized consultation.

Table from ACOG Practice Bulletin No. 234: (1)

Table 1. Screening and Interventions for Prevention of Preterm Birth

Cervical length ultrasound	IM 17-OHPC	Vaginal progesterone	Ultrasound-indicated cerclage	Physical examination-indicated cerclage	Cervical pessary
Singleton pregnancy, no prior preterm birth					
Cervix should be visualized at the time of the 18 0/7–22 6/7 weeks of gestation anatomy assessment	Not indicated	Recommended for cervical length less than 25 mm	Insufficient data; possibly of benefit if the cervical length is less than 10 mm	Consider	Not indicated
Singleton pregnancy, prior spontaneous preterm birth					
Serial (every 1–4 weeks) endovaginal ultrasound measurement of cervical length beginning at 16 0/7 and repeated until 24 0/7 weeks of gestation	Offer progesterone supplementation (either 17-OHPC or vaginal progesterone)	Offer progesterone supplementation (either 17-OHPC or vaginal progesterone) If not on progesterone already, consider with a cervical length less than 25 mm (versus cerclage)	Consider with a cervical length less than 25 mm (versus vaginal progesterone if not already on progesterone supplementation)	Consider	Not indicated
Multiple gestation					
Cervix should be visualized at the time of the 18 0/7–22 6/7 weeks of gestation anatomy assessment	Not indicated	Insufficient data	Insufficient data	Consider	Not indicated

Abbreviations: IM, intramuscular; 17-OHPC, 17-alpha hydroxyprogesterone caproate.

UC Health pharmacy formulary status comment regarding 17-OHPC (Makena™):

Outpatients: Restricted to outpatients with confirmation of payer status and reimbursement
Inpatient: No formal restriction but, limited to:

1. Continuation of home therapy in patients who will be hospitalized when due for next dose.
2. For inpatients, delay initiation of progesterone to the outpatient setting to the extent possible, unless anticipated discharge is greater than one week from order date, or if near end of window for initiation of therapy.

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