

Advances in Preterm Birth Prevention,
Subcutaneous Versus Intramuscular Dosing of
17 Alpha-hydroxyprogesterone Caproate:
Pharmacokinetic Profile, Patient and
Practitioner Impact

Objectives

- Incorporate strategies for providing optimal clinical management to women at risk for PTB, based on SMFM, ACOG, and ACNM recommendations
- Define the bioavailability and bioequivalence data regarding subcutaneous administration of 17-OHPC compared with intramuscular administration
- Describe the impact of subcutaneous dosing of 17-OHPC on patient and practitioner parameters

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Dr. Sibai has nothing to disclose.

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Dr. Smith receives consulting fees from Clovis
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Society Guidelines: Progesterone to Prevent Preterm Birth

SMFM

SMFM CLINICAL GUIDELINE www.ACOG.org

Progesterone and preterm birth prevention: translating clinical trial data into clinical practice

Source: Society for Maternal-Fetal Medicine (SMFM), published in *Obstetrics and Gynecology*, 2012

Objective: To update clinical practice recommendations regarding the use of progesterone to prevent preterm birth.

Background: Recent evidence of a potential benefit for the reduction of obstetric morbidity and mortality associated with preterm birth has led to a renewed interest in the use of progesterone for the prevention of preterm birth. However, the clinical practice implications of this evidence are unclear. This guideline provides an update on the current evidence regarding the use of progesterone for the prevention of preterm birth.

Key Points: The use of progesterone for the prevention of preterm birth is supported by clinical trial data. However, the clinical practice implications of this evidence are unclear. This guideline provides an update on the current evidence regarding the use of progesterone for the prevention of preterm birth.

Recommendations: The use of progesterone for the prevention of preterm birth is supported by clinical trial data. However, the clinical practice implications of this evidence are unclear. This guideline provides an update on the current evidence regarding the use of progesterone for the prevention of preterm birth.

ACOG

Practitioner College of Obstetricians and Gynecologists

PRACTICE BULLETIN

Volume 138, October 2012

Prediction and Prevention of Preterm Birth

Background: Preterm birth is the leading cause of neonatal mortality in the United States, and preterm birth prevention is a high priority for obstetricians and gynecologists. This practice bulletin provides an update on the current evidence regarding the use of progesterone for the prevention of preterm birth.

Key Points: The use of progesterone for the prevention of preterm birth is supported by clinical trial data. However, the clinical practice implications of this evidence are unclear. This guideline provides an update on the current evidence regarding the use of progesterone for the prevention of preterm birth.

Recommendations: The use of progesterone for the prevention of preterm birth is supported by clinical trial data. However, the clinical practice implications of this evidence are unclear. This guideline provides an update on the current evidence regarding the use of progesterone for the prevention of preterm birth.

ACNM

POSITION STATEMENT

Prenatal Use of Progesterone to Prevent Preterm Birth

The American College of Nurse-Midwives (ACNM) affirms the following:

- 1. Obstetric history and exam at each prenatal visit provide essential baseline for the midwife and society. This baseline places the patient at risk of preterm birth and guides the management of pregnancy.
- 2. Early prenatal history and exam, including obstetric history, obstetric exam, and pelvic exam, are essential for the midwife to identify and manage risk factors for preterm birth. Midwives should be alert to signs and symptoms of preterm labor.
- 3. All providers of obstetric care should offer comprehensive education regarding prevention of preterm birth, including evidence-based strategies and treatment options.
- 4. In addition to education, midwives should offer comprehensive education regarding prevention of preterm birth, including evidence-based strategies and treatment options.
- 5. Application of evidence-based strategies to prevent preterm birth is essential to the midwife's role in the prevention of preterm birth. This includes the use of progesterone for the prevention of preterm birth.
- 6. Obstetric history, physical exam, and pelvic exam are essential for the midwife to identify and manage risk factors for preterm birth. This includes the use of progesterone for the prevention of preterm birth.

Background: Preterm birth is the leading cause of neonatal mortality in the United States, and preterm birth prevention is a high priority for obstetricians and gynecologists. This practice bulletin provides an update on the current evidence regarding the use of progesterone for the prevention of preterm birth.

Pharmacokinetic Properties of 17-OHPC After a Single Dose via Subcutaneous or Intramuscular Administration

Variable	Subcutaneous Injection (n=45)	Intramuscular Injection (n=45)
C _{max} (ng/mL)	7.9	6.9
t _{max} (ng/mL)	48.1	49.7
AUC 0-168 hrs (ng•h/mL)	813	790
t _{1/2} , h	212	185

Treatment-emergent Adverse Events (TEAEs)

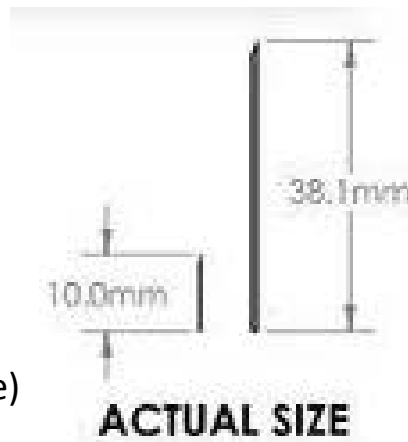
Most Common Treatment Emergent Adverse Events	Subcutaneous Injection (n=57)	Intramuscular Injection (n=60)
	Number (%) of subjects	Number (%) of subjects
Injection site pain	22 (37.3)	5 (8.2)
Headache	9 (15.3)	10 (16.4)
Dizziness	1 (1.7)	1 (1.6)
Diarrhea	3 (5.1)	1 (1.6)
Nausea	1 (1.7)	1 (1.6)
Upper respiratory tract infections	1 (1.7)	3 (4.9)

Comparison of Pharmacokinetic Properties After Single Dose of Hydroxyprogesterone Caproate in Post-menopausal Women and Pregnant Women

Note that the higher levels for second and third trimester are due to reaching steady state and having some accumulation from weekly dosing

Group (N)	C _{max} , ng/mL (CV%)	T _{max} , h (range)	AUC (0-t), ng•h/mL (CV%)
Post-menopausal women IM study arm (n=45)	6.9 (62.9)	49.7 (2-336)	2098 (27.7)
First trimester pregnant women IM (n=6)	5.0 (1.5)	132 (48-168)	571.4 (195.2)
Second trimester pregnant women IM (n=8)	12.5 (3.9)	24 (21.6-45.6)	1269.6 (285.0)
Third trimester pregnant women IM (n=11)	12.3 (4.9)	48 ((24-72)	1268 (511.6)

Auto-Injector



Sub-cu Needle (27 gauge)

IM Needle (21 gauge)

Auto-Injector

- Identify injection location in the back of either upper arm. Disinfect injection site and allow to air dry.
- Place device at a 90 degree angle while supporting patient's arm. Push down, listen for click, and hold device firmly against arm.
- To ensure full dose, verify window is completely orange before removing device.



17-OHPC Subcutaneous/IM Features Comparison Table

Product Feature	Subcutaneous 17-OHPC	Intramuscular 17-OHPC
Packaging	Pre-filled/single-use	Single-use vials/multi-dose vials
Location of injection	Back of arm	Buttock
Needle gauge	27 gauge/0.5" SQ	21 gauge/1.5"
Duration of injection	15 seconds	≥1 minute
Needle visibility	Hidden	Viewable
Safety shield	Yes	No