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Advances in Preterm Birth Prevention: Subcutaneous vs. Intramuscular Dosing of 17-OHPC – Pharmacokinetic Profile, Patient and Practitioner Impact

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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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Faculty Information

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Dr. Sibai has nothing to disclose.

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Society Guidelines: Progesterone to Prevent Preterm Birth

SMFM


SMFM Clinical Guideline

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

ACOG


PRACTICE BULLETIN

Prediction and Prevention of Preterm Birth

ACNM


POSITION STATEMENT

Bioequivalence

Drug demonstrates the absence of a significant difference between both the rate and the extent of which it becomes available at the site of action when administered at the same concentration or same dose in an appropriate designed study

Bioavailability

The degree at which the rate of the drug is absorbed and available at the physiological site of action, and this is often described as the total exposure or area under the curve – AUC

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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
$t_{½}$, h	212	185

Krop et al, Clinical Therapeutics 2018; 39(12):2345-2354.

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Treatment-emergent Adverse Events (TEAEs)

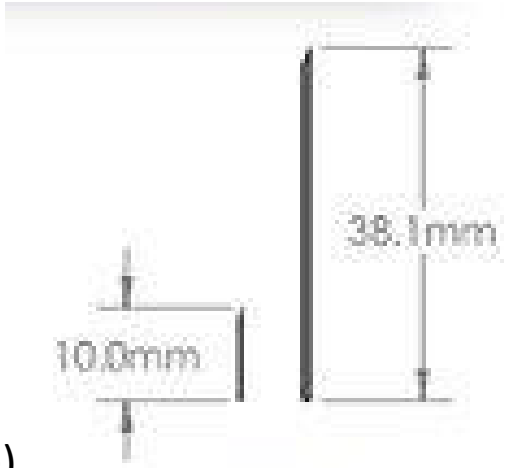
Most Common Treatment Emergent Adverse Events	Subcutaneous Injection (n=57)	Intramuscular Injection (n=60)
	Number (%) of subjects	Number (%) of subjects
Injection site pain	22 (37.3)	5 (8.2)
Headache	9 (15.3)	10 (16.4)
Dizziness	1 (1.7)	1 (1.6)
Diarrhea	3 (5.1)	1 (1.6)
Nausea	1 (1.7)	1 (1.6)
Upper respiratory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

Krop et al, Clinical Therapeutics 2018; 39(12):2345-2354.

Evolution of 17-OHPC

- Approved in 2011
- Administered as 1-mL (250-mg) solution via IM injection in the upper-outer quadrant of gluteus maximus muscle using 21-gauge needle syringe
- HCPs were required to draw the drug from a vial using a large-gauge needle and then switch needles to administer the dose with a smaller-gauge needle
- February 2018, FDA-approval for a single-use autoinjector for subcutaneous dosing of 17-OHPC 1-mL (275-mg)
- Rationale for developing an autoinjector for subcutaneous administration of 17-OHPC included increased convenience and safety of administration
  - Potential reduction in dosing errors, needle sticks, injection-related pain/anxiety for the patient – without compromising its bioavailability and other PK characteristics

Auto-Injector



IM Needle (21 gauge)

Sub-cu Needle (27 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.

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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

Adapted from Krop et al, Clinical Therapeutics 2018; 39(12):2345-2354.