

## **A guide to the cost of progesterone for prevention of preterm labor**

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Progesterone, in various forms, has been the sole pharmacologic weapon against preterm labor supported by randomized controlled trials since the groundbreaking work of da Fonseca<sup>1</sup> and Meis<sup>2</sup> in the early 2000s.

Progesterone is indicated in preventing recurrent preterm labor and preterm delivery in the setting of a history preterm delivery due to cervical insufficiency or unexplained preterm delivery. This is what the evidence supports. However, many investigators are trying to expand the indications for the use of progesterone. These include using progesterone in twin pregnancies and in the setting of a short cervix. To date, no investigator has published data supporting the use of progesterone in multiple gestations. However, there is good evidence to support the use of progesterone in women with a short cervix.

This was recently reaffirmed by work done by Hassan, et al as part of the PREGNANT trial.<sup>3</sup> Furthermore, a decision and cost analysis by Cahill, et al showed that universal screening for a short cervix and treatment with vaginal progesterone was cost effective.<sup>4</sup> However, the most recent ACOG guidelines only support the use of progesterone in women with an *incidentally* found short cervix.<sup>5</sup>

Nightly vaginal suppositories and weekly injections were the first forms of progesterone proved to be effective in preventing preterm labor. The effectiveness of nightly vaginal gel was then demonstrated by O'Brien<sup>6</sup>. These options are all relatively affordable. Suppositories and gel are only available in branded forms under the names Endometrin, Crinone and Prochieve. Until recently the intramuscular injection form was only available from compounding pharmacies.

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K-V Pharmaceutical, through its wholly owned subsidiary, Ther-Rx Corporation, recently brought Makena to the market. This is an FDA-approved once weekly injection of 17-alpha-OH-progesterone caproate intended for the prevention of preterm labor. Although having this available in retail pharmacies would make prescribing progesterone for patients easier in some circumstances, the cost was widely felt to be prohibitively expensive for the vast majority of patients - \$1500 per injection. Therefore, the total retail price of prescribing Makena for weeks 16 through 36 in a pregnancy would be \$31,500. Makena was met with much resistance from the OBGYN community for this reason. The situation was particularly frightening because the manufacturer of Makena had sent cease and desist orders to compounding pharmacies that made progesterone injections. Thus, the only option for injectable progesterone would have been inaccessible to most patients due to cost.

After much lobbying from the American College of Obstetricians and Gynecologists (ACOG), the Society for Maternal-Fetal Medicine, and other societies, the FDA made an unprecedented statement on

March 30<sup>th</sup> of this year. They announced that the FDA “does not intend to take enforcement action against pharmacies that compound hydroxyprogesterone caproate.”<sup>7</sup> K-V Pharmaceutical announced on April 1<sup>st</sup> that it would lower the price of Makena from \$1500 to \$690 per dose. Presumably, this was in response to the backlash that the company received from the OBGYN community, the FDA and the press.<sup>8</sup> However, according to ACOG, this price reduction remains a “woefully inadequate response.”<sup>9</sup>

Fortunately, there are other forms of progesterone available, at very reasonable prices, for preterm labor prophylaxis. Table 1 is a guide to the various forms of progesterone currently available. The total cost is based on a 21-week course of treatment, starting at 16 weeks gestation and continuing until 36 completed weeks. Several factors must be considered when choosing a product for a patient. These include route of administration, patient preference, local availability and cost.

It is hoped that the information provided in this review will be helpful to practitioners who care for at risk women.

Table 1: Various forms of progesterone and associated costs for 21-week course of treatment

Formulation	Dosing	Retail price	Price per dose	Total cost for 21 weeks of treatment
Endometrin	100 mg vaginal insert nightly	\$157 per 21 insert pack	\$7.48	\$1,099.56
Prometrium	100 mg vaginal capsule nightly	\$69 per 30 capsules	\$2.30	\$338.10
Crinone	90 mg vaginal gel nightly	\$170 per 10 tubes	\$17.00	\$2,499.00
Prochieve	90 mg vaginal gel nightly	\$221 per 18 tubes	\$12.28	\$1,805.16
Makena	250 mg intramuscular weekly	\$690 per injection	\$690.00	\$14,490.00
Compounded 17-alpha-OH-progesterone caproate*	250 mg intramuscular weekly	\$136 per 10 injections	\$13.60	\$285.60

Retail pricing according to [www.drugstore.com](http://www.drugstore.com)

\*Pricing from Wedgewood Pharmacy, Swedesboro, NJ, USA

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