MEDICATION COVERAGE POLICY

PHARMACY AND THERAPEUTICS ADVISORY COMMITTEE

POLICY:	Women's Health	**P&T DATE:**	12/9/2025
CLASS:	Endocrine	**REVIEW HISTORY** (MONTH/YEAR)	12/24, 1/24, 12/22, 12/21, 12/20, 12/19, 12/18, 5/17, 2/17, 2/16
LOB:	Medi-Cal		

This policy has been developed through review of medical literature, consideration of medical necessity, generally accepted medical practice standards, and approved by the Health Plan of San Joaquin/Mountain Valley Health Plan (Health Plan) Pharmacy and Therapeutic Advisory Committee.

Effective 1/1/2022, the Pharmacy Benefit is regulated by Medi-Cal Rx. Please visit https://medi-calrx.dhcs.ca.gov/home/ for portal access, formulary details, pharmacy network information, and updates to the pharmacy benefit.
All medical claims require that an NDC is also submitted with the claim. If a physician administered medication has a specific assigned CPT code, that code must be billed with the correlating NDC. If there is not a specific CPT code available for a physician administered medication, the use of unclassified CPT codes is appropriate when billed with the correlating NDC.
For agents listed for coverage under the medical benefit, this coverage is specific to outpatient coverage only (excludes emergency room and inpatient coverage).
This coverage policy is updated on an annual basis. For more recent or up-to-date criteria, reference the Medi-Cal Provider Manual and/or the Medicare National Coverage Determination/Local Coverage Determination (NCD/LCD) for specific criteria. If the Medi-Cal Provider Manual and/or the Medicare NCD/LCD do not have medical necessity criteria, please refer to the "Evaluation Criteria" section in this policy for specific criteria. It is also important to reference the Medicare Benefit Manuals - Chapter 15 and Chapter 16 - when determining benefit coverage and criteria for review of physician administered drugs on the Medicare benefit.

OVERVIEW

This document is intended to explain the Health Plan contraceptive benefit. Health Plan covers implantable, injectable, and intrauterine birth control agents.

Preterm birth (PTB), or birth at less than 37 gestational weeks, is the leading cause of neonatal mortality in the United States and is associated with long-term neurological disabilities such as developmental delays and cerebral palsy. Each year, preterm birth affects nearly 500,000 infants – or 1 in every 8 born in the United States.[2] Major risk factors for preterm birth include history of spontaneous preterm labor and a short cervix (< 25mm) in the mid-trimester.

The Society of Maternal-Fetal Medicine (SMFM) and American Congress of Obstetricians and Gynecologists (ACOG) publish guidelines and practice bulletins that address the major risk factors and role of progesterone and its synthetic derivative in prevention of preterm birth (https://core.ac.uk/reader/46968129?utm_source=linkout, https://www.acog.org/clinical/clinical-guidance/practice-bulletin/articles/2021/08/prediction-and-prevention-of-spontaneous-preterm-birth).[11,62] Progesterone is a steroidal hormone essential for the maintenance of pregnancy—by preventing preterm birth in women with identified risk factors and reducing risks in women with history of recurrent miscarriages.

Historically, progesterone oral capsules are administered as vaginal suppository. This route exhibits a substantially higher concentration of progesterone in the endometrial tissues and is more effective than systemic administration for prevention of preterm labor. Newer formulations include Crinone (progesterone) vaginal gel, progesterone in oil injection, and Makena (hydroxyprogesterone caproate) injection. However, the FDA withdrew the approval of Makena for prevention of preterm birth in 2023 (https://www.fda.gov/news-events/press-announcements/fda-commissioner-and-chief-scientist-announce-decision-withdraw-approval-makena#:~:text=The%20decision%20was%20issued%20jointly,be%20distributed%20in%20interstate%20commerce).[53]

According to ACOG, The Endocrine Society, and the American Association of Clinical Endocrinologists (AACE), the most effective therapy for vasomotor symptoms is systemic hormone therapy (estrogen with or without

progestin), although there is evidence supporting the use of SSRIs, SNRIs, clonidine, and gabapentin. Vaginal symptoms are also best managed with hormone therapy, but topical methods are preferred due to having fewer side effects (https://pubmed.ncbi.nlm.nih.gov/24463691/, https://pubmed.ncbi.nlm.nih.gov/26444994/, https://pubmed.ncbi.nlm.nih.gov/22193047/).[3-5]

For a complete list of drugs and contraceptive supplies reimbursed by the Family PACT Program, refer to the Family PACT Pharmacy Formulary on the Medi-Cal Rx website (https://medi-calrx.dhcs.ca.gov) and the Clinic Formulary section in this manual: https://files.medi-cal.ca.gov/pubsdoco/publications/masters-mtp/fpact/benfam.pdf.

EVALUATION CRITERIA FOR APPROVAL/EXCEPTION CONSIDERATION

Below are the coverage criteria and required information for agents with medical benefit restrictions. This coverage criteria has been reviewed and approved by the Health Plan Pharmacy & Therapeutics (P&T) Advisory Committee. For agents that do not have established prior authorization criteria, Health Plan will make the determination based on Medical Necessity criteria as described in Health Plan Medical Review Guidelines (UM06).

Progestin
Hydroxyprogesterone caproate (Makena)

- ❒ **Coverage Criteria**: Requests for hydroxyprogesterone caproate will not be approved for the prevention of pre-term delivery due to FDA withdrawal.

Post Partum Depression Agent
Brexanolone (Zulresso)

- ❒ **Coverage Criteria:** Brexanolone is reserved for ALL of the following:
  - Age 15 years or older
  - Diagnosis of moderate to severe postpartum depression with symptom onset during the third trimester of pregnancy up to 4 weeks post delivery
  - Patient is less than or equal to 6 months postpartum
  - Patient is not currently pregnant
- ❒ **Limits:** Limited to one infusion per pregnancy. Must be prescribed by a specialist.
- ❒ **Required Information for Approval:** N/A
- ❒ **Other Notes:** Avoid use in patients with eGFR of < 15 mL/minute/1.73 m^2

REFERENCES

1. DHCS All Plan Letter (APL) 16-003. 18-019
2. Preterm birth. Centers for Disease Control and Prevention Web Site. https://www.cdc.gov/reproductive health/maternalinfanthealth/pretermbirth.htm. Updated November 10, 2016. Accessed January 15, 2017.
3. Management of menopausal symptoms. Practice Bulletin No. 141. American College of Obstetricians and Gynecologists. Obstet Gynecol 2014;123:202–16.
4. Cynthia A. Stuenkel, Susan R. Davis, Anne Gompel, Mary Ann Lumsden, M. Hassan Murad, JoAnn V. Pinkerton, Richard J. Santen; Treatment of Symptoms of the Menopause: An Endocrine Society Clinical Practice Guideline, The Journal of Clinical Endocrinology & Metabolism, Volume 100, Issue 11, 1 November 2015, Pages 3975–4011.
5. American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for the Diagnosis and Treatment of Menopause. AACE. *Endocrine Practice*. 2011;17(Suppl 6):1-25. https://www.cdc.gov/reproductivehealth/contraception/index.htm. Updated December 3 2018. Accessed December 10 2018.
6. Reproductive Health: Contraception. Centers for Disease Control and Prevention Web Site.
7. https://files.medi-cal.ca.gov/pubsdoco/outreach_education/workbooks/modules/hap/fpactbil_hap.pdf
8. FDA Statement on Makena. U.S. Department of Health & Human Services. http://www.fda.gov/Drugs/ GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm402614.htm Updated December 9, 2014. Access January 15, 2017.
9. Farine D, Mundle WR, Dodd J, et al. The use of progesterone for prevention of preterm birth. *J Obstet Gynecol Can*. 2008;30(1): 67-71
10. O'Brien JM, Adair CD, Lewis DF. Progesterone vaginal gel for the reduction of recurrent preterm birth: primary results from a randomized, double-blind, placebo-controlled trial. *Ultrasound in Obstet Gynecol*. 2007;30(5):687-696
11. SMFM: Progesterone and preterm birth prevention: translating clinical trials data into clinical practice. *Am J Obstet Gynecol*. 2012; 376-383
12. Romero R, Nicolaides KH, Conde-Agudelo A, et al. Vaginal progesterone decreases preterm birth ≤ 34 weeks of gestation: a singleton pregnancy and a short cervix: an updated meta-analysis from the OPPTIMUM study. *Ultrasound Obstet Gynecol*. 2016; 48(3): 308-17.

13. Hassan SS, Romero R, Vidyadhari D, et al. Vaginal progesterone reduces the rate of preterm birth in women with a sonographic short cervix: a multicenter randomized, double-blind, placebo-controlled trial. *Ultrasound Obstet Gynecol*. 2011; 38:18-31.
14. Pirjani R, Heidari R, Rahimi A, et al. 17-alpha-hydroxyprogesterone caproate versus vaginal progesterone suppository for the prevention of preterm birth in women with a sonographically short cervix: A randomized controlled trial. *J. Obstet Gynecol Res.* 2017; 43(1): 57-64
15. Winer N, Bretelle F, Senat MV, et al. 17 alpha-hydroxyprogesterone caproate does not prolong pregnancy or reduce the rate of preterm birth in women at high risk for preterm delivery and a short cervix: a randomized controlled trial. *Am J Obstet Gynecol*. 2015; 212(4):485.e1-485.e10.
16. Fonseca EB, Bittar RE, Carvalho MH, et al. Prophylactic administration of progesterone by vaginal suppository to reduce the incidence of spontaneous preterm birth in women at increased risk: a randomized placebo-controlled double-blind study. Am J Obstet Gynecol. Feb 2003;188(2):419-424
17. Elimian A, Smith K, Williams M, et al. A randomized controlled trial of intramuscular versus vaginal progesterone for the prevention of recurrent preterm birth. *Int J. Gyneco Obstet*. 2016; 134(2):169-72.
18. How HY, Barton JR, Istwan NB, Rhea DJ, Stanziano GJ. Prophylaxis with 17 alpha-Hydroxyprogesterone caproate for prevention of recurrent preterm delivery: does gestational age at initiation of treatment matter? *Am J Obstet Gynecol*. 2007;197:260.e1-260.e4
19. Meis PJ, Klebanoff M, Thom E, et al. Prevention of Recurrent Preterm Delivery by 17 Alpha-Hydroxyprogesterone Caproate. *NEJM*. 2003;348:2379-2385
20. Coomarasamy A, Williams H, Truchanowicz E, et al. A randomized trial of progesterone in women with recurrent miscarriages. *N ENGL J MED.* 2015;373(22): 2141-8.
21. Roeckner JT, Sanchez-Ramos. The comparative efficacy of cervical pessary, cerclage, vaginal and parenteral progesterone for the prevention of preterm birth in women with a sonographic short cervix and a singleton gestation: a systemic review and network meta-analysis. *Am J Obstet Gynecol.* 2017;S382
22. Gonzalez-Quintero VH, Istwan NB, Rhea DJ. Gestational age at initiation of 17-hydroxyprogesterone caproate (17P) and recurrent preterm delivery. *Journal of Maternal-Fetal & Neonatal Medicine.* 2007;20:249-252
23. Haas DM, Ransey PS. Progestogen for preventing miscarriage. *Cochrane Library*. 2013
24. Stephenson MD, McQueen D, Winter M, Kliman HJ. Luteal start vaginal micronized progesterone improves pregnancy success in women with recurrent pregnancy loss. *Fertility and Sterility*.
25. Fonseca EB, Celik E, Parra M, et al. Progesterone and the risk of preterm birth among women with a short cervix. *NEJM.* 2007;357(5):462-469
26. Bagga R, Jalra J, Sharma M, et al. Intravaginal use of natural micronised progesterone to prevent pre-term birth: A randomised trial in India. *Journal of Obstet and Gynecol*. 2009; 29(6): 493-498
27. El-refaie W, Abdelhafez MS, Badawy A. Vaginal progesterone for prevention of preterm labor in asymptomatic twin pregnancies with sonographic short cervix: a randomized clinical trial of efficacy and safety.
28. Berghella V, Figueroa D, Szychowski JM, et al. 17-alpha-hydroxyprogesterone caproate for the prevention of preterm birth in women with prior preterm birth and a short cervical length. *Am J Obstet Gynecol*. 2010; 202:351e1-351e6
29. Brizot ML, Hernandez W, Liao AW, et al. Vaginal progesterone for the prevention of preterm birth in twin gestations: a randomized placebo-controlled double-blind study. *Am J Obstet Gynecol.* 2015;213(1):82.e1-82.e9
30. Serra V, Perales A, Meseguer J, et al. Increased doses of vaginal progesterone for the prevention of preterm birth in twin pregnancies: A randomized controlled double-blind multicenter trial. *BJOG An International J Obstret Gyneco.* 2012; 50-57
31. Rode L, Klein K, Nicolaides KH, et al. Prevention of preterm delivery in twin gestations (PREDICT): a multicenter, randomized, placebo-controlled trial on the effect of vaginal micronized progesterone. *Ultrasound Obstet Gynecol*. 2011; 38:272-280
32. Romero R, Conde-Agudelo A, El-Refaie W. Vaginal progesterone decreases preterm birth and neonatal morbidity and mortality in women with a twin gestation and a short cervix: An updated meta-analysis of individual patient data. *Ultrasound Obstet Gynecol*. 2017
33. Zafran N. Comparing Double Dose of Vaginal Progesterone to no treatment for prevention of preterm birth in twins and short cervix. Website: https://clinicaltrials.gov/ct2/show/record/NCT02329535
34. Grobman WA, Thom EA, Spong CY, et al. 17 alpha-Hydroxyprogesterone caproate to prevent prematurity in nulliparas with cervical length less than 30mm. Am J Obstet Gynecol. 2012; 207(5):1.e1-1.e8
35. Saccone G, Khalifeh A, Elimian A. Vaginal progesterone compared to intramuscular 17-alpha-hydroxyprogesterone caproate for prevention of recurrent spontaneous preterm birth in singleton gestations: a systematic review and meta-analysis of randomized controlled trials. Ultrasound Obstet Gynecol. 2016
36. Northen AT, Norman GS, Anderson K, et al. Follow-up of Children Exposed In Utero to 17 α-Hydroxyprogesterone Caproate Compared With Placebo. Obstet Gynecol. 2007;110(4):865-872
37. Keeler SM, Kiefer D, Rochon M, et al. A randomized trial of cerclage vs. 17 α-hydroxyprogesterone caproate for treatment of short cervix. J of Perinatal Medicine. 2009;37(5):473-479
38. Shah DS. Monophasic versus multiphasic oral contraceptives: RHL commentary (last revised: 23 June 2009). *The WHO Reproductive Health Library*; Geneva: World Health Organization.
39. van Vliet HAAM, Grimes DA, Helmerhorst FM, Schulz KF. Biphasic versus monophasic oral contraceptives for contraception. *Cochrane Database of Systematic Reviews*;Issue 3, 2006.
40. van Vliet HAAM, Grimes DA, Lopez LM, Schulz KF, Helmerhorst FM. Triphasic versus monophasic oral contraceptives for contraception. *Cochrane Database of Systematic Reviews*;Issue 3, 2006.
41. van Vliet HAAM, Grimes DA, Helmerhorst FM, Schulz KF. Biphasic versus triphasic oral contraceptives for contraception. *Cochrane Database of Systematic Reviews*;Issue 3, 2006.
42. Belsey EM, Farley TMM. The analysis of menstrual bleeding patterns: a review. *Contraception* 1988;38:129-156.
43. FDA Board Recommends Withdrawing Progesterone Therapy for Preterm Birth. Pharmacy Times website. Published October 30, 2019. https://www.pharmacytimes.com/news/fda-advisory-board-votes-to-recommend-withdrawing-progesterone-therapy-for-preterm-birth. Accessed November 17, 2019.
44. Cyklokapron (tranexamic acid injection) [prescribing information]. New York, NY: Pfizer; January 2011.

45. Mirena (levonorgestrel-releasing intrauterine system) [prescribing information]. Wayne, NJ: Bayer HealthCare Pharmaceuticals; July 2008.
46. Prometrium (Progesterone) [prescribing information]. St. Petersburg, FL: Catalent Pharma Solutions; 2011.
47. Cobin RH, Goodman NF, American Association of Clinical Endocrinologists and American College of Endocrinology Position Statement on Menopause- 2017 Update: Endocr Pract 2017;23(7):869-880.
48. Fournier A, Fabre A, Mesrine S, et al. Use of different postmenopausal hormone therapies and risk of histology- and hormone receptor-defined invasive breast cancer. J Clin Oncol. 2008; 26: 1260– 1268.
49. North American Menopause Society. The 2017 hormone therapy position statement of: The North American Menopause Society. Menopause 2017; 10:1097.
50. U.S. Food and Drug Administration. October 5, 2020. Makena Withdrawal Request. Available at: https://www.fda.gov/drugs/drug-safety-and-availability/cder-proposes-withdrawal-approval-makena#:~:text=%5B10%2F5%2F2020%5D,concluded%20that%20the%20available%20evidence. Accessed November 4, 2020.
51. Makena (Medroxyprogesterone caproate injection) [prescribing information]. McPherson, KS: Hospira, Inc.; 1956.
52. How HY, Barton JR, Istwan NB, Rhea DJ, Stanziano GJ. Prophylaxis with 17 alpha-hydroxyprogesterone caproate for prevention of recurrent preterm delivery: does gestational age at initiation of treatment matter? Am J Obstet Gynecol. 2007 Sep;197(3):260.e1-4. doi: 10.1016/j.ajog.2007.07.013. PMID: 17826411.
53. FDA Commissioner and Chief Scientist Announce Decision to Withdraw Approval of Makena. FDA website. Published April 6, 2023. https://www.fda.gov/news-events/press-announcements/fda-commissioner-and-chief-scientist-announce-decision-withdraw-approval-makena#:~:text=The%20decision%20was%20issued%20jointly,be%20distributed%20in%20interstate%20commerce.
54. ACOG Statement on the FDA Withdrawal of 17-OHPC. ACOG website. Published April 7, 2023. https://www.acog.org/news/news-releases/2023/04/acog-statement-on-the-fda-withdrawal-of-17-ohpc.
55. Zulresso (brexanolone) [prescribing information]. Cambridge, MA: Sage Therapeutics, Inc.; 2019.
56. Hutcherson TC, Cieri-Hutcherson NE, Gosciak MF. Brexanolone for postpartum depression. American Journal of Health-System Pharmacy 2020;77(5):336-345. DOI: 10.1093/ajhp/zxz333.
57. Meltzer-Brody S, et al. Brexanolone injection in post-partum depression: two multicentre, double-blind, randomised, placebo-controlled, phase 3 trials. Lancet 2018;392(10152):1058-1070. DOI: 10.1016/S0140-6736(18)31551-4.)
58. Treatment and Management of Mental Health Conditions During Pregnancy and Postpartum: ACOG Clinical Practice Guideline No. 5. Obstet Gynecol 2023; 141:1262.
59. Zuranolone for the treatment of postpartum depression. ACOG website. 2023. Accessed October 9, 2024. https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2023/08/zuranolone-for-the-treatment-of-postpartum-depression.
60. Zurzuvae (zuranolone) [prescribing information]. Cambridge, MA: Biogen Inc. and Sage Therapeutics, Inc.; 2023.
61. FASTSTATS - body measurements. Centers for Disease Control and Prevention. September 10, 2021. Accessed October 11, 2024. https://www.cdc.gov/nchs/fastats/body-measurements.htm.
62. Prediction and Prevention of Spontaneous Preterm Birth: ACOG Clinical Practice Guideline No. 234. Obstet Gynecol 2021.

REVIEW & EDIT HISTORY

Document Changes	Reference	Date	P&T Chairman
Creation of Policy	Contraceptives May09_JHP01 draft from MI.doc	4/2009	Allen Shek, PharmD
Update to Policy	Contraceptives May09_JHP01 5-11-09.doc	5/2009	Allen Shek, PharmD
Update to Policy	OC Class Review 9-20-11.docx	9/2011	Allen Shek, PharmD
Update to Policy	Formulary Realignment 9-18-12.xlsx	9/2012	Allen Shek, PharmD
Update to Policy	Oral Contraceptive Formulary Realignment 2-2016_update.docx	2/2016	Johnathan Yeh, PharmD
Update to Policy	HPSJ Coverage Policy – Endocrine – Hormonal Contraception 2016-05.docx	5/2016	Johnathan Yeh, PharmD
Creation of Policy	HPSJ Coverage Policy – Women's Health – Preterm Birth Prevention 2017-02.docx	2/2017	Johnathan Yeh, PharmD
Update to Policy	HPSJ Coverage Policy – Endocrine – Hormonal Contraception 2017-05.docx	5/2017	Johnathan Yeh, PharmD
Update to Policy	HPSJ Coverage Policy – Endocrine – Women's Health 2018-12.docx	12/2018	Matthew Garrett, PharmD
Update to Policy	HPSJ Coverage Policy – Endocrine – Women's Health 2019-12.docx	12/2019	Matthew Garrett, PharmD
Update to Policy	HPSJ Coverage Policy – Endocrine – Women's Health 2020-12.docx	12/2020	Matthew Garrett, PharmD
Review of Policy	Women's Health	12/2021	Matthew Garrett, PharmD
Review of Policy	Women's Health	12/2022	Matthew Garrett, PharmD
Review of Policy	Women's Health	1/2024	Matthew Garrett, PharmD
Review of Policy	Women's Health	12/2024	Matthew Garrett, PharmD
Review of Policy	Women's Health	12/2025	Matthew Garrett, PharmD

Note: All changes are approved by the Health Plan P&T Committee before incorporation into the utilization policy

- Agents used to **promote fertility** are excluded from coverage. This is based **on Title XIX, Social Security Act, Section 1927(d)(2).**