MERCI Brief
February 2025

MEDICAID EVIDENCE REVIEW AND COST INITIATIVE BRIEF

Hydroxyprogesterone Caproate (Makena) for Reducing the Risk of Preterm Birth

OVERVIEW

In 2011, the US Food and Drug Administration (FDA) gave hydroxyprogesterone caproate (HPC; branded as Makena), accelerated approval to reduce the risk of preterm birth in women with a singleton pregnancy who have a history of singleton spontaneous preterm birth.[1,2] The confirmatory study requested by the FDA did not verify clinical benefit, and the FDA's Center for Drug Evaluation and Research proposed withdrawing the drug's approval in 2020.[3] In 2023, following a public hearing process, the FDA withdrew approval of Makena and its generics.[1,3]

Preterm birth is a birth that occurs before 37 weeks of gestation.[4] Preterm birth is the most common cause of infant death and is the leading cause of long-term disability in children.[5]

According to 2022 data, the Centers for Disease Control and Prevention (CDC) estimates that 1 in every 10 infants are born preterm in the US.[4] The rate of preterm birth is higher among Black women (14.6%) when compared with White or

MERCI Aims

The Medicaid Evidence and Review of Cost Initiative (MERCI) describes policy considerations for drugs approved by the US Food and Drug Administration (FDA) through the accelerated approval pathway. This brief provides information on:

- The estimated prevalence of target diagnoses (the accelerated approval drug's indication[s]) among Medicaid members;
- The clinical trial population used to support FDA approval, and how similar it is to Medicaid members overall; and
- Projected drug costs for state Medicaid programs, including a breakdown of state and federal funds using the Federal Medical Assistance Percentage (FMAP).

MERCI analyses include national and state-level data where available to inform budget and policy decisions by state and federal policymakers.

Hispanic women (9.4% and 10.1% respectively).[4] Women with lower incomes are also at higher risk for early deliveries.[4]

In 2019, when the results of the confirmatory trial were published, Medicaid was covering 42% of all deliveries among pregnant women.[6] Between 2019 and 2021, at least 66,000 nondually eligible female Medicaid members aged 16 to 49 years has at least 1 claim for HPC. From 2019 through 2021, total Medicaid spending on HPC is estimated at $362.3 million nationally, with $354.8 million on Makena and $7.4 million on generic HPC.

What Is Preterm Birth?

Preterm birth is a birth that occurs before 37 weeks (259 days) of gestation, in contrast to the typical duration of pregnancy of 40 weeks (280 days).[4,5,7] About one-quarter of preterm births are intentional, with a delivery to address a maternal or fetal indication.[8] The remainder are following spontaneous preterm labor or premature prelabor rupture of membranes.[8] Spontaneous preterm births can be related to a history of prior preterm births, pregnancy complications (preeclampsia, placenta previa, hypertension, diabetes during pregnancy), medical conditions (infections, inflammation), younger or older maternal age, multiple gestations, substance use (smoking, alcohol, drugs) during pregnancy, overweight or underweight during pregnancy, or a pregnancy resulting from invitro fertilization.[4,5,9] However, in most cases the causes of preterm labor or birth remain largely unknown.[4]

Preterm birth is the most common cause of infant death and is the leading cause of long-term disability in children.[5] Infants born prematurely are at risk of developing neurological developmental delays and are at high risk for cerebral palsy.[5] In addition, preterm births are one of the main risk factors for neonatal mortality.[10] In 2021, 65% of infant deaths occurred among infants born preterm.[11]

How Many Preterm Births Are There in the US?

In 2023, around 1 in every 10 infants (approximately 364,000) was born preterm in the US.[12] Preterm birth rates vary among races and ethnic groups.[4] The rate of preterm birth tends to be higher among Black women (14.6% in 2022) when compared with White or Hispanic women (9.4% and 10.1% respectively).[4] Black, Native Hawaiian or other Pacific Islander, and American Indian or Alaska Native women are among the ethnic groups at higher risk to deliver preterm babies.[4] Women with low income or poor socioeconomic status are also at higher risk for early deliveries.[4,11]

Infant mortality is twice as high among non-Hispanic Black infants compared with non-Hispanic White infants.[13] Sociodemographic and prenatal health factors such as maternal education, marital status or paternity acknowledgment, source of delivery payment, hypertension in pregnancy, and the experience of racial discrimination may contribute to the disparities in preterm labor between non-Hispanic Black and non-Hispanic White women.[14,15]

According to CDC WONDER data for 2021, Mississippi had the highest rates of preterm births (15.0%), followed by Louisiana (13.5%) and Alabama (13.1%).[4] Meanwhile, Vermont (8.0%), New Hampshire (8.5%), Oregon (8.9%), Washington (8.9%), and Idaho (9.0%) had the lowest preterm birth rates.[4]

In 2019, Medicaid covered 42% of all births.[6] This amounts to 65.1% of births among non-Hispanic Black women, 59% of Hispanic women, and 29.4% of non-Hispanic White women.[6]

How Is Preterm Birth Prevented?

Gestational length results from a complex interplay of many biological, psychosocial and environmental factors.[16,17] Some risk factors for preterm birth, such as prepregnancy weight, smoking, unintended pregnancy, and short interpregnancy interval, are modifiable and can be addressed

through high-quality preconception and perinatal care.[8,16] Appropriate prevention and management of chronic conditions, such as hypertension and diabetes, before and during pregnancy can also reduce the risk of preterm birth.[16] The strongest predictors of preterm birth, however, are a history of preterm birth, multiple gestations (twins, triplets, or more), and certain cervical or uterine anomalies.[16,18] Some women with a short or weak cervix can be treated with vaginal progesterone or a surgical procedure (cervical cerclage), temporarily closing the cervix with stitches, to prevent early labor.[5] There are no evidence-based interventions that achieve the original indication of Makena, which was prevention of recurrent spontaneous preterm birth in singleton pregnancies.[16]

How Much Does Preterm Birth Cost?

Preterm births can take both an emotional and financial toll on families.[4] The total cost of preterm birth for the 2016 US birth cohort was estimated to be $25.2 billion: $17.1 billion for medical care of infants born preterm, $2.0 billion for delivery care, $1.3 billion for early intervention and special education, and $4.8 billion in lost productivity due to associated disabilities in adults born prematurely.[19] The average cost of single preterm birth in 2016 was $64,815 per birth.[19]

Preterm birth can also result in long-term health consequences for these children who are at risk for breathing problems, feeding difficulties, intellectual and developmental disabilities, and vision and hearing problems. These long term-health consequences of preterm birth lead to an estimated annual cost in the US of $32.4 billion in 2017.[13]

DRUG INFORMATION

Hydroxyprogesterone caproate is a synthetic progestin hormone.[20,21] Prior to 2011, HPC was available as a non–FDA-approved compounded drug.[1] In 2011, HPC under the brand name Makena received accelerated FDA approval using a clinical endpoint of reduction in deliveries before 37 weeks.[1,2,20] However, the FDA withdrew approval of Makena and its generics 12 years later on April 6, 2023, because the required postmarket study failed to verify clinical benefit, concluding that the available evidence did not show Makena is effective for its approved use.[3,20]

What Evidence Was Used by the FDA to Approve Makena?

Exhibit 1 summarizes the studies used to approve Makena.

Why Did the FDA Grant Accelerated Approval?

The FDA approved Makena based on a multicenter, randomized, double-blind, placebo-controlled clinical trial in women with a singleton pregnancy (aged 16 to 43 years) who had a documented history of prior singleton spontaneous preterm birth.[20] The primary outcome of interest was the proportion of women who delivered at less than 37 weeks of gestation. The outcome also included assessment in both groups at less than 35 weeks and less than 32 weeks gestation.[20]

The proportion of women delivering at less than 37 weeks was significantly lower in the Makena group when compared with placebo; 37.1% versus 54.9% (a reduction of 17.8%; 95% confidence interval [CI], 7.4% to 28.0%).[20] This evidence was deemed sufficient to support accelerated approval, with a confirmatory trial requested by the FDA. However, concerns were raised about the evidence used to support effectiveness for use in the US, and these concerns remained until withdrawal.[26]

While Makena was approved in February 2011, the FDA released information the next month (March 2011) announcing that it did not plan to take enforcement action when pharmacies compounded HPC based on a valid prescription for an individual patient.[27] The Centers for Medicare & Medicaid Services (CMS) issued a concurrent clarification that state Medicaid agencies could cover compounded HPC without any change to the State Plan.[27]

HYDROXYPROGESTERONE CAPROATE Makena®

DRUG SUMMARY

BASIC INFORMATION

DRUG CLASS
Synthetic progestin

MANUFACTURER
Covis Pharma (Amag Pharmaceuticals)

PRICE PER PATIENT
$803 per 1 mL, administered weekly[22-24]

FDA APPROVAL

PATHWAY Accelerated approval

DATE February 2011

PRESCRIBING LABEL
https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/021945s013lbl.pdf

WITHDRAWN DATE April 2023

WITHDRAWL REASON
No clinical benefit

SAFETY

ADVERSE REACTIONS
Injection site reactions (pain, swelling, itching, nodule, hives), nausea, and diarrhea

APPROVED INDICATION(S)

Prevention of recurrent spontaneous preterm births

DOSING

ROUTE Intramuscular, subcutaneous

FORMULATION
- Auto-injector for subcutaneous use
- Single-dose vial for intramuscular use

INFORMATION
- Makena auto-injector: Administer subcutaneously using Makena auto injector at a dose of 275 mg (1.1 mL) once weekly, in the back of either upper arm
- Makena (single-dose and multidose vials): Administer intramuscularly at a dose of 250 mg (1 mL) once weekly in the upper outer quadrant of the gluteus maximus

STRENGTH
- 1.1 mL single-use auto-injector for subcutaneous use contains 275 mg of hydroxyprogesterone caproate (250 mg/mL)
- 1-mL single-dose vial for intramuscular use contains 250 mg of hydroxyprogesterone caproate (250 mg/mL)
- 5-mL multidose vial for intramuscular use contains 1,250 mg of hydroxyprogesterone caproate (250 mg/mL)

Sources. IPD Analytics and the US Food and Drug Administration (FDA).
Abbreviations. FDA: US Food and Drug Administration.

EXHIBIT 1

Summary characteristics of the study used to support efficacy of Makena (17P)

	17P study[25]
Official title	Prevention of recurrent preterm delivery by 17 alpha-hydroxyprogesterone caproate
ClinicalTrials.gov ID	Not reported
Study design	Randomized, double-blind, placebo-controlled trial
Clinical trial phase	Not reported
Study population description	463 pregnant women with a history of spontaneous preterm delivery in a previous pregnancy and a current pregnancy gestation between 15 weeks and 20 weeks, 3 days
Intervention	17P 250 mg intramuscularly once per week
Control	Placebo (castor oil)
Primary outcome used for accelerated approval	Proportion of deliveries at less than 37 weeks
Trial funding	National Institute of Child Health and Human Development

Sources. This information is taken from the trial publications and may vary to that reported in the prescribing label.
Abbreviation. 17P: 17 alpha-hydroxyprogesterone caproate; Makena: brand-name hydroxyprogesterone caproate.

What Studies Were Requested to Convert Makena to Full Approval?

As part of accelerated approval, the FDA requested a confirmatory trial to assess the efficacy of HPC on both preterm birth and neonatal morbidity, and to further evaluate safety based on fetal or early infant death.[28,29]

The Progestin's Role in Optimizing Neonatal Gestation (PROLONG) study (NCT01004029) was a multicenter, placebo-controlled double-blinded trial that randomly allocated 1,708 women in a 2:1 ratio to receive HPC or placebo once per week from the time of enrollment and randomization through 36 weeks or delivery.[28]

The PROLONG study was designed with the efficacy objective of assessing whether HPC decreases recurrent preterm birth and neonatal morbidity in women with a prior spontaneous preterm birth in a singleton gestation, and a safety objective to rule out an increase in the risk of fetal or early infant death.[28,30] The primary outcome measures include rate of preterm birth before 35 weeks and composite neonatal morbidity and mortality index.[28] Exhibit 2 summarizes the PROLONG study.

What Study Results Led the FDA to Withdraw Approval?

In PROLONG, there was no significant difference in preterm birth between the Makena group and the placebo group (11.0% vs. 11.5 %; relative risk [RR], 0.95; 95% CI, 0.71 to 1.26).[28] Given the results, in September 2020 the FDA's Center for Drug Evaluation and Research proposed that the FDA withdraw approval of Makena.[31] On April 6, 2023, the FDA issued the decision of withdrawing Makena and its generics from the market.[3]

EXHIBIT 2

Summary characteristics of the study requested for confirmatory results

	PROLONG[28,30]
Official title	A phase 3b, multicenter, randomized, double-blind study of hydroxyprogesterone caproate (HPC) injection, 250 mg/ml, versus vehicle for the prevention of preterm birth in women with a previous singleton spontaneous preterm delivery
ClinicalTrials.gov ID	NCT01004029
Study design	Randomized, double-blind, placebo-controlled trial
Study population description	1,740 women with a singleton pregnancy who had a documented previous pregnancy complicated by a singleton spontaneous preterm birth and who were 16 weeks, 0 days to 20 weeks, 6 days in the current pregnancy
Study arms	2 study arms
Intervention	17P 250 mg IM weekly
Control	Placebo (inert oil)
Study duration	Weekly injections given from time of enrollment and continued until 36 weeks of gestation or delivery
Study sites	93 sites located in 9 countries, including the US
Trial funding	AMAG Pharmaceuticals
Primary outcome	Preterm birth at less than 35 weeks, composite neonatal morbidity and mortality index
Status of requested study	Completed; published in October, 2019
Primary completion date	October 2018 (actual)

Sources. This information is taken from the trial publications and ClinicalTrials.gov trial registry records and may vary from that reported in the accelerated approval record.
Abbreviations. 17P: 17 alpha-hydroxyprogesterone caproate; IM: intramuscular.

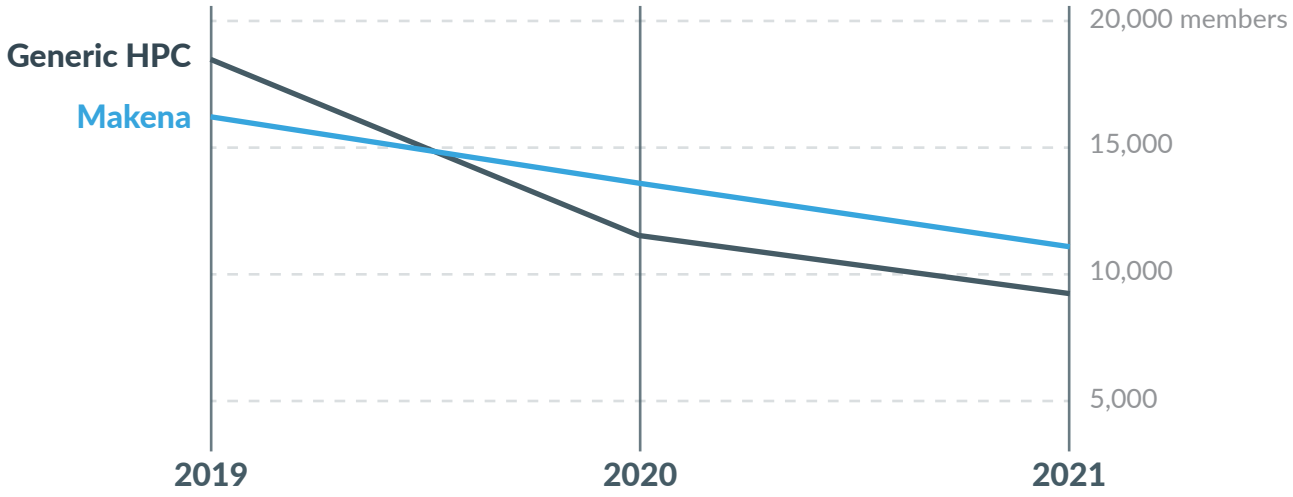
How Common Was Use of HPC Among Medicaid Members?

We identified 66,260 nondually eligible female Medicaid members aged 16 to 49 years with at least 1 claim for HPC from 2019 to 2021 (members in Alabama, Illinois, Mississippi, New York, and Utah were excluded because of data availability concerns). These members had a total of 334,618 outpatient and pharmacy HPC claims over 3 years; 44.2% of these claims were for Makena and 55.8% were for generic non-Makena HPC. The decline in HPC usage between 2019 and 2021 coincides with both the start of the COVID-19 public health emergency and the publishing of Makena's confirmatory trial results in 2020.

While overall HPC usage declined, more members had at least 1 Makena claim compared with members with at least 1 claim for generic HPC in 2020 and 2021 (Exhibit 3). A small fraction (about 5%) of these members had claims for both Makena and generic HPC. (See Exhibit 3; also see the number of HPC claims in each year by Makena vs. generics in Appendix B.)

EXHIBIT 3

Number of Medicaid members (nondually eligible, female, aged 16 to 49 years) with at least 1 HPC claim, 2019-2021



Abbreviations. HPC: hydroxyprogesterone caproate; Makena: brand-name HPC.

DATA METHODS SUMMARY

Hydroxyprogesterone caproate (HPC) is indicated for prevention of preterm birth in women with a singleton pregnancy who have a history of singleton spontaneous preterm birth. Researchers at the Center for Evidence-based Policy (Center) used Centers for Medicare & Medicaid Services (CMS) Transformed Medicaid Statistical Information System (T-MSIS) analytic files to identify Medicaid members who had at least 1 claim for this treatment.

Specifically, we identified female members aged 16 to 49 years with at least 1 pharmacy or outpatient claim with a procedure code or National Drug Code (NDC) for HPC in the years 2019, 2020, and 2021. As our focus was on Medicaid expenditures, and members with both Medicaid and Medicare (i.e., dual-eligible) have pharmacy benefits under Medicare Part D, we excluded members with evidence of dual enrollment. Using these criteria, Alabama and Utah were excluded as these states do not report dual-enrollment status using this method. Other state-based analysis exclusions were determined using recommendations from the CMS Data Quality Atlas, which reports state-specific data availability and completeness; we generally did not report data elements for states identified as "unusable" or of "high concern" data quality according to the Data Quality Atlas. Due to unusable data quality for matching claims files with demographic and enrollment files in Mississippi and the procedure codes in institutional outpatient claims submitted in New York and Illinois, we excluded those 3 states from the analysis.

Our cost model estimated annual cost for HPC based on drug uptake and treatment patterns observed in the data, as well as average drug acquisition costs and statutorily required rebates. Refer to Appendix A for additional detail on how we conducted this study.

Non-Hispanic White, Hispanic, and non-Hispanic Black Medicaid members made up the bulk of members with a claim for HPC (35%, 33%, and 27.4%, respectively, totaling 95.4%). Use of HPC was most common among women between the ages of 25 and 34 years (62.1%; Exhibit 4). Hispanic individuals were more likely to have claims for Makena than for the generics; the pattern was reversed for non-Hispanic White and non-Hispanic Black members, who were more likely to use the generic versions (Exhibit 4).

The number of nondually eligible female members aged 16 to 49 years with any HPC claim in 2021 varied among the states with available data, from fewer than 2 members per 10,000 in Arkansas and Hawaii, to more than 20 members per 10,000 in Louisiana and Texas (Exhibit 5). The distribution of members with claims for Makena versus generics also varied across states in 2021. All or nearly all members with HPC claims in Missouri, Vermont, and West Virginia received Makena, whereas Hawaii, Idaho, and Washington DC had the lowest proportion that received Makena at 6% or less (Exhibit 6). Both the geographic distribution of people receiving HPC and the proportions of members receiving Makena versus generics in the states were similar in 2019 and 2020, and the national downward trend in total number of people receiving HPC over time was observed in all states (see Appendix D for detail).

EXHIBIT 4

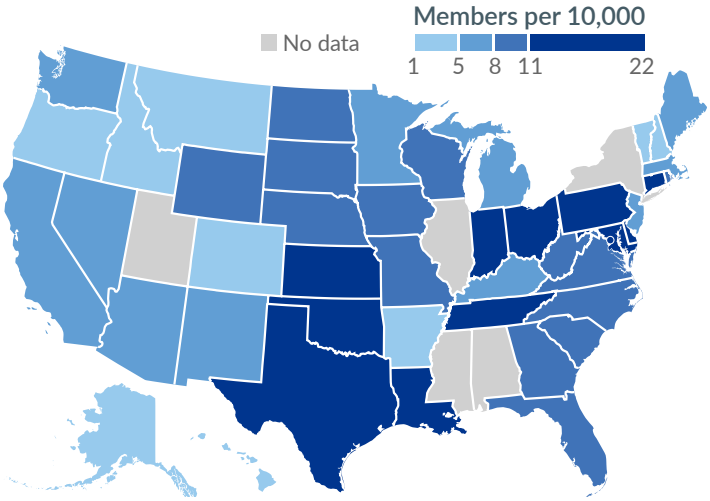
Characteristics of female Medicaid members aged 16 to 49 years with at least 1 HPC claim, 2019-2021

	has ≥ 1 HPC claim[a]	%[b]	has ≥ 1 Makena claim[a,c]	%[b]	has ≥ 1 generic HPC claim[a,c]	%[b]
Total members	*66,260*	-	*36,550*	-	*34,683*	-
Pregnancy status						
Pregnant	65,670	99.1	36,047	98.6	34,593	99.7
Age, in years						
16 to 24	12,581	19.0	7,195	19.7	6,202	17.9
25 to 34	41,134	62.1	22,583	61.8	21,700	62.6
35 to 49	12,545	18.9	6,772	18.5	6,781	19.6
Race and ethnicity						
American Indian or Alaska Native, non-Hispanic	584	1.2	289	1.1	327	1.3
Asian, non-Hispanic	1,091	2.3	567	2.1	618	2.4
Black, non-Hispanic	13,299	27.4	6,421	24.1	7,771	30.8
Hispanic	16,011	33.0	10,088	37.8	7,092	28.1
Native Hawaiian or Pacific Islander, non-Hispanic	246	< 1	100	< 1	168	< 1
White, non-Hispanic	16,986	35.0	9,059	33.9	9,127	36.2
Multiracial or other race or ethnicity	271	< 1	164	< 1	123	< 1

Notes. [a] Excludes dually eligible members and members in Alabama, Illinois, Mississippi, New York, and Utah. [b] Percentage of members with nonmissing data on demographic characteristics; 48,488 (73.2%) of members with at least 1 HPC claim had nonmissing race *or* ethnicity data. For more detail see Appendix C. [c] Includes members who had claims for both Makena and generics during the same pregnancy or across different pregnancies over the 3 years. [d] As reported at the time of last treatment.
Abbreviations. HPC: hydroxyprogesterone caproate; Makena: brand-name HPC.

EXHIBIT 5

Prevalence of HPC[a] in Medicaid per 10,000 female members aged 16 to 49 years, by state, 2021[b]



Note. [a] Usage is defined as at least 1 claim for HPC. [b] Data not available for Alabama, Illinois, Mississippi, New York, and Utah. Abbreviation. HPC: hydroxyprogesterone caproate.

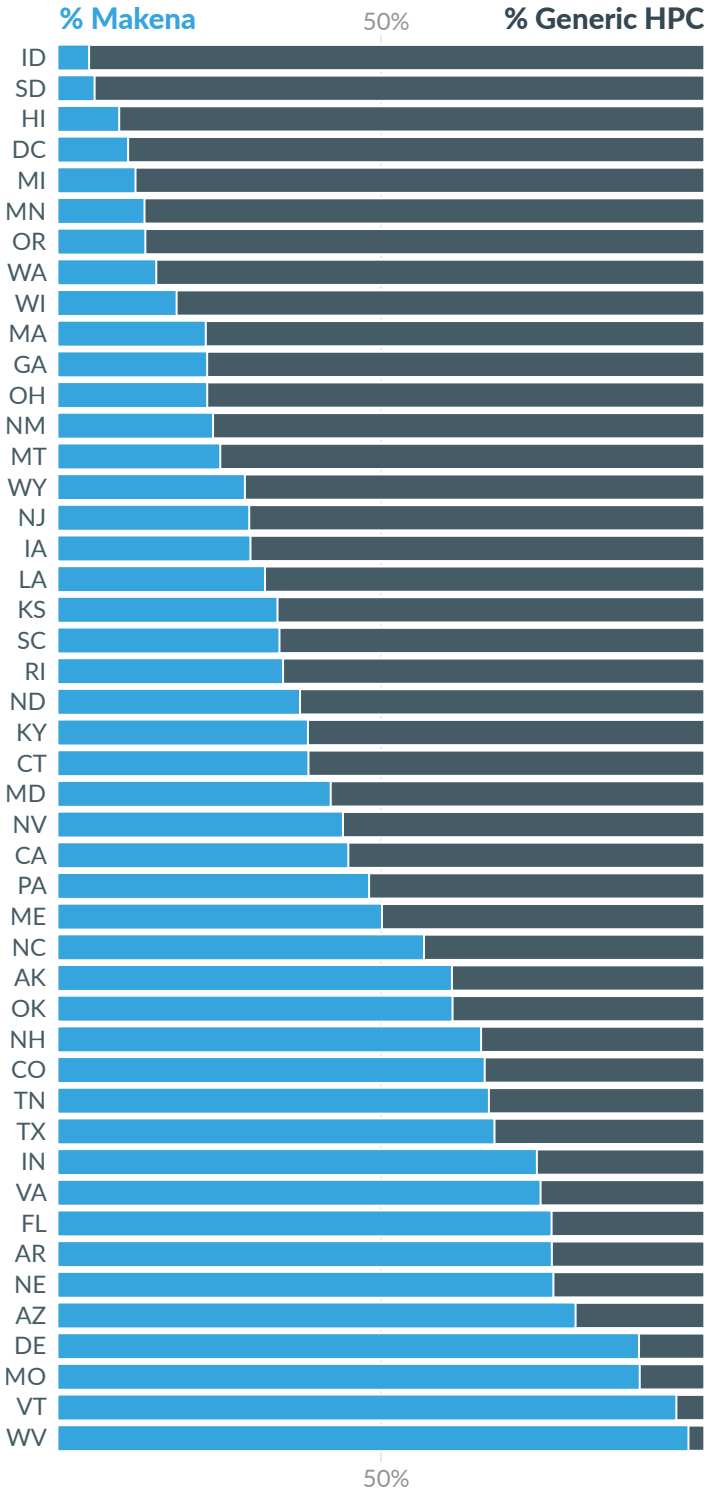
How Do Medicaid Members With HPC Claims Compare With Trial Populations?

The demographic characteristics of patients included in the drug trial varied substantially from our Medicaid cohort in terms of racial and ethnic composition. The Makena study cohort was predominantly Black (54%) with only 13.9% of the participants identifying as Hispanic, while 24.1% of the Medicaid members with Makena claims were Black and 37.8% were Hispanic.

Exhibit 7 describes the most common body system-level impairments and medical conditions among female Medicaid members with a history of HPC claims. We identified body-system impairments using Chronic Disability Payment System methodology[32]; other select conditions were added based on peer-reviewed literature on this population.[33-35] The most commonly affected systems were psychological, genital, and cardio-vascular.

EXHIBIT 6

Percentage of Medicaid HPC claims by Makena vs. generics by state, 2019-2021[a]



Notes. States are identified by 2-letter postal abbreviations. [a] Data not available for Alabama, Illinois, Mississippi, New York, and Utah. Abbreviations. HPC: hydroxyprogesterone caproate; Makena: brand-name HPC.

EXHIBIT 7

Prevalence of affected body systems in female Medicaid members aged 16 to 49 years with HPC claims, 2021

	Medicaid members with at least 1 claim for HPC	
System or condition	N	%[a]
Total members[a]	*19,845*	-
Asthma	11,342	17.1
Bleeding disorder	2,366	3.6
BMI > 40	2,904	4.4
Cardiovascular	13,302	20.1
Chronic hypertension	7,932	12.0
Gastrointestinal	12,225	18.5
Genital system	13,410	20.3
Gestational diabetes	10,299	15.6
HIV	238	0.4
Psychological	20,806	31.4
Pulmonary	12,056	18.2
Skeletal	8,560	12.9
Substance use disorder	6,543	9.9
Type 2 diabetes	5,552	8.4

Note. [a] Members included in this calculation are those with at least 1 inpatient or 1 outpatient claim between 2019 and 2021. There were 53 members who did not have claims appropriate for inclusion in this calculation and are excluded from these estimates. Abbreviations. BMI: body mass index; HPC: hydroxyprogesterone caproate.

What Was the Impact of HPC on State Medicaid Spending in 2019 through 2021?

We estimate that total Medicaid spending on HPC was $362.3 million nationally in 2019 to 2021 (95% confidence bounds, $338.7 million and $820.4 million), with $354.8 million spent on Makena and $7.4 million spent on generics. We estimated these costs by identifying Makena and generic HPC claims in pharmacy and outpatient claims records based on the NDCs (National Drug Codes), and converting the total number of days' supply in these claims into a dollar cost using the average price of Makena and the generic HPCs. The total estimated cost equates to a per-member per-month cost of $0.15 (95% confidence bounds, $0.14 and $0.35) for all Medicaid members. Based on the enrollment composition of members with HPC claims in CHIP (Children's Health Insurance Program) and Medicaid expansion, and the weighted national average of corresponding federal match rates, we estimate $251.7 million of the total cost came from federal funds and the remaining $110.6 million from state funds. Refer to Appendix A for additional detail on how the costs were calculated.

CONSIDERATIONS

Makena's accelerated approval in 2011 and withdrawal of approval in 2023 highlight gaps in the FDA's authority both to require timely completion of confirmatory trials and to quickly remove an ineffective drug from the market. Taking 8 years to complete, Makena's confirmatory study was first published 2019.[31] The results did not demonstrate a clinical benefit and the FDA proposed withdrawing the drug's approval in 2020.[3] In 2023, following a public hearing process, the FDA finally withdrew approval of Makena and its generics.[1,3]

The 12 years between initial approval and withdrawal affected a large number of Medicaid members with high-risk pregnancies, their families, and clinicians. Our analysis found that more than 66,000 Medicaid members received HPC in the 3-year period of 2019 through 2021. Extrapolating, it is possible that 200,000 or more Medicaid members may have received the drug during the 12 years it was FDA-approved. In addition to the potential harms of an ineffective treatment, the expenditures incurred to cover HCP represent a significant opportunity cost to state Medicaid programs.

As Medicaid is required to cover all FDA-approved drugs where the manufacturer has entered into a rebate agreement with the Department of Health

and Human Services, the delay of Makena's withdrawal from the market is particularly troubling. In 2019, Medicaid paid for 42% of deliveries among pregnant women in the US.[6] Knowing that the drug had not proven effective, Medicaid was still required to cover Makena in the years 2020, 2021, 2022, and 2023, spending hundreds of millions of taxpayer dollars and exposing individuals with high-risk pregnancy to ineffective care.

With this example in mind, state and federal policymakers should explore how the FDA's authority can be adjusted to expedite the withdrawal process and speed the completion of confirmatory trials and the public disclosure of the results. Moreover, policymakers should explore how Medicaid may be able to deny coverage of a drug when a FDA-required confirmatory trial has failed to demonstrate clinical benefit. The safety of patients and the stewardship of taxpayer dollars should be superseded by drug manufacturer attempts to enforce coverage of a drug without proven clinical benefit.

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APPENDIX A

METHODS

See attachment for a full description of the methods used to prepare this brief.

APPENDIX B

HYDROXYPROGESTERONE CAPROATE CLAIMS

See attachment for a figure showing the hydroxyprogesterone caproate claims each year 2019 through 2021, divided by brand name (Makena) and generics claims.

APPENDIX C

DEMOGRAPHIC INFORMATION

See attachment for a table describing the availability of demographic information of Medicaid members included in our study.

APPENDIX D

MEDICAID MEMBERS WITH AND WITHOUT CLAIMS FOR HPC, 2019-2021

See attachment for this table.

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