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A REPORT TO THE 2023–2024 CALIFORNIA STATE LEGISLATURE

Analysis of California Assembly Bill 2467 Menopause

APRIL 16, 2024



California Health Benefits Review Program (CHBRP)
Office of Research, University of California, Berkeley

www.chbrp.org

Analysis of California Assembly Bill 2467

Menopause

Summary to the 2023-2024 California State Legislature, April 16, 2024



Summary

AB 2467 would require coverage for treatment of menopause symptoms, including but not limited to one particular drug and multiple bill-identified therapeutic categories of drugs.

Benefit Coverage: At baseline, 13,162,000 enrollees have an outpatient pharmacy benefit regulated by the Department of Managed Health Care (DMHC) or California Department of Insurance (CDI). Among them, at baseline, 7% have coverage for fezolinetant and 15% have coverage for ospemifene. For other drugs and categories, baseline coverage ranges from 92% to 100%. Postmandate, coverage for these drugs and categories would be 100%.

Medical Effectiveness: There is a *preponderance of evidence* for the effectiveness of fezolinetant as well as ospemifene, and *limited evidence* for the effectiveness of high-dose vaginal estrogen. More broadly, commonly referenced clinical guidelines indicate that systemic hormonal therapy and nonhormonal therapy can be effective.

Cost and Health Impact: Utilization of other drugs is expected to increase in proportion to the increase in benefit coverage, so greatest for fezolinetant as well as ospemifene. This would result in an increase of total net annual expenditures for enrollees with DMHC-regulated plans and CDI-regulated policies of \$3,993,000 (0.0025%). Within the first year postmandate, CHBRP finds that AB 2467 would improve the health of the women receiving the 15,880 (30-day) prescriptions under new coverage (which might translate to ~1,323 women, assuming each received one prescription for 12 consecutive months).

Context

Menopause is part of the normal aging process. Perimenopause is the period of 1 to 3 years when menstruation becomes irregular, and menopause is when menstruation has ceased for 12 consecutive months. This transition to a new stage of life (rather than a condition or disease) is experienced by every woman and most often occurs naturally between ages 45 and 55 years but may occur between ages 40 and 64 years (median age 51 years). During the menopause transition, the ovaries produce less estrogen and progesterone as they stop releasing eggs. Menopause can also begin with surgical removal of the ovaries. The decrease in the hormonal levels may lead to moderate-to-severe symptoms prompting requests for treatment.

Bill Summary

AB 2467 would require coverage for treatment of menopause symptoms, including but not limited to one particular drug and multiple bill-identified therapeutic categories of drugs.

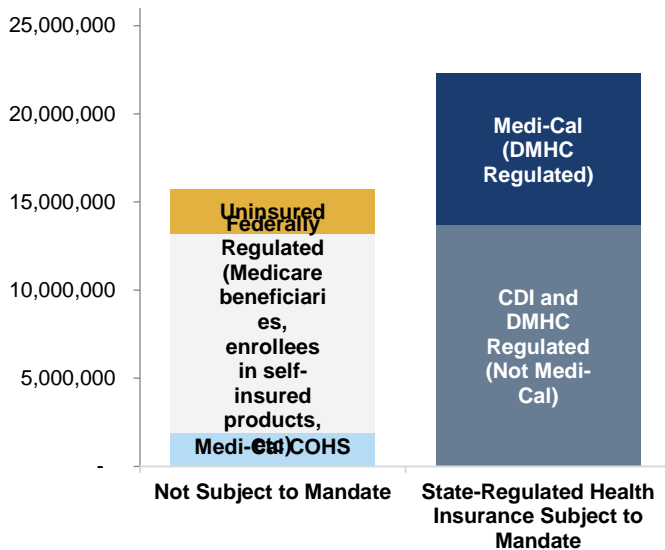
Analytic Approach

Almost all (96.2%) commercial/CalPERS enrollees have a pharmacy benefit regulated by DMHC or CDI that covers both generic and brand-name outpatient prescription drugs.¹ CHBRP has assumed that AB 2467 would not require creation of a pharmacy benefit and so baseline benefit coverage for enrollees would be compliant so long as they (1) are without a pharmacy benefit or (2) their pharmacy benefit is not regulated by DMHC or CDI. The latter group includes all Medi-Cal beneficiaries enrolled in DMHC-regulated plans, as their pharmacy benefit is through the Medi-Cal program (not the DMHC-regulated plan). So, although all 22.3 million enrollees in plans and policies regulated by DMHC or CDI have health insurance that would be subject to AB 2467 (see Figure A), impacts would only among the 13.2

¹ For more detail, see CHBRP's resource *Pharmacy Benefit Coverage in State-Regulated Health Insurance*, available at www.chbrp.org/other-publications/resources.

million who currently have a pharmacy benefit regulated by DMHC or CDI.

Figure A. 2025 Health Insurance in CA



Source: California Health Benefits Review Program, 2024.
 Key: CDI = California Department of Insurance; COHS = County Organized Health System; DMHC = Department of Managed Health Care.

CHBRP has assumed that plans and policies with a pharmacy benefit regulated by DMHC or CDI would be compliant postmandate if at least one drug per therapeutic category is covered.

CHBRP has restricted utilization estimates to women aged 40 to 64. Older women are not included because the benefit coverage of Medicare beneficiaries would not be affected by AB 2467.

Medical Effectiveness

Commonly referenced guidelines indicate that hormone therapy remains the most effective treatment for vasomotor symptoms (VMS) and genitourinary syndrome of menopause (GSM), and has been shown to prevent bone loss and fractures. Hormone therapy risks depend on type, dose, duration of use, route of administration, timing of initiation, and whether a progestogen is used.

There is *clear and convincing evidence* that low-dose vaginal estrogen for the treatment of GSM is effective.

There is *limited evidence* that high-dose vaginal estrogen is effective at treating VMS (hot flashes).

There is *limited evidence* that compounded bioidentical hormones are effective treatment for menopause symptoms. Use of compounded bioidentical hormones is only recommended for patients with an allergy to an active pharmaceutical ingredient or inactive ingredient of a drug product approved by the FDA or documented requirement for a different dosage form than available. This is due to serious concerns about the safety, efficacy, and standardization of these drugs, which are not regulated by the FDA.

There is a *preponderance of evidence* that fezolinetant is effective for treatment of VMS.

There is a *preponderance of evidence* that ospemifene improved symptoms GSM.

Impacts

Benefit Coverage

At baseline, 13.2 million enrollees have an outpatient pharmacy benefit regulated by DMHC or CDI. Among the specific drugs that CHBRP identified as treatments for menopause symptoms, an estimated 7% of enrollees in DMHC-regulated plans and CDI-regulated policies have coverage for fezolinetant and 15% have coverage for ospemifene at baseline. For other drugs and categories, baseline coverage ranges from 92% to 100%, and would increase to or remain at 100% for all if AB 2467 were enacted.

Utilization

Because CHBRP is concerned with estimating the marginal impact of AB 2467, the utilization analyses focus on drugs and treatments for which enrollees in DMHC-regulated plans and CDI-regulated policies did not have 100% coverage at baseline. As current utilization for both is nearly entirely as a noncovered benefit, the increase in benefit coverage would be expected to increase utilization for fezolinetant (231%) and ospemifene (187%). Utilization of other drugs and treatments would be expected to increase in proportion to the increase in benefit coverage.

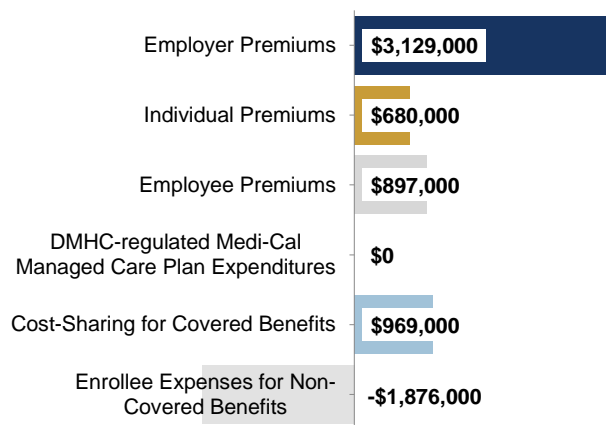
Expenditures

For enrollees in DMHC-regulated plans and CDI-regulated policies, AB 2467 would increase total premiums paid (by employers and enrollees) and cost sharing, though it would decrease expenses for

noncovered benefits (see Figure B). This would result in an increase of total net annual expenditures for enrollees with DMHC-regulated plans and CDI-regulated policies of \$3,993,000 (0.0025%).

CHBRP projects no change to copayments or coinsurance rates but does project increases in utilization of some drugs and therefore an increase in enrollee cost sharing. Increases in utilization of covered benefits are a combination of reductions in utilization that was paid for out of pocket at baseline that would be covered under AB 2467 postmandate and new utilization due to increased take-up with increases in coverage.

Figure B. Expenditure Impacts of AB 2467



Source: California Health Benefits Review Program, 2024.
Key: DMHC = Department of Managed Health Care.

Public Health

Within the first year postmandate, CHBRP finds that AB 2467 would reduce or abate menopause symptoms for women receiving the additional 15,400 (30-day) prescriptions (which might translate to ~1,250 women, assuming each received one prescription for 12 consecutive months).

Long-Term Impacts

CHBRP does not anticipate any additional changes postmandate that are different from the new levels of coverage established under AB 2467. If a lower-cost drug option were to become available, DMHC-regulated plans and CDI-regulated policies could shift to covering those options, which would potentially reduce overall costs. Additionally, if in the future more DMHC-regulated Medi-Cal plans began including an outpatient pharmacy benefit, that cost increase would include compliance with AB 2467.

The long-term public health impacts of AB 2467 are expected to be similar to those described in the short-term impact section. Most bill-specified drug categories (where most prescriptions are concentrated) are already covered at baseline. Therefore, CHBRP anticipates that a limited number of women (especially those with hormone-sensitive cancer experience) will continue to access the newly covered categories.

About CHBRP

The California Health Benefits Review Program (CHBRP) was established in 2002. As per its authorizing statute, CHBRP provides the California Legislature with independent analysis of the medical, financial, and public health impacts of proposed health insurance benefit-related legislation.

The state funds CHBRP through an annual assessment on health plans and insurers in California.

An analytic staff based at the University of California, Berkeley, supports a task force of faculty and research staff from multiple University of California campuses to complete each CHBRP analysis. A strict conflict-of-interest policy ensures that the analyses are undertaken without bias. A certified, independent actuary helps to estimate the financial impact. Content experts with comprehensive subject-matter expertise are consulted to provide essential background and input on the analytic approach for each report.

More detailed information on CHBRP's analysis methodology, authorizing statute, as well as all CHBRP reports and other publications, are available at www.chbrp.org.

Table of Contents

| | |
|---|------------|
| Policy Context | 1 |
| Background on Menopause | 4 |
| What Is Menopause? | 4 |
| Estimated Number of Californians Who May Experience Menopause Symptoms | 4 |
| Symptoms of Menopause | 4 |
| Treatments for Menopause Symptoms | 6 |
| Treatment Preferences and Barriers | 9 |
| Societal Impact of Menopause | 9 |
| Medical Effectiveness | 11 |
| Research Approach and Methods | 11 |
| Benefit Coverage, Utilization, and Cost Impacts | 20 |
| Analytic Approach and Key Assumptions | 20 |
| Baseline and Postmandate Benefit Coverage | 21 |
| Baseline and Postmandate Utilization and Unit Cost | 22 |
| Baseline and Postmandate Expenditures | 23 |
| Other Considerations for Policymakers | 25 |
| Public Health Impacts | 30 |
| Short-Term Public Health Impacts | 30 |
| Long-Term Impacts | 31 |
| Long-Term Utilization and Cost Impacts | 31 |
| Appendix A. Text of Bill Analyzed | A-1 |
| Appendix B. Literature Review Methods Specifications | B-1 |
| Appendix C. Cost Impact Analysis: Data Sources, Caveats, and Assumptions | C-1 |
| Appendix D. Examples of Treatments for Menopause Symptoms | D-1 |

References

California Health Benefits Review Program Committees and Staff

Acknowledgments

Lists of Tables and Figures

| | |
|---|-----|
| Table 1. Common Symptoms Related to Menopause..... | 5 |
| Table 2. Description of Drug Categories in AB 2467 and Menopause Symptoms Treated | 7 |
| Table 3. Impacts of AB 2467 on Benefit Coverage, 2025..... | 21 |
| Table 4. Impacts of AB 2467 on Utilization and Unit Cost, 2025..... | 22 |
| Table 5. Impacts of AB 2467 on Expenditures, 2025..... | 23 |
| Table 6. Baseline Per Member Per Month Premiums and Total Expenditures by Market Segment, California, 2025..... | 26 |
| Table 7. Postmandate Change in Per Member Per Month Premiums and Total Expenditures by Market Segment, California, 2025..... | 28 |
| Table 8. Treatments Considered in the Cost Impact Analysis for AB 2467 | C-3 |
| Table 9. Drug Therapy for Menopause Symptoms and Conditions Associated with Menopause by Therapeutic Category | D-1 |
| | |
| Figure 1. Findings Regarding the Effectiveness of Low-Dose Vaginal Estrogen on Treatment GSM Symptoms of Menopause..... | 14 |
| Figure 2. Findings Regarding the Effectiveness of High-Dose Vaginal Estrogen on Treatment of Menopause Symptoms | 14 |
| Figure 3. Findings Regarding the Effectiveness of Compounded Bioidentical Hormones on Treatment of Menopause Symptoms (Vaginal Atrophy) | 15 |
| Figure 4. Findings Regarding the Effectiveness of Compounded Bioidentical Hormones on Treatment of Menopause Symptoms (VMS)..... | 15 |

Policy Context

The California Assembly Committee on Health has requested that the California Health Benefits Review Program (CHBRP)² conduct an evidence-based assessment of the medical, financial, and public health impacts of Assembly Bill (AB) 2467, Menopause.

Bill-Specific Analysis of AB 2467, Menopause

Bill Language

AB 2467 would require coverage for treatment of menopause symptoms, including but not limited to the following:

- Hormone therapy
 - Combination estrogen and hormone
 - Combination estrogen and progestin
 - Estrogen-only medicines
- Low-dose antidepressants
- Anticonvulsants
- Vaginal estrogen
- Medications to prevent or treat osteoporosis
- Fezolinetant (Veoza) (hormone-free option)
- Topical hormone therapy
- Bioidentical hormones

The full text of AB 2467 can be found in Appendix A.

California Regulating Agencies

DMHC: California Department of Managed Health Care

CDI: California Department of Insurance

DHCS: Department of Health Care Services, which administers Medi-Cal

Relevant Populations

If enacted, AB 2467 would apply to the health insurance of approximately 22.3 million enrollees (58.6% of all Californians). This represents those who have commercial or CalPERS health insurance regulated by DMHC and CDI and Medi-Cal beneficiaries enrolled in DMHC-regulated plans. However, CHBRP expects impacts only among the 13.2 million enrollees who have a pharmacy benefit regulated by DMHC or CDI (see assumptions, below).

Analytic Approach and Key Assumptions

For this analysis, CHBRP has assumed that mandates that reference plans and policies that cover prescription drugs are relevant to pharmacy benefit coverage. Drugs that are physician-ordered and administered under the supervision of a physician (generally in a hospital, a provider's office, infusion center, or similar medical facility), along with the hospital stay or office visit, are generally covered through a medical benefit. Pharmacy benefits cover outpatient prescription drugs by covering prescriptions that are generally filled at a retail pharmacy, a mail-order pharmacy, or a specialty pharmacy.

For this analysis, CHBRP has assumed that plans and policies that would not have covered both generic and brand-name outpatient prescription drugs³ would not be required to do so for drugs prescribed as treatment for menopause symptoms.

² CHBRP's authorizing statute is available at www.chbrp.org/about/faqs.

³ See CHBRP's resource *Pharmacy Benefit Coverage in State-Regulated Health Insurance*, available at <https://www.chbrp.org/other-publications/resources>

Almost all (96.2%) commercial/CalPERS enrollees in plans and policies regulated by DMHC or CDI have an outpatient pharmacy benefit regulated by DMHC or CDI that covers both generic and brand-name outpatient prescription drugs; there is no pharmacy benefit for 1.2%, and 2.6% have a pharmacy benefit that is not regulated by DMHC or CDI.

As of January 1, 2022, outpatient prescription drugs are covered on a fee-for-service basis by DHCS for all Medi-Cal beneficiaries through the Medi-Cal Rx program.⁴ Their pharmacy benefit is “carved out” of the coverage provided by Medi-Cal managed care plans, and so AB 2467 would not be expected to impact their benefit coverage.

For this analysis, CHBRP has assumed that on-formulary coverage for certain drugs and on-formulary coverage of an example drug within certain categories of drugs (see Appendix D for categories and examples) would comply with the mandate.

AB 2467 addresses one particular drug and multiple bill-identified therapeutic categories of drugs. For the reasons noted below, CHBRP considered some subcategories and some additional drugs.

CHBRP approached the bill-identified therapeutic category “bioidentical hormones” as two subcategories: compounded bioidenticals and manufactured bioidenticals. CHBRP did so because manufactured bioidenticals have approval from the Food and Drug Administration (FDA), though compounded bioidenticals do not, and clinical recommendations are very different for the two subcategories (see *Medical Effectiveness* section).

Within the bill-identified therapeutic category “vaginal estrogen,” CHBRP included multiple particular drugs because one example, estradiol ring (Femring), is a high-dose vaginal estrogen. As a treatment, it is not interchangeable with the other examples of vaginal estrogen (see *Medical Effectiveness* section), which are low-dose estrogen.

Although it does not fit into a bill-defined therapeutic category, CHBRP has included a focus on ospemifene because it is the only nonhormonal, oral alternative to low-dose vaginal estrogen for the treatment of genitourinary syndrome of menopause (GSM).

The bill-identified therapeutic category “hormone therapy” specifies combination estrogen and progestin as a treatment as well as estrogen-only drugs. Estrogen-only drugs are often accompanied by a progestin-only prescription (separate pills that are, effectively, the combination treatment) and so CHBRP has included progestin-only drugs as a focus in this analysis.

Interaction With Existing State and Federal Requirements

Health benefit mandates may interact and align with the following state and federal mandates or provisions.

California Policy Landscape

California law and regulations

The California health insurance benefit mandate requiring coverage of contraception⁵ prohibits denial of contraception when the contraception is a treatment for menopause symptoms.

⁴ For more on outpatient prescription drug coverage among Californians with state-regulated health insurance, see CHBRP’s resource *Pharmacy Benefit Coverage in State-Regulated Health Insurance*, available at www.chbrp.org/other-publications/resources.

⁵ HSC 1367.25 and INS 10123.196

Similar requirements in other states

Nevada requires that health insurance that covers prescription drugs or devices include coverage for any type of hormone replacement therapy that is approved by the FDA and is lawfully prescribed or ordered in Nevada.⁶

Illinois requires coverage for “medically necessary hormone therapy treatment to treat menopause that has been induced by a hysterectomy.”⁷

Federal Policy Landscape

Affordable Care Act

A number of Affordable Care Act (ACA) provisions have the potential to or do interact with state benefit mandates. Below is an analysis of how AB 2467 may interact with requirements of the ACA as presently exist in federal law, including the requirement for certain health insurance to cover essential health benefits (EHBs).^{8,9}

Essential Health Benefits

In California, nongrandfathered¹⁰ individual and small-group health insurance is generally required to cover EHBs.¹¹ In 2025, approximately 11.5% of all Californians will be enrolled in a plan or policy that must cover EHBs.¹²

States may require state-regulated health insurance to offer benefits that exceed EHBs.^{13,14,15} Should California do so, the state could be required to defray the cost of additionally mandated benefits for enrollees in health plans or policies purchased through Covered California, the state’s health insurance marketplace. However, state benefit mandates specifying provider types, cost sharing, or other details of existing benefit coverage would not meet the definition of state benefit mandates that could exceed EHBs.^{16,17}

As AB 2467 would not require coverage for a new state benefit, it appears not to exceed the definition of EHBs in California.

⁶ NRS 689A.0415

⁷ Sec. 356z.53 – source: P.A. 102-804, eff. 1-1-23

⁸ The ACA requires nongrandfathered small-group and individual market health insurance — including but not limited to qualified health plans sold in Covered California — to cover 10 specified categories of EHBs. Policy and issue briefs on EHBs and other ACA impacts are available on the CHBRP website: www.chbrp.org/other-publications/issue-briefs.

⁹ Although many provisions of the ACA have been codified in California law, the ACA was established by the federal government, and therefore, CHBRP generally discusses the ACA as a federal law.

¹⁰ A grandfathered health plan is “a group health plan that was created — or an individual health insurance policy that was purchased — on or before March 23, 2010. Plans or policies may lose their ‘grandfathered’ status if they make certain significant changes that reduce benefits or increase costs to consumers.” Available at: www.healthcare.gov/glossary/grandfathered-health-plan.

¹¹ For more detail, see CHBRP’s issue brief *Essential Health Benefits: An Overview of Benefits, Benchmark Plan Options, and EHBs in California*, available at www.chbrp.org/other-publications/issue-briefshttps://chbrp.org/other_publications/index.php.

¹² See CHBRP’s resource *Sources of Health Insurance in California*, available at www.chbrp.org/other-publications/resources.

¹³ ACA Section 1311(d)(3).

¹⁴ State benefit mandates enacted on or before December 31, 2011, may be included in a state’s EHBs, according to the U.S. Department of Health and Human Services (HHS). Patient Protection and Affordable Care Act; Standards Related to Essential Health Benefits, Actuarial Value, and Accreditation. Final Rule. Federal Register, Vol. 78, No. 37. February 25, 2013. Available at: www.gpo.gov/fdsys/pkg/FR-2013-02-25/pdf/2013-04084.pdf.

¹⁵ However, as laid out in the Final Rule on EHBs U.S. Department of Health and Human Services (HHS) released in February 2013, state benefit mandates enacted on or before December 31, 2011, would be included in the state’s EHBs, and there would be no requirement that the state defray the costs of those state-mandated benefits. For state benefit mandates enacted after December 31, 2011, that are identified as exceeding EHBs, the state would be required to defray the cost.

¹⁶ Essential Health Benefits. Final Rule. A state’s health insurance marketplace would be responsible for determining when a state benefit mandate exceeds EHBs, and qualified health plan issuers would be responsible for calculating the cost that must be defrayed. Patient Protection and Affordable Care Act; Standards Related to Essential Health Benefits, Actuarial Value, and Accreditation. Final Rule. Federal Register, Vol. 78, No. 37. February 25, 2013. Available at: www.gpo.gov/fdsys/pkg/FR-2013-02-25/pdf/2013-04084.pdf.

¹⁷ Both Massachusetts and Utah currently pay defrayment costs for exceeding EHBs. For more information about defrayal, refer to CHBRP’s issue brief *Essential Health Benefits: Exceeding EHBs and they Defrayal Requirement*, available at: www.chbrp.org/other-publications/issue-briefs

Background on Menopause

AB 2367 would mandate coverage of specified prescription drugs and therapeutic categories of drugs used to treat menopause symptoms. This section provides contextual information defining menopause, the symptoms that may accompany the menopause stages, the percent of people potentially affected by symptoms, and pharmacologic treatments for symptoms. It also summarizes disparities among women experiencing menopause, barriers to treating the symptoms and estimates of societal burden associated with menopause.

What Is Menopause?

Menopause is part of the normal aging process in which menstruation has ceased for 12 consecutive months (Endocrine Society, 2022). This transition to a new stage of life (rather than a condition or disease) is experienced by every woman¹⁸ and most often occurs naturally between ages 45 and 55 years but may occur between ages 40 and 64 years (median age 51 years) (A.D.A.M., 2023).

There are three clinical stages of the menopause transition:

- Perimenopause: menstruation becomes irregular in frequency, duration, and bleeding intensity for an average of 1 to 3 years before periods stop completely.
- Menopause is the complete cessation of menstruation for 12 consecutive months; average at menopause: 51 years.
- Postmenopause is defined as the point after which no menstruation has occurred for one year. See below for symptom descriptions.

Types of Menopause

- **Natural:** median age 51 years.
- **Clinically induced:** May occur at any age due to some prescription drug treatments (e.g., chemotherapy or hormone therapy used to treat breast cancer) or surgical removal of the ovaries (oophorectomy).

For simplicity in this report, CHBRP will use “menopause” to describe the perimenopause, menopause, and postmenopause stages, unless otherwise specified.

Physiologically, during the menopause transition (whether naturally or clinically induced), the ovaries produce less estrogen and progesterone as they stop releasing eggs. Once a woman achieves menopause, she can no longer become pregnant without significant medical intervention (Casper et al., 2024). The decrease in the hormonal levels may lead to bothersome symptoms prompting requests for treatment.

Estimated Number of Californians Who May Experience Menopause Symptoms

There are approximately 5 million women aged 40 to 64 years in California, many of whom experience mild, moderate, or severe menopause symptoms for a few months to more than 12 years (Avis et al., 2015; CHIS, 2024; NIA, 2021).

Symptoms of Menopause

Diminished estrogen and progesterone production can produce a wide variety of symptoms across all stages of menopause (NIA, 2021). Symptoms can affect women differently by type, intensity, and duration during any menopause stage. See the Disparities section for discussion of differences in symptoms by race/ethnicity.

¹⁸ CHBRP refers to women in the discussion of menopause, but recognizes that individuals with female reproductive organs who identify as male or nonbinary also experience menopause.

The longitudinal *Study of Women’s Health Across the Nation (SWAN)* released findings that differentiated between symptoms attributable to menopause and those attributable to the general aging process. Table 1 describes common menopause symptoms and their estimated prevalence (when available). Genitourinary (vaginal atrophy and/or dryness) and vasomotor symptoms (night sweats, hot flashes [colloquially called hot flashes]) are the two most commonly reported symptoms and can occur throughout the menopausal stages. The genitourinary syndrome of menopause (GSM) includes symptoms such as dysuria (burning, stinging, itching during urination), and dyspareunia (painful intercourse due to vaginal dryness or atrophy) (SWAN, 2023). For those who experience moderate-to-severe vasomotor symptoms (VMS), sleep disruption and insomnia can occur which, in turn, may affect memory, cognition, and mood (irritability or depression). Memory and cognition (without sleep disruption) may decline during the early menopausal stage, but decrements can reverse during later menopause. There is mixed evidence as to whether menopause reduces physical functioning, changes to skin and hair, and decreased libido. Urinary incontinence and urinary tract infections may be related to the general aging process or to changes during menopause transition (Casper et al., 2024; SWAN, 2023).

Table 1. Common Symptoms Related to Menopause

| Symptom | Description/Duration | Estimated National Prevalence |
|---|--|---|
| Genitourinary syndrome of menopause^a (GSM) | Vaginal dryness and/or vulvovaginal atrophy can result in vaginal discomfort, burning, stinging, and itching during urination; frequent urination; recurrent urinary tract infections; and/or painful intercourse. | Prevalence of vaginal dryness ranges between 30% and 50% of menopausal women. Symptoms persist in more than 25% of women in later stages of menopause. |
| Vasomotor symptoms (VMS) Hot flashes/flashes/night sweats | Hot flashes/night sweats are due to sudden body temperature dysregulation. They last for 2 to 4 minutes and may be associated with sweating and palpitations, sometimes followed by chills and/or a sensation of anxiety. Hot flashes that occur during sleep are called night sweats. Frequency varies from 1 to 2 per day to 1 to 2 per hour and may last a few months to many years. Frequent severe hot flashes may impact sleep, concentration, mood, energy, and sexual activity, and may last longer for those experiencing stress, anxiety, or depression. | 80% of women experience some hot flashes/night sweats. Can last 7+ years for about 50% of women. Prevalence of moderate-to-severe hot flashes in U.S. is 35%. An estimated 20%-30% of women seek medical attention. |
| Memory and cognition | Menopausal memory concerns, which generally occur in earlier menopausal stages, can reverse in later stages of menopause. Sleep disruption and depression, also menopause symptoms, can affect memory and cognition. | An estimated 65% women reported memory complaints during menopause transition. |
| Depression | Feelings of sadness, feeling down, tired, and helpless or hopeless are not uncommon, especially during transition to menopause as production of progesterone ends. Sleep disturbance from vasomotor symptoms may also affect mood. | Unknown. Significant increased risk of new-onset depression in women during the menopausal transition with risk decreasing in into later menopause stage. |

| Symptom | Description/Duration | Estimated National Prevalence |
|----------------------|---|--|
| Sleeplessness | Difficulty staying asleep and waking too early; symptoms are most frequent in the early menopause stage and may stabilize or improve later. Night sweats caused by vasomotor symptoms can disrupt sleep. | An estimated 50% of women reported sleep problems during early menopause compared to 30% before menopause. |
| Bone loss | Accelerated loss of bone density and strength occurs in early menopause but slows during the later stages; menopause experienced at younger ages produces lower bone density as women age, which results in more fractures. | About 13% of women aged 50-64 years have bone loss (osteoporosis) and increases to 27% for those 65 years and older; some may be age-related rather than menopause-specific. |

Source: California Health Benefits Review Program, 2024, based on Deecher and Dorries, 2007; Green and Santoro, 2009; Martin et al., 2024; Sarafrazui et al., 2021; SWAN, 2023.

Note: (a) Urinary incontinence is not a symptom of menopause; it is aging related. Other aspects of sexual health such as desire, arousal and emotional satisfaction are reported to be more related to older age, fair or poor health, depressive symptoms, and anxiety.

Treatments for Menopause Symptoms

AB 2367 lists overlapping categories of drugs for the treatment of menopause symptoms (see *Policy Context* section). Table 2 matches the bill-specified language to the therapeutic drug categories CHBRP uses to explain the drugs, their routes of administration, and the symptoms the drugs treat.

Hormone therapy treats the two primary symptoms of menopause: VMS and GSM. VMS (i.e., hot flashes/night sweats) are treated with higher-dose systemic hormone therapy (which also may reduce bone loss) while GSM symptoms are treated with low-dose vaginal estrogen (Martin et al., 2024). Nonhormonal treatments can also treat VMS (e.g., antidepressants, anticonvulsants) and GSM (ospemifene) (Table 2).

Potential Hormone Therapy Side Effects

Note that some women may experience side effects from systemic hormone therapy, prefer not to take hormone therapy, or have other conditions (such as high risk for or a history of breast cancer) that preclude use of hormone therapy. There are a number of documented side effects from systemic hormone therapy that may affect patients (e.g., breast tenderness, headache, heavy nonmenstrual vaginal bleeding, upset stomach, vomiting, fluid retention, and swelling) (Martin et al., 2024; NLM, 2018). Potential side effects from low-dose hormone therapy include those for high-dose systemic therapy as well as weight gain, fatigue, cold-/flu-like symptoms, hair loss, etc. (NLM, 2023). Estrogen plus progestin treatments are known to increase the risk of blood clots, heart attack, and stroke, especially in older women, and may increase the risk of breast cancer. See the *Medical Effectiveness* section for information about effectiveness and harms, such as increased risk of certain types of cancer.

Some nonpharmacologic treatments such as cognitive behavioral therapy, hypnosis, and mindfulness-based stress reduction may have beneficial effects on menopause symptoms (SWAN, 2023).

Formulations & Routes of Administration

Drugs can come in one or more *formulations*: tablet/capsule; transdermal patch, topical spray, cream/gel/ lotion; or vaginal suppository, cream, or silicone ring.

Drugs can be delivered by different *routes of administration*: oral, topical, vaginal, subcutaneous, injectable, or intravenous (IV).

Dosage Levels

Hormone therapy is available in *high-dose formulations*, which has a systemic effect that treats VMS. *Low-dose formulations* produce local effects and are prescribed most often to treat GSM symptoms.

Table 2. Description of Drug Categories in AB 2467 and Menopause Symptoms Treated

| AB 2467-Specified Language for Drug Treatments of Menopause Symptoms | Therapeutic Categories Assigned by CHBRP for Analysis | Routes of Administration & Dosage Form | Menopause Symptoms Treated | Notes |
|---|---|---|---------------------------------|--|
| Hormonal Drug Therapy | | | | |
| Hormone therapy (e.g., combination estrogen and hormone drugs, combination estrogen and progestin, and estrogen only) | <ul style="list-style-type: none"> Oral systemic <ul style="list-style-type: none"> Estrogen only Progesterone only (co-prescribed with estrogen) Combination estrogen and hormone | Oral tablet or capsule | VMS, GSM | <p>Systemic treatment. Estrogen-only drugs recommended only for women who have had a hysterectomy because of the marked increased risk of uterine cancer when estrogen is taken alone.</p> <p>Progesterone-only drugs are co-prescribed with estrogen-only drugs to reduce risk of uterine cancer.</p> <p>Combination hormone can have significant negative side effects; can have side benefit of reducing bone loss.</p> |
| Topical estrogen | <ul style="list-style-type: none"> Transdermal systemic | Transdermal patch, spray, cream/gel/ lotion | VMS, GSM | Systemic treatment. |
| Vaginal estrogen | <ul style="list-style-type: none"> Vaginal estrogen <ul style="list-style-type: none"> High dose Low dose | <p>Vaginal silicone ring only</p> <p>Vaginal silicone ring, suppository, or cream</p> | <p>VMS, GMS</p> <p>GSM only</p> | <p>Only one vaginal ring product uses high-dose estrogen that absorbs systemically to treat VMS.</p> <p>Most vaginal estrogens are locally applied and have a lower dose that has local effects.</p> |
| Bioidentical hormones ^a | <ul style="list-style-type: none"> Compounded bioidentical hormones | Oral tablet/capsule, spray, cream/gel, lotion | VMS, GSM | Custom compounded at a compounding pharmacy that are plant-derived natural hormones (not FDA regulated); may vary in doses across and between pharmacies. |
| Nonhormonal Drug Therapy | | | | |
| Other hormone-free options | Ospemifene | Oral tablet | GSM | Systemic treatment. May increase risk of blood clots. |
| Fezolinetant | Fezolinetant | Oral tablet | VMS only | Appropriate for women wanting treatment for VMS who have contraindication to hormone therapy due to high risk of or have/had hormone-sensitive cancers. |
| Low-dose antidepressants | Antidepressants (SSRI and SNRI) | Oral tablet/capsule | VMS only | Appropriate for women wanting treatment for VMS who have contraindications to hormone |

| | | | | |
|--|--|---|-----------|---|
| | | | | therapy (high risk due to hormone-sensitive cancers). |
| Anticonvulsants | Anticonvulsants | Oral tablet/capsule | VMS only | Appropriate for women wanting treatment for VMS who have contraindications to hormone therapy (high risk due to hormone-sensitive cancers). |
| Medications to prevent or treat osteoporosis | Medications to prevent or treat osteoporosis | Oral tablet/capsule, injection, intravenous, subcutaneous | Bone loss | Slow bone loss or encourage bone regrowth by improving bone density and strength. Side effects may include stomach upset, heart burn, and other serious outcomes. |

Source: California Health Benefits Review Program, 2024, based on Martin et al, 2024; Stanczyk et al., 2019;

Note: (a) Compounded bioidentical hormone formulations are composed of plant-derived natural hormones and are not FDA-regulated. Manufactured compounded hormone formulations are also composed of plant-derived natural hormones but are FDA-approved and manufactured in standard doses; these are not included in the compounded bioidentical hormone category for this analysis (see Appendix C for more details).
 Key: GSM = genitourinary syndrome of menopause; SNRI = serotonin-norepinephrine reuptake inhibitors; SSRI = selective serotonin reuptake inhibitors; VMS = vasomotor symptoms.

Disparities¹⁹ in Menopause Symptoms and Treatment

Disparities are noticeable and preventable or modifiable differences between groups of people. Health insurance benefit mandates or related legislation may impact disparities.

Race or Ethnicity

There is considerable variation in the prevalence and treatment of menopause symptoms among racial/ethnic groups. Fact sheets produced by SWAN (based on its longitudinal study and other literature) state that Native American and Black women report the most frequent and most bothersome hot flashes of all groups studied with Black women 50% more likely to report hot flashes than White women (Hispanic women reported similar rates to White women and Asian women reported the lowest rates) (Harlow, et al., 2022; Reed et al., 2014; SWAN, 2023). The fact sheets also reported that Black women were more likely to experience depressive symptoms than White women. Despite the disparate symptom burdens, Black women were about half as likely as White women to use menopause hormone therapy (SWAN, 2023). Other evidence indicates that clinicians are less likely to prescribe menopause hormone therapy for Black women (Blanken et al., 2022).

Other studies produced similar evidence of disparities in symptoms among different races and ethnicities. For example, Green and Santoro (2009) found that Black (46.5%) and Hispanic (49.4%) women report vaginal symptoms more often than White, Japanese, and Chinese women (28.9%, 34.3%, and 36.6% respectively). Similar findings were reported for VMS with Black women reporting the longest duration and Chinese and Japanese women reporting the shortest duration (Avis et al., 2015). A review of literature about Black women’s experience with menopause found that Black women reported most GSM symptoms less often than White women, but reported vaginal dryness more often (Williams et al., 2022). Hispanic women reported more genitourinary symptoms overall. No evidence was found regarding disparities in treatment for VMS.

Sleep disruption also differs among women with different racial/ethnic heritage. For instance, Harlow and colleagues (2022) found that Black, Chinese, Japanese, and Hispanic/Latinx women experience more interrupted sleep and poorer sleep quality relative to White women, and Black women are less likely to be treated for depression. No evidence of disparities in treatment for sleep disturbance was found. Race/ethnic differences in menopause symptoms may be related

¹⁹ Several competing definitions of “health disparities” exist. CHBRP relies on the following definition: Health disparity is defined as the differences, whether unjust or not, in health status or outcomes within a population (Wyatt et al., 2016).

to racial/ethnic differences in health problems, physical inactivity, stress, financial strain, and discrimination (Green and Santoro, 2009).

Treatment Preferences and Barriers

Patient Preferences

As noted, the types, severity, and duration of menopause symptom varies among women as they advance through the menopause stages. Some women who experience symptoms do not seek prescription drug therapy because their symptoms are mild enough without any treatment or symptoms may be attenuated by over-the-counter products (e.g., vaginal lubricants for vaginal dryness, sleep aids for sleeplessness), or because negative side effects from drug treatments (e.g., nausea, bloating, irregular uterine bleeding) outweigh reductions in the menopause symptom(s).

Barriers: Patient and Clinician Perspectives

In addition to patient preferences affecting uptake of treatment for symptoms, research shows other potential barriers to treating symptoms. A 2023 qualitative study identified several barriers preventing menopausal women from seeking help for symptoms including lack of knowledge about menopause (including the range of symptoms related to menopause and the length of time symptoms may last) or misattribution of symptoms to another cause. Additional barriers included stigma or embarrassment, as well as normalization of symptoms or cultural norms around menopause (Barber and Charles, 2023). Barriers to accessing or accepting hormone therapy treatment included perceptions of hormone therapy and beliefs about the risk of breast cancer, as well as having received limited or no information to support the decision to use hormone therapy (including how long to take it, long-term safety, long-term benefits, or that their concerns were not addressed) (Barber and Charles, 2023). A study by DePree et al. (2023) of clinician-perceived barriers to patients initiating care focused on concerns about the risks of treatment and financial considerations. The clinicians also noted that most patients waited several months before notifying their clinicians about their symptoms.

Additionally, the 2002 Women's Health Initiative (WHI) study had an impact on hormone therapy use among menopausal women both for patients and clinicians. The large clinical trial reported that postmenopausal women taking combination hormone therapy had an increased risk for breast cancer, heart disease, stroke, blood clots, and urinary incontinence (Office on Women's Health, 2020). The WHI produced a significant and longstanding decrease in the use of hormone therapy in the U.S. (Cagnacci and Venier, 2019). Crawford et al. (2018) analyzed SWAN data and found a significant decrease in hormone therapy initiation (from 8.6% pre-WHI to 2.8% post-WHI) and in hormone therapy continuation (from 84.0% to 62.0%) after 2002. These studies reported reasons for women declining initiation or discontinuing hormone therapy largely reflected concerns highlighted by the WHI results (such as concerns about risks of heart disease, cancer, and side effects), as well as media reports and provider advice. Similarly, clinicians were redirected away from hormone replacement therapy for a period of years based on the WHI results (Cagnacci and Venier, 2019). With the advent of low-dose estrogen and hormone combination therapies, and subsequent research that informed changes in clinical practice guidelines, the prescribing trend has reversed over the last 15 years (Cho et al., 2023).

Societal Impact of Menopause

Menopause occurs during a significant portion of a woman's work life. Evidence of the effect of menopause on direct and indirect economic and societal costs varies. CHBRP found several studies that estimated financial impacts of menopause symptoms on productivity ranging between \$1.8 billion and \$2.2 billion annually. For example, a 2016 review of 75 studies on experiences of menopausal women in the workplace identified studies that indicate VMS have a negative impact on productivity, capacity to work, and work experience, although this was not a uniform finding (Jack et al., 2016). The review also found that physical and psychosocial factors in the workplace also can also affect the relationship between symptoms

and work. A 2013 study of 3,000 women found that moderate and severe VMS were associated with lower work productivity compared to mild symptoms (Whiteley et al., 2013).

A more recent study (2021) study of 4,000 women attending Mayo Clinic sites found that menopause symptoms resulted in an average of three missed workdays in the previous 12 months among 11% of women, a cutback in hours worked among 5% of women, quitting/retiring among 1% of women, and layoffs or firings among 0.3% of women (Faubion et al., 2023). The authors estimated menopause-related productivity losses of about \$1.8 billion annually assuming 11% of women aged 40 to 60 years missed three workdays/year. This estimate excludes reduced work hours, loss of employment, or changing jobs (Faubion et al., 2023).

Finally, a 2021 study using SWAN survey data examined the impact of sleep disturbances among women of menopausal age on employment and work productivity. The study found that risk of unemployment was 31% higher for women with new-onset sleep disturbances. Although the study did not find significant associations between sleep disturbances and reduction in work time, the authors estimated that sleep problems could be associated with a reduction in 0.44 hours of work per week. Based on this finding, the authors estimate around \$2.2 billion in lost productivity among women aged 42 to 64 in the United States (Kagan et al., 2021). (Please note, the societal impact discussed here is relevant to a broader population than those covered by AB 2467; see the *Benefit Coverage, Utilization, and Cost Impacts* section for estimates of direct cost impacts for the specific population targeted by AB 2467.)

The societal impact of menopause is beginning to be publicly acknowledged by employers as well. CHBRP found reports by several large companies surveying their workforce about the effect of menopause in the workplace and suggested employer-based supports (Bank of America, 2024; Carrot Fertility, 2022).

Medical Effectiveness

As discussed in the *Policy Context* section, AB 2467 would mandate coverage of treatment of menopause symptoms that includes but is not limited to:

- Hormone therapy
 - Combination estrogen and hormone
 - Combination estrogen and progestin
 - Estrogen-only medicines
- Low-dose antidepressants
- Anticonvulsants
- Vaginal estrogen
- Medications to prevent or treat osteoporosis
- Fezolinetant (Veoza) (hormone-free option)
- Topical hormone therapy
- Bioidentical hormones

Additional information on menopause is included in the *Background* section.

Research Approach and Methods

The medical effectiveness review summarizes findings from evidence²⁰ on the effectiveness of drugs that may not be commonly covered by insurance (see *Benefit Coverage, Utilization, and Cost Impacts* section) and that may be appropriate for patients who have significant risk factors, such as high risk or history of breast cancer that make systemic hormone therapy inadvisable and therefore, need alternate drugs, including vaginal estrogen, compounded bioidentical hormones, and hormone-free therapies including fezolinetant and ospemifene during menopause.

CHBRP's review of literature does not include other treatments for menopause symptoms including hormonal therapy (including but not limited to combination estrogen and hormone, combination estrogen and progestin, and estrogen-only drugs), low-dose antidepressants, anticonvulsants, drugs to prevent or treat osteoporosis, and topical hormone therapy. For these treatments, CHBRP relied on systematic reviews and clinical guidelines because there is already broad coverage for these drugs, such that AB 2467 is not expected to change benefit coverage for them (see *Benefit Coverage, Utilization, and Cost Impacts* section).

The search was limited to studies published from 2019 to present. A total of 23 studies were included in the medical effectiveness review for this report. Articles were eliminated because they did not focus on drugs that are used to treat menopause symptoms, were of poor quality, or did not report findings from clinical research studies. A more thorough description of the methods used to conduct the medical effectiveness review and the process used to grade the evidence for each outcome measure is presented in Appendix B.

²⁰ Much of the discussion in this section is focused on reviews of available literature. However, as noted in the section on Implementing the Hierarchy of Evidence in CHBRP's *Medical Effectiveness Analysis and Research Approach* document (posted at www.chbrp.org/about/analysis-methodology/medical-effectiveness-analysis), in the absence of fully applicable to the analysis peer-reviewed literature on well-designed randomized controlled trials (RCTs), CHBRP's hierarchy of evidence allows for the inclusion of other evidence.

The conclusions below are based on the best available evidence from peer-reviewed and grey literature.²¹ Unpublished studies are not reviewed because the results of such studies, if they exist, cannot be obtained within the 60-day timeframe for CHBRP reports.

Key Questions

1. In menopausal women, what is the effect of high-dose and low-dose vaginal estrogen on reduction in menopause symptoms compared with no intervention?
2. In menopausal women, what is the effect of compounded bioidentical hormones on reduction in menopause symptoms compared with no intervention?
3. In menopausal women, what is the effect of fezolinetant on reduction in menopause symptoms compared with no intervention?
4. In menopausal women, what is the effect ospemifene reduction in menopause symptoms compared with no intervention?

Outcomes Assessed

The outcomes of interest for the medical effectiveness review include vasomotor symptoms (VMS) associated with menopause, including hot flashes or flushes and night sweats, and genitourinary syndrome of menopause (GSM), which includes symptoms of sexual dysfunction, sexual well-being, dyspareunia, and urinary symptoms (including dysuria, urgency and frequency of urination, recurrent urinary tract infections [UTIs], and urinary incontinence).

CHBRP also reviewed evidence on the harms of treatment for menopause symptoms, which include elevated risks of endometrial hyperplasia and endometrial cancer when systemic estrogen is given without progesterone to women with a uterus, cardiovascular events, and risk of breast cancer. Additional harms assessed include changes of total cholesterol, triglycerides, LDL or HDL, fasting glucose, insulin, or insulin resistance, and liver enzyme elevations with use of compounded bioidentical hormones.

Study Findings

This following section summarizes CHBRP's findings regarding the strength of evidence for the effectiveness of treatments addressed by AB 2467. Each section is accompanied by a corresponding figure. The title of the figure indicates the test, treatment, or service for which evidence is summarized. The statement in the box above the figure presents CHBRP's conclusion regarding the strength of evidence about the effect of a particular test, treatment, or service based on a specific relevant outcome and the number of studies on which CHBRP's conclusion is based. Definitions of CHBRP's grading scale terms is included in the box below, and more information is included in Appendix B.

The following terms are used to characterize the body of evidence regarding an outcome:

Clear and convincing evidence indicates that there are multiple studies of a treatment and that the large majority of studies are of high quality and consistently find that the treatment is either effective or not effective.

Preponderance of evidence indicates that the majority of the studies reviewed are consistent in their findings that treatment is either effective or not effective.

Limited evidence indicates that the studies have limited generalizability to the population of interest and/or the studies have a fatal flaw in research design or implementation.

²¹ Grey literature consists of material that is not published commercially or indexed systematically in bibliographic databases. For more information on CHBRP's use of grey literature, visit www.chbrp.org/about/analysis-methodology/medical-effectiveness-analysis.

Inconclusive evidence indicates that although some studies included in the medical effectiveness review find that a treatment is effective, a similar number of studies of equal quality suggest the treatment is not effective.

Insufficient evidence indicates that there is not enough evidence available to know whether or not a treatment is effective, either because there are too few studies of the treatment or because the available studies are not of high quality. It does not indicate that a treatment is not effective.

More information is available in Appendix B.

Findings on the Effectiveness of Vaginally Administered Estrogen on Treatment of Menopause Symptoms

Vaginal low-dose local estrogen

A systematic review of 30 randomized controlled trials (RCTs) examining the effect of hormone therapy on urinary symptoms (including dysuria, urgency and frequency of urination, recurrent UTIs, and urinary incontinence) in menopause included five RCTs examining vaginal low-dose local estrogen compared to placebo (Christmas et al., 2023; 32,204 subjects). The authors reported significant improvements in dysuria, incontinence, frequency of UTIs, and decreased UTI in patients that were treated with vaginal low-dose estrogen compared to placebo. One trial reported that vaginal low-dose estrogen showed significant improvement in dysuria, incontinence, urinary frequency, and decreased UTI. Another trial reported a significant decrease incidence of stress urinary incontinence and UTI in patients treated with vaginal estrogen. Another RCT showed a significant reduction in urinary urgency with 25 µg vaginal estradiol but no improvement in urinary frequency or incontinence. An RCT of postmenopausal women with history of recurrent UTIs comparing 2 mg vaginal estradiol ring to placebo reported significant improvement in urge urinary incontinence, stress urinary incontinence, and higher incidence of being UTI-free but no significant difference in dysuria, frequency, or urgency. Two RCTs of postmenopausal women with recurrent UTIs reported a significant lower incidence of UTIs in the treatment group (over 6 to 8 months) and an 8-month-long RCT reported significantly lower days of antibiotic use in the vaginal low-dose estrogen treatment group than placebo (6.9 ± 1.1 versus 32.0 ± 7.8 days).

Another systematic review (Biehl²² et al., 2019; 53 RCTs; N = 32,204) evaluated the effect of hormone therapy on urinary symptoms in menopause and included 24 trials that compared vaginal low-dose estrogen therapy to placebo. The authors reported that vaginal low-dose estrogen significantly reduced urinary frequency, urgency, urge and stress incontinence, and recurrent urinary tract infections. All studies showed superiority of vaginal low-dose estrogen products when compared with placebo in outcomes including maturation of the vaginal epithelium, reduction of vaginal pH, and symptoms of dyspareunia (6 studies), vaginal dryness (7 studies) and alleviation of urogenital symptoms (2 studies) including reduced urinary urgency and decreased incidence of cystitis.

A more recent small, participant-masked, RCT (n=39) comparing the effect estrogen-containing vaginal ring to a placebo vaginal ring on vaginal or urinary Lactobacillus relative abundance, researchers reported no significant difference or changes in vaginal or urinary Lactobacillus relative abundance, vulvovaginal dryness, urinary frequency painful intercourse, and urinary urgency at 12-week follow-up (Lillemon et al., 2022).

Summary of findings regarding the effectiveness of low-dose vaginal estrogen on treatment GSM symptoms of menopause: There is *clear and convincing evidence* that low-dose vaginal estrogen for the treatment of menopausal GSM (including dysuria, urgency and frequency of urination, recurrent UTIs, and urinary incontinence) is effective, based on 20 studies.

²² Cardozo, 2021, and Simunić et al., 2003, are in both Christmas et al., 2023, and Biehl et al., 2019, systematic reviews.

Figure 1. Findings Regarding the Effectiveness of Low-Dose Vaginal Estrogen on Treatment GSM Symptoms of Menopause



Vaginal high-dose systemic estrogen

High-dose vaginal estrogen, FDA approved for the relief of moderate-to-severe VMS and GSM in menopausal women in 2003, is a prescription vaginal ring that contains estradiol (an estrogen hormone) with the goal of systemic distribution.

One RCTs (Speroff et al., 2003; 225 subjects) reported that 50 or 100 mcg per day of vaginally administered estradiol, significantly reduced moderate-to-severe VMS and improved urogenital symptoms in menopausal women, compared with placebo, at 13 weeks follow-up.

Summary of findings regarding the effectiveness of high-dose vaginal estrogen on treatment of perimenopausal and menopause symptoms: There is *limited evidence* that high-dose vaginally administered estrogen for the treatment of menopausal VMS is effective, based on one RCT.

Figure 2. Findings Regarding the Effectiveness of High-Dose Vaginal Estrogen on Treatment of Menopause Symptoms



Findings on the Effectiveness of Compounded Bioidentical Hormones on Treatment of Menopause Symptoms

Bioidentical hormones (estradiol and progesterone) are chemically identical to those produced by the ovaries. These are derived from plant sources such as soy or yams and are often considered “natural” hormones. Bioidentical hormones are available as manufactured FDA-approved drugs in a wide range of doses that can be tailored to patient needs and prescribed as patches, pills, gels, sprays, or vaginal rings with tested efficacy.²³ Compounded bioidentical hormones include these two plant-based hormones (and sometimes others) that are customizable (custom compounded in a compounding pharmacy) for patients. Compounded bioidentical hormones are often falsely advertised as safer alternatives to FDA-approved pharmaceutical bioidentical options (Constantine et al., 2016). Compounded drugs are not subject to the same FDA regulations or oversight as other manufactured noncompounded products and are not routinely tested by any regulatory agency for quality, purity, or potency (Bhavnani and Stanczyk, 2012).

The North American Menopause Society (NAMS) and the American College of Obstetricians and Gynecologists (ACOG) state that, because of the lack of FDA oversight and safety and efficacy concerns — including lack of standardization due to product-to-product variability — compounded bioidentical hormone drugs should be reserved for patients with an allergy to an active pharmaceutical ingredient or inactive ingredient of an FDA-approved drug product or documented requirement for a different dosage form than available (ACOG, 2023).

A literature review (13 studies) by the National Academies of Sciences, Engineering, and Medicine (NAEM, 2020) concluded that there is insufficient evidence to support the medical value of compounded bioidentical hormones as a treatment for menopause symptoms because of the lack of high-quality, rigorous studies on the efficacy and harms of these drugs.

²³ See appendix D for examples of manufactured FDA-approved bioidentical hormones.

CHBRP found one network meta-analysis²⁴ of studies with short-term follow-up (a year or less) that compared compounded bioidentical hormonal therapy including vaginal estradiol, vaginal testosterone, vaginal DHEA, or oral DHEA, to placebo. Liu et al. (2022) reported that compounded bioidentical hormones in the form of compounded vaginal androgen was found to significantly improve vaginal atrophy symptoms, measured by the Female Sexual Function Index (FSFI)²⁵ (5 studies; n=598).

Liu (2022) also reported that two studies in the systematic review reported inconclusive evidence of compounded bioidentical hormones on VMS in menopause. One study (Leonetti et al., 1999; n=90) reported significantly improved VMS in most patients at 1 year with topical progesterone therapy. Another study (Thomas et al., 2014; 13 patients) examining oral combined estrogen plus progesterone reported no significant symptom relief after 2 months, compared to placebo. There was inadequate data to perform meta-analysis.

Summary of findings regarding the effectiveness of compounded bioidentical hormones on treatment of perimenopausal and menopause symptoms: There is *limited evidence* based on five studies that compounded vaginal androgen improved vaginal atrophy symptoms. There is *inconclusive evidence* that compounded bioidentical hormones are effective treatment for VMS based on two small studies. One study (n=90) reported significantly improved VMS in most patients at 1 year with topical progesterone therapy and another very small study (n=13) examining oral combined estrogen plus progesterone reported no significant symptom relief after 2 months, compared to placebo.

Figure 3. Findings Regarding the Effectiveness of Compounded Bioidentical Hormones on Treatment of Menopause Symptoms (Vaginal Atrophy)



Figure 4. Findings Regarding the Effectiveness of Compounded Bioidentical Hormones on Treatment of Menopause Symptoms (VMS)



Findings on the Effectiveness of Fezolinetant on Treatment of Menopause Symptoms

Vasomotor symptoms

Fezolinetant is a nonhormone neurokinin 3 receptor antagonist that was approved in 2023 by the FDA for treatment of moderate-to-severe VMS due to menopause. This drug is indicated for women with a high risk or history of breast cancer or other hormonal dependent cancer that are very strongly recommended not to use hormone therapy due to its associated increased risk of breast cancer. Although there are other nonhormonal treatments for VMS, fezolinetant fills a gap for women in this group with moderate-to-severe VMS whose symptoms are not alleviated by other nonhormonal treatments.

In a systematic review and meta-analysis, Bonga et al., 2024 (5 RCTs; 2,168 subjects) included RCTs that compared fezolinetant to placebo for the treatment of menopause-associated VMS lasting for 12 weeks or longer. This meta-analysis reported that fezolinetant significantly reduced VMS frequency²⁶ (4 studies, n=860) and was significantly more

²⁴ Network meta-analysis is method for comparing multiple treatments (in this case drugs) by combining direct and indirect evidence of effectiveness.

²⁵ The change of FSFI and other female sexual function scores can be surrogate measures for the change of vaginal atrophy.

²⁶ VMS frequency was defined as the number of VMS, such as night sweats and hot flashes, experienced by postmenopausal women in a day.

likely to show a reduction of at least 75% in frequency of moderate-to-severe VMS compared with placebo (167/388 versus 81/385 participants) (3 studies; n=773).

Psychological symptoms

One meta-analysis reported that fezolinetant significantly improved menopause quality-of-life scores. Bonga et al., 2024 (5 RCTs; 2,168 subjects) reported significantly improved menopause quality-of-life scores relative to placebo (3 studies; n=773).

Sleep outcomes

In the Bonga et al., 2024, meta-analysis, two studies (685 subjects) evaluated sleep using the Patient Global Impression of Severity in Sleep Disturbance (PGI-C SD).²⁷ Improved PGI-C SD scores were significantly higher in the fezolinetant group (267/343) compared with the placebo group (204/342).

Summary of findings regarding the effectiveness of fezolinetant on treatment of menopause symptoms: There is a *preponderance of evidence* that fezolinetant is effective for treatment of VMS due to menopause based on one systematic review of five RCTs that compared it to placebo.

Figure 4. Findings Regarding the Effectiveness of Fezolinetant on Treatment of Menopause Symptoms



Findings on the Effectiveness of Ospemifene on Treatment of Menopause Symptoms

Ospemifene is a selective estrogen receptor modulator (SERM) that was approved in 2013 by the FDA for the treatment of vulvar and vaginal atrophy due to menopause, including moderate-to-severe symptoms of dyspareunia and/or vaginal dryness and physiological changes (parabasal cells, superficial cells, and pH).

In a systematic review and network meta-analysis, Simon et al., 2023 (44 RCTs; 12,637 participants) reported that ospemifene showed significant improvements in vaginal dryness compared to placebo and vaginal estradiol inserts and similar symptom relief compared to conjugated equine estrogens (CEE) vaginal cream (high and low doses²⁸), prasterone vaginal ovule (DHEA), and vaginal estrogen cream. The effects of ospemifene on dyspareunia (painful intercourse), ospemifene were similar to those of other active treatments — including CEE vaginal cream (high and low doses²⁹), DHEA, vaginal estradiol inserts, and vaginal estrogen cream — and compared to placebo.

In one RCT, Goldstein et al., 2019 (631 participants; ospemifene 316, placebo 315) reported that ospemifene significantly improved total scores for severe vaginal dryness from baseline to week 12, with significant improvement reported by 4 weeks.

The network meta-analysis (Simon et al., 2023) reported that ospemifene (60 mg) was associated with an increase in the risk of hot flashes versus placebo and DHEA 6.5 mg. There was no statistically significant difference in the risk of hot flashes associated with ospemifene 60 mg and other treatments.

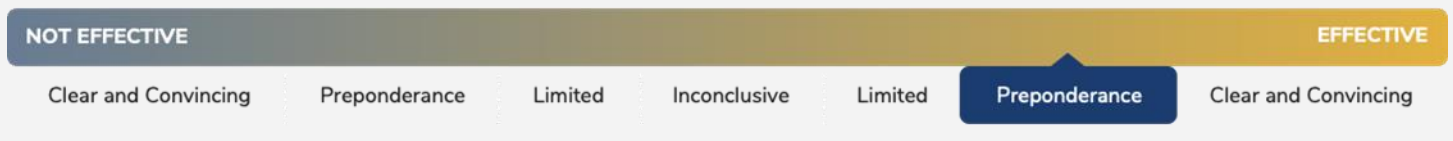
²⁷ Patients were asked to rate how well they were sleeping at that timepoint compared with the start of the study by using a scale ranging from 1 (much better) to 7 (much worse).

²⁸ CEE vaginal cream dosages were separated as low (twice weekly, 0.3–0.625 mg) and high doses (daily for 21 d, 7 d off, 0.3–1.25 mg)

²⁹ CEE vaginal cream dosages were separated as low (twice weekly, 0.3–0.625 mg) and high doses (daily for 21 d, 7 d off, 0.3–1.25 mg)

Summary of findings regarding the effectiveness of ospemifene on treatment of menopause symptoms: There is a *preponderance of evidence* that ospemifene improved symptoms of vaginal dryness and dyspareunia (painful intercourse) in menopausal women compared to placebo. Evidence suggests that the effects of ospemifene on dyspareunia (painful intercourse) and vaginal dryness are similar to those of other treatments including CEE vaginal cream (high and low doses³⁰), DHEA, estrogen vaginal inserts, and estrogen vaginal cream on scores of.

Figure 5. Findings Regarding the Effectiveness of Ospemifene on Treatment of Menopause Symptoms



Harms

Vaginal estrogen

Low-dose vaginal estrogen

A systematic review of low-dose vaginal estrogens using endometrial histology (Constantine et al., 2019; 20 RCTs; 2,983 unique women exposed to vaginal estrogen products for up to 1 year) reported no evidence of increased risk of endometrial hyperplasia or endometrial cancer with low-dose vaginal estrogen alone.

High-dose vaginal estrogen

CHBRP did not find any studies that reported harms or adverse effects of high-dose vaginal estrogen.

Compounded bioidentical hormones

As noted previously, NAMS, ACOG, and the FDA have raised concerns about inconsistency in doses of and consistency of estradiol and progesterone found in compounded forms of oral capsules and transdermal cream formulations (Stanczyk et al., 2019)

In a systematic review and meta-analysis of short-term (1-week to 1-year follow-up) use of compounded bioidentical hormones, Liu et al. (2022; 7 RCTs, 237 patients) reported that there are insufficient RCTs currently available to assess effects on clinical risk of breast cancer, endometrial cancer, or cardiovascular disease. Overall, the meta-analysis showed no significant adverse effects of compounded bioidenticals on lipid profile or glucose metabolism (including changes of total cholesterol, triglycerides, LDL or HDL, fasting glucose, insulin, or insulin resistance) compared with placebo. There was no change in endometrial thickness or serious adverse events (Liu et al., 2022; 19 RCTs; 1,373 patients).

Fezolinetant

Bonga et al., 2024, reported no significant difference between fezolinetant and placebo in liver function assessments (5 RCTs; 2,080 subjects). Meta-analyses Bonga et al., 2024 (5 RCTs; 2,168 subjects) and Rahman et al., 2023 (5 studies; 4,064 subjects) reported no significant difference in all adverse events or study dropouts due to treatment-ending adverse events (TEAEs) between fezolinetant and placebo. Rahman et al., 2023, reported no significant differences in endometrial hyperplasia/tumors (4 studies; 3,621 subjects) or uterine bleeding (4 studies; 3,707 subjects) compared to placebo.

Ospemifene

The Simon et al., 2023, network meta-analysis reported no statistically significant difference between ospemifene 60 mg and other tested therapies for most safety outcomes. There were no statistically significant differences in serious TEAEs between patients taking 60 mg ospemifene and other comparator treatments including CEE and DHEA 3.25,6.5, estrogen cream, vaginal estrogen insert. However, TEAE were significantly less likely to occur with estradiol capsules (4, 10, 25 µg)

and placebo than ospemifene. There were no cases of endometrial carcinoma or hyperplasia (12 studies), nor polyps with atypical hyperplasia (7 studies) or cancer in ospemifene trials (12 studies) at up to 52 weeks of treatment.

Clinical Practice Guidelines for Menopause Symptoms

Systemic hormonal therapy

In a 2022 evidence-based position statement, NAMS states that “Hormone therapy remains the most effective treatment for vasomotor symptoms (VMS) and the genitourinary syndrome of menopause (GSM) and has been shown to prevent bone loss and fracture. Hormone therapy risks depend on type, dose, duration of use, route of administration, timing of initiation, and whether a progestogen is used. For women aged younger than 60 years or who are within 10 years of menopause onset and have no contraindications, the NAMS states that the benefit-risk ratio is beneficial for treatment of VMS and prevention of bone loss. For women who initiate hormone therapy more than 10 years from menopause onset or who are aged older than 60 years, the NAMS states that the benefit-risk ratio is less advantageous because of the greater absolute risks of coronary heart disease, stroke, venous thromboembolism, and dementia” (NAMS, 2022).

The 2015 Endocrine Society clinical practice guidelines recommend women with a uterus who decide to undergo menopausal hormone therapy with estrogen and progestogen understand risks and benefits, including possible increased risk of breast cancer during and after discontinuing treatment. Transdermal estrogen therapy by patch, gel, or spray is recommended for women who request menopausal hormone therapy and have an increased risk of venous thromboembolism. Progestogen treatment is recommended to prevent uterine cancer for women taking estrogen for VMS relief but unnecessary for women who have undergone a hysterectomy. Low-dose vaginal estrogen therapy is recommended to treat women for GSM (Stuenkel et al., 2015).

Nonhormonal therapy

While systemic hormone therapy remains the most effective treatment for vasomotor symptoms and should be considered in menopausal women within 10 years of their menopause onset, NAMS also recommended the following nonhormone therapies: cognitive-behavioral therapy, clinical hypnosis, selective serotonin reuptake inhibitors/serotonin-norepinephrine reuptake inhibitors, gabapentin, fezolinetant (Level I); oxybutynin (Levels I-II); stellate ganglion block (Levels II-III) (NAMS, 2023) for women who want drugs to manage moderate-to-severe VMS, but don't want to take hormone therapy or have significant risk factors such as high risk or history of breast cancer that make hormone therapy inadvisable.

Summary of Findings

CHBRP relied on systematic reviews and clinical guidelines for findings regarding treatments for menopause symptoms that are already covered and are typically prescribed for menopause symptoms as standards of care backed by strong scientific evidence, as previously discussed in the clinical guidelines.

The medical effectiveness review includes findings from evidence on the effectiveness of high- and low-dose vaginal estrogens, compounded bioidentical hormones, and hormone-free therapies including fezolinetant and ospemifene. Hormone-free drugs may be appropriate for patients with significant risk factors including high risk or history of breast cancer or other estrogen dependent cancers that make hormone therapy inadvisable and therefore, alternate drugs are needed.

There is *clear and convincing evidence* that low-dose vaginal estrogen is an effective treatment for GSM (including dysuria, urgency and frequency of urination, recurrent UTIs, and urinary incontinence). Additionally, a systematic review reported no evidence of increased risk of endometrial hyperplasia or endometrial cancer with low-dose vaginal estrogen alone.

There is *limited evidence* that high-dose vaginal estrogen is effective at treating VMS. CHBRP did not find any studies that reported harms or adverse effects of high-dose vaginal estrogen.

There is *inconclusive evidence* that compounded bioidentical hormones are effective treatment for VMS based on two small studies. One study (n=90) reported significantly improved VMS in most patients at 1 year with topical progesterone therapy and another very small study (n=13) examining oral combined estrogen plus progesterone reported no significant symptom relief after 2 months, compared to placebo.

There is limited evidence based on five studies that compounded vaginal androgen improved vaginal atrophy symptoms.

However, NAMS and ACOG state that, because of the lack of FDA oversight and safety and efficacy concerns — including lack of standardization due to product-to-product variability — compounded bioidentical hormone therapy drugs should be reserved for patients with an allergy to an active pharmaceutical ingredient or inactive ingredient of a FDA-approved drug product or documented requirement for a different dosage form than available (ACOG, 2023).

There is a *preponderance of evidence* that fezolinetant is effective for treatment of VMS due to menopause based on seven RCTs. There were no reported significant differences in all adverse events or study dropouts due to treatment-ending adverse reactions.

There is a *preponderance of evidence* that ospemifene improved symptoms of dryness and dyspareunia (painful intercourse) in menopausal women compared to placebo. Evidence also suggests that the effects of ospemifene on dyspareunia (painful intercourse) and vaginal dryness are similar to the effects of CEE vaginal cream (high and low doses), DHEA, estrogen vaginal insert, and estrogen vaginal cream. There were no reported statistically significant differences between ospemifene 60 mg and other tested therapies for most safety outcomes. CHBRP also reviewed systematic reviews and clinical guidelines regarding other drugs used to treat menopause symptoms. These guidelines recommend hormone therapy (including but not limited to combination estrogen and hormone, combination estrogen and progestin, and estrogen-only drugs), low-dose antidepressants, anticonvulsants, drugs to prevent or treat osteoporosis, topical hormone therapy, and manufactured FDA-approved bioidentical hormones.

Benefit Coverage, Utilization, and Cost Impacts

As discussed in the *Policy Context* section, AB 2467 would mandate health plans and health policies regulated by DMHC or CDI to cover specific prescription drugs and therapeutic categories of drugs for the treatment of menopause symptoms. See Appendix D for examples of drugs in the categories listed in the Analytic Approach section below.

This section reports the potential incremental impacts of AB 2467 on estimated baseline benefit coverage, utilization, and overall cost.

Analytic Approach and Key Assumptions

To estimate the impact of AB 2467, if enacted, CHBRP assumes that DMHC-regulated plans and CDI-regulated policies would continue their current practice of covering prescription drugs for treatment of menopause symptoms. CHBRP assumes that AB 2467 would not require benefit coverage to be extended to every drug within the bill-specified therapeutic categories; therefore, CHBRP assumes that DMHC-regulated plans and CDI-regulated policies would be compliant postmandate if at least one example drug per therapeutic category is covered. CHBRP also acknowledges that these therapeutic categories and specific drugs treat different menopause symptoms and are not interchangeable (see *Background* section for more information).

In addition to commercial enrollees, 74% of enrollees associated with the California Public Employees' Retirement System (CalPERS) and 80% of Medi-Cal beneficiaries are enrolled in DMHC-regulated plans.³¹ As noted in the *Policy Context* section, AB 2467 would impact these CalPERS enrollees' and Medi-Cal beneficiaries' benefit coverage only if there is an existing outpatient pharmacy benefit. Almost all (96.2%) commercial/CalPERS enrollees have a pharmacy benefit regulated by DMHC or CDI that covers both generic and brand-name outpatient prescription drugs.³² Of the remaining commercial/CalPERS enrollees, 1.2% do not have a pharmacy benefit, while 2.6% have a pharmacy benefit that is not regulated by DMHC or CDI. For Medi-Cal beneficiaries in DMHC-regulated managed care plans, the pharmacy benefit is separate and administered by the Department of Health Care Services (DHCS) under the Medi-Cal Rx program; therefore, it is not subject to DMHC regulation. Because AB 2467 would not require creation of a pharmacy benefit, baseline benefit coverage for enrollees is compliant if they are either without a pharmacy benefit or the pharmacy benefit is not regulated by DMHC or CDI. Being compliant with AB 2467 at baseline does not necessarily mean that these Medi-Cal plans have a pharmacy benefit that includes coverage for treatments of menopause symptoms, as CHBRP did not survey DMHC-regulated Medi-Cal plans.

CHBRP restricts utilization estimates to women aged 40 to 64 years as the range around the average age of menopause at 51 (see *Background* section), and because CHBRP does not calculate estimates for the population covered under Medicare. CHBRP also assumes that prescribing will follow clinical guidelines and coverage for non-hormonal therapies will be limited to those who are not able to tolerate hormonal therapies (NAMS, 2023), with hormonal therapies remaining the main type of treatment.

In estimating the cost impacts of AB 2467, CHBRP assumes that DMHC-plans and CDI-policies with an outpatient pharmacy benefit will continue their current cost-sharing requirements, and that compliance with AB 2467 will require on-formulary coverage.

For further details on the underlying data sources and methods used in this analysis, please see Appendix C.

³¹ For more detail, see CHBRP's resource *Sources of Health Insurance in California*, available at www.chbrp.org/other-publications/resources.

³² For more detail, see CHBRP's resource *Pharmacy Benefit Coverage in State-Regulated Health Insurance*, available at www.chbrp.org/other-publications/resources.

Baseline and Postmandate Benefit Coverage

Below, Table 3 provides estimates of how many Californians have health insurance that would have to comply with AB 2467 in terms of benefit coverage.³³

Table 3. Impacts of AB 2467 on Benefit Coverage, 2025

| | Baseline | Postmandate | Increase/ Decrease | Percentage Change |
|---|------------|-------------|-----------------------|----------------------|
| Total enrollees with health insurance subject to state benefit mandates | 22,297,000 | 22,297,000 | 0 | 0.00% |
| Total enrollees with health insurance subject to AB 2467 | 22,297,000 | 22,297,000 | 0 | 0.00% |
| Total enrollees with health insurance subject to AB 2467 with a pharmacy benefit regulated by DMHC or CDI (a) | 13,162,000 | 13,162,000 | 0 | 0.00% |
| Enrollees with coverage for treatment of menopause symptoms that includes (b): | | | | |
| <u>On-formulary coverage for hormonal drug therapies:</u> | | | | |
| <i>Oral systemic</i> | | | | |
| Estrogen only | 100% | 100% | 0% | 0% |
| Progesterone only | 100% | 100% | 0% | 0% |
| Combination estrogen-hormone | 100% | 100% | 0% | 0% |
| <i>Topical systemic</i> | 100% | 100% | 0% | 0% |
| <i>Vaginal estrogen</i> | | | | |
| High dose - ring | 8% | 100% | 92% | 1132% |
| Low dose | 100% | 100% | 0% | 0% |
| Compounded bioidentical hormones | 91% | 100% | 9% | 10% |
| <u>On-formulary coverage for nonhormonal drug therapies:</u> | | | | |
| Fezolinetant | 7% | 100% | 93% | 1336% |
| Ospemifene | 13% | 100% | 87% | 665% |
| Low-dose antidepressants | 100% | 100% | 0% | 0% |
| Anticonvulsants | 100% | 100% | 0% | 0% |
| Drugs to prevent or treat osteoporosis | 100% | 100% | 0% | 0% |

Source: California Health Benefits Review Program, 2024.

Notes: (a) See CHBRP's resource Pharmacy Benefit Coverage in State-Regulated Health Insurance, available at <https://www.chbrp.org/other-publications/resources>. (b) Examples of drugs in these categories can be found in Appendix D.

Key: CDI = California Department of Insurance; DMHC = Department of Managed Health Care.

³³ For more detail, see CHBRP's resource, *Sources of Health Insurance in California*, available at www.chbrp.org/other-publications/resources.

At baseline, CHBRP estimates that 13,162,000 enrollees have DMHC-regulated or CDI-regulated coverage that includes an outpatient pharmacy benefit. Among hormonal therapies that CHBRP identified as treatments for menopause symptoms, an estimated 8% of enrollees in DMHC-regulated plans and CDI-regulated policies have coverage for the high dose ring form of vaginal estrogen. For nonhormonal therapies, 7% of enrollees in DMHC-regulated plans and CDI-regulated policies have coverage for fezolinetant, and 13% have coverage for ospemifene at baseline (see Table 3). For other drugs and categories, baseline coverage ranges from 91% to 100%, and would increase to or remain at 100% for all if AB 2467 were enacted (Table 3).

Baseline and Postmandate Utilization and Unit Cost

Below, Table 4 provides estimates of the impacts of AB 2467 on utilization as a covered benefit and unit cost of drugs and treatments for menopause symptoms.

Table 4. Impacts of AB 2467 on Utilization and Unit Cost, 2025

| | Baseline | Postmandate | Increase/ Decrease | Percentage Change |
|---|-----------|-------------|-----------------------|----------------------|
| Total enrollees that are women aged 40-64 with an outpatient drug benefit | 2,972,000 | 2,972,000 | 0 | 0.00% |
| Annual number of 30-day menopause prescriptions for women aged 40-64 | | | | |
| <u>Hormonal drug therapies</u> | | | | |
| High dose vaginal estrogen ring | 1,182 | 3,802 | 2,620 | 221.66% |
| Compounded bioidentical hormones | 77,073 | 82,595 | 5,522 | 7.16% |
| <u>Nonhormonal drug therapies</u> | | | | |
| Fezolinetant | 2,496 | 8,260 | 5,764 | 230.93% |
| Ospemifene | 1,054 | 3,028 | 1,974 | 187.29% |
| Average per unit cost | | | | |
| <u>Hormonal drug therapies</u> | | | | |
| High dose vaginal estrogen ring | \$145 | \$145 | \$0 | 0.00% |
| Compounded bioidentical hormones | \$243 | \$243 | \$0 | 0.00% |
| <u>Non-hormonal drug therapies</u> | | | | |
| Fezolinetant | \$337 | \$337 | \$0 | 0.00% |
| Ospemifene | \$168 | \$168 | \$0 | 0.00% |

Source: California Health Benefits Review Program, 2024.

Because CHBRP is concerned with estimating the marginal impact of AB 2467, the utilization analyses focuses on drugs and treatments for which enrollees in DMHC-regulated plans and CDI-regulated policies did not have 100% coverage at baseline. Utilization for the high-dose vaginal estrogen ring, fezolinetant, and ospemifene is expected to increase substantially as current utilization is nearly entirely as a noncovered benefit. Utilization of other drugs and treatments are expected to increase in proportion to the increase in benefit coverage (see Table 4).

CHBRP does not anticipate that the increases in utilization will affect the per-unit cost, postmandate. Per-unit costs range from \$145 for a high-dose vaginal estrogen ring to \$337 per unit for a fezolinetant prescription.

Baseline and Postmandate Expenditures

Below, Table 5 provides estimates of the impacts of AB 2467 on expenditures, which include premiums, enrollee cost sharing, and enrollee expenses for noncovered benefits.

Table 5. Impacts of AB 2467 on Expenditures, 2025

| | Baseline | Postmandate | Increase/ Decrease | Percentage Change |
|---|--------------------------|--------------------------|-----------------------|----------------------|
| Premiums | | | | |
| Employer-sponsored (a) | \$64,203,365,000 | \$64,206,270,000 | \$2,905,000 | 0.00% |
| CalPERS employer (b) | \$6,974,311,000 | \$6,974,651,000 | \$340,000 | 0.00% |
| Medi-Cal (excludes COHS) (c) | \$30,043,243,000 | \$30,043,243,000 | \$0 | 0.00% |
| Enrollee premiums | | | | |
| Enrollees, individually purchased insurance | \$20,751,015,000 | \$20,751,687,000 | \$672,000 | 0.00% |
| Outside Covered California | \$5,089,510,000 | \$5,089,670,000 | \$160,000 | 0.00% |
| Through Covered California | \$15,661,505,000 | \$15,662,017,000 | \$512,000 | 0.00% |
| Enrollees, group insurance (d) | \$20,397,418,000 | \$20,398,335,000 | \$917,000 | 0.00% |
| Enrollee out-of-pocket expenses | | | | |
| Cost sharing for covered benefits (deductibles, copays, etc.) | \$15,689,351,000 | \$15,690,433,000 | \$1,082,000 | 0.01% |
| Expenses for noncovered benefits (e) (f) | \$1,923,000 | \$0 | -\$1,923,000 | -100.00% |
| Total expenditures | \$158,060,626,000 | \$158,064,619,000 | \$3,993,000 | 0.0025% |

Source: California Health Benefits Review Program, 2024.

Notes: (a) In some cases, a union or other organization. Excludes CalPERS.

(b) Includes only CalPERS enrollees in DMHC-regulated plans. Approximately 51.6% are state retirees, state employees, or their dependents. About one in five of these enrollees has a pharmacy benefit not subject to DMHC.³⁴ CHBRP has projected no impact for those enrollees. However, CalPERS could, postmandate, require equivalent coverage for all its members (which could increase the total impact on CalPERS).

(c) Includes only Medi-Cal beneficiaries enrolled in DMHC-regulated plans. In addition, it seems likely that there would also be a proportional increase of \$0 for Medi-Cal beneficiaries enrolled in COHS managed care.

(d) Enrollee premium expenditures include contributions by enrollees to employer (or union or other organization)-sponsored health insurance, health insurance purchased through Covered California, and any contributions to enrollment through Medi-Cal to a DMHC-regulated plan.

(e) Includes only expenses paid directly by enrollees (or other sources) to providers for services related to the mandated benefit that are not covered by insurance at baseline. This only includes those expenses that will be newly covered postmandate. Other components of expenditures in this table include all health care services covered by insurance.

(f) For covered benefits, such expenses would be eliminated, although enrollees with newly compliant benefit coverage might pay some expenses if benefit coverage is denied (through utilization management review).

Key: CalPERS = California Public Employees' Retirement System; CDI = California Department of Insurance; COHS = County Organized Health Systems; DMHC = Department of Managed Health Care.

For DMHC-regulated plans and CDI-regulated policies, AB 2467 would increase total premiums and out-of-pocket expenses for covered benefits paid by employers and enrollees for newly covered benefits by \$5,916,000 (Table 5). Enrollee expenses for covered and/or noncovered benefits would decrease overall by \$1,923,000. This would result in an increase of total net annual expenditures for enrollees with DMHC-regulated plans and CDI-regulated policies of \$3,993,000 (0.0025%; Table 5).

³⁴ For more detail, see CHBRP's resource *Pharmacy Benefit Coverage in State-Regulated Health Insurance*, available at www.chbrp.org/other-publications/resources.

Premiums

At the end of this section, Table 6 and Table 7 present baseline and postmandate expenditures by market segment for DMHC-regulated plans and CDI-regulated policies. The tables present per member per month (PMPM) premiums, enrollee expenses for both covered and noncovered benefits, and total expenditures (premiums as well as enrollee expenses).

Changes in premiums as a result of AB 2467 would vary by market segment. Note that such changes are related to the number of enrollees (see Table 5, Table 6, and Table 7), with health insurance that would be subject to AB 2467.

Premiums are expected to increase among DMHC-regulated plans, ranging from \$0.0232 PMPM for individual plans to \$0.0312 PMPM for large group plans. Among CDI-regulated policies, premiums are expected to increase from \$0.0201 PMPM for individual plans to \$0.0269 PMPM for large-group plans.

For enrollees associated with CalPERS in DMHC-regulated plans, CHBRP estimates that premiums will increase by \$0.0381 PMPM.

For Medi-Cal beneficiaries enrolled in DMHC-regulated plans, CHBRP estimates no impact as these plans do not currently include an outpatient prescription drug benefit regulated by DMHC and therefore are currently compliant with AB 2467 at baseline.

Enrollee Expenses

AB 2467-related changes in cost sharing for covered benefits (deductibles, copays, etc.) and out-of-pocket expenses for noncovered benefits would vary by market segment. Note that such changes are related to the number of enrollees (see Table 5, Table 6, and Table 7) with health insurance that would be subject to AB 2467 expected to use prescription drugs and treatments for menopause symptoms during the year after enactment.

CHBRP projects no change to copayments or coinsurance rates but does project increases in utilization of some drugs (see Table 4) and therefore an increase in enrollee cost sharing. Increases in utilization of covered benefits are comprised of a combination of reductions in utilization that was paid for out of pocket at baseline that would be covered under AB 2467 postmandate combined with new utilization due to increased take-up with increases in coverage.

It is possible that some enrollees incurred expenses related to drugs and treatments for menopause symptoms for which coverage was denied, but CHBRP cannot estimate the frequency with which such situations occur and cannot estimate a calculation of the impact.

Enrollee expenses for cost sharing for covered benefits will increase overall by \$1,082,000, ranging from increases of \$0.0035 PMPM for enrollees in DMHC-regulated large group plans to \$0.0129 PMPM for enrollees in CDI-regulated small group policies. These increases will be offset by a \$1,923,000 decrease in out-of-pocket costs postmandate in aggregate, with decreases ranging from \$0.0096 PMPM for enrollees in CDI-regulated small group plans to \$0.0143 PMPM for DMHC-regulated CalPERS plans and policies. In aggregate, enrollee cost sharing for covered benefits is estimated to decrease by \$841,000 postmandate.

Postmandate Administrative Expenses and Other Expenses

CHBRP estimates that the increase in administrative costs of DMHC-regulated plans and/or CDI-regulated policies will remain proportional to the increase in premiums. CHBRP assumes that if health care costs increase as a result of increased utilization or changes in unit costs, there is a corresponding proportional increase in administrative costs. CHBRP assumes that the administrative cost portion of premiums is unchanged. All health plans and insurers include a component for administration and profit in their premiums.

Other Considerations for Policymakers

In addition to the impacts a bill may have on benefit coverage, utilization, and cost, related considerations for policymakers are discussed below.

Postmandate Changes in the Number of Uninsured Persons

Because the change in average premiums does not exceed 1% for any market segment (see Table 6 and Table 7), CHBRP would expect no measurable change in the number of uninsured persons due to the enactment of AB 2467.

Changes in Public Program Enrollment

CHBRP estimates that the mandate would produce no measurable impact on enrollment in publicly funded insurance programs due to the enactment of AB 2467.

How Lack of Benefit Coverage Results in Cost Shifts to Other Payers

CHBRP has found no other payers that would be affected by the enactment of AB 2467.

Table 6. Baseline Per Member Per Month Premiums and Total Expenditures by Market Segment, California, 2025

| | DMHC-Regulated | | | | | | CDI-Regulated | | | Total |
|---|-------------------------------------|-----------------|-----------------|-----------------------|---------------------------------|-----------------|--|-----------------|-----------------|--------------------------|
| | Commercial Plans (by Market) (a) | | | Publicly Funded Plans | | | Commercial Policies (by Market) (a) | | | |
| | Large Group | Small Group | Individual | CalPERS (b) | Medi-Cal (Excludes COHS) (c) | | Large Group | Small Group | Individual | |
| | | | | Under 65 | 65+ | | | | | |
| Enrollee counts | | | | | | | | | | |
| Total enrollees in plans/policies subject to state mandates (d) | 7,864,000 | 2,161,000 | 2,378,000 | 894,000 | 7,791,000 | 818,000 | 293,000 | 62,000 | 36,000 | 22,297,000 |
| Total enrollees in plans/policies subject to Ab 2467 | 7,864,000 | 2,161,000 | 2,378,000 | 894,000 | 0 | 0 | 293,000 | 62,000 | 36,000 | 13,688,000 |
| Premiums | | | | | | | | | | |
| Average portion of premium paid by employer (e) | \$527.59 | \$461.25 | \$0.00 | \$650.10 | \$263.09 | \$554.83 | \$585.36 | \$533.03 | \$0.00 | \$101,220,919,000 |
| Average portion of premium paid by enrollee | \$138.26 | \$193.80 | \$716.04 | \$133.99 | \$0.00 | \$0.00 | \$215.50 | \$174.12 | \$736.61 | \$41,148,433,000 |
| Total premium | \$665.85 | \$655.05 | \$716.04 | \$784.09 | \$263.09 | \$554.83 | \$800.87 | \$707.15 | \$736.61 | \$142,369,352,000 |
| Enrollee expenses | | | | | | | | | | |
| Cost sharing for covered benefits (deductibles, copays, etc.) | \$48.82 | \$146.52 | \$209.79 | \$56.41 | \$0.00 | \$0.00 | \$119.25 | \$246.95 | \$203.25 | \$15,689,351,000 |
| Expenses for noncovered benefits (f) | \$0.01 | \$0.01 | \$0.01 | \$0.01 | \$0.00 | \$0.00 | \$0.01 | \$0.01 | \$0.01 | \$1,923,000 |
| Total expenditures | \$714.68 | \$801.58 | \$925.84 | \$840.52 | \$263.09 | \$554.83 | \$920.13 | \$954.11 | \$939.87 | \$158,060,626,000 |

Source: California Health Benefits Review Program, 2024.

Notes: (a) Includes enrollees with grandfathered and nongrandfathered health insurance acquired outside or through Covered California (the state’s health insurance marketplace).

(b) Includes only CalPERS enrollees in DMHC-regulated plans. Approximately 51.6% are state retirees, state employees, or their dependents. About one in five of these enrollees has a pharmacy benefit not subject to DMHC.³⁵ CHBRP has projected no impact for those enrollees. However, CalPERS could, postmandate, require equivalent coverage for all its members (which could increase the total impact on CalPERS).

(c) Includes only Medi-Cal beneficiaries enrolled in DMHC-regulated plans. Includes those who are also Medicare beneficiaries.

(d) Enrollees in plans and policies regulated by DMHC or CDI. Includes those associated with Covered California, CalPERS, or Medi-Cal.³⁶

(e) In some cases, a union or other organization, or Medi-Cal for its beneficiaries.

(f) Includes only those expenses that are paid directly by enrollees (or other sources) to providers for services related to the mandated benefit that are not covered by insurance at baseline. This only includes those expenses that will be newly covered, postmandate. Other components of expenditures in this table include all health care services covered by insurance.

³⁵ For more detail, see CHBRP’s resource *Estimates of Pharmacy Benefit Coverage in State-Regulated Health Insurance*, available at <https://www.chbrp.org/other-publications/resources>.

³⁶ For more detail, see CHBRP’s resource *Sources of Health Insurance in California*, available at www.chbrp.org/other-publications/resources.

Key: CalPERS = California Public Employees' Retirement System; CDI = California Department of Insurance; COHS = County Organized Health Systems; DMHC = Department of Managed Health Care.

Table 7. Postmandate Change in Per Member Per Month Premiums and Total Expenditures by Market Segment, California, 2025

| | DMHC-Regulated | | | | | | CDI-Regulated | | | Total |
|---|-------------------------------------|----------------|------------|-----------------------|---------------------------------|----------|--|----------------|------------|--------------------|
| | Commercial Plans (by Market) (a) | | | Publicly Funded Plans | | | Commercial Policies (by Market) (a) | | | |
| | Large Group | Small Group | Individual | CalPERS (b) | Medi-Cal (Excludes COHS) (c) | | Large Group | Small Group | Individual | |
| | | | | Under 65 | 65+ | | | | | |
| Enrollee counts | | | | | | | | | | |
| Total enrollees in plans/policies subject to state mandates (d) | 7,864,000 | 2,161,000 | 2,378,000 | 894,000 | 7,791,000 | 818,000 | 293,000 | 62,000 | 36,000 | 22,297,000 |
| Total enrollees in plans/policies subject to AB 2467 | 7,864,000 | 2,161,000 | 2,378,000 | 894,000 | 0 | 0 | 293,000 | 62,000 | 36,000 | 13,688,000 |
| Premiums | | | | | | | | | | |
| Average portion of premium paid by employer (e) | \$0.0247 | \$0.0189 | \$0.0000 | \$0.0316 | \$0.0000 | \$0.0000 | \$0.0197 | \$0.0157 | \$0.0000 | \$3,245,000 |
| Average portion of premium paid by enrollee | \$0.0065 | \$0.0080 | \$0.0232 | \$0.0065 | \$0.0000 | \$0.0000 | \$0.0072 | \$0.0051 | \$0.0201 | \$1,589,000 |
| Total premium | \$0.0312 | \$0.0269 | \$0.0232 | \$0.0381 | \$0.0000 | \$0.0000 | \$0.0269 | \$0.0208 | \$0.0201 | \$4,833,000 |
| Enrollee expenses | | | | | | | | | | |
| Cost sharing for covered benefits (deductibles, copays, etc.) | \$0.0035 | \$0.0099 | \$0.0117 | \$0.0120 | \$0.0000 | \$0.0000 | \$0.0064 | \$0.0129 | \$0.0095 | \$1,082,000 |
| Expenses for noncovered benefits (f) | -\$0.0114 | -\$0.0118 | -\$0.0118 | -\$0.0143 | \$0.0000 | \$0.0000 | -\$0.0109 | -\$0.0118 | -\$0.0096 | -\$1,923,000 |
| Total expenditures | \$0.0233 | \$0.0250 | \$0.0231 | \$0.0358 | \$0.0000 | \$0.0000 | \$0.0224 | \$0.0219 | \$0.0200 | \$3,993,000 |
| Percent change | | | | | | | | | | |
| Premiums | 0.0047% | 0.0041% | 0.0032% | 0.0049% | 0.0000% | 0.0000% | 0.0034% | 0.0029% | 0.0027% | 0.0034% |
| Total expenditures | 0.0033% | 0.0031% | 0.0025% | 0.0043% | 0.0000% | 0.0000% | 0.0024% | 0.0023% | 0.0021% | 0.0025% |

Source: California Health Benefits Review Program, 2024.

Notes: (a) Includes enrollees with grandfathered and nongrandfathered health insurance acquired outside or through Covered California (the state's health insurance marketplace).

(b) Includes only CalPERS enrollees in DMHC-regulated plans. Approximately 51.6% are state retirees, state employees, or their dependents. About one in five of these enrollees has a pharmacy benefit not subject to DMHC.³⁷ CHBRP has projected no impact for those enrollees. However, CalPERS could, postmandate, require equivalent coverage for all its members (which could increase the total impact on CalPERS).

(c) Includes only Medi-Cal beneficiaries enrolled in DMHC-regulated plans. Includes those who are also Medicare beneficiaries.

(d) Enrollees in plans and policies regulated by DMHC or CDI. Includes those associated with Covered California, CalPERS, or Medi-Cal.³⁸

(e) In some cases, a union or other organization – or Medi-Cal for its beneficiaries.

(f) Includes only those expenses that are paid directly by enrollees (or other sources) to providers for services related to the mandated benefit that are not covered by insurance at baseline. This only includes those expenses that will be newly covered, postmandate. Other components of expenditures in this table include all health care services covered by insurance.

Key: CalPERS = California Public Employees' Retirement System; CDI = California Department of Insurance; COHS = County Organized Health Systems; DMHC = Department of Managed Health Care.

³⁷ For more detail, see CHBRP's resource *Pharmacy Benefit Coverage in State-Regulated Health Insurance*, available at www.chbrp.org/other-publications/resources.

³⁸ For more detail, see CHBRP's resource *Sources of Health Insurance in California*, available at www.chbrp.org/other-publications/resources.

Public Health Impacts

As discussed in the *Policy Context* section, AB 2467 would mandate coverage of specified hormone drug therapies (oral systemic, transdermal, vaginal estrogen, and compounded bioidentical hormones), and nonhormone drug therapies (fezolinetant, ospemifene, antidepressants, anticonvulsants, and medications to prevent or treat osteoporosis) for the treatment of menopause symptoms.

As presented in the *Medical Effectiveness* section, these therapeutic categories are effective in reducing the menopause symptoms for which they are FDA approved. There is limited evidence that compounded bioidentical hormones, which are not FDA-approved, are effective in managing vaginal atrophy; however, several medical societies recommend reserving compounded agents for women with allergies to commercially manufactured drug ingredients. The cautious recommendations are due to the lack of FDA oversight and standardization of compounded formulations that may result in prescription-to-prescription variability.

As presented in the *Benefit Coverage, Utilization, and Cost Impacts* section, there is 100% coverage at baseline among most of the bill-specific therapeutic categories. CHBRP projects that the categories with less than 100% coverage at baseline would result in an additional 15,880 (30-day) prescriptions being dispensed in the first year postmandate. These new prescriptions would include high-dose vaginal estrogen rings, hormone-free treatments (fezolinetant and ospemifene), and compounded bioidentical hormones. CHBRP estimates that the enrollees purchasing these newly covered prescriptions would see an out-of-pocket savings of about \$841,000.

Short-Term Public Health Impacts

Within the first year postmandate, CHBRP finds that AB 2467 would improve the health of the women receiving the 15,880 (30-day) prescriptions under new coverage (which might translate to ~1,323 women, assuming each received one prescription for 12 consecutive months). Health impacts include improved quality of life through reduction in genitourinary syndrome of menopause (GSM) symptoms (e.g., vaginal dryness, vulvovaginal atrophy, burning and itching during urination, and/or painful intercourse) and/or vasomotor symptoms (VMS) such as hot flashes/night sweats. As discussed in the *Background* section, VMS can cause or exacerbate sleep problems and memory/cognitive function. Furthermore, some women experiencing moderate-to-severe VMS may experience reduced productivity, capacity to work, and poorer work experience. Use of the newly covered drugs may improve sleep and memory/cognitive function as symptoms abate. Additionally, some of these women may experience improved productivity or presenteeism as their VMS subside (and sleep improves). Note that these women may also experience drug side effects, which may or may not influence decisions to continue the drug therapy.

The impact of AB 2467 on disparities in the treatment of symptoms is unknown among racial/ethnic groups and different socioeconomic groups in California.

Potential Harms from AB 2467

As described in the *Medical Effectiveness Harms* section, there is evidence of side effects and potential harms from drugs that treat menopause symptoms. However, **for FDA-approved drugs, there is evidence that the benefits of symptom relief outweigh the potential harms** (assuming the drugs are appropriately prescribed, and patients are monitored properly). **CHBRP is unable to project whether the benefits of compounded bioidentical hormonal treatments outweigh the potential harms due to limited evidence and clinical practice guidelines that generally recommend against the use of such treatments.**

Long-Term Impacts

In this section, CHBRP estimates the long-term impact of AB 2467 which CHBRP defines as impacts occurring beyond the first 12 months after implementation. These estimates are qualitative and based on the existing evidence available in the literature. CHBRP does not provide quantitative estimates of long-term impacts because of unknown improvements in clinical care, changes in prices, implementation of other complementary or conflicting policies, and other unexpected factors.

Long-Term Utilization and Cost Impacts

Utilization Impacts

CHBRP does not anticipate changes to utilization patterns that are markedly different beyond the first year postmandate.

Cost Impacts

CHBRP does not anticipate any additional changes postmandate that are different from the new levels of 100% coverage established under AB 2467. If a lower-cost option were to become available, DMHC-regulated plans and CDI-regulated policies would shift to covering those options and would potentially reduce overall costs. Additionally, if in the future DMHC-regulated Medi-Cal plans began including an outpatient pharmacy benefit, then any menopause drugs or categories not covered for this population at baseline would be required to be covered under AB 2467, resulting in associated cost increases.

Public Health Impacts

The long-term public health impacts (including disparities) of AB 2467 are expected to be similar to those described in the short-term impact section. Most bill-specified drug categories (where most prescriptions are concentrated) are already covered at baseline. Therefore, CHBRP anticipates that a limited number of women (especially those with high risk for or history of hormone-sensitive cancers) will continue to access the newly covered categories. These women would be expected to experience reductions in or abatement of moderate-to-severe vasomotor symptoms (VMS) and genitourinary syndrome of menopause (GSM) over the course of their treatment, which might last 4 to 12 years after they start menopause (Avis et al., 2015). These treatments rarely have negative long-term effects, so no population-level harms are expected in the long-term.

Non-bill related factors that influence treatment uptake would remain unaffected by AB 2467 including patient knowledge of menopause, and comfort or confidence in discussing bothersome symptoms with clinicians. Note that existing cost-sharing and utilization management protocols related to these therapeutic categories would still apply.

Appendix A. Text of Bill Analyzed

On February 23, 2024, the California Assembly Committee on Health requested that CHBRP analyze AB 2467.

AMENDED IN ASSEMBLY MARCH 4, 2024

California Legislature—2023–24 regular session

ASSEMBLY BILL

NO. 2467

Introduced by Assembly Member Bauer-Kahan

February 13, 2024

An act to add Section 1367.252 to the Health and Safety Code, and to add Section 10123.1962 to the Insurance Code, relating to ~~public health~~ health care coverage.

LEGISLATIVE COUNSEL'S DIGEST

AB 2467, as introduced, Bauer-Kahan—~~Menopause~~. Health care coverage for menopause.

Existing law, the Knox-Keene Health Care Service Plan Act of 1975, provides for the licensure and regulation of health care service plans by the Department of Managed Health Care and makes a willful violation of the act a crime. Existing law also provides for the regulation of health insurers by the Department of Insurance. Existing law sets forth specified coverage requirements for health care service plan contracts and health insurance policies.

This bill would require a health care service plan contract or health insurance policy, except for a specialized contract or policy, that is issued, amended, or renewed on or after January 1, 2025, to include coverage for treatment of perimenopause and menopause. Because a willful violation of these provisions by a health care service plan would be a crime, the bill would impose a state-mandated local program.

The California Constitution requires the state to reimburse local agencies and school districts for certain costs mandated by the state. Statutory provisions establish procedures for making that reimbursement.

This bill would provide that no reimbursement is required by this act for a specified reason.

~~Existing law establishes various programs to support the health of Californians, including programs to support the health of pregnant women, children, and older adults.~~

~~This bill would state the intent of the Legislature to enact legislation relating to menopause.~~

Vote: majority Appropriation: no Fiscal Committee: ~~no~~-yes Local Program: ~~no~~-yes

THE PEOPLE OF THE STATE OF CALIFORNIA DO ENACT AS FOLLOWS:

SECTION 1. Section 1367.252 is added to the Health and Safety Code, to read:

1367.252. A health care service plan contract, except for a specialized health care service plan contract, that is issued, amended, or renewed on or after January 1, 2025, shall include coverage for treatment of perimenopause and menopause that includes, but is not limited to, all of the following:

- (a) Hormone therapy, including, but not limited to, combination estrogen and hormone medicines, combination estrogen and progestin medicines, and estrogen-only medicines.
- (b) Low-dose antidepressants.
- (c) Anticonvulsants.
- (d) Vaginal estrogen.
- (e) Medications to prevent or treat osteoporosis.
- (f) Fezolinetant (Veozah) or other hormone-free options.
- (g) Topical hormone therapy.
- (h) Bioidentical hormones.

SEC. 2. Section 10123.1962 is added to the Insurance Code, to read:

10123.1962. A health insurance policy, except for a specialized health insurance policy, that is issued, amended, or renewed on or after January 1, 2025, shall include coverage for treatment of perimenopause and menopause that includes, but is not limited to, all of the following:

- (a) Hormone therapy, including, but not limited to, combination estrogen and hormone medicines, combination estrogen and progestin medicines, and estrogen-only medicines.
- (b) Low-dose antidepressants.
- (c) Anticonvulsants.
- (d) Vaginal estrogen.
- (e) Medications to prevent or treat osteoporosis.
- (f) Fezolinetant (Veozah) or other hormone-free options.
- (g) Topical hormone therapy.
- (h) Bioidentical hormones.

SEC. 3. No reimbursement is required by this act pursuant to Section 6 of Article XIII B of the California Constitution because the only costs that may be incurred by a local agency or school district will be incurred because this act creates a new crime or infraction, eliminates a crime or infraction, or changes the penalty for a crime or infraction, within the meaning of Section 17556 of the Government Code, or changes the definition of a crime within the meaning of Section 6 of Article XIII B of the California Constitution.

~~SECTION 1. It is the intent of the Legislature to enact legislation relating to menopause.~~

Appendix B. Literature Review Methods Specifications

This appendix describes methods used in the literature review conducted for this report.

Studies of the effects of vaginal estrogen (low dose for treatment of genitourinary syndrome of menopause [GSM] and high dose for treatment of vasomotor symptoms [VMS]), compounded bioidentical hormones, fezolinetant, and ospemifene that the bill addresses were identified through searches of PubMed, the Cochrane Library, Web of Science, the Cumulative Index of Nursing and Allied Health Literature (CINAHL). Websites maintained by the following organizations were also searched: the Agency for Healthcare Research and Quality (AHRQ), the National Institute for Health and Clinical Excellence (NICE), U.S. Preventive Services Task Force (USPSTF), World Health Organization (WHO), and the Scottish Intercollegiate Guideline Network. The search was limited to abstracts of studies published in English. The search was limited to studies published from 2019 to present. CHBRP's review of literature does not include treatments for the symptoms of menopause including hormonal therapy (including but not limited to combination estrogen and hormone, combination estrogen and progestin, and estrogen-only drugs), low-dose antidepressants, anticonvulsants, drugs to prevent or treat osteoporosis, and topical hormone therapy, because AB 2467 will not affect coverage for these drugs.

Reviewers screened the title and abstract of each citation retrieved by the literature search to determine eligibility for inclusion. The reviewers acquired the full text of articles that were deemed eligible for inclusion in the review and reapplied the initial eligibility criteria.

A total of 23 studies were included in the medical effectiveness review for AB 2467

Medical Effectiveness Evidence Grading System

In making a "call" for each outcome measure, the medical effectiveness lead and the content expert consider the number of studies as well as the strength of the evidence. Further information about the criteria CHBRP uses to evaluate evidence of medical effectiveness can be found in CHBRP's *Medical Effectiveness Analysis Research Approach*.³⁹ To grade the evidence for each outcome measured, the team uses a grading system that has the following categories:

- Research design;
- Statistical significance;
- Direction of effect;
- Size of effect; and
- Generalizability of findings.

The grading system also contains an overall conclusion that encompasses findings in these five domains. The conclusion is a statement that captures the strength and consistency of the evidence of an intervention's effect on an outcome. The following terms are used to characterize the body of evidence regarding an outcome:

- *Clear and convincing evidence* indicates that there are multiple studies of a treatment and that the *large majority* of studies are of high quality and consistently find that the treatment is either effective or not effective.
- *Preponderance of evidence* indicates that there are multiple studies of a treatment and that the *large majority* of studies are of high quality and consistently find that the treatment is either effective or not effective.

³⁹ Available at: www.chbrp.org/about/analysis-methodology/medical-effectiveness-analysis.

- *Limited evidence* indicates that the studies had limited generalizability to the population of interest and/or the studies had a fatal flaw in research design or implementation.
- *Inconclusive evidence* indicates that although some studies included in the medical effectiveness review find that a treatment is effective, a similar number of studies of equal quality suggest the treatment is not effective.
- *Insufficient evidence* indicates that there is not enough evidence available to know whether or not a treatment is effective, either because there are too few studies of the treatment or because the available studies are not of high quality. It does not indicate that a treatment is not effective.

Appendix C. Cost Impact Analysis: Data Sources, Caveats, and Assumptions

With the assistance of CHBRP's contracted actuarial firm, Milliman, the cost analysis presented in this report was prepared by the faculty and researchers connected to CHBRP's Task Force with expertise in health economics.⁴⁰ Information on the generally used data sources and estimation methods, as well as caveats and assumptions generally applicable to CHBRP's cost impact analyses are available at CHBRP's website.⁴¹

Analysis-Specific Data Sources

Current coverage of menopause treatment for commercial enrollees was determined by a survey of the largest (by enrollment) providers of health insurance in California. Responses to this survey represent approximately 14% of the CDI-regulated market and 65% of the DMHC-regulated market. Combined, responses to this survey represent 63% of enrollees in the privately funded market subject to state mandates. In addition, CalPERS was queried regarding related benefit coverage.

For this analysis, CHBRP relied on Current Procedural Terminology (CPT®) codes to identify relevant services: CPT copyright 2022 American Medical Association (AMA). All rights reserved. Fee schedules, relative value units, conversion factors, and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. CPT is a registered trademark of the AMA.

Health Cost Guidelines

The health cost guidelines (HCGs) are a health care pricing tool used by actuaries in many of the major health plans in the United States. The guidelines provide a flexible but consistent basis for estimating health care costs for a wide variety of commercial health insurance plans. It is likely that these organizations use the HCGs, among other tools, to determine the initial premium impact of any new mandate. Thus, in addition to producing accurate estimates of the costs of a mandate, we believe the HCG-based values are also good estimates of the premium impact as estimated by the HMOs and insurance companies.

The highlights of the commercial HCGs include:

- Specific major medical, managed care, and prescription drug rating sections and guidance with step-by-step rating instructions.
- Other helpful analysis resources, such as inpatient length of stay distribution tables, Medicare Severity-Adjusted Diagnosis Related Group (MS-DRG) models, and supplementary sections addressing EHBs and mandated benefits, experience rating, and individual and small-group rating considerations.
- Presentation of loosely and well-managed nationwide utilization and cost information by Milliman benefit-aligned service categories used throughout the Rating Structures — inpatient hospital services for both loosely and well-managed are also supported by DRG level utilization and cost benchmarks.
- Annual updates address emerging regulatory considerations such as health care reform and mental health parity requirements.
- Annually updated benefit descriptions used in the HCG service categories.

⁴⁰ CHBRP's authorizing statute, available at https://chbrp.org/about_chbrp/index.php, requires that CHBRP use a certified actuary or "other person with relevant knowledge and expertise" to determine financial impact.

⁴¹ See method documents posted at <https://www.chbrp.org/about/analysis-methodology/cost-impact-analysis.php>; in particular, see Cost Analyses: Data Sources, Caveats, and Assumptions.

- Annually updated medical trend assumptions and considerations.
- Presentation of two sets of nationwide area factors to facilitate development of area-specific claim costs, including separate utilization and charge level factors by type of benefit, state and Metropolitan Statistical Area for first-dollar coverage, and composite factors by deductible amount.
- Claim Probability Distributions (CPDs) by type of coverage that contain distributions of claim severity patterns for unique combinations of benefits and member types (adult, child, composite member).
- The Prescription Drug Rating Model (RXRM), an automated rating tool that provides a detailed analysis of prescription drug costs and benefits.

Consolidated Health Cost Guidelines Sources Database

Milliman maintains benchmarking and analytic databases that include health care claims data for nearly 60 million commercial lives and over 3 million lives of Medicaid managed care data. This dataset is routinely used to evaluate program impacts on cost and other outcomes.

Detailed Cost Notes Regarding Analysis-Specific Caveats and Assumptions

The analytic approach and key assumptions are determined by the subject matter and language of the bill being analyzed. As a result, analytic approaches may differ between topically similar analyses, and therefore the approach and findings may not be directly comparable.

Methodology and Assumptions for Baseline Benefit Coverage

- The population subject to the mandated offering includes individuals covered by DMHC-regulated commercial insurance plans, CDI-regulated policies, and CalPERS plans subject to the requirements of the Knox-Keene Health Care Service Plan Act.
- CHBRP assumes that the bill will have no impact on plans without an outpatient prescription drug benefit or whose outpatient prescription drug benefit is not regulated by DMHC or CDI and as such, these plans have not been considered in the analysis. Approximately 40% of enrollees are excluded from the analysis due to not having an outpatient drug benefit. This comprises all Medi-Cal enrollees, approximately 20% of CalPERS enrollees, and approximately 3% of enrollees in other commercial plans with no outpatient prescription drug benefit.
- CHBRP assumes additional utilization due to the enactment of this bill will occur amongst women aged 40 to 64, as this is the age range where women are expected to seek treatment for naturally occurring menopause. This assumption was confirmed by the content expert.
- CHBRP surveyed the carriers to determine the percentage of the population with on-formulary coverage for various treatments of menopause symptoms. The types of treatments included in the survey were consistent with those listed in the bill language for AB 2467, with the following adjustments:
 - CHBRP added ospemifene to the list of specific drugs since this is a treatment option for genitourinary syndrome of menopause (GSM) symptoms that does not fit into any of the therapeutic categories listed in the bill language for AB 2467.
 - CHBRP expanded certain treatment categories where different treatments within the categories have different indications.
 - Some treatment categories listed in the bill language are already covered on-formulary. CHBRP assumes that coverage is compliant with AB 2467 if at least one drug in the listed category is covered on-formulary by the carriers' plans. Therefore, CHBRP only modeled select treatment types with anticipated coverage changes resulting from AB 2467. The list of treatments considered in the analysis is shown in the table below.

Table 8. Treatments Considered in the Cost Impact Analysis for AB 2467

| Treatment | Included in AB 2467 Bill Language |
|--|---|
| On-formulary coverage for hormonal drug therapies | |
| Oral systemic | |
| Estrogen only | Yes |
| Progesterone only | Yes |
| Combination estrogen-hormone | Yes |
| Topical systemic | Yes |
| Vaginal estrogen | |
| High dose ring | Yes. Expanded from vaginal estrogen category since this is a different form of treatment compared to other vaginal estrogen treatments and is used to treat hot flashes in addition to vaginal dryness. |
| Low dose | Yes. Expanded from vaginal estrogen category. |
| Compounded bioidentical hormones | Yes. AB 2467 mandates coverage of bioidentical hormones. CHBRP’s analysis considers compounded bioidentical hormones separately since manufactured bioidentical hormones are already included in the other treatment categories considered. |
| On-formulary coverage for non-hormonal drug therapies | |
| Fezolinetant | Yes |
| Ospemifene | No. CHBRP anticipates coverage for ospemifene would expand as a result of this legislation, since it is a treatment for GSM symptoms. |
| Low-dose antidepressants | Yes |
| Anticonvulsants | Yes |
| Medications to prevent or treat osteoporosis | Yes |

Source: California Health Benefits Review Program, 2024.

Methodology and Assumptions for Baseline Utilization

On-formulary coverage for the treatment of menopause symptoms

- Baseline utilization (measured as the number of scripts) was only estimated for treatments where less than 100% of enrollees have coverage premandate. For treatments where 100% of enrollees have coverage, CHBRP assumes that there is no cost or utilization impact postmandate. Enrollees with coverage are those with health insurance subject to AB 2467 with an outpatient prescription drug benefit regulated by DMHC or CDI.
- Baseline utilization for high dose vaginal estrogen and ospemifene was estimated using Milliman’s proprietary 2022 Consolidated Health Cost Guidelines™ Sources Database (CHSD). The data was limited to California commercial enrollees.
 - Fezolinetant and compounded bioidentical hormones:

- The content expert estimated that 1% of women seeking treatment for menopause symptoms would use fezolinetant and that 10 to 20% of women seeking treatment for menopause symptoms are currently using compounded bioidentical hormones. CHBRP assumed that for enrollees with coverage, the utilization of hormone treatments observed in the claims data for women aged 40 to 64 represents 89% of total utilization, with the remaining 11% being made up of fezolinetant (1%) and compounded bioidentical hormones (10%).
 - Fezolinetant: CHBRP assumed no baseline utilization of this drug since it is a new drug that was approved for medical use in 2023 and is not currently on-formulary for any of the carriers CHBRP surveyed. The utilization assumption provided by the content expert is used to estimate postmandate utilization of this drug.
 - Compounded bioidentical hormones: Since there are no specific national drug codes (NDCs) assigned to compounded bioidentical hormones, it is not straightforward to identify them in claims data and as such, the content expert's estimate was used. Baseline utilization is calculated for the proportion of enrollees that have coverage according to the carrier survey responses (91% of enrollees).
- Utilization was trended to 2025 at 1.6% per year. This trend is based on the 2023 Milliman Health Cost Guidelines.

Utilization of mandated treatments for noncovered benefits

- CHBRP assumed that women aged 40 to 64 without coverage for treatment of menopause symptoms utilize treatments at 25% of the rate of women who do have coverage, based on an estimate provided by the content expert. The content expert's estimate represents an average for all treatments for menopause symptoms but the actual utilization for noncovered benefits will vary by treatment effectiveness and cost.

Methodology and Assumptions for Baseline Cost

- CHBRP used Milliman's proprietary 2022 CHSD to calculate the cost per script for high dose vaginal estrogen rings and ospemifene. Although the vaginal estrogen rings are typically used for 90 days at a time, the cost per script has been adjusted to reflect a 30-day time period for consistency with other treatments considered in the analysis.
 - CHBRP assumed a \$562 cost per script (gross of rebates) for fezolinetant based on feedback collected in the carrier surveys.
 - The cost per script for compounded bioidenticals of \$243 was calculated by using the ratio of the cost of compounded bioidentical hormones to the "average price of FDA-approved postmenopausal hormone therapy prescriptions" based on results from a 2017 national survey⁴². The ratio of \$88 to \$49 was applied to the average cost per script of treatments for menopause symptoms from the 2022 claims data and trended to 2025.
 - The average cost per script was trended to 2025 using a 4.0% annual trend. This trend is based on the 2023 Milliman Health Cost Guidelines.
 - The average cost per script (gross of rebates) for noncompounded brand drugs was reduced by 40% to reflect rebate payments from pharmaceutical manufacturers. Actual rebate payments are proprietary and the 40% estimate reflects the average observed rebate percentage observed in the Milliman Health Cost Guidelines for brand drugs. No rebate adjustment was applied to the cost of compounded bioidentical hormones since these are not considered brand drugs.

Methodology and Assumptions for Baseline Cost Sharing

- CHBRP assumed the cost sharing for treatments for menopause symptoms is the same as major medical cost sharing. Major medical cost sharing was estimated based on metal tier actuarial values and sample plans. Cost

⁴² The Use of Compounded Bioidentical Hormone Therapy - The Clinical Utility of Compounded Bioidentical Hormone Therapy - NCBI Bookshelf (nih.gov)

sharing for CalPERS plans was assumed to be the same as the average cost sharing for large group commercial plans.

- CHBRP assumes that any enrollee who does not have on-formulary coverage for a particular product would pay 100% of the average cost per script (prior to rebates) at baseline.

Methodology and Assumptions for Postmandate Utilization

- CHBRP assumed the utilization rate for enrollees with coverage postmandate is equal to the utilization rate for enrollees with coverage at baseline.
- CHBRP assumed that increased coverage of fezolinetant and compounded bioidentical hormones would not lead to a reduction in utilization of other hormone treatments that are covered at baseline. This assumption is based on information provided by the content expert:
 - Per the content expert, fezolinetant is a hormone-free treatment that is less effective than the available hormone treatments. Fezolinetant is targeted at a smaller subset of women who are unable to take hormone treatments (for example, women who have a history of cancer) or those who do not want to take hormone treatments. The content expert does not expect that fezolinetant coverage will replace existing utilization of hormone treatments.
 - The content expert does not expect that increased coverage of compounded bioidentical hormones will replace utilization of other hormone treatments since these drugs are not FDA-approved.
- CHBRP assumed that on-formulary utilization of fezolinetant would comprise 1% of the total postmandate hormone treatments for menopause symptoms, per the content expert.

Methodology and Assumptions for Postmandate Cost

- CHBRP assumed the average cost per script would not change as a result of AB 2467.

Methodology and Assumptions for Postmandate Cost Sharing

- CHBRP assumed the average cost sharing per script for enrollees with coverage would be the same postmandate as baseline. Total cost sharing will increase to the extent that total utilization will increase but cost sharing per script will remain the same.

Determining Public Demand for the Proposed Mandate

CHBRP reviews public demand for benefits by comparing the benefits provided by self-insured health plans or policies (which are not regulated by the DMHC or CDI and therefore not subject to state-level mandates) with the benefits that are provided by plans or policies that would be subject to the mandate.

Among publicly funded self-insured health insurance policies, the preferred provider organization (PPO) plans offered by CalPERS have the largest number of enrollees. The CalPERS PPOs currently provide benefit coverage similar to what is available through group health insurance plans and policies that would be subject to the mandate.

To further investigate public demand, CHBRP used the bill-specific coverage survey to ask plans and insurers who act as third-party administrators for (non-CalPERS) self-insured group health insurance programs whether the relevant benefit coverage differed from what is offered in group market plans or policies that would be subject to the mandate. The responses indicated that there were no substantive differences.

Second-Year Impacts on Benefit Coverage, Utilization, and Cost

CHBRP has considered whether continued implementation during the second year of the benefit coverage requirements of AB 2467 would have a substantially different impact on utilization of either the tests, treatments, or services for which coverage was directly addressed, the utilization of any indirectly affected utilization, or both. CHBRP reviewed the literature and consulted content experts about the possibility of varied second-year impacts and determined the second year's impacts of AB 2467 would be substantially the same as the impacts in the first year (see Table 5, Table 6, and Table 7. Minor changes to utilization and expenditures are due to population changes between the first year postmandate and the second year postmandate.

Appendix D. Examples of Treatments for Menopause Symptoms

Table 9. Drug Therapy for Menopause Symptoms and Conditions Associated with Menopause by Therapeutic Category

| Hormonal Drug Therapy |
|---|
| Oral systemic |
| Estrogen only <ul style="list-style-type: none"> • Estradiol* (Estrace, generics) • Conjugated estrogens (Premarin) • Esterified estrogen (Menest) |
| Progesterone only <ul style="list-style-type: none"> • Progesterone (Prometrium, generics) • Medroxyprogesterone (Provera, generics) |
| Combination estrogen-progesterone <ul style="list-style-type: none"> • Conjugated estrogens and medroxyprogesterone (Premphase and Prempro) • Estradiol and norethindrone acetate (Activella, Amabelz, Lopreeza, Mimvey, generic) • Estradiol drospirenone (Angeliq) • Estradiol and progesterone* (Bijuva) |
| Combination Estrogen and SERM <ul style="list-style-type: none"> • Conjugated/equine estrogen and bazedoxifene (Duavee) |
| Combination Estrogen and Androgens <ul style="list-style-type: none"> • Esterified estrogen and methyltestosterone (Covaryx, Covaryx HS, EEMT, EEMT HS, Est Estrogen-Methyltest DS, Est Estrogen-Methyltest HS) |
| Topical systemic |
| Estrogen only <ul style="list-style-type: none"> • Estradiol gel/cream* (Divigel, Elestrin, Estrogel) • Estradiol spray* (Evamist) |
| Progesterone only <ul style="list-style-type: none"> • Progesterone gel (Crinone) |
| Transdermal systemic |
| Estrogen only <ul style="list-style-type: none"> • Estradiol patch* (Alora, Estradot, Climara, MiniVelle, Oesclim, Menostar, Dotti, Lyllana, generics) |
| Combination estrogen-progesterone <ul style="list-style-type: none"> • Estradiol and levonorgestrel (Climara Pro) • Estradiol and norethindrone (CombiPatch) |

Vaginal high-dose systemic (one FDA-approved ring)

Estrogen only

- Estradiol acetate ring* (Femring)

Vaginal low-dose local (cream, tablet, insert, ring)

Estrogen only

- Estradiol ring* (Estring)
- Estradiol cream* (Estrace)
- Conjugated/equine estrogen cream (Premarin)
- Estradiol vaginal insert* (Imvexxy)
- Estradiol vaginal tablets* (Vagifem, Yuvafem)

Compounded bioidentical hormones (oral, topical, and vaginal) – Non-FDA–approved products

Nonhormonal Drug Therapy

Neurokinin 3 (NK3) receptor antagonist

Fezolinetant (Veozah)

Selective estrogen receptor modulator (SERM)

Ospemifene (Osphena)

Antidepressants

Selective Serotonin Reuptake Inhibitors (SSRIs)

- Paroxetine (Brisdelle, Paxil)
- Escitalopram (Lexapro)
- Citalopram (Celexa)
- Fluoxetine (Prozac)
- Sertraline (Zoloft)
- Fluvoxamine (Luvox)

Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)

- Venlafaxine (Effexor)
- Desvenlafaxine (Pristiq)

Anticonvulsants

GABA analog

- Gabapentin (Neurontin)
- Pregabalin (Lyrica)

Drugs to prevent or treat bone loss

Bisphosphonates

- Alendronate (Fosomax)
- Risedronate (Actonel, Atyelvia)
- Ibandronate (Boniva)
- Zoledronic acid (Reclast)

Selective estrogen receptor modulators (SERMs)

- Reloxifene (Evista)

Synthetic parathyroid hormone

- Teriparatide (Forteo)
- Abaloparatide (Tymlos)

Monoclonal antibodies

- Denosumab (Prolia and Xgeva)

Calcitonin (Miacalcin, Fortical)

Source: California Health Benefits Review Program, 2024.

Note: *Denotes manufactured FDA-approved bioidentical hormone.

References

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A group of faculty, researchers, and staff complete the analysis that informs California Health Benefits Review Program (CHBRP) reports. The CHBRP **Faculty Task Force** comprises rotating senior faculty from University of California (UC) campuses. In addition to these representatives, there are other ongoing researchers and analysts who are **Task Force Contributors** to CHBRP from UC that conduct much of the analysis. The **CHBRP staff** coordinates the efforts of the Faculty Task Force, works with Task Force members in preparing parts of the analysis, and manages all external communications, including those with the California Legislature. As required by CHBRP's authorizing legislation, UC contracts with a certified actuary, **Milliman**, to assist in assessing the financial impact of each legislative proposal mandating or repealing a health insurance benefit.

The National Advisory Council provides expert reviews of draft analyses and offers general guidance on the program to CHBRP staff and the Faculty Task Force. CHBRP is grateful for the valuable assistance of its National Advisory Council. CHBRP assumes full responsibility for the report and the accuracy of its contents.

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CHBRP assumes full responsibility for the report and the accuracy of its contents. All CHBRP bill analyses and other publications are available at www.chbrp.org.

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