CALIFORNIA
HEALTH BENEFITS REVIEW PROGRAM

Analysis

California Senate Bill 1191 Medi-Cal: Pharmacogenomic Testing

Summary to the 2021–2022
California State Legislature
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SUMMARY

The California Senate Committee on Health requested that the California Health Benefits Review Program (CHBRP) conduct an evidence-based assessment of California Senate Bill (SB) 1191, Pharmacogenomic Testing as amended on March 16th and April 19th. SB 1191 would require Medi-Cal coverage of pharmacogenomic testing for new and currently used medications with a clinically actionable pharmacogenomic association identified by the U.S. Food and Drug Administration (FDA) or a Clinical Pharmacogenetics Implementation Consortium (CPIC) recommendation of A, A/B, or B.

Background on Pharmacogenomics.

Pharmacogenomics (sometimes called pharmacogenetics) is the study of how genes affect a person's response to medications. Because every person's genes are unique, depending on one's genetic makeup, the effectiveness of drug therapies may vary across individuals. There are different types of pharmacogenomic testing, including (1) necessary pharmacogenomic testing for one specific drug (known as a companion diagnostic), (2) pharmacogenomic testing for a specific gene-drug pair but not a required companion diagnostic, (3) pharmacogenomic multigene panel tests to evaluate metabolic response to a medication, and (4) preemptive testing using multigene panels[1] across genes-drugs. Preemptive testing can be done before a provider and patient are considering a specific medication, or before a provider and patient are considering any medication. Because the genes relevant to pharmacogenomic testing do not change over time, the testing would only need to be completed once and the results would be accessible within a patient's medical records.

More recently, the use of pharmacogenomics in conjunction with a comprehensive medication management program has been shown to help identify medication appropriateness, improve adherence, and reduce adverse reactions in a more comprehensive way than either of these approaches can alone.

More than 90% of patients are thought to carry at least one genetic variant that should prompt a change in dosing or medication if certain medications are prescribed.

Pharmacogenomic testing is a type of biomarker test and is performed using a cheek swab or blood sample, which is then sent to a laboratory for analysis. There are two major sources of pharmacogenomic testing recommendations: The FDA and the CPIC.

Effectiveness, Clinical Utility, and Cost-Effectiveness of Pharmacogenomic Testing.

Evidence on the effectiveness and clinical utility of pharmacogenomic testing varies significantly across conditions. Some studies have found that pharmacogenomic testing leads to changes in medications and a reduction in hospital admissions. While the studies identified by CHBRP show that pharmacogenomic testing may result in changes to medication for some patients, especially to prevent adverse reactions, most patients who receive pharmacogenomic testing remain on their previously prescribed medication regimen.

Similarly, there is some evidence that the use of pharmacogenomic testing for specific types of diseases is cost-effective, but this varies significantly by disease, treatment, and outcomes assessed. However, systematic reviews have also described the weakness of the literature as having insufficient sensitivity analyses, heterogeneity in study designs and populations, and low quality of data and methodologies utilized.

Relevant Populations.

If enacted, SB 1191 would apply to the Medi-Cal coverage of approximately 9,747,000 beneficiaries (25% of all Californians) in 2023. This represents Californians who will access benefits through Medi-Cal, including

[1] Multigene panels allow simultaneous testing of at least two genes, and could include more than 150 genes.

beneficiaries enrolled in Department of Managed Health Care (DMHC)-regulated Medi-Cal managed care plans, beneficiaries enrolled in County Organized Health Systems (COHS), and enrollees accessing full-scope benefits through the fee-for-service program administered by the Department of Health Care Services (DHCS).

Benefit Coverage.

Broadly speaking, all beneficiaries with health insurance subject to SB 1191 have coverage for biomarker testing,[2] including pharmacogenomic testing, that is supported by medical and scientific evidence and is determined medically necessary. Pharmacogenomic testing can be performed before a beneficiary begins taking a medication with a companion diagnostic indication (as listed by the FDA); before a beneficiary begins taking — or concurrently with — a medication with a significant biomarker reference in the FDA drug label; as a panel; or preemptively. However, according to subject matter experts, pharmacogenomic testing is not as commonly performed preemptively as compared to the other reasons for testing. Because SB 1191 would clarify existing benefit coverage, it would, in essence, act as a new benefit coverage mandate.

Utilization and Expenditure Impacts.

Approximately 30% of Medi-Cal beneficiaries use medications with a clinically actionable FDA-identified pharmacogenomic association or CPIC A, A/B, or B recommendation at baseline. Of these beneficiaries, 0.9% (25,900 beneficiaries) received a test at baseline. This equates to approximately 0.3% of the total Medi-Cal population receiving pharmacogenomic testing.

Additionally, approximately 16,500 (64%) beneficiaries receive one single-gene test on one day, 9,100 (35%) beneficiaries receive multiple single-gene tests on one day, and 3,400 (13%) beneficiaries receive at least one multigene panel test on a one day. Some beneficiaries may receive both multigene panels and single-gene tests on one day, or across multiple days, and therefore will be present in multiple categories.

Due to the clarification of existing Medi-Cal coverage policies, CHBRP assumes there would be an increase in utilization for some pharmacogenomic testing. CHBRP has assumed utilization of pharmacogenomic tests would increase from 0.3% of the population to 0.8% of the population. Among beneficiaries using medications with a clinically actionable pharmacogenomic association, utilization would increase from 0.9% at baseline to 2.6% postmandate. This increase in utilization would result in an additional 51,900 beneficiaries receiving pharmacogenomic testing postmandate.

To estimate potential impacts of SB 1191, CHBRP provides three scenarios:

- Scenario 1: Utilization of pharmacogenomic testing would increase because of clarification of existing benefit coverage; billing patterns would remain the same as at baseline (i.e., single-gene vs. multigene panel tests).
- Scenario 2: Utilization of pharmacogenomic testing would increase because of clarification of existing benefit coverage; multiple single-gene tests billed on the same day would be billed as ONE multigene panel test postmandate.
- Scenario 3: Utilization of pharmacogenomic testing would increase because of clarification of existing benefit coverage; multiple single-gene tests billed on the same day would be billed as *multiple* multigene panel tests postmandate (a one-to-one transfer of single-gene tests to multigene panel tests).

Total expenditure increases for each scenario are:

- Scenario 1: Total expenditures would increase by almost $22,000,000 (0.07%) due to new utilization. Per member per month (PMPM), Medi-Cal premiums would increase by $0.19 (0.07%).
- Scenario 2: Total expenditures would increase by almost $18,000,000 (0.06%) due to new utilization and a shift in

[2] Biomarker tests are a way to measure and quantify biomarkers, which are characteristics that can be measured to specify normal or abnormal health processes or to indicate a condition or disease.

billing practices. PMPM, Medi-Cal premiums would increase by $0.15 (0.06%)

- Scenario 3: Total expenditures would increase by more than $54,000,000 (0.18%) due to new utilization and a shift in billing practices. PMPM, Medi-Cal premiums would increase by $0.46 (0.18%). Approximately 60% of the increase in expenditures is due to changes in billing practices, and 40% of the increase in expenditures is due to the increase in utilization.

As discussed in this analysis, several studies have found that pharmacogenomic testing can lead to offsets, including a reduction in emergency room utilization, unplanned hospital admissions, and outpatient visits. While other studies have found that for most patients who receive pharmacogenomic testing, no changes are made to their medications. Due to insufficient evidence, CHBRP is unable to project offsets as a result of SB 1191.

Public Health Implications.

CHBRP projects no measurable public health impact at the population level due to the increase in utilization for a relatively small number of beneficiaries and indeterminate offsets. However, SB 1191 may yield individual-level health improvements for beneficiaries with reduced utilization of other health care services such as emergency room visits, unplanned hospital admissions, and outpatient visits.

There is also no measurable impact on disparities identified in pharmacogenomic testing, including disparities by race and ethnicity, age, and socioeconomic status, despite an estimated utilization increase. Additionally, studies have suggested that clinician barriers — including familiarity with guidelines and knowledge of best practices for use of biomarker testing, expertise in genomic testing, or access to a multidisciplinary specialty team — impact whether patients receive testing. There is literature indicating that disparities could widen inequities in utilization of pharmacogenomic testing if not specifically addressed.

Long-Term Implications.

CHBRP assumes it is likely DMHC-regulated Medi-Cal managed care plans, COHS, and DHCS will continue to incorporate new clinical guidelines and practice standards as they become available in future years. As noted previously, some evidence suggests that pharmacogenomic testing is cost-effective, which could contribute to offsets in health care expenditures or improved quality of life for beneficiaries. Additionally, prescribing practices of providers, including pharmacists, could shift towards requiring pharmacogenomic testing prior to prescribing common medications, such as ibuprofen and codeine. This would contribute to greater utilization over time.

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BACKGROUND ON PHARMACOGENOMIC TESTING

Senate Bill (SB) 1191 would require Medi-Cal coverage for a subtype of biomarker testing, pharmacogenomics, when a medication is being considered for use, or is already being administered, in treating a Medi-Cal beneficiary's condition and is known to have a gene-drug or drug-drug-gene interaction that has been demonstrated to be clinically actionable. This section provides an overview of pharmacogenomic testing and how it is used for treatment decisions in clinical practice.

Biomarker Testing

A *biomarker* is a characteristic that can be measured to specify normal or abnormal health processes or to indicate a condition or disease. These measurements can also be used to determine the effects a treatment is having on a patient. Examples of biomarkers are varied and include measures such as blood pressure and heart rate; basic metabolic studies such as HbA1c; x-ray findings; and complex histologic values examining genes, proteins, or other molecules that may be a sign of a disease (FDA-NIH, 2016). Biomarkers can be categorized as molecular, histologic, radiographic, or physiologic (e.g., blood glucose is a molecular characteristic, while blood pressure is physiologic) (FDA-NIH, 2016; IOM, 2010).

Biomarker tests are a way to measure and quantify biomarkers. Nonphysiologic tests are often done in a laboratory using samples of blood, tissue, or other clinical samples to quantify and evaluate the biomarker. In recent years, biomarker testing has been used in the expansion of precision medicine, an approach in which treatment and prevention are based on patients' genetic, environmental, and lifestyle factors rather than a single approach to a disease or condition for all patients (FDA, 2018). Biomarkers can be tested a variety of ways, including individually (single-analyte tests) or within a multigene panel test.

Pharmacogenomics

Pharmacogenomics is the study of how genes affect a person's response to medications. Because every person's genes are unique, depending on one's genetic makeup, the effectiveness of drug therapies may vary across individuals. There are different types of pharmacogenomic testing, including (1) necessary pharmacogenomic testing for one specific drug (known as a companion diagnostic[3]), (2) pharmacogenomic testing for a specific gene-drug pair but not a required companion diagnostic, (3) pharmacogenomic multigene panel tests[4] to evaluate metabolic response to a medication; and (4) preemptive testing using multigene panels across genes-drugs. Preemptive testing can be done before a provider and patient are considering a specific medication, or before a provider and patient are considering any medication. Because the genes relevant to pharmacogenomic testing do not change over time, the testing would only need to be completed once and the results would be accessible within a patient's medical records.

Pharmacogenomic testing can also be a tool in reducing adverse drug reactions (ADRs) by helping to predict the best medications to use, or by adjusting current/future medication doses. ADRs are best defined as unintended negative health reactions caused by medications. ADRs are classified as either mild, moderate, severe, or lethal and are associated with a wide range of harmful side effects (Marsh,

[3] Tests that are essential for the safe and effective use of a therapeutic product (i.e., a medication), including those that identify patients for which the drug is contraindicated, are companion diagnostics.
[4] Multigene panels allow simultaneous testing of at least two genes, and could include more than 150 genes. There are two types of multigene panels: (1) Off the shelf: Designed by a laboratory to include genes commonly associated with a broad phenotype or a recognizable syndrome with genetic heterogeneity; or (2) Custom designed: Includes genes selected by a clinician for analysis by clinical sequencing. Results for each gene on the custom multigene panel are reported to the ordering clinician, whereas the results from the remaining genes sequenced (but not requested by the clinician) are not analyzed or included in the final laboratory report.

2016). Most common side effects are digestive disturbances including nausea, vomiting, loss of appetite, constipation, diarrhea, abdominal pain, dyspepsia, and anorexia (Marsh, 2016).

Pharmacogenomic testing can be used to help identify responders and nonresponders to optimize medication dose (Jarvis et al., 2022). More recently, the use of pharmacogenomics in conjunction with a comprehensive medication management program has been shown to help identify medication appropriateness, improve adherence, and reduce adverse reactions in a more comprehensive way than either of these approaches can alone (Jarvis et al., 2022).

More than 90% of patients are thought to carry at least one genetic variant that should prompt a change in dosing or medication if certain medications are prescribed (Hockings et al., 2020).

Pharmacogenomic testing is a type of biomarker test and is performed using a cheek swab or blood sample, which is then sent to a laboratory for analysis. There are two major sources of pharmacogenomic testing recommendations: The U.S. Food and Drug Administration (FDA) and the Clinical Pharmacogenetics Implementation Consortium (CPIC).

U.S. Food and Drug Administration (FDA) List of Medications with Pharmacogenetic Associations

The FDA compiles a list of medications with pharmacogenetic[5] associations (FDA, 2021). Pharmacogenetic associations on the FDA's list have been evaluated and the FDA believes there is sufficient evidence to suggest that some patients with certain genetic variants, or genetic variant-inferred phenotypes, are likely to have altered drug metabolism, and in certain cases, differential therapeutic effects, including differences in the risks of adverse events (FDA, 2021). Medications are classified in three ways:

1. Pharmacogenomic associations for which the data support therapeutic management recommendations

2. Pharmacacogenomic associations for which the data indicate a potential impact on safety or response; and

3. Pharmacogenomic associations for which the data demonstrate a potential impact on pharmacokinetic properties only (the way in which a drug is metabolized)- the impact of these genetic variants on the safety or response of the corresponding medication has not been established.

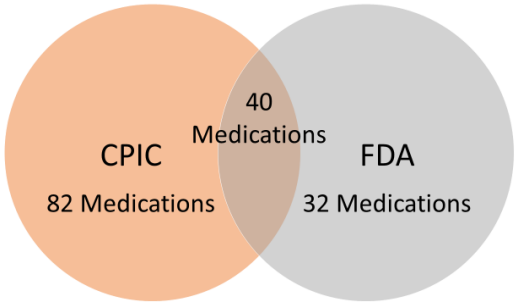
[5] Pharmacogenetics is the study of genetic causes of individual variations in drug response.

The FDA notes that while specific information regarding therapeutic management is provided for some pharmacogenomics associations, most of the associations listed have not been evaluated in terms of impact of genetic testing on clinical outcomes. Additionally, the FDA states that "the fact that the FDA has included a particular gene-drug interaction in the table does not necessarily mean the FDA advocates using a pharmacogenetic test before prescribing the corresponding medication, unless the test is a companion diagnostic" (FDA, 2021).

Clinical Pharmacogenetics Implementation Consortium (CPIC)

The Clinical Pharmacogenetics Implementation Consortium (CPIC) publishes clinical guidelines designed to help clinicians understand how available genetic test results should be used to optimize drug therapy (CPIC, 2021c). These guidelines may be relied on, in addition to the official pharmacogenomic indications included on medication labels approved by the FDA and the above described lists. CPIC assigns recommendation levels to gene/drug pairs. As discussed in the Policy Context section below, SB 1191 specifies pharmacogenomics testing should be covered if the drug/gene pair has a CPIC recommendation of A, A/B, or B. Definitions for these ratings are included in Table 1.

Figure 1. Overlap of Medications with CPIC Recommendations and on the FDA's list



Source: California Health Benefits Review Program, 2022.

Table 1. Level Definitions for CPIC Genes/Drugs

CPIC Level	Clinical Context	Level of Evidence	Strength of Recommendation
A	Genetic information should be used to change prescribing of affected drug	Preponderance of evidence is high or moderate in favor of changing prescribing of affected drug	At least one moderate or strong action (change in prescribing) recommended
A/B	Preliminary review indicates it is likely that the definitive CPIC level will be either A or B	Full evidence review needed to assess level of evidence, but prescribing actionability is likely	Full review by expert guideline group to assign strength of recommendation
B	Genetic information could be used to change prescribing of affected drug because alternative therapies/dosing are extremely likely to be as effective and as safe as nongenetically based dosing	Preponderance of evidence is weak with little conflicting data	At least one optional action (change in prescribing) is recommended

Source: CPIC, 2021b.

Key: CPIC = Clinical Pharmacogenetics Implementation Consortium.

A few examples of common drug-gene pairs are included in Table 2. As shown in Figure 1, CHBRP identified 32 unique medications on the FDA's list, 82 unique medications on CPIC's guidelines, and 40 medications on both lists.

Table 2. Examples of Common Drug-Gene Pairs

Drug	Relevant Clinical Areas	Genotype	Phenotype Implications	CPIC Recommendations

Abacavir	Infectious disease	HLA-B*57:01	Significantly increased risk of Abacavir hypersensitivity	Abacavir is not recommended
Warfarin	Cardiovascular	VKORC1 1639G>A	Increased sensitivity	Calculate dose based on published pharmacogenomic algorithms
SSRIs	Psychiatric/mental health	CYP2D6*1/*1	Normal metabolism	Initiate therapy with recommended starting dose
Ibuprofen	Chronic pain	CYP2C9	Normal metabolism	Calculate dose based on guidelines
Codeine	Acute & chronic pain	CYP2D6	Normal metabolism	Calculate dose based on guidelines

Source: California Health Benefits Review Program, 2022. Adapted from CPIC, 2021a.
Key: SSRI = selective serotonin reuptake inhibitor.

Effectiveness and Clinical Utility of Pharmacogenomics

As mentioned previously, pharmacogenomics uses variations in a patient's genes to guide therapeutic recommendations or medication selections. Evidence on the effectiveness and clinical utility of pharmacogenomic testing varies significantly across conditions. In a review of pharmacogenomic biomarkers in FDA-approved drug labels, Kim et al. (2021) compared the clinical actionability[6] of pharmacogenomic information included in drug labels across therapeutic areas from 2000 to 2020. Overall, the annual proportion of new drugs approved containing pharmacogenomic information has increased to nearly 30%. However, clinically actionable information was observed significantly more frequently in biomarker drug pairs associated with cancer drugs than those for other therapeutic areas (59.7% vs. 40.3%, respectively).

In a recent systematic review, David et al. (2021) examined the overall literature, across conditions, on the impact of pharmacogenomic testing on medication changes and hospital admissions. Their review included a total of five studies that compared medication changes and five that compared hospitalization rates between pharmacogenomic-tested patients with patients receiving treatment as usual (TAU). In their analysis of the studies that compared medication changes, including 749 patients in the pharmacogenomic-tested arm and 825 patients in the TAU arm, they found a 32% increase in medication changes for patients who had received pharmacogenomic testing. For the outcome of hospital admission, the review also found that unplanned hospital admission occurred significantly less in the pharmacogenomic-tested arm. In the pharmacogenomic-tested arm, 11.5% of patients (340 out of 2,957) had a hospital admission, compared to 20.1% of patients (1,365 out of 6,783) with a hospital admission in the TAU arm. Though this review showed positive results for pharmacogenomic testing on medication changes and hospital admissions, the authors note that the literature is limited by the small number of studies that include these clinical outcomes, the heterogeneity of settings and study designs, and low-quality study methodology. A recent study found results in line with the David et al. (2021) review, with about 30% of pharmacogenomic testing indicating recommended changes to optimize therapy (Steinbach et al., 2022). The most common recommendations were to monitor for possible adverse drug reaction or to consider discontinuation of the medication. It is worth noting that while the studies presented show that pharmacogenomic testing may result in recommendations and changes to medication for some patients,

[6] Kim et al. (2021) defined clinical actionability as follows: Considered clinically actionable if they were categorized as "required genetic testing," "recommended genetic testing," or "actionable PGx." Biomarker–drug pairs were considered to lack actionability if they were assigned an "informative PGx" level by PharmGKB; examples of "informative" biomarker–drug pairs include those with labels that only describe the role of a variant in the drug's metabolism or state that dose adjustment or other actions were not necessary for a particular variant.

especially to prevent adverse reactions, most patients who receive pharmacogenomic testing remain on their previously prescribed medication regimen.

The majority of literature on the clinical effectiveness and utility of pharmacogenomic testing is condition-specific and spans across a wide variety of medical conditions, most notably for cancer and chemotherapy treatments. A systematic review by Yang et al. (2021) evaluated the correlation between genomic variants that can be tested for in a panel and chemotherapy-induced cadiotoxicity (CIC) (i.e., adverse reactions to chemotherapy treatment). In their review of 41 studies, they concluded six genetic variants to be significantly associated with increased risk for CIC, including CYBA, RAC2, CYP3A5, ABCC1, ABCC2, and HER2. The authors concluded that this shows promising benefits of pharmacogenomic screening before a patient begins chemotherapy to minimize possible adverse reactions, but further research is needed to confirm these benefits in practice. Relatedly, Faruque et al. (2019) report in their systematic review on the value of pharmacogenomic testing for cancer drugs that the degree of utility for clinical efficacy or safety outcomes varies based on specific gene-drug pairs, with some providing more value for guiding cancer treatment than others.

Other common conditions for which there is literature on pharmacogenomic testing include depression and other psychiatric conditions and cardiovascular disease. For example, a systematic review by Aboelbaha et al. (2021) analyzed the effects of pharmacogenomic tests on depression outcomes from six previous systematic reviews and three RCTs. The overall results provided some evidence for the efficacy of pharmacogenomic testing in patients with moderate to severe depression. The results from the more recent high-quality RCTs included in the review show stronger evidence for clinical efficacy, especially for patients taking medications for which there is a known gene-drug interactions. The evidence on the effectiveness of pharmacogenomic testing for cardiovascular disease is mixed. While multiple studies have provided evidence to support the clinical utility of testing for one specific gene-drug pair (warfarin-CYP2C9/VKORC1), other studies on multigene panel pharmacogenomic testing found that testing did not improve outcomes (Billings et al., 2018; Zhu et al., 2020).

Cost-Effectiveness of Pharmacogenomic Testing

There is some evidence that the use of pharmacogenomic testing for specific types of diseases is cost-effective, but this varies significantly by disease, treatment, and outcomes assessed. In 2013, Varbleen et al. reviewed the overall literature on cost-effectiveness of pharmacogenomic testing. This review found that economic evaluations for pharmacogenomic testing were only available for 10 out of 68 drugs. Fifty-seven percent of the studies had results that favored pharmacogenomic testing (i.e., cost-effective or cost saving). This increased to 75% if the genetic information was already known (i.e., had already been collected as part of other treatment). Similarly, Berm et al. reviewed 80 studies on pharmacogenomic testing and found that most studies indicated a favorable cost-effectiveness (Berm et al., 2016). In addition, a systematic review of 59 economic evaluations of pharmacogenomic testing for prevention of adverse drug reactions reported the quality and strength of evidence in favor of pharmacogenomic testing varied by condition and treatment (Turongkaravee et al., 2021). These reviews also described the weakness of the literature as having insufficient sensitivity analyses, heterogeneity in study designs and populations, and low quality of data and methodologies utilized (Berm et al., 2016; Kasztura et al., 2019; Verbelen et al., 2017).

Systematic reviews have also been conducted on the use of pharmacogenomic testing for specific conditions. For example, one systematic review of 18 studies of pharmacogenomic testing prior to treatment of psychiatric conditions, found that that the vast majority (89%) of economic evaluations favored the use of pharmacogenomic testing (Karamperis et al., 2021). While a separate review by Peterson et al. concluded that the cost-effectiveness of pharmacogenomic testing for treatment of major depressive disorder was unclear (Peterson et al., 2017). In addition, a systematic review of 46 studies on treatment for cardiovascular disease by Zhu et al. found that two thirds of the studies showed pharmacogenomic testing to be cost-effective, but the results varied by specific drugs and conditions (Zhu et al., 2020).

There is additionally a large amount of literature on the use of pharmacogenomic testing for cancer treatment. One systematic review of pharmacogenomic testing for cancer drugs by Faruque and colleagues demonstrated inconsistencies in the summary of results depending on the type of economic analysis performed (Faruque et al., 2019). For example, while 89% of studies reporting cost-minimization comparisons found that pharmacogenomics was cost saving, only 21% of comparisons of cost per quality adjusted life year found pharmacogenomic testing to be dominant (i.e., clinically superior and cost saving to the alternative) (Faruque et al., 2019). The overall conclusions were highly dependent on specific treatments and outcomes assessed. Treatment for other conditions with pharmacogenomics, such as colorectal cancer, was deemed inconclusive due to a lack of high-quality evidence (Guglielmo et al., 2018).

POLICY CONTEXT

The California Senate Committee on Health has requested that the California Health Benefits Review Program (CHBRP)[7] conduct an evidence-based assessment of the medical, financial, and public health impacts of Senate Bill (SB) 1191 as amended on March 16th and April 19th, which would require Medi-Cal coverage of pharmacogenomic testing.

Bill-Specific Analysis of SB 1191, Pharmacogenomic Testing

Relevant Populations

If enacted, SB 1191 would apply to the Medi-Cal coverage of approximately 9,747,000 beneficiaries (25% of all Californians) in 2023. This represents Californians who will access benefits through Medi-Cal, including beneficiaries enrolled in Department of Managed Health Care (DMHC)-regulated Medi-Cal managed care plans, beneficiaries enrolled in County Organized Health Systems (COHS), and enrollees accessing full-scope benefits through the fee-for-service program administered by the Department of Health Care Services (DHCS).

Bill Language

SB 1191 would require Medi-Cal coverage of pharmacogenomic testing when a medication is being considered for use — or is already being administered — in treating a Medi-Cal beneficiary's condition and is known to have a gene-drug or drug-drug-gene interaction that has been demonstrated to be clinically actionable. The bill states "clinically actionable" can be defined by either the U.S. Food and Drug Administration (FDA) or by the Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines for level A, A/B, or B.

Medications must be approved for use to treat the beneficiary's condition and must be ordered by an enrolled Medi-Cal clinician or pharmacist.

SB 1191 prohibits clinicians from submitting claims for multiple billing codes in lieu of a single billing code for a multigene panel test.

Sample collection for purposes of performing pharmacogenomic testing may be completed at home, within a pharmacy, or at a health facility. Medi-Cal reimbursement shall not be impacted by the location of sample collection.

SB 1191 provides the following definitions:

- "Pharmacogenomics" means the evaluation of how a person's genes affect how the person responds to medications. Pharmacogenomics enables the selection of drugs and doses best suited to reduce toxicity and adverse drug events, including treatment failures, severe harm, or even death.
- "Pharmacogenomics testing" means laboratory genetic panel testing by a Clinical Laboratory Improvement Amendment (CLIA)- and California-licensed, College of American Pathologists (CAP)-accredited laboratory to identify how a person's genetics may impact the efficacy, toxicity, and safety of medications.

The full text of SB 1191 can be found in Appendix A.

[7] CHBRP's authorizing statute is available at www.chbrp.org/about_chbrp/faqs/index.php.

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

Under existing law, DMHC-regulated plans, including DMHC-regulated Medi-Cal managed care plans, are required to cover medically necessary diagnostic lab services and ongoing disease management services.[8] Medi-Cal covers medically necessary tests, treatments, and services (DHCS, 2021).

Existing law prohibits use of prior authorization for biomarker testing for enrollees with advanced or metastatic stage three or four cancer, including for cancer progression or recurrence for these enrollees.[9] SB 912 would direct the Welfare and Institutions Code to incorporate prior authorization prohibitions mentioned in the existing law. Should the biomarker test fall under the purview of pharmacogenomics, prior authorization would be prohibited for Medi-Cal beneficiaries.

SB 912, introduced in 2022, would require coverage of biomarker testing for enrollees in commercial and CalPERS plans and policies, as well as for Medi-Cal beneficiaries. CHBRP's analysis of this bill was published in April 2022 (CHBRP, 2022).

Similar requirements in other states

Illinois passed similar legislation to SB 912 in 2021.[10] Louisiana passed a bill in 2021 that requires coverage of genetic or molecular testing, including pharmacogenomic testing, for cancer.[11] In 2019, Connecticut introduced a bill that would prohibit prior authorization for pharmacogenomics tests for Medicaid beneficiaries.[12]

Federal Policy Landscape

Federal legislation

The 117th Congress has introduced one bill related to pharmacogenomic testing. House Resolution 6875 or The Right Drug Dose Now Act, would update the National Action Plan for Adverse Drug Event Prevention to provide educational information on adverse drug events and pharmacogenomic testing, to improve electronic health records for pharmacogenomic information, and for other purposes.[13]

Federal regulation of biomarker tests

The FDA has cleared and approved over 40 biomarker tests (FDA, 2022). The FDA reviews these tests for safety and effectiveness by assessing their analytical and clinical validity (Cancer Action Network, 2020).

[8] HSC 1345 and 1367.005; IC 10112.281.
[9] Health and Safety Code 1367.665; Insurance Code 10123.20.
[10] Illinois House Bill 1779, 102nd General Assembly. Available at https://www.ilga.gov/legislation/publicacts/fulltext.asp?Name=102-0203.
[11] Louisiana Senate Bill 84, 2021. Available at http://www.legis.la.gov/legis/BillInfo.aspx?s=21rs&b=SB84&sbi=y.
[12] Connecticut Senate Bill 820, 2019. Available at https://www.cga.ct.gov/2019/TOB/s/pdf/2019SB-00820-R00-SB.PDF.
[13] HR 6875, Right Drug Dose Now Act, 117th Congress (2021-2022). Available at: https://www.congress.gov/bill/117th-congress/house-bill/6875/text.

Additionally, hospitals and other laboratories can produce their own category of diagnostic test, known as laboratory-developed tests (Cancer Action Network, 2020). While not reviewed by the FDA, the laboratories are required to meet certain criteria under CLIA, including an inspection that reviews analytical validity of laboratory-developed tests.

Analytic Approach and Key Assumptions

CHBRP makes the following assumptions and approach decisions for the analysis of SB 1191:

- Utilization management policies, such as prior authorization, are allowed under SB 1191, except where prohibited by current law (see above).
- Although SB 1191 defines pharmacogenomic testing as "laboratory genetic panel testing," CHBRP does not assume that pharmacogenomic testing performed as a single-gene test would be prohibited and required to be billed as a multigene panel (unless multiple single-gene tests were billed on the same day, which would need to billed as a panel test). Recent developments and trends in pharmacogenomic testing have been shifting more towards using multigene panel tests instead of single-gene tests. Should regulators interpret this definition to only require coverage of panel tests, additional expenditures would be expected.
- SB 1191 does not define "clinically actionable." Additionally, this term is not used by the FDA to describe pharmacogenomic associations. CHBRP assumes "clinically actionable" to mean that prescribing patterns can change based on the results of the pharmacogenomics test, be it whether a patient receives or does not receive a medication, or dosing is adjusted. While the FDA does provide a list of gene/drug pairs for which metabolic associations have been determined, neither the FDA nor the FDA-approved drug labels provide recommendations for how to adjust the dose of the medication. CPIC may provide such recommendations. There may be some medications with a pharmacogenomic association for which there are no clinically actionable recommendations. However, because the FDA does not use the terminology "clinically actionable," CHBRP is unable to parse out which medications on the FDA's list would meet this criterion and has therefore included medications with a pharmacogenomic association in categories (1) and (2) as described in U.S. Food and Drug Administration (FDA) List of Medications with Pharmacogenetic Associations in the *Background* section. Category (3) was excluded because although there is an association, the FDA states "the impact of these genetic variants or genetic variant inferred phenotypes on the safety or response of the corresponding drug has not been established."
- As discussed in the *Background* section, preemptive testing can be done before a provider and patient are considering a specific medication, or before a provider and patient are considering any medication. CHBRP assumes the type of pharmacogenomic testing in the first instance would be covered under SB 1191, but the second type of testing would not.

CHBRP analyzed related bill language, SB 912, in 2022 concurrently with this analysis. Where applicable, this analysis incorporates information from the analysis of SB 912.

Beginning in 2022, DHCS began implementing the California Advancing and Innovating Medi-Cal (CalAIM) initiative.[14] To the extent possible as of this analysis, CHBRP has incorporated known CalAIM changes into its methods and approach.

[14] More information about CalAIM is available at https://www.dhcs.ca.gov/CalAIM/Pages/calaim.aspx.

BENEFIT COVERAGE, UTILIZATION, AND COST IMPACTS

As discussed in the *Policy Context* section, SB 1191 would require Medi-Cal coverage of pharmacogenomic testing for new and currently used medications with an FDA-identified pharmacogenomic association or a CPIC recommendation of A, A/B, or B.

Analytic Approach and Key Assumptions

CHBRP identified medications identified by the FDA with a pharmacogenomic association, as well as medications with a Clinical Pharmacogenetics Implementation Consortium (CPIC) recommendation of A, A/B, or B. As mentioned in the *Policy Context* section, CHBRP identified medications that may be clinically actionable, and therefore excluded a portion of medications on the FDA's list of pharmacogenetic associations. From there, CHBRP identified utilization of these medications among Medi-Cal beneficiaries and whether beneficiaries received any biomarker tests.

Claims data was analyzed using Milliman's 2019 Consolidated Health Cost Guidelines Sources Database (CHSD). Biomarker testing is a rapidly evolving field and the claims captured by CHBRP's analysis does not include more recently added biomarker tests or utilization. Utilization may also be higher or different than what CHBRP displays below, which is using 2019 claims data to project utilization in 2023.

Because SB 1191 would require pharmacogenomic testing to be billed as a panel test, CHBRP makes the following distinctions regarding how pharmacogenomics tests are billed currently:

- Beneficiaries with **one single-gene test** billed on one day
- Beneficiaries with **multiple single-gene tests** billed on one day
- Beneficiaries with at least one **multigene panel test(s)** billed on one day

CHBRP assumes SB 1191 would require tests currently billed as multiple single-gene tests on the same day would be required to be billed as a multigene panel test. Single-gene tests would continue to be permissible, despite the definition of "pharmacogenomic testing" in the bill language. However, there are several reasons why providers may bill for multiple single-gene tests at baseline. Some providers will submit claims to insurers for multiple single-gene tests when a multigene panel test was run because an insurer may not provide reimbursement for a panel that includes non–medically indicated tests, because no billing code exists for the panel test that was run, or there is not a panel available that includes the desired biomarker tests.[15]

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

Benefit Coverage

As part of CHBRP's analysis of SB 912, CHBRP queried DMHC-regulated Medi-Cal managed care plans to determine baseline benefit coverage of biomarker testing. **Broadly speaking, all beneficiaries with health insurance subject to SB 1191 have coverage for biomarker testing, including pharmacogenomic testing, that is supported by medical and scientific evidence and is determined medically necessary.[16]** Pharmacogenomic testing can be performed before a beneficiary begins taking a

[15] This has been confirmed through CHBRP's survey of insurers in California, as well as multiple subject matter experts.

[16] To further investigate whether benefit coverage existed at baseline, CHBRP examined the utilization of tests that are likely for pharmacogenomics purposes between Medi-Cal beneficiaries and commercial enrollees in California. Utilization between the two groups was similar, indicating that there is benefit coverage for these biomarker tests in DMHC-regulated Medi-Cal managed care plans. CHBRP is unable to determine whether benefit coverage for

medication with a companion diagnostic indication (as listed by the FDA); before a beneficiary begins taking — or concurrently with — a medication with a significant biomarker reference in the FDA drug label; as a panel; or preemptively. However, according to subject matter experts, pharmacogenomic testing is not as commonly performed preemptively as compared to the other reasons for testing. Because SB 1191 would clarify existing benefit coverage, it would, in essence, act as a new benefit coverage mandate.

As reported in CHBRP's analysis of SB 912, whether or not insurers place prior authorization requirements on biomarker testing varied (CHBRP, 2022). Some beneficiaries in DMHC-regulated Medi-Cal managed care plans subject to SB 912 had prior authorization requirements, while others did not. Insurers and DHCS may use prior authorization requirements as a way to confirm medical necessity of requested tests.

To estimate potential impacts of SB 1191, CHBRP provides three scenarios:

- Scenario 1: Utilization of pharmacogenomic testing will increase because of clarification of existing benefit coverage; billing patterns remain the same as at baseline (i.e., single-gene vs. multigene panel tests).
- Scenario 2: Utilization of pharmacogenomic testing will increase because of clarification of existing benefit coverage; multiple single-gene tests billed on the same day will be billed as ONE multigene panel test postmandate.
- Scenario 3: Utilization of pharmacogenomic testing will increase because of clarification of existing benefit coverage; multiple single-gene tests billed on the same day will be billed as *multiple* multigene panel tests postmandate (a one-to-one transfer of single-gene tests to multigene panel tests).

Baseline Utilization and Per-Unit Cost

Approximately 30% of Medi-Cal beneficiaries use medications with a clinically actionable FDA-identified pharmacogenomic association or CPIC A, A/B, or B recommendation at baseline. Of these beneficiaries, 0.9% (25,900 beneficiaries) received a test at baseline. This equates to approximately 0.3% of the total Medi-Cal population receiving pharmacogenomic testing.

Additionally, approximately 16,500 (64%) beneficiaries receive one single-gene test on one day, 9,100 (35%) beneficiaries receive multiple single-gene tests on one day, and 3,400 (13%) beneficiaries receive at least one panel test on a one day. Some beneficiaries may receive both multigene panels and single-gene tests on one day, or across multiple days, and therefore will be present in multiple categories.

At baseline, the average annual cost per user of pharmacogenomics tests is $380.

Postmandate Utilization

Due to the clarification of existing Medi-Cal coverage policies, CHBRP assumes there would be an increase in utilization for some pharmacogenomic testing.

CHBRP has assumed utilization of pharmacogenomics tests would increase from 0.3% of the population to 0.8% of the population. Among beneficiaries using medications with a clinically actionable pharmacogenomic association, utilization would increase from 0.9% at baseline to 2.6% postmandate. This assumption is supported by a recent study by Jarvis et al. (2022), in which a large state retirement system offered pharmacogenomic testing plus comprehensive medication management to retirees over age 65. About 18% of enrollees voluntarily participated in this program (5,288/28,619) when it was

biomarker tests differs between DMCH-regulated Medi-Cal managed care plans and COHS, which have near-identical standard contracts from DHCS.

offered. California's Medi-Cal population is substantially younger, on average, and includes large portions of children and adults under the age of 65. However, the large share of beneficiaries who take medications for which there are pharmacogenomic associations and the growing movement in pharmacogenomic testing leads CHBRP to assume that interest in this type of testing would lead to increased utilization postmandate.

This increase in utilization would result in an additional 51,900 beneficiaries receiving pharmacogenomic testing postmandate. This is a 200% increase from the 25,900 beneficiaries receiving pharmacogenomic testing at baseline.

Scenario 1: Increase in Utilization Only

The increase in utilization of pharmacogenomic testing would not result in any change to the average annual costs per user of pharmacogenomics tests (Table 3). While there is an increase in the number of tests performed, because the increase is experienced evenly by the type of testing, the average does not change. Total expenditures would increase by almost $22,000,000 (0.07%) due to new utilization. Per member per month (PMPM), Medi-Cal premiums would increase by $0.19 (0.07%).

Due to the increase in utilization, approximately 49,500 (64%) beneficiaries would receive one single-gene test on one day, 27,300 (35%) beneficiaries would receive multiple single-gene tests on one day, and 10,300 (13%) beneficiaries would receive at least one panel test on a one day (Table 6).

Table 3. SB 1191 Impacts on Utilization and Cost, 2023; Scenario 1 Increase in Utilization Only

	Baseline (2023)	Postmandate Year 1 (2023)	Increase/ Decrease	Change Postmandate
Utilization and cost				
Number of enrollees utilizing biomarker tests	25,900	77,800	51,900	200%
Annual costs per user of biomarker tests	$380	$380	$0	0%
Expenditures				
Medi-Cal expenditures (a)	$30,895,981,000	$30,917,691,000	$21,710,000	0.07%

Source: California Health Benefits Review Program, 2022.
Notes: (a) Includes expenditures for DMHC-regulated Medi-Cal managed care plans and COHS. CHBRP assumes COHS plan expenditures are similar to under 65 Medi-Cal managed care enrollee expenditures on a PMPM basis.
Key: COHS = County Organized Health Systems; PMPM = per member per month.

Scenario 2: Increase in Utilization and Multiple Single-Gene Tests Would be Billed as One Multigene Panel Test

In addition to the increase in utilization of pharmacogenomic testing postmandate, billing practices would also shift based on the implementation of SB 1191. Postmandate, billing for multiple single-gene tests on the same day would transition to being billed as one multigene panel test. This assumes that there is a multigene panel available and with a Current Procedural Terminology (CPT)[17] or Healthcare Common Procedure Coding System (HCPCS) code that meets the providers' and beneficiaries' needs regarding which tests are needed.

The increase in utilization of pharmacogenomic testing and the shift in billing practices would lead to a $45 reduction in average annual costs per user of pharmacogenomics tests (a 12% reduction) (Table 4). The reduction in average annual costs of biomarker testing for users of FDA medications is because beneficiaries with multiple single-gene tests on one day would transition to a single multigene panel test, indicating that the panel test may be less expensive than the sum of the multiple single-gene tests. However, CHBRP is unable to determine whether the average cost of a multigene panel test would be an

[17] CPT copyright 2022 American Medical Association.

accurate amount for a panel test that would include the multiple single-gene tests previously billed individually, as the cost of panel tests varies.

Total expenditures would increase by almost $18,000,000 (0.06%) due to new utilization and a shift in billing practices. Per member per month (PMPM), Medi-Cal premiums would increase by $0.15 (0.06%).

Due to the increase in utilization, approximately 49,500 (64%) beneficiaries would receive one single-gene test on one day, and 29,300 (38%) beneficiaries would receive at least one panel test on a one day (Table 6).

Table 4. SB 1191 Impacts on Utilization and Cost, 2023; Scenario 2 Increase in Utilization; Multiple Single-Gene Tests Billed as One Multigene Panel Test

	Baseline (2023)	Postmandate Year 1 (2023)	Increase/ Decrease	Change Postmandate
Utilization and Cost				
Number of enrollees utilizing biomarker tests	25,900	77,800	51,900	200%
Annual costs per user of biomarker tests	$380	$335	($45)	-12%
Expenditures				
Medi-Cal expenditures (a)	$30,895,981,000	$30,913,570,000	$17,589,000	0.06%

Source: California Health Benefits Review Program, 2022.

Notes: (a) Includes expenditures for DMHC-regulated Medi-Cal managed care plans and COHS. CHBRP assumes COHS plan expenditures are similar to under 65 Medi-Cal managed care enrollee expenditures on a PMPM basis.

Key: COHS = County Organized Health Systems; PMPM = per member per month.

Scenario 3: Increase in Utilization and Multiple Single-Gene Tests Would be Billed as Multiple Multigene Panel Tests

In addition to the increase in utilization of pharmacogenomic testing postmandate, billing practices would also shift based on the implementation of SB 1191. Postmandate, billing for multiple single-gene tests on the same day would transition to being billed as multiple multigene panel tests. This assumes that there is *not* a panel available with all of the tested-for biomarker that meets the providers' and beneficiaries' needs and therefore each single-gene test is billed as an individual multigene panel test. This is a high-impact estimate.

The increase in utilization of pharmacogenomic testing and the shift in billing practices would lead to a $380 increase in average annual costs per user of pharmacogenomics tests (a 100% increase) (Table 5). Total expenditures would increase by more than $54,000,000 (0.18%) due to new utilization and a shift in billing practices. Per member per month (PMPM), Medi-Cal premiums would increase by $0.46 (0.18%). Approximately 60% of the increase in expenditures is due to changes in billing practices, and 40% of the increase in expenditures is due to the increase in utilization.

Due to the increase in utilization, approximately 49,500 (64%) beneficiaries would receive one single-gene test on one day, and 29,300 (38%) beneficiaries would receive at least one panel test on a one day (Table 6).

Table 5. SB 1191 Impacts on Utilization and Cost, 2023; Scenario 3 Increase in Utilization; Multiple Single-Gene Tests Billed as Multiple Multigene Panel Tests

	Baseline (2023)	Postmandate Year 1 (2023)	Increase/ Decrease	Change Postmandate
Utilization and Cost				
Number of enrollees utilizing biomarker tests	25,900	77,800	51,900	200%
Annual costs per user of biomarker tests	$380	$760	$380	100%
Expenditures				
Medi-Cal expenditures (a)	$30,895,981,000	$30,950,189,000	$54,208,000	0.18%

Source: California Health Benefits Review Program, 2022.

Notes: (a) Includes expenditures for DMHC-regulated Medi-Cal managed care plans and COHS. CHBRP assumes COHS plan expenditures are similar to under 65 Medi-Cal managed care enrollee expenditures on a PMPM basis.

Key: COHS = County Organized Health Systems. PMPM = per member per month.

Table 6. User Count by Type of Biomarker Tests, Baseline and Postmandate Scenarios

	One Single-Gene Test	Multiple Single-Gene Tests	Multigene Panel Tests
Baseline			
User Count (a)	16,500	9,100	3,400
Percentage	64%	35%	13%
Scenario 1: Increase in utilization only			
User Count (a)	49,500	27,300	10,300
Percentage	64%	35%	13%
Scenario 2: Multiple single-gene tests become one multigene panel test			
User Count (a)	49,500	0	29,300
Percentage	64%	0%	38%
Scenario 3: Multiple single-gene tests become multiple multigene panel tests			
User Count (a)	49,500	0	29,300
Percentage	64%	0%	38%

Source: California Health Benefits Review Program, 2022.

Notes: (a) Users may be in more than one biomarker type category. Biomarker type is determined by services received in a day and users may have multiple services over different days. Additionally, the users who had one single-gene test may have also had a panel test the same day. CHBRP assumed the single-gene test remained outside of the panel because a panel test does not exist.

Potential Offsets From Increased Utilization of Pharmacogenomic Testing

As discussed previously in this analysis, several studies have found that pharmacogenomic testing can lead to offsets, including a reduction in emergency room utilization, unplanned hospital admissions, and outpatient visits (Brixner, 2016; David et al., 2021; Elliott, 2017; Jarvis et al., 2022; Steinbach et al., 2022). Other studies have found that for most patients who receive pharmacogenomic testing, no changes are made to their medications (David et al., 2021; Steinbach et al., 2022) or the testing did not lead to improved outcomes (Billings et al., 2018; Zhu et al., 2020).

One study that reviewed the effectiveness of a pharmacogenomics and comprehensive medication management program found that the most common pharmacist recommendation was “monitor” (78.8%), followed by mentions of future concerns (22.1%), recommendation to discontinue medication (15.6%),

modify prescription (14.3%), or initiate new medication (12.3%). Jarvis et al. (2022) does not document whether the recommendations provided by pharmacists to the patient's prescribing provider of record were acted upon. Additionally, it is not clear for which types of medications these recommendations were related to, and whether the reductions in other health care utilization was due to this comprehensive medication management. Therefore, CHBRP is unable to project offsets as a result of SB 1191.

PUBLIC HEALTH IMPLICATIONS

As discussed in the *Policy Context* section, SB 1191 would mandate coverage of pharmacogenomic testing for Medi-Cal beneficiaries for the purpose of identifying how a person's genetics may impact the efficacy, toxicity, and safety of medications.

This section provides an overview of public health implications related to pharmacogenomic testing including disparities and social determinants of health contributing to inequities in its utilization.

Estimated Public Health Outcomes

As presented in the *Benefit Coverage, Utilization, and Cost Impacts* section, utilization of pharmacogenomic tests would increase threefold, from 0.3% to 0.8% of the population postmandate. Due to a small projected increase, as well as indeterminate offsets due to other healthcare utilization, CHBRP projects no measurable public health impact at the population level.

As discussed in *Background on Pharmacogenomic Testing*, evidence of the effectiveness and clinical utility of pharmacogenomic testing varies significantly across conditions. There is some evidence of clinically actionable information resulting from this testing, but also some evidence that there is no recommended change to treatment. Further, there may be offsets due to reductions in utilization of other health care resources such as emergency room visits, unplanned hospital admissions, and outpatient visits. Because the evidence is not directly attributable to pharmacogenomic testing use, CHBRP is unable to project offsets as a result of SB 1191. However, there may be impacts for individuals who receive pharmacogenomic testing and change medications or doses, and these changes may result in any of the potential related outcomes.

CHBRP projects no measurable public health impact at the population level due to the increase in utilization for a relatively small number of beneficiaries and indeterminate offsets. However, SB 1191 may yield individual-level health improvements for beneficiaries with reduced utilization of other health care services such as emergency room visits, unplanned hospital admissions, and outpatient visits.

Disparities[18] and Social Determinants of Health[19] in Pharmacogenomic Testing

Per statute, CHBRP includes discussion of disparities and social determinants of health (SDOH) as it relates to pharmacogenomic testing. Disparities are noticeable and preventable differences between groups of people. CHBRP found literature identifying disparities in pharmacogenomic testing by race and ethnicity, socioeconomic status, health literacy, and geographic location.

[18] 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).

[19] CHBRP defines social determinants of health as conditions in which people are born, grow, live, work, learn, and age. These social determinants of health (economic factors, social factors, education, physical environment) are shaped by the distribution of money, power, and resources and impacted by policy (adapted from: CDC, 2014; Office of Disease Prevention and Health Promotion, 2019).

Disparities

Race or ethnicity

It is widely stated that studies of genetic variation and diversity have focused on those of European descent and that not enough is known about genetic variation in other populations. A recent review of pharmacogenomics and health equality showed that there are limited studies specific to pharmacogenomics in the literature (Magavern et al., 2022). The authors cite that race, ethnicity, and ancestral lineage all form the basis for pharmacogenomics and can have clinically significant impacts on efficacy and safety. The existing research on primarily non-Hispanic Whites cannot be applied universally, which speaks to the inaccessibility of genetic diagnoses for underrepresented groups and need for race/ethnic-specific genetic research (Smith et al., 2016). It has been reported that underrepresented racial/ethnic groups may still have inconclusive results even if genetic services are provided due to reduced ability to interpret pathogenicity of variants found in populations categorized by ancestry, contributing further to disparities in diagnostic rates (Fraiman and Wojcik, 2021).

In a 2021 review article, McAlarnen et al. found that despite an increase in genetic testing in the United States, disparities exist among racial and ethnic groups when it comes to awareness and utilization of this type of testing. For example, significantly more White participants were aware of cancer risk than Hispanic, African American, or Asian participants. Some studies in this review found that there was a lack of trust regarding how genetic information would be used, and a lack of confidence in the validity and utilization of the results (Allford et al., 2014; Saulsberry and Terry, 2013). Other themes that emerged from the reviewed studies and may contribute to persistent health disparities in genetic services for cancer were lack of provider recommendation and equal access to specialized care.

The gap in genomic testing utilization by race/ethnicity will continue to be exacerbated as the lack of data gathered from representative populations limits the generalizability of current genomic research. This is particularly of concern for development of guideline recommendations which may not necessarily be reflective of the diversity of the population (Jooma et al., 2019; McAlarnen et al., 2021). These findings have been supported in other studies (Kehl et al., 2019; Lynch et al., 2018).

Clinical Disparities and Barriers

Many pharmacogenomics tests are relatively new clinical tools and are part of a rapidly evolving field. Because of this there may be clinical and implementation considerations involved in uptake and utilization of these tests. Studies have suggested that clinician barriers including familiarity with guidelines and knowledge of best practices for use of pharmacogenomic testing, expertise in genomic testing, or access to a multidisciplinary specialty team impact whether patients receive testing (Martin et al., 2017). Relatedly, studies consistently report higher rates of genetic and genomic testing at academic medical centers compared to community sites (Boehmer et al., 2021; Wilson et al., 2018). Routine clinical uptake of pharmacogenomic testing has encountered barriers such as concerns over the clinical validity/utility for some pharmacogenomic tests, lack of professional education and guidelines, and logistics of implementation (Abul-Husn, 2014). These disparities and barriers in clinical practice may be limiting factors in more widespread and equitable implementation of pharmacogenomic testing.

Social Determinants of Health

Social determinants of health (SDOH) include factors outside of the traditional medical care system that influence health status and health outcomes (e.g., income, education, geography). CHBRP found literature citing differences in biomarker testing by socioeconomic status, health literacy, and geographic location.

Socioeconomic status

Socioeconomic status is strongly associated with morbidity and mortality across the income distribution. Lower incomes are associated with lower life expectancy, higher rates of chronic disease and physical limitations, and worse self-reported health status (Khullar and Chokshi, 2018). Additionally, poor health contributes to reduced income, creating a negative feedback loop (Khullar and Chokshi, 2018).

In a 2020 systematic review and meta-analysis, Norris and colleagues examined the role of socioeconomic status and utilization of predictive biomarker tests and/or precision therapies in different types of cancers. The analysis included 11 studies that reported data on predictive biomarker testing and 40 studies including data on utilization of biological and precision therapy. The authors found statistically significant differences in biological and precision therapy utilization: those with low socioeconomic status were 17% less likely to be treated with precision therapies. This finding is consistent with previously published studies on cancer treatment inequalities by socioeconomic status (Aarts et al., 2010; Forrest et al., 2013) and inequalities in time to screening and diagnosis of various types of cancers (Lyratzopoulos et al., 2013; Hayes et al., 2021). The overall pooled odds ratio (OR) for receipt of biological and precision therapy for patients from low socioeconomic status was 0.83 (95% CI, 0.75–0.91). Associations with therapy utilization were strongest in lung cancer (OR 0.75; 95% CI, 0.51–1.00) and weakest in breast cancer (OR 0.93; 95% CI, 0.78–1.10).

Health literacy

Health literacy, a person's capacity to access, understand, appraise, and apply information for healthcare decisions, may impact how patients utilize healthcare and biomarker testing. Health literacy plays a role in awareness, access, and interpretation of personalized medicine results (Williams et al., 2018; Rostamzadeh et al., 2020). Familiarity with more recent precision medicine terms including "pharmacogenomics" is low, even among those with higher health literacy (Williams et al., 2018). Williams found that in general, most patients reported low familiarity with precision medicine concepts, but those with higher health literacy gave significantly greater importance to provider trust than those with lower levels ($p \leq .008$). It was concluded that culturally sensitive efforts tailored to health literacy level should be implemented to enhance equitable utilization of precision medicine as a healthcare tool. A recent meta-analysis of 36 studies similarly found limited health literacy among patients in pharmacogenomic testing, indicating a need for "universal precaution" with regard to this kind of testing (Veilleux et al., 2020). Despite health literacy being generally low, it is possible that those with higher health literacy would be more likely to have pharmacogenomic testing as part of their medication management. Based on these recent studies, efforts to tailor pharmacogenomic testing information to health literacy level could prevent disparities from widening.

Geographic location

As reported in CHBRP's analysis of SB 912, rural-urban disparities exist for time to diagnosis and treatment of certain cancers (Bergin et al., 2018). Because clinical guidelines for biomarker and pharmacogenomic testing exist for many types of cancer, among other diseases/conditions, this disparity is carried forward to treatment decisions resulting from pharmacogenomic testing (Greenbaum et al., 2017). Furthermore, implementation differences were found to exist between small metropolitan, rural, and tribal communities with regards to acceptability, uptake, and cost associated with travel (Dorfman et al., 2015; Stegelmeier et al., 2020). Greater outreach might be required to inform the more rural-dwelling public about pharmacogenomic testing (Stegelmeier et al., 2020).

Because there is no measurable public health impact for SB 1191, there is no projected impact on disparities. There is literature indicating that disparities could widen inequities in utilization of pharmacogenomic testing if not specifically addressed.

LONG-TERM IMPLICATIONS

In this section, CHBRP estimates the long-term impact of SB 1191, 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.

A changing landscape exists for pharmacogenomic testing as new drug/gene pairs are identified and tested. Utilization of pharmacogenomic testing is also increasing, and clinical practice standards are changing when these tests are being performed and how the information is being used. CHBRP assumes it is likely DMHC-regulated Medi-Cal managed care plans, COHS, and DHCS will continue to incorporate new clinical guidelines and practice standards as they become available in future years. As noted previously, some evidence supports cost-effectiveness of pharmacogenomic testing, which could contribute to offsets in health care expenditures or improved quality of life for beneficiaries. Additionally, prescribing practices of providers, including pharmacists, could shift towards requiring pharmacogenomic testing prior to prescribing common medications, such as ibuprofen and codeine. This would contribute to greater utilization over time.

APPENDIX A TEXT OF BILL ANALYZED

On March 17, 2022, the California Senate Committee on Health requested that CHBRP analyze SB 1191.

SENATE BILL **NO. 1191**

Introduced by Senator Bates

February 17, 2022
Amended March 16, 2022
Amended April 19, 2022

An act to amend Section 14132 ~~of, and to add Section 14137.9 to,~~ *of* the Welfare and Institutions Code, relating to Medi-Cal.

LEGISLATIVE COUNSEL'S DIGEST

SB 1191, as amended, Bates. Medi-Cal: pharmacogenomic testing.

Existing law establishes the Medi-Cal program, which is administered by the State Department of Health Care Services and under which qualified low-income individuals receive health care services. The Medi-Cal program is, in part, governed and funded by federal Medicaid program provisions. Existing law sets forth a schedule of covered benefits under the Medi-Cal program.

This bill, to be known as the Utilizing Pharmacogenomics to Greatly Reduce Adverse Drug Events (UPGRADE) Act, would add pharmacogenomic testing as a covered benefit under Medi-Cal. The bill would define pharmacogenomic testing as laboratory genetic panel testing, by a laboratory with specified licensing and accreditation, to identify how a person's genetics may impact the efficacy, toxicity, and safety of medications. The bill would cover the benefit under Medi-Cal if a medication is being considered for use, or is already being administered, and is approved for use, in treating a Medi-Cal beneficiary's condition and is known to have a gene-drug or drug-drug-gene interaction that has been demonstrated to be clinically actionable, as specified, if the medication is ordered by an enrolled Medi-Cal clinician or pharmacist.

The bill would authorize the department to implement the above-described provisions through all-county or plan letters, or similar instructions, ~~without taking any further regulatory action.~~ *until the department promulgates regulations.*

~~The bill, subject to implementation of the provisions above, and in collaboration with certain stakeholders, would require the Department of Health Care Access and Information to assess the impact of Medi-Cal coverage of pharmacogenomic testing and to annually prepare and publish a~~

~~report on its internet website. The bill would require the annual reports to include an assessment of health economics and health outcomes of the benefit coverage, as specified.~~

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

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

SECTION 1. This act shall be known, and may be cited, as the Utilizing Pharmacogenomics to Greatly Reduce Adverse Drug Events (UPGRADE) Act.

SEC. 2. Section 14132 of the Welfare and Institutions Code is amended to read:

14132. The following is the schedule of benefits under this chapter:

[Sections (a) through (af) remain unchanged]

(ag) (1) Pharmacogenomic testing is covered when a medication is being considered for use, or is already being administered, and is approved for use, in treating a Medi-Cal beneficiary's condition and is known to have a gene-drug or drug-drug-gene interaction that has been demonstrated to be clinically actionable, as defined by the United States Food and Drug Administration or by the Clinical Pharmacogenetics Implementation Consortium (CPIC) Guidelines for Level A, A/B, or B, if the medication is ordered by an enrolled Medi-Cal clinician or pharmacist pursuant to paragraph (12) of subdivision (a) of Section 4052 of the Business and Professions Code.

(2) (A) Medi-Cal reimbursement for pharmacogenomic testing is subject to the use of only one Current Procedural Terminology (CPT) code, or only one Healthcare Common Procedure Coding System (HCPCS) code, for the panel test. Each individual gene shall not be billed with multiple CPT or HCPCS codes.

(B) Sample collection for purposes of performing pharmacogenomic testing may be completed at home, within a pharmacy, or at a health facility. The location of sample collection shall not impact Medi-Cal reimbursement for pharmacogenomic testing.

(3) Notwithstanding Chapter 3.5 (commencing with Section 11340) of Part 1 of Division 3 of Title 2 of the Government Code, the department may implement this subdivision by means of all-county letters, plan letters, plan or provider bulletins, or similar instructions,~~without taking any further regulatory action.~~ *until the department promulgates regulations.*

(4) For purposes of this subdivision, the following definitions apply:

(A) "Pharmacogenomics" means the evaluation of how a person's genes affect how the person responds to medications. Pharmacogenomics enables the selection of drugs and doses best suited to reduce toxicity and adverse drug events, including treatment failures, severe harm, or even death.

(B) “Pharmacogenomic testing” means laboratory genetic panel testing by a CLIA- and California-licensed, College of American Pathologists (CAP)-accredited laboratory to identify how a person’s genetics may impact the efficacy, toxicity, and safety of medications.

~~SEC. 3.Section 14137.9 is added to the Welfare and Institutions Code, to read:~~

~~14137.9. (a) Subject to implementation of Medi-Cal coverage of pharmacogenomic testing pursuant to subdivision (ag) of Section 14132, and in collaboration with stakeholders from the pharmacogenomics field, the Clinical Pharmacogenetics Implementation Consortium, the diagnostics industry, and the patient community, the Department of Health Care Access and Information shall assess the impact of Medi-Cal coverage of pharmacogenomic testing and shall annually prepare and publish a report on its internet website, commencing no later than one year following implementation of that Medi-Cal coverage.~~

~~(b)The annual reports described in subdivision (a) shall include an assessment of health economics and health outcomes of Medi-Cal coverage of pharmacogenomic testing, covering all of the following components:~~

~~(1)Evaluation of cost savings and health outcomes associated with avoidance of adverse drug events and usage of ineffective drugs, including reductions in emergency room visits, hospitalizations, readmissions, and mortality.~~

~~(2)Evaluation of a change in prescription or dose based on a pharmacogenomic result, including, but not limited to, how claims data could be used to risk-adjust populations and track pharmacogenomic ordering and changes in prescriptions.~~

~~(3)Evaluation of clinical care improvements with enhanced genetic information and prescription of appropriate medication.~~

~~(4)Investigation into shortcomings, if any, resulting from a lack of interoperability and data sharing of patient records.~~

~~(5)Assessment of advancements in health equity and reduced disparities related to medication management and pharmacogenomic risks.~~

~~(c)For purposes of this section, the following definitions apply:~~

~~(1)“Pharmacogenomics” means the evaluation of how a person’s genes affect how the person responds to medications. Pharmacogenomics enables the selection of drugs and doses best suited to reduce toxicity and adverse drug events, including treatment failures, severe harm, or even death.~~

~~(2)“Pharmacogenomic testing” means laboratory genetic panel testing by a CLIA- and California-licensed, College of American Pathologists (CAP)-accredited laboratory to identify how a person’s genetics may impact the efficacy, toxicity, and safety of medications.~~

APPENDIX B COST IMPACT ANALYSIS: DATA SOURCES, CAVEATS, AND ASSUMPTIONS

With the assistance of CHBRP's contracted actuarial firm, Milliman, Inc, 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.[20] Information on the generally used data sources and estimation methods, as well as caveats and assumptions generally applicable to CHBRP's cost impacts analyses are available at CHBRP's website.[21]

This appendix describes analysis-specific data sources, estimation methods, caveats, and assumptions used in preparing this cost impact analysis.

Analysis-Specific Data Sources

Current coverage of biomarker testing for commercial and Medi-Cal enrollees was determined by a survey of the largest (by enrollment) providers of health insurance in California. Responses to this survey represented 66% of commercial enrollees with health insurance that can be subject to state benefit mandates. Responses to this survey represented 39% of Medi-Cal enrollees with health insurance that can be subject to state benefit mandates. In addition, CalPERS and DHCS were queried regarding related benefit coverage.

For this analysis, CHBRP relied on CPT® codes to identify services related to SB 1191.

Analysis-Specific Caveats and Assumptions

The analytic approach and key assumptions are determined by the subject matter and language of the bill being analyzed by CHBRP. 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 mandate includes individuals enrolled in MediCal HMO and County Organized Health System (COHS) Medi-Cal plans.
- CHBRP assumed COHS expenditures are the same as the per enrollee per month expenditures for the under 65 Medi-Cal managed care population.
- CHBRP assumed 100% of the population has coverage for pharmacogenomic testing.

Methodology and Assumptions for Baseline Utilization and Cost

- Drugs and biologicals included in the analysis were drawn from two FDA categories:
    - Pharmacogenetic associations for which the data support therapeutic management recommendations; and

[20] 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.
[21] See method documents posted at http://chbrp.com/analysis_methodology/cost_impact_analysis.php; in particular, see *2023 Cost Analyses: Data Sources, Caveats, and Assumptions*.

    - Pharmacogenetic associations for which the data indicate a potential impact on safety or response.
- Drugs and biologicals identified by the Clinical Pharmacogenetics Implementation Consortium (CPIC) as level A, B, or A/B that were not included in the FDA drug list were identified as CPIC drugs. The full list of FDA and CPIC drugs and biologicals can be found in Table 7**.**
- Enrollees who utilized at least one of the FDA or CPIC drugs were identified in Milliman's 2019 Consolidated Health Cost Guidelines Sources Database (CHSD). The data was limited to Medi-Cal enrollees. Biomarker test utilization for enrollees who used an FDA or CPIC drug were identified in CHSD.
- CHBRP identified procedure codes specific to biomarker tests that may be used for pharmacogenomic testing. The biomarker test list includes only those tests that could be reported for the specific genes identified for the FDA and CPIC drugs. Biomarker tests can be found in Table 8.
- The Medi-Cal–allowed costs for biomarker tests are based on the February 2022 Medi-Cal fee-for-service reimbursement rates. For services where a fee-for-service rate is not available, the Medi-Cal rate is calculated as 60% of the commercial rate. This discount was determined by comparing the commercial and Medi-Cal rates of the biomarker tests and related services where fee-for-service rates were available.
- Utilization of biomarker tests and drugs were trended from 2019 to 2023 using 1% annual trend. Allowed costs per user of biomarker tests were trended from 2019 to 2023 using 0% trend.
- The trends applied reflect typical medical service trends and do not consider the rapid growth in this area.

Methodology and Assumptions for Baseline Cost Sharing

- CHBRP assumed the Medi-Cal population does not have cost sharing for biomarker testing.

Methodology and Assumptions for Postmandate Utilization and Cost

- As a result of SB 1191, provider reimbursement would only be allowed for a single procedure code that describes a multigene panel test. At baseline, there are several reasons multiple single-gene test codes may be reported on a day for a single patient:
    - Panel tests may be available, but single-gene tests are performed.
    - A specific multigene panel test HCPCS code for the biomarkers included in the multigene panel test is not available in the HCPCS code set.
    - Payer guidance to facilitate payment for covered services may require separate reporting of multiple single-gene test codes provided as part of a single multigene panel so that it can cover and pay for the single-gene tests with an evidence base and non-cover, and not pay for other gene tests in the multigene panel where the payer determines that the evidence is insufficient for coverage.
- To address the uncertainty around the reasons for the utilization of multiple single-gene tests on the same day by the same patient that appears in the claims data, CHBRP modeled three scenarios.
- At baseline, CHBRP assumed that biomarker testing is performed on users if there was a concern about the dosing or a reaction to a medication. Postmandate, CHBRP assumed that as a result of SB 1191, physicians may become more proactive about ordering biomarker testing for enrollees prior to prescribing drugs. For all scenarios, CHBRP assumed utilization of biomarker testing would triple postmandate.

Scenario 1: No billing change. Single-gene tests are billed multiple times because panels do not exist.

- This scenario assumed single-gene tests were billed multiple times because multigene panel tests did not exist for the biomarkers tested.

- All single-gene tests remained single-gene tests postmandate.
- The cost per single-gene test remained unchanged postmandate.

Scenario 2: Multiple single-gene tests become one multigene panel test.

- This scenario assumed that if more than one single-gene test was performed on the same day for a single patient at baseline, all the utilization for the patient's single-gene tests would be captured by one multigene panel test that could be reported for all of the single-gene tests performed. This is likely an underestimate of postmandate utilization of multigene panel tests since all single-gene tests utilized on one day may not be available on one multigene panel.
- For single-gene tests at baseline that became a multigene panel test postmandate, the average cost of a multigene panel test was assumed.
- If an enrollee utilized only one single-gene test on a single day at baseline, CHBRP assumed it remained a single-gene test postmandate. The cost per test remained unchanged postmandate.
- If an enrollee utilized multigene panel tests at baseline, CHBRP assumed they remained multigene panels postmandate. The price of these multigene panel tests remained unchanged postmandate.
- CHBRP assumed the multigene panel tests are fully covered even though the multigene test panel may include some tests for gene markers without an evidence base. The estimated expenditures may be overstated if enrollees must pay for those gene marker tests within the multigene test panel without an evidence base that payers do not cover.

Scenario 3: Multiple single-gene tests become multiple multigene panel tests

- This scenario assumed that if more than one single-gene test was performed on the same day for a single patient at baseline, it was because a single multigene panel test for all of the gene biomarkers did not exist. This scenario also assumed that a multigene panel test exists for each gene biomarker being tested on the day, but no multigene panel includes more than one of the gene biomarkers being tested. Therefore, each unit of the single-gene tests became one unit of multigene panel testing. This is likely an overestimate of postmandate utilization of multigene panel tests as some of the single genes may be able to be tested on the same multigene panel test.
- For single-gene tests at baseline that became multigene panel tests postmandate, the average cost of a panel for a biomarker test was assumed.
- If an enrollee utilized only one single-gene test on a single day at baseline, it remained a single-gene test postmandate. The cost per test remained unchanged postmandate.
- If an enrollee utilized multigene panel tests at baseline, they remained multigene panel tests postmandate. The price of these multigene panel tests remained unchanged postmandate.
- CHBRP assumed the multigene panel tests are fully covered even though the multigene panel test may include tests for gene markers without an evidence base. The estimated expenditures may be overstated if enrollees must pay for those gene marker tests within the multigene panel test without an evidence base that payers do not cover.

Methodology and Assumptions for Postmandate Cost Sharing

- CHBRP assumed the Medi-Cal population does not have cost sharing for biomarker testing.
- CHBRP assumed the multigene panel tests are covered even though the multigene panel test may include tests without evidence base. The estimated cost sharing may be underestimated if enrollees must pay for those gene marker tests within the multigene test panel without an evidence base.

Table 7. FDA and CPIC Drugs

Category	Generic Name
CPIC	Abacavir, Acenocoumarol, Allopurinol, Amikacin, Amitriptyline, Aripiprazole, Aspirin, Atazanavir, Atomoxetine, Atorvastatin, Azathioprine, Belinostat, Brivaracetam, Capecitabine, Carbamazepine, Carglumic Acid, Celecoxib, Chloramphenicol, Chlorpropamide, Ciprofloxacin, Citalopram, Clomipramine, Clopidogrel, Codeine, Dapsone, Desflurane, Desipramine, Dexlansoprazole, Dimercaprol, Divalproex Sodium, Doxepin, Efavirenz, Eliglustat, Enflurane, Escitalopram, Fluorouracil, Flurbiprofen, Fluvastatin, Fluvoxamine, Fosphenytoin, Gentamicin, Glibenclamide, Glimepiride, Glipizide, Halothane, Hydralazine, Hydrocodone, Ibuprofen, Imipramine, Irinotecan, Isoflurane, Ivacaftor, Kanamycin, Lansoprazole, Lornoxicam, Lovastatin, Mafenide, Meloxicam, Mercaptopurine, Mesalazine, Methadone, Methoxyflurane, Methylene Blue, Moxifloxacin, Mycophenolic Acid, Nalidixic Acid, Nitrofurantoin, Norfloxacin, Nortriptyline, Oliceridine, Omeprazole, Ondansetron, Oxcarbazepine, Pantoprazole, Paromomycin, Paroxetine, Peginterferon Alfa-2A, Peginterferon Alfa-2B, Pegloticase, Phenazopyridine, Phenprocoumon, Phenytoin, Pimozide, Piroxicam, Pitavastatin, Pitolisant, Plazomicin, Pravastatin, Primaquine, Probenecid, Quinine, Rasburicase, Risperidone, Rosuvastatin, Sertraline, Sevoflurane, Simvastatin, Siponimod, Sodium Nitrite, Streptomycin, Succinylcholine, Sulfacetamide, Sulfadiazine, Sulfamethoxazole / Trimethoprim, Sulfasalazine, Sulfisoxazole, Tacrolimus, Tafenoquine, Tamoxifen, Tenoxicam, Tetrabenazine, Thioguanine, Tobramycin, Tramadol, Trimipramine, Tropisetron, Valproic Acid, Velaglucerase Alfa, Venlafaxine, Voriconazole, Vortioxetine, Warfarin
FDA	Abacavir, Allopurinol, Amifampridine, Amifampridine Phosphate, Amphetamine, Aripiprazole, Aripiprazole Lauroxil, Atomoxetine, Azathioprine, Belinostat, Brexpiprazole, Brivaracetam, Capecitabine, Carbamazepine, Carvedilol, Celecoxib, Cevimeline, Citalopram, Clobazam, Clopidogrel, Clozapine, Codeine, Deutetrabenazine, Dronabinol, Efavirenz, Eliglustat, Erdafitinib, Flibanserin, Fluorouracil, Flurbiprofen, Fosphenytoin, Gefitinib, Iloperidone, Irinotecan, Isoniazid, Lapatinib, Lofexidine, Meclizine, Meloxicam, Mercaptopurine, Metoclopramide, Mivacurium, Nilotinib, Oliceridine, Oxcarbazepine, Pantoprazole, Pazopanib, Perphenazine, Phenytoin, Pimozide, Piroxicam, Pitolisant, Procainamide, Propafenone, Sacituzumab Govitecan-Hziy, Simvastatin, Siponimod, Succinylcholine, Sulfamethoxazole / Trimethoprim, Sulfasalazine, Tacrolimus, Tetrabenazine, Thioguanine, Thioridazine, Tolterodine, Tramadol, Valbenazine, Venlafaxine, Voriconazole, Vortioxetine, Warfarin

Source: California Health Benefits Review Program, 2022.
Key: CPIC = Clinical Pharmacogenetics Implementation Consortium; FDA = U.S. Food and Drug Administration.

Table 8. Biomarker Procedure Codes

Category	List of CPT/HCPCS
Single Gene	81220 - 81224, 81405, 81404, 81402, 0030U, 0029U, 81232, 81247 - 81249, 81251, 81283, 81306, 81328, 81335, 81346, 81350, 81355, 81373 - 81374, 81376 - 81377, 81380 - 81383, 81400 - 81401, 81231, 81403, 81230, 81226, 81479, 81599, 82955, 84431, 0074U, 0073U, 0072U, 0075U, 0032U, 0033U, 0034U, 0076U, 0071U, 0028U, 0070U, 81227, 81225, 0031U
Multiple Genes	81370 - 81372, 81374 - 81375, 81378 - 81379, 81406 - 81408, 81419, 81430, 81440, 0015U, 0078U, 0169U, 0173U, 0175U, 0237U

Source: California Health Benefits Review Program, 2022.
Note: CPT copyright 2022 American Medical Association. All rights reserved.
Key: CPT = Current Procedural Terminology; HCPCS = Healthcare Common Procedure Coding System.

Determining Public Demand for the Proposed Mandate

CHBRP reviews public demand for benefits relevant to a proposed mandate in two ways. CHBRP:

- Considers the bargaining history of organized labor; and

- Compares the benefits provided by self-insured health plans or policies (which are not regulated by 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.

On the basis of conversations with the largest collective bargaining agents in California, CHBRP concluded that in general, unions negotiate for broader contract provisions such as coverage for dependents, premiums, deductibles, and broad coinsurance levels.

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 carriers 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.

APPENDIX C INFORMATION SUBMITTED BY OUTSIDE PARTIES

In accordance with the California Health Benefits Review Program (CHBRP) policy to analyze information submitted by outside parties during the first 2 weeks of the CHBRP review, the following parties chose to submit information.

> Invitae submitted multiple pieces of information to CHBRP in March 2022. These items include background information, studies on the effectiveness and cost-effectiveness of biomarker testing, information types of tests, and information on potential cost savings due to increased benefit coverage and utilization.

Submitted information is available upon request. For information on the processes for submitting information to CHBRP for review and consideration please visit: www.chbrp.org/requests.html.

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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.

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** works with Task Force members in preparing parts of the analysis, and manages 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. Information on CHBRP's analysis methodology, authorizing statute, as well as all CHBRP reports and other publications, are available at www.chbrp.org.

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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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