MEDICAL POLICY

POLICY TITLE	**GENETIC TESTING FOR DIAGNOSIS AND MANAGEMENT OF MENTAL HEALTH CONDITIONS**
POLICY NUMBER	**MP 2.264**

CLINICAL BENEFIT	☐ MINIMIZE SAFETY RISK OR CONCERN. ☒ MINIMIZE HARMFUL OR INEFFECTIVE INTERVENTIONS. ☐ ASSURE APPROPRIATE LEVEL OF CARE. ☐ ASSURE APPROPRIATE DURATION OF SERVICE FOR INTERVENTIONS. ☒ ASSURE THAT RECOMMENDED MEDICAL PREREQUISITES HAVE BEEN MET. ☐ ASSURE APPROPRIATE SITE OF TREATMENT OR SERVICE.
Effective Date:	**3/1/2024**

I. POLICY

Genetic testing (pharmacogenomic Multi-Gene Panels) for the management of mental health disorders may be considered **medically necessary** when ALL of the following criteria are met:

- The individual has a diagnosis of major depressive disorder or generalized anxiety disorder; and
- The individual has not been adequately treated with, or has been intolerant to, at least one prior medication; and
- The Multi-Gene Panel uses combinatorial genetics and the reports include only FDA reviewed guidance as well as drug/gene and drug/drug interaction.

Covered test Multi-gene Panels under this policy are: LifeKit® PreScript®

Pharmacogenomic screening in the general population is considered **not medically necessary**.

Genetic testing for diagnosis of mental health disorders is considered **investigational** in all situations, including but not limited to the following:

- To confirm a diagnosis of a mental health disorder in an individual with symptoms; **or**
- To predict future risk of a mental health disorder in an asymptomatic individual**.**

There is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with this procedure.

Genetic testing panels for mental health disorders, including but not limited to the Genecept Assay, STA^{2}R test, the GeneSight Psychotropic panel, the Proove Narcotic Risk assay, the MindX blood tests for mood disorders, and the Mental Health DNA Insight Panel, are considered

investigational for all indications. There is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with this procedure.

Policy Guidelines

Pharmacogenomics Nomenclature Update

The International Conference on Harmonisation (ICH), a world-wide consortium of regulatory agencies, has defined "pharmacogenomics" as the study of variations of DNA and RNA characteristics as related to drug response, and "pharmacogenetics" as the study of variations in DNA sequence as related to drug response.

Pharmacogenetics adopted a "star" nomenclature (e.g. *CYP2C19*2*) to describe variants in genes (sometimes termed "pharmacogenes") underlying variability in drug response. Some star alleles may include more than one variant; for example, *TPMT*3A* designates an allele defined by the presence of two single nucleotide polymorphisms (SNPs), and distinguishing this allele from those carrying only one of the SNPs can be challenging. While the star nomenclature persists, attempts are being made to reconcile the notation with alternate variant nomenclature such as the conventional "rs" designation.

The field is also adopting a standard set of definitions of pharmacogenetic phenotypes; for pharmacokinetic genes, these include "normal metabolizers" (NMs), "poor metabolizers" (PMs, carrying two loss-of-function alleles), "intermediate metabolizers" (IMs, carrying one loss-of-function allele), and "ultrarapid metabolizers" (UMs, carrying gain-of-function alleles or gene duplications), and for pharmacodynamic genes, designations such as positive or negative for high risk alleles. These are convenient shorthand designations and there is often some overlap in drug response.

Cross-references:

MP 2.234 Cytochrome p450 Genotype Guided Treatment Strategy
MP 2.253 Genetic Testing for Inherited Thrombophilia

MP 2.323 General Approach to Evaluating the Utility of Genetic Panels

II. PRODUCT VARIATIONS TOP

This policy is only applicable to certain programs and products administered by Capital Blue Cross and subject to benefit variations as discussed in Section VI. Please see additional information below.

FEP PPO - Refer to FEP Medical Policy Manual. The FEP Medical Policy manual can be found at: https://www.fepblue.org/benefit-plans/medical-policies-and-utilization-management-guidelines/medical-policies

III. DESCRIPTION/BACKGROUND TOP

Mental Health Disorders

POLICY TITLE	GENETIC TESTING FOR DIAGNOSIS AND MANAGEMENT OF MENTAL HEALTH CONDITIONS
POLICY NUMBER	MP 2.264

Psychiatric disorders cover a wide range of clinical phenotypes and are generally classified by symptomatology in systems such as the classification outlined in the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5). In addition to counseling and other forms of behavioral treatment, treatment commonly involves one or more psychotropic medications that are aimed at alleviating symptoms of the disorder. Although there are a wide variety of effective medications, treatment of psychiatric disease is characterized by relatively high rates of inadequate response. This often necessitates numerous trials of individual agents and combinations of medications in order to achieve optimal response.

Knowledge of the physiologic and genetic underpinnings of mental health disorders is advancing rapidly and may substantially alter the way these disorders are classified and treated. Genetic testing could be used in several ways, including stratifying patients' risks of developing a particular disorder, aiding diagnosis, targeting medication therapy, and optimally dosing medication.

Drug Efficacy and Toxicity

Drug efficacy and toxicity vary substantially across individuals. Because drugs and doses are typically adjusted, if needed, by trial-and-error, clinical consequences may include a prolonged time to optimal therapy. In some cases, serious adverse events may result.

Multiple factors may influence the variability of drug effects, including age, liver function, concomitant diseases, nutrition, smoking, and drug-drug interactions. Inherited (germline) DNA sequence variation in genes coding for drug metabolizing enzymes, drug receptors, drug transporters, and molecules involved in signal transduction pathways also may have major effects on the activity of those molecules and thus on the efficacy or toxicity of a drug.

Pharmacogenomics studies how an individual's genetic inheritance affects the body's response to drugs. It may be possible to predict therapeutic failures or severe adverse drug reactions in individual patients by testing for important DNA variants (genotyping) in genes related to the metabolic pathway (pharmacokinetics) or signal transduction pathway (pharmacodynamics) of the drug. Potentially, test results could be used to optimize drug choice and/or dose for more effective therapy, avoid serious adverse events, and decrease medical costs.

REGULATORY STATUS

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments. The tests discussed in this section are available under the auspices of the Clinical Laboratory Improvement Amendments. Laboratories that offer laboratory-developed tests must be licensed by the Clinical Laboratory Improvement Amendments for high-complexity testing. To date, the U.S. Food and Drug Administration has chosen not to require any regulatory review of this test.

Examples of commercially available panels include the following:

- Genecept™ Assay (Genomind);

- STA^{2}R test (SureGene Test for Antipsychotic and Antidepressant Response; Clinical Reference Laboratory). Specific variants included in the panel were not easily identified from the manufacturer's website.
- GeneSight® Psychotropic panel (Assurex Health);
- Mental Health DNA Insight™ panel (Pathway Genomics);
- IDgenetix-branded tests (AltheaDx).

Also, many labs offer genetic testing for individual genes, including *MTFHR* (GeneSight Rx and other laboratories), cytochrome P450 variants, and *SULT4A1.*

AltheaDx offers a number of IDgenetix-branded tests, which include several panels focusing on variants that affect medication pharmacokinetics for a variety of disorders, including psychiatric disorders.

IV. RATIONALE

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SUMMARY OF EVIDENCE

The Pharmacogenomics Knowledge for Personalized Medicine database (PharmGKB) is a NIH-funded resource that provides information about how human genetic variation affects response to medications, and provides a centralized resource of international gene-drug professional society prescribing guidelines, FDA label information on gene-drug recommendations, and evidence based clinical curations (Whirl-Carillo et al., 2012, 2021).

Table 1 lists genes that can inform antidepressants and antipsychotics that are found in PharmGKB with an evidence level of 2B (moderate evidence of an association) or better (PharmGKB, 2019a and 2019b).

Table 1: Antidepressant, Antipsychotic Drugs, and Associated Genes

Drug	Genes	Selected Associated References
Citalopram	CYP2C19, SLC6A4, GRIK4, HTR2A, FKBP5, COMT, TXNRD2	CPIC Guideline for CYP2D6 and CYP2C19 Genotypes and Dosing of Selective Serotonin Reuptake Inhibitors (Hicks et al., 2015)
		Polymorphisms in GRIK4, HTR2A, and FKBP5 Show Interactive Effects in Predicting Remission to Antidepressant Treatment (Horstmann et al., 2010)
Escitalopram	CYP2C19, SLC6A4, COMT, TXNRD2	CPIC Guideline for CYP2D6 and CYP2C19 Genotypes and Dosing of Selective Serotonin Reuptake Inhibitors (Hicks et al., 2015)
		Interaction between serotonin transporter gene variants and life events predicts response to antidepressants in the GENDEP project (Keers et al., 2011)
Fluoxetine	FKBP5, COMT, TXNRD2	Polymorphisms in GRIK4, HTR2A, and FKBP5 Show Interactive Effects in Predicting Remission to Antidepressant Treatment (Horstmann et al., 2010)

Paroxetine	CYP2D6, HTR1A, FKBP5, COMT, TXNRD2	CPIC Guideline for CYP2D6 and CYP2C19 Genotypes and Dosing of Selective Serotonin Reuptake Inhibitors (Hicks et al., 2015)
		Polymorphisms in GRIK4, HTR2A, and FKBP5 Show Interactive Effects in Predicting Remission to Antidepressant Treatment (Horstmann, et al., 2010)
		SSRI response and HTR1A (Yevtushenko et al., 2010)
Fluvoxamine	CYP2D6, COMT, TXNRD2	CPIC Guideline for CYP2D6 and CYP2C19 Genotypes and Dosing of Selective Serotonin Reuptake Inhibitors (Hicks et al., 2015)
Venlafaxine	CYP2D6, FKBP5	Polymorphisms in GRIK4, HTR2A, and FKBP5 Show Interactive Effects in Predicting Remission to Antidepressant Treatment (Horstmann et al., 2010)
Amitriptyline	CYP2C19, 2D6	CPIC Guideline for CYP2D6 and CYP2C19 Genotypes and Dosing of Tricyclic Antidepressants (Hicks et al., 2017)
Nortriptyline	CYP2D6	CPIC Guideline for CYP2D6 and CYP2C19 Genotypes and Dosing of Tricyclic Antidepressants (Hicks et al., 2017)
Clomipramine	CYP2C19, 2D6	CPIC Guideline for CYP2D6 and CYP2C19 Genotypes and Dosing of Selective Serotonin Reuptake Inhibitors (Hicks et al., 2015)
Doxepin	CYP2C19, 2D6	CPIC Guideline for CYP2D6 and CYP2C19 Genotypes and Dosing of Tricyclic Antidepressants (Hicks et al., 2017)
Imipramine	CYP2C19, 2D6	CPIC Guideline for CYP2D6 and CYP2C19 Genotypes and Dosing of Tricyclic Antidepressants (Hicks et al., 2017)
Olanzapine	ANKK1, DRD2, MCR4, HTR2C	Genetic variation and the D2 dopamine receptor: implications for the treatment of neuropsychiatric disease (Mickey et al., 2016)
		Pharmacogenetic Associations of Antipsychotic Drug-Related Weight Gain: A Systematic Review and Meta-analysis (Zhang et al., 2016)
Clozapine	ANKK1, DRD2, MCR4, HTR2C	Genetic variation and the D2 dopamine receptor: implications for the treatment of neuropsychiatric disease (Mickey et al.,2016)
		The combined effect of CYP2D6 and DRD2 Taq1A polymorphisms on the antipsychotics daily doses and hospital stay duration in schizophrenia inpatients (Kurylev et al., 2018)

		Pharmacogenetic Associations of Antipsychotic Drug-Related Weight Gain: A Systematic Review and Meta-analysis (Zhang et al., 2016)
Risperidone	CYP2D6, ANKK1, DRD2, MCR4, HTR2C	DPWG Guideline for risperidone and CYP2D6 (Swen et al., 2011)
		Genetic variation and the D2 dopamine receptor: implications for the treatment of neuropsychiatric disease (Mickey et al., 2016)
		Pharmacogenetic Associations of Antipsychotic Drug-Related Weight Gain: A Systematic Review and Meta-analysis (Zhang et al., 2016)
Mirtazapine	CYP2D6, FKBP5	Multicenter study on the clinical effectiveness, pharmacokinetics, and pharmacogenetics of mirtazapine in depression (Jaquenoud Sirot et al., 2012) Polymorphisms in GRIK4, HTR2A, and FKBP5 Show Interactive Effects in Predicting Remission to Antidepressant Treatment (Horstmann et al., 2010)
Desipramine	CYP2D6	CPIC Guideline for CYP2D6 and CYP2C19 Genotypes and Dosing of Tricyclic Antidepressants (Hicks et al., 2017)
Trimipramine	CYP2C19, 2D6	CPIC Guideline for CYP2D6 and CYP2C19 Genotypes and Dosing of Tricyclic Antidepressants (Hicks et al., 2017)

Up to 42% of variance in therapy response for major depressive disorders (MDD) can be explained by genetic variation, which has led to the development of pharmacogenetic tests to inform the use of certain psychiatric medications. Prospective randomized clinical trials have been performed to validate the clinical validity and utility of a number of pharmacogenetics (PGx) multi-gene panels.

In a prospective evaluation of pharmacogenetic guided treatment decisions for major depressive disorder, Brown et al. (2020) et al. calculated the overall mean effect of symptom improvement and relative risk ratio (RR) of response and remission referencing four studies and 1,556 patients. When care was guided by combinatorial pharmacogenetics results, significant patient outcomes were reported as Δ=10.08%, 95% CI: 1.67-18.50; p=0.019; response RR=1.40, 95% CI: 1.17-1.67; p<0.001; remission RR=1.49, 95% CI: 1.17-1.89; p=0.001). The authors summarized that for MDD patients who have had at least one medication failure, guided treatment demonstrated significant clinical utility.

Bousman et al. (2019) conducted a systematic review of the literature and meta-analysis of prospective, randomized controlled (RCT) trials on the use of PGx multi-gene panels that had included a decision support tool to guide clinicians in the use of the results for MDD. RCTs were evaluated using the Cochrane criteria. A total of five RCTs representing 1737 patients were identified. Individuals receiving PGx testing with physicians utilizing a guided decision support

tool (n=887) were 1.17 times more likely (p=.005) than the treatment as usual (TAU) group (n=850) to report symptom remission. Similarly, Rosenblat et al. (2018) conducted a meta-analysis on the use of PGx multi-gene panels to guide treatment of MDD. Article databases were searched up to December 2017 on the human clinical utility of pharmacogenetics for the treatment of MDD. Four randomized clinical trials and two open-label controlled cohort studies were included. The outcomes analyzed were response and remission between PGx and TAU groups. The pooled risk ratio for overall treatment response was 1.36 in favor of PGx guided treatment compared to TAU, and 1.74 for PGx for remission when compare to TAU. The studies were heterogeneous across population, criteria, and PGx testing used.

Menchon et al. (2019) examined the influence of patient characteristics such as age, baseline severity, and duration of episode on the clinical utility of PGx testing for psychiatric drugs from the AB-GEN study, a randomized 12-week long study comparing TAU toPGx guided therapy selection in 280 adults with MDD. The primary outcomes analyzed were the Patient Global Impression of Improvement (PGI-I) scale and the Hamilton Depression Rating Scale (HAM-D17). Patients generally showed no difference in sustained response at the 12-week end point between the TAU and PGx group (Perez, et al., 2017). However, the PGx group had a higher response rate than TAU, and when subjects were removed whose physicians did not follow the genetic testing recommendations, the response rate improved further. Side effects were less in the PGx group by 6 weeks, and this was maintained at week 12. The primary dependent variable identified was the number of previously failed medication trials. In the Menchon et al. (2019) reanalysis by patient demographics, additional important variables were identified. Age was important as PGx testing significantly improved outcomes in those under age 60, but not over age 60. Outcomes were also improved in those with moderate to severe depression, but not those with mild depression. Genetic testing improved PGI-I in one year or less from diagnosis, but not HAM-D17. The effect on HAM-D17 was not significant until the cutoff from time of diagnosis was increased to 5 years. After this, however, a null effect was seen, and individuals who were more than 5 years from their diagnosis were actually worse off in the PGx arm than TAU. To determine which type of patient is most likely to benefit from pharmacogenetic testing for psychiatric therapies, more prospective, randomized trials are needed.

GUIDED is a 24 week RCT conducted between April 2014 and February 2017 comparing active treatment groups guided by PGx information, to active treatment groups receiving usual care (TAU) for MDD (Greden et al., 2019). Sixty sites participated, and patients were referred to the study when it was self- or clinician reported to have inadequate response to at least one antidepressant. The average number of medications failed in the cohort was three, making this a difficult to treat population. Genotyping was for eight genes, *CYP1A2, CYP2C9, CYP2C19, CYP3A4, CYP2B6, CYP2D6, HTR2A,* and *SLC6A4,* and results were evaluated and reported using a proprietary pharmacogenetic algorithm from Assurex Health. Participants were blinded to the study arm but clinicians were not, since they needed to consult the PGx results to guide treatment. Using the results to guide treatment was not mandated. Patients were assessed at 4, 8, 12, and 24 weeks using the HAM-D17, which was administered by blinded raters. A total of 1167 enrolled patients made it through week 8 with 607 in TAU and 560 in PGx guided. HAM-

D17 scores decreased in the TAU arm by 24% and in the PGx arm by 27%, but the difference was not statistically significant. Treatment response, defined as ≥50% decrease in depression, was greater in the PGx arm (26%) than TAU (20%). The depression remission rate, defined as score of ≤7 for HAM-D17, was 10% with TAW and 15% with PGx (p=.007). Additionally, at week 8, there was no difference between the groups in reported side effects. When patients taking incongruent medications were evaluated as a separate cohort, those who switched to congruent medications by week 8 experienced significantly fewer side effects. Medication prescriptions that aligned with PGx results at baseline were 77% in the TAU group and 79% in the PGx group. By week 8, the PGx group increased to 91%, and the TAU group was unchanged. After 8 weeks, clinicians in the TAU arm were unblinded and could use the PGx results if they chose. A total of 913 participants completed through week 24 with 456 in TAU and 457 in the PGx guided arm. Overall, in the PGx group, HAM-D17 scores decreased by 43% at week 24 relative to baseline. Response and remission increased by 70% and 100%, respectively, from week 8 to week 24. While the primary outcome being analyzed, symptom improvement at week 8, was not different between the two groups, there was significant difference in response and remission in the PGx group on other measures.

A panel of ten genes with select polymorphisms combined with a proprietary algorithm, the NeuroIDgenetix® _Test, was the subject of a RCT to evaluate clinical utility for guiding treatment for depression and anxiety (Bradley et al., 2018). Genes included *CYP1A2, CYP2C9, CYP2C19, CYP2D6, CYP3A4, CYP3A5, SLC6A4, COMT, HTR2A,* and *MTHFR.* Participants were identified from 20 independent clinical sites in the US that represented psychiatry, internal medicine, family medicine, and obstetrics and gynecology. A total of 685 patients were included in the study, ranging in age from 19 to 87, and all had a diagnosis of depression or anxiety using the DSM-V criteria and verified by the MINI Psychiatric Interview. Most were female (73%) with diagnoses of depression (n=246), anxiety (n=235) or both (n=204) Participants were either ‘New to Treatment’ (newly diagnosed or taking medications for less than 6 weeks) or ‘Inadequately Controlled’ with medications as defined by lack of efficacy or treatment discontinuation due to adverse events or intolerability; although the authors did not report the distribution. PGx testing was performed in all subjects but was only shared with the physicians of those in the PGx arm. Patients were assessed at 4, 8, and 12 weeks using the HAM-D17 and the Hamilton Rating Scale for Anxiety (HAM-A), with their physicians blinded to the results. Adverse events were captured via the Adverse Drug Event form developed by external psychiatric consultants, and a blinded clinician ranked the adverse events on a severity scale. The PGx testing group showed a greater response and remission rate with odds ratios of 4.72 and 3.54 respectively, than the TAU group at 12 weeks. In the anxiety group, those that received testing had a higher response rate at 8 and 12 weeks with an odds ratio of 1.76, compared to the TAU group. Physicians made at least one medication change in 81% of those receiving testing than the control group (64%) at the two-week time point when results were returned to physicians. No difference was found in adverse drug events between the two treatment groups. In a post-hoc analysis on the ‘Inadequately Controlled’ cohort remission rates (42% vs. 27%, p =0.03) and response rates (62% vs. 44%, p=0.01) response rates were greater with PGx than TAU.

Jung et al. (2017) conducted a genome-wide association study (GWAS) in Generalized Anxiety Disorder (GAD) to identify potential predictors of venlafaxine XR treatment outcome. Ninety-eight European American patients participated in a venlafaxine XR clinical trial for GAD, with Hamilton Anxiety Scale (HAM-A) response/remission at 24 weeks as the primary outcome measure. All participants were genotyped with the Illumina PsychChip, and 266,820 common single nucleotide polymorphisms (SNPs) were analyzed. Although no SNPs reached genome-wide significance, eight SNPs were marginally associated with treatment response/remission and HAM-A reduction at week 12 and 24 ($p<0.00001$). The authors concluded that several identified genes may indicate markers crossing neuropsychiatric diagnostic categories. The authors acknowledged that the limitations of this study include small sample size and the lack of statistical power for a GWAS. Areas for future research include the replication of results with larger samples sizes to increase statistical power and further elucidate the treatment effects of antidepressant venlafaxine XR on GAD.

Researchers enrolled 528 (outpatients and inpatients) from 18 hospitals and associated mental health centers in Spain from July 2014 to June 2015 in the AB-GEN study, a 12-week, double-blind, parallel, multi-center RCT to evaluate the effectiveness of PGx testing for drug therapy guidance for MDD. Patients with a CGI-S ≥ 4 and requiring antidepressant medication de novo or changes in their medication were randomized to a PGx or TAU group. PGx testing was conducted by Neuropharmagen, and results were reported using their web-based clinical decision support tool. Thirty genes and relevant single nucleotide polymorphisms were analyzed. The primary endpoint was measuring a sustained response on the Patient Global Impression of Improvement (PGI-I) of ≤ 2 within the 12-week follow-up. Follow up was conducted by phone, and the interviewer was blinded to the participant's study arm. A patient was considered to have a sustained response with a PGI-I score of 2 or less if they reported their condition to be "much better" or "very much better." Only 280 of 528 patients completed the study. A difference in sustained response was not observed between PGx and TAU at 12 weeks. Overall the PGx group had a much higher response rate, and this improved when removing the patients whose physicians did not follow the PGx recommendations. Effects were greatest in patients who had failed up to three prior medications. Of those who reported side effects at baseline, the PGx group was more likely to report fewer side effects than the TAU group (Perez et al., 2017). This study is interesting as it uses real world practices and clinicians, a heterogeneous population with variable disease states and prior treatment failures, and clinicians could choose to not follow the PGx recommendations. Additional studies are needed to replicate these findings across larger, ethnically diverse study groups.

Perlis et al. (2017) reported on a propensity-score matched case-control analysis of health claims data from a US payer that examined the longitudinal claims of individuals with a mood or anxiety disorder. Claims from individuals who had received the Genecept pharmacogenetic ten gene test from Genomind were compared to case-matched controls who matched on gender, age, and diagnosis who did not receive testing. Diagnoses that were included were depressive disorders, any anxiety diagnosis, bipolar disorder, and any substance abuse diagnosis. Co-morbidities that were accounted for in the analysis included hyperlipidemia, low back pain, hypertension, migraine and other headaches, diabetes mellitus, and any mental health visit. Of

the 1639 individuals who received genetic testing, it was possible to match 817. Patients who had PGx testing had 40% fewer emergency room visit for any cause and 58% fewer hospitalizations for any cause. There was no difference between the groups in the number of psychiatric medications prescribed, or mood disorder related inpatient hospitalizations. Selection bias, since this was an observational study, was a physician that ordered genetic testing might, in theory, be more aggressive in patient management. The study's authors concluded that randomized prospective clinical trials are needed to further validate the clinical utility of genetic testing for psychiatric disorders.

V. DEFINITIONS

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N/A

VI. BENEFIT VARIATIONS

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The existence of this medical policy does not mean that this service is a covered benefit under the member's health benefit plan. Benefit determinations should be based in all cases on the applicable health benefit plan language. Medical policies do not constitute a description of benefits. A member's health benefit plan governs which services are covered, which are excluded, which are subject to benefit limits and which require preauthorization. There are different benefit plan designs in each product administered by Capital Blue Cross. Members and providers should consult the member's health benefit plan for information or contact Capital Blue Cross for benefit information.

VII. DISCLAIMER

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Capital Blue Cross's medical policies are developed to assist in administering a member's benefits, do not constitute medical advice, and are subject to change. Treating providers are solely responsible for medical advice and treatment of members. Members should discuss any medical policy related to their coverage or condition with their provider and consult their benefit information to determine if the service is covered. If there is a discrepancy between this medical policy and a member's benefit information, the benefit information will govern. If a provider or a member has a question concerning the application of this medical policy to a specific member's plan of benefits, please contact Capital Blue Cross' Provider Services or Member Services. Capital Blue Cross considers the information contained in this medical policy to be proprietary and it may only be disseminated as permitted by law.

VIII. CODING INFORMATION

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Note: This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.

Covered when medically necessary for LifeKit® PreScript®

Procedure Codes								
81599	0392U							

Genetic testing for mutations associated with mental health disorders, including but not limited to the Genecept Assay, STA2R test, the GeneSight Psychotropic panel, the Proove Narcotic Risk assay, MindX blood tests, and the Mental Health DNA Insight Panel, are Investigational; therefore, not covered:

Procedure Codes								
0032U	0033U	0175U	81225	81226	81230	81231	81291	81401
81479	0290U	0291U	0292U	0293U	0345U	0347U	0348U	0349U
0380U	0411U	0419U	0423U	0437U	0434U	0438U		

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X. POLICY HISTORY

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MP- 2.264	**04/21/2020 Consensus review**. Policy statement unchanged. Policy guideline, Background, Rationale, and References updated. Coding reviewed.

POLICY TITLE	GENETIC TESTING FOR DIAGNOSIS AND MANAGEMENT OF MENTAL HEALTH CONDITIONS
POLICY NUMBER	MP 2.264

	05/20/2020 Administrative update. New code 0175U added to the policy. Product Variation, Benefit Variation, and Disclaimer updated.
	02/25/2021: Major review. Policy statement updated to include LifeKit Prescript as MN. Rationale, Background, coding, and references updated.
	12/01/2021 Administrative update. Added 0290U-0293U
	04/07/2022 Minor review. MindX blood tests for mood disorders added to policy as INV. Policy guidelines, Product Variations, and Summary of Evidence updated. References added.
	9/12/2022 Administrative update. New Codes 0345U, 0347U, 0348U & 0349U added
	3/16/2023 Administrative update. New Code 0380U added.
	6/13/2023 Administrative update. New Code 0392U added.
	8/11/2023 Consensus review. Regulatory status updated. References reviewed and updated. Coding reviewed.
	9/7/2023 Administrative update. New Codes 0411U, 0419U added.
	12/13/2023 Administrative update. New codes added:0423U, 0437U, 0434U, & 0438U
	1/19/2024 Administrative update. Clinical benefit added.

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