5.01.35	Digital Health Therapies for Substance Use Disorders		
Original Policy Date:	June 1, 2022	**Effective Date:**	March 1, 2023
Section:	5.0 Prescription Drug	**Page:**	Page 1 of 20

Policy Statement

I. Digital health therapies for individuals with substance use disorders are considered **investigational**.

NOTE: Refer to Appendix A to see the policy statement changes (if any) from the previous version.

Policy Guidelines

Vorvida® and Modia® (Orexo) provide support for individuals with problematic drinking and opioid use disorder. These digital technologies have not received marketing clearance by U.S. Food and Drug Administration and are not reviewed here. They are currently available in the U.S. through the Enforcement Policy for Digital Health Devices for Treating Psychiatric Disorders During COVID19 (U.S. Food and Drug Administration, 2020).

Coding

Effective April 1, 2022, there is a new CPT code that represents reSET by Pear Therapeutics. Per the manufacturer, reSET is prescription digital therapeutics and is a cognitive behavioral therapy, indicated for patients 18 years of age and older who are enrolled in outpatient treatment under the supervision of a clinician. It is indicated as a twelve-week prescription-only treatment for patients with substance use disorder who are not currently on opioid replacement therapy, who do not abuse alcohol solely or who do not abuse opioids as their primary substance of abuse. It is intended to increase abstinence from a patient's substances of abuse during treatment and increase retention in the outpatient treatment program

- **A9291**: Prescription digital behavioral therapy, FDA-cleared, per course of treatment

Effective January 1, 2023, the following codes have been **deleted**:

- **0702T**: Remote therapeutic monitoring of a standardized online digital cognitive behavioral therapy program ordered by a physician or other qualified health care professional; supply and technical support, per 30 days
- **0703T**: Remote therapeutic monitoring of a standardized online digital cognitive behavioral therapy program ordered by a physician or other qualified health care professional; management services by physician or other qualified health care professional, per calendar month

Effective January 1, 2023, this Category I code is replacing Category III codes 0702T and 0703T which are being deleted. This service represents online computer-based cognitive behavioral therapy that can be used for a range of disorders, including substance use.

- **98978:** Remote therapeutic monitoring (e.g., therapy adherence, therapy response); device(s) supply with scheduled (e.g., daily) recording(s) and/or programmed alert(s) transmission to monitor cognitive behavioral therapy, each 30 days

Description

The World Health Organization defines substance use disorder as "the harmful or hazardous use of psychoactive substances", which include alcohol, cocaine, marijuana, stimulants, benzodiazepines and opiates. Treatments for drug addiction include behavioral counseling and skills training, which can be given as part of a cognitive-behavioral approach. The first prescription mobile app,

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developed to supplement or replace individual or group therapy, delivers a cognitive-behavioral approach developed specifically for substance use disorder in a series of interactive lessons.

Related Policies

- Drug Testing in Pain Management and Substance Use Disorder Treatment

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates (e.g., Federal Employee Program [FEP]) prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

Regulatory Status

In 2017, reSET® (Pear Therapeutics), received de novo marketing clearance from the FDA to provide CBT as an adjunct to contingency management, for patients with SUD who are enrolled in outpatient treatment under the supervision of a clinician (DEN160018). This is the first prescription digital therapeutic to be approved by the FDA. reSET is indicated as a 12-week (90 days) prescription-only treatment intended to increase abstinence from a patient's substances of abuse during treatment, and increase retention in the outpatient treatment. FDA product code: PWE

In 2018, reSET-O® (Pear Therapeutics) was cleared for marketing by the FDA through the 510(k) pathway as a prescription-only digital therapeutic to "increase retention of patients with opioid use disorder (OUD) in outpatient treatment by providing cognitive behavioral therapy, as an adjunct to outpatient treatment that includes transmucosal buprenorphine and contingency management" (K173681). FDA determined that this device was substantially equivalent to existing devices. The predicate device was reSET.

Vorvida® and Modia® (Orexo) provide support for individuals with problematic drinking and OUD. These digital technologies have not received marketing clearance by U.S. Food and Drug Administration and are not reviewed here. They are currently available in the U.S. through the Enforcement Policy for Digital Health Devices for Treating Psychiatric Disorders During COVID-19.[7,]

Rationale

Background

Substance Use Disorder

The World Health Organization defines substance use disorder as "the harmful or hazardous use of psychoactive substances, including alcohol and illicit drugs", which include alcohol, cocaine, marijuana, stimulants, benzodiazepines and opiates. The American Psychiatric Association, in the Diagnostic and Statistical Manual of Mental Disorders, details 11 problematic patterns of use that lead to clinically significant impairment or distress. Mild substance use disorder (SUD) is defined as meeting 2 to 3 criteria, moderate as 4 to 5 criteria, and severe as 6 or more criteria.

1. Often taken in larger amounts or over a longer period than was intended.
2. A persistent desire or unsuccessful efforts to cut down or control use.

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3. A great deal of time is spent in activities necessary to obtain, use, or recover from the substance's effects.
4. Craving or a strong desire or urge to use the substance.
5. Recurrent use resulting in a failure to fulfill major role obligations at work, school, or home.
6. Continued use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by its effects.
7. Important social, occupational, or recreational activities are given up or reduced because of use.
8. Recurrent use in situations in which it is physically hazardous.
9. Continued use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance.
10. Tolerance.
11. Withdrawal.

Treatment

Treatments for substance use disorder include behavioral counseling, skills training, medication, treatment for withdrawal symptoms, treatment for co-occurring mental health issues, and long-term follow-up to prevent relapse. For patients with primary opioid use disorder (OUD), medication-assisted treatment is the most common approach. U.S. Food and Drug Administration (FDA)-approved drugs for opioid use treatment include a full opioid agonist (methadone), a partial opioid agonist (buprenorphine), and an opioid antagonist (naltrexone). These are used to suppress withdrawal symptoms and reduce cravings, and may be used in combination with counseling and behavioral therapies.

One common psychosocial intervention is cognitive-behavioral therapy (CBT). CBT is an established therapy based on social learning theory that addresses a patient's thinking and behavior. CBT has proven positive effects for the treatment of SUD.[1,] There are 2 main goals of CBT: first, recognize thoughts and behaviors that are associated with substance abuse, and second, expand the repertoire of effective coping responses. Specific goals for SUD and OUD include a better understanding of risk factors for use, more accurate attributions of cause and effect, increased belief in the ability to address problems, and coping skills. Specific skills may include motivation, drink/drug refusal skills, communication, coping with anger and depression, dealing with interpersonal problems, and managing stress.

The community reinforcement approach is a form of CBT that has a goal of making abstinence more rewarding than continued use. Community reinforcement approach increases non-drug reinforcement by teaching skills and encouraging behaviors that help improve employment status, family/social relations and recreational activities. Community reinforcement approach was originally developed for alcohol dependence and cocaine use, and has been shown to be more effective than usual care in reducing the number of substance use days.

Contingency management may also be a component of addiction treatment. Contingency management, also known as motivational incentives, provides immediate positive reinforcement to encourage abstinence and attendance. Positive reinforcement may range from a verbal/text acknowledgement of completion of a task to monetary payment for drug-negative urine specimens. Contingency management is based on the principles of operant conditioning as formulated by B.F. Skinner, which posits that rewarding a behavior will increase the frequency of that behavior. Contingency management is typically used to augment a psychosocial treatment such as community reinforcement approach.

The combination of community reinforcement approach plus contingency management was shown in a 2018 network meta-analysis of 50 RCTs to be the most efficacious and accepted intervention among 12 structured psychosocial interventions, including contingency management alone, in individuals with cocaine or amphetamine addiction.[2,] Positive reinforcement with voucher draws (e.g.,

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from a fishbowl) of variable worth that range from a congratulatory message to an occasional high dollar value are as effective as constant monetary vouchers. Studies conducted by the National Drug Abuse Treatment Clinical Trials Network have shown that intermittent reinforcement with incentives totaling $250 to $300 over 8 to 12 weeks both increases retention in a treatment program and reduces stimulant drug use during treatment.[3,]

Software as a Medical Device

The International Medical Device Regulators Forum, a consortium of medical device regulators from around the world which is led by the FDA, distinguishes between 1) software in a medical device and 2) software as a medical device (SaMD). The Forum defines SaMD as "software that is intended to be used for one or more medical purposes that perform those purposes without being part of a hardware medical device".[4,]

FDA's Center for Devices and Radiological Health is taking a risk-based approach to regulating SaMD. Medical software that "supports administrative functions, encourages a healthy lifestyle, serves as electronic patient records, assists in displaying or storing data, or provides limited clinical decision support, is no longer considered to be and regulated as a medical device".[5,]

Regulatory review will focus on mobile medical apps that present a higher risk to patients.

- Notably, FDA will not enforce compliance for lower risk mobile apps such as those that address general wellness.
- FDA will also not address technologies that receive, transmit, store, or display data from medical devices.

The agency has launched a software pre- certification pilot program for SaMD that entered its test phase in 2019. Key features of the regulatory model include the approval of manufacturers prior to evaluation of a product, which is based on a standardized "Excellence Appraisal" of an organization, and its commitment to monitor product performance after introduction to the U.S. market. Criteria include excelling in software design, development, and validation. Companies that obtain pre-certification participate in a streamlined pre-market review of the SaMD. Pre-certified organizations might also be able to market lower-risk devices without additional review. In 2017, FDA selected 9 companies to participate in the pilot program, including Pear Therapeutics.

BCBSA Evaluation Framework for Digital Health Technologies

SaMDs, as defined by FDA, are subject to the same evaluation standards as other devices; the Blue Cross and Blue Shield Association Technology Evaluation Criterion are as follows:

1. The technology must have final approval from the appropriate governmental regulatory bodies.
2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes.
3. The technology must improve the net health outcome.[a]
4. The technology must be as beneficial as any established alternatives.
5. The improvement must be attainable outside the investigational settings.[b]

[a] The technology must assure protection of sensitive patient health information as per the requirements of The Health Insurance Portability and Accountability Act of 1996 (HIPAA)
[b] The technology must demonstrate usability in a real-world setting

Other regulatory authorities such as the United Kingdom's National Institute for Health and Care Excellence (NICE) have proposed standards to evaluate SaMD.[6,]

Literature Review

Evidence reviews assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are the length of life, quality of life, and

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ability to function including benefits and harms. Every clinical condition has specific outcomes that are important to patients and managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent 1 or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Digital Health Technologies for Substance Use Disorders Other than Opioid Use Disorder

Clinical Context and Therapy Purpose

Substance use disorder(SUD) is a serious health problem in the U.S. A 2019 survey from the Substance Abuse and Mental Health Services Administration found that 20.4 million people age 12 years or older in the U.S., or 7.4 percent of the U.S. population, had SUD, but only 1.5 million people were enrolled in substance use treatment.[8,] The most common substances reported in the survey are alcohol, followed by tobacco and marijuana. Illicit drug use and prescription drug misuse occur in a lower percentage of the population.

A computer-delivered cognitive-behavioral therapy (CBT) program named CBT4CBT (Computer-Based Training for Cognitive Behavioral Therapy) has been developed to provide therapy for patients with substance abuse. The program includes 7 core CBT skills delivered by on-screen narration, graphic animation, quizzes, and interactive exercises. In a 2018 RCT, both clinician and computer delivery of CBT reduced the frequency of substance use more than treatment as usual.[9,] In addition, patients who received the computer-based CBT with minimal monitoring had the best treatment retention, learning of CBT concepts, and 6 month outcomes compared to either clinician-delivered CBT or treatment as usual. A computer-based community reinforcement approach (CRA) plus vouchers was reported in a 2008 study to lead to similar levels of abstinence as patients who received clinician-guided CRA plus vouchers.[10,] These results suggest that computerized CRA (CCRA) could potentially substitute for clinician-guided therapy and increase access to treatment.

In 2017 and 2018, the first prescription mobile apps (i.e., reSET and reSET-O) were cleared for marketing by the U.S. Food and Drug Administration (FDA). These 2 apps are intended to provide CCRA as an addition to traditional therapy in the context of an outpatient program.

The question addressed in this evidence review is: do prescription mobile apps that provide CCRA improve the net health outcome in patients with SUDs other than opioid use disorder (OUD)?
The following PICO was used to select literature to inform this review.

Populations

ReSET is indicated for adult patients with SUD, who are not currently on opioid replacement therapy, who do not abuse alcohol solely, or who do not abuse opioids as their primary substance of abuse. Individuals with SUD should be enrolled in outpatient treatment under the supervision of a clinician.

Interventions

ReSET and ReSET-O are prescription-based mobile device apps that deliver behavioral therapy in a series of interactive therapy lessons. The lessons include a CBT component and skill building

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exercises, which may be delivered with videos, animations, and graphics. Both apps are modeled on the CRA. The mobile apps provide a way for patients to self-report cravings and triggers, and in the case of ReSET-O, buprenorphine use. The module sequence and progress with the lesson modules can be selected and viewed by the treating clinician.

Comparators

The comparator is treatment as usual in a clinician supervised outpatient program. In the pivotal study described below, treatment as usual for SUD consisted of group or individual therapy sessions for 4 to 6 hours per week and urine drug testing.

Outcomes

The outcome which is most frequently cited as the most important outcome for patients is abstinence from the substance of abuse.[11,] This primary outcome should be measured during therapy, at the end of therapy, and at longer-term (e.g., 3-, 6-, and 12- month) follow-up to assess the durability of the treatment.

Other outcomes that have been reported as important to patients are drug craving, employment, and stable relationships. A semi-structured assessment of 7 potential problem areas in individuals with SUD is the Addiction Severity Index.[12,] The domains are medical status, employment and support, drug use, alcohol use, legal status, family/social status, and psychiatric status. The Addiction Severity Index provides severity ratings of the client's need for treatment and composite scores which measure problem severity during the prior 30 days.

The Maudsley Addiction Profile is a brief standardized interview that assesses treatment outcomes in domains of substance abuse, health risk behavior, physical and psychological health, and personal social functioning.[13,]

Retention in a treatment program is commonly used in addiction research but is an indirect measure of treatment success. Although retention is necessary, it is not sufficient to assess effectiveness and additional outcome measures are needed. Observational data from the Drug Abuse Treatment Outcome Studies suggest that most addicted individuals need at least 3 months in treatment to significantly reduce or stop their drug use and that the best outcomes occur in patients who participate in longer treatment.[14,15,]

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse effects, single-arm studies that capture longer periods of follow-up and/or larger populations were sought;
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Randomized Controlled Trial

The pivotal RCT for the prescription digital apps for SUD (resSET) is described below and in Tables 1 and 2. The technology was developed by the National Institute of Drug Abuse-funded Center for Technology and Behavioral Health as the Therapeutic Education System, which was subsequently submitted to the FDA for a mobile platform by Pear Therapeutics.

Campbell et al (2014) reported the pivotal multicenter trial for reSET, in which patients with SUD or OUD completed 20 to 30 minutes of multimedia modules on a desktop while in the clinic or at home.[16,17,] The active treatment was the Therapeutic Education System, which combined CCRA plus

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contingency management, and was compared to treatment as usual (therapy alone) at 10 community-based outpatient treatment programs as part of the National Drug Abuse Clinical Trials Network. Clinicians were able to access reports on computer activity and discussed module completion in the individual therapy sessions. Contingency management consisted of random selection of vouchers, which ranged from a congratulatory message to $100 cash, for module completion and negative urine drug results. The mean dollars earned was $277 (standard deviation [SD] $226) over the 12 weeks. Although the study was intended to replace some of the hours of therapy, the Therapeutic Education System group received the same number of therapy session as the control group, so the combined program was effectively in addition to counseling alone.

The co-primary outcomes were abstinence from drug/heavy alcohol use in the last 4 weeks of treatment and retention in the treatment program. In the analysis by Campbell et al (2004)[16], the Therapeutic Education System reduced drop-out from the treatment program (hazard ratio, 0.72; 95% confidence interval [CI], 0.57 to 0.92; p=.010), and the odds of achieving abstinence was 1.62 fold greater in the group with CCRA and contingency management group (p=.010). However, the beneficial effect of the Therapeutic Education System was observed only in patients who were not abstinent at baseline. For patients who were abstinent at baseline, the Therapeutic Education System did not increase abstinence, and at 3 and 6 month follow-up, the effect of Therapeutic Education System was no longer significant. Subsequent analyses of the trial found that the Therapeutic Education System was not associated with improvements in social functioning compared to standard outpatient care.[18]

In the FDA analyses of the trial[17], results were analyzed for the entire cohort and for cohorts that excluded patients who reported opioid use. Abstinence during weeks 9 to 12 and total abstinence with CCRA plus contingency management was significantly greater in the cohort as a whole and more so in the analyses that excluded primary opioid users. For example, abstinence during weeks 9 to 12 was 40.3% in the SUD subgroup who received CCRA plus vouchers compared to 17.6% in the group who received only therapy (p<.001). Total abstinence, defined as the number of half weeks with a negative urine drug test, was 11.9 half weeks in the SUD subgroup who received the experimental treatment and 8.8 half weeks in controls (p=.003).

There was a significant increase in retention during the 12 week program. The SUD subgroup had a 23.8% drop out rate compared to 36.8% in the control group (p=.004).

Maricich et al (2022) published a post hoc secondary analysis of data from the trial, excluding participants with OUD (n=399 individuals with SUD related to alcohol, cannabis, cocaine, or other stimulants). Abstinence was significantly higher than treatment as usual in the reSET group (40.3% vs. 17.6%; *p*<.001) as was retention in therapy (76.2% vs. 63.2%; p=.004).[19]

Table 1. Summary of Key Randomized Controlled Trial Characteristics

Study; Trial	Countries	Sites	Participants	Interventions	
				Active[a]	*Comparator*
Campbell et al (2014); FDA Submission DEN160018 [16,17]	U.S.	10	507 adult patients with self-report of drug use, with a subset of 305 who did not have primary use of opioids treated at community health centers	12 weeks of treatment as usual + CCRA (62 modules on a desktop) + contingency management for module completion and negative drug screen (n=255)	12 weeks of treatment as usual consisting ≥2 individual or group therapy sessions per week (n=252)

CCRA: computer-based community reinforcement approach.
[a]CCRA consisted of 20 to 30 min multimedia computer modules. Patients completed a mean of 36.6 (standard deviation, 18.1) out of 62 total CCRA modules in the study by Campbell et al.

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Table 2. Summary of Key Randomized Controlled Trial Results

Study	Abstinence		Total Abstinence		Retention		Dropping Out of Treatment	
Campbell et al (2014); FDA Submission DEN160018 [16,17]	Rate During Weeks 9-12		Half weeks					
	Entire Cohort (n=507)	*Excluding Primary Opioid Abusers (n=399)*	*Entire Cohort (n=507)*	*Excluding Primary Opioid Abusers (n=399)*	*Entire Cohort (n=507)*	*Excluding Primary Opioid Abusers (n=399)*	*Entire Cohort (n=507)*	*Excluding Primary Opioid Abusers (n=399)*
Treatment as usual + CCRA + contingency management	29.7%	40.3%	10.9	11.9	72.2%	76.2%	27.8%	23.8%
Treatment as usual	16.0%	17.6%	8.6	8.8	63.5%	63.2%	36.5%	36.8%
p	.008	<.001	.002	.003			.03	.004

C CRA: computer-based community reinforcement approach.

The trial had a number of limitations in relevance and in design and conduct that preclude determination of the effect of the intervention on relevant health outcomes (Tables 3 and 4).

- The experimental group received both the web-based CCRA and a reward for a negative drug test. The trial was designed to assess the combined treatment approach, and not specifically the CCRA program. Because a reward for a negative drug screen is known by itself to increase both retention and abstinence during a trial,[3,] the contribution of the digital technology to the increase in abstinence in patients with SUD cannot be determined. Notably, abstinence was not improved at the 3 and 6 month follow-up, raising further questions about whether the increase in abstinence during the trial was due to contingency management rather than the CCRA.
- The choice (e.g., retention) and timing (e.g., during treatment) of the outcome measures. Abstinence after a treatment program is a main objective of therapy. Abstinence was greater during the trial, but not improved at the 3 and 6 month follow-up.
- The potential for performance bias among the volunteers in this unblinded study. Nearly half of patients who qualified for the study chose not to participate. There may have been greater motivation to use the new technology in patients who agreed to participate in the study. While acknowledging the difficulty of blinding with this type of intervention, providing a control intervention of similar intensity, such as computer time that is not based on CRA, is feasible.

Given these limitations, further study in well designed trials is needed to determine the effects of the technology on addiction.

Table 3. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Campbell et al (2014); FDA Submission DEN16001 [16,17]	4. The study volunteers may not be representative of the general population with substance use disorder.	2. Intervention was conducted in the clinic	3. The comparator did not include contingency management with vouchers. Delivery was not a similar intensity as the intervention.	1. Uncertain significance of retention as an outcome.	1. Duration of follow-up not sufficient to assess durability.

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The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 4. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Campbell et al (2014); FDA Submission DEN160018 [16,17]		1. Participants and investigators were not blinded to treatment assignment.	2. Subgroup analyses in the FDA Summary were not pre-specified			

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

Observational Study

In a retrospective analyses of data from the pivotal trial, Luderer et al (2022) found an association between engagement with the app (i.e., total number of modules completed) and abstinence during weeks 9 to 12.[20]

Section Summary: Digital Health Technologies for Substance Use Disorders Other than Opioid Use Disorder

Mobile digital technology is proposed as an adjunct to outpatient treatment; however, there are a number of limitations in the current evidence base that limit any conclusions regarding efficacy. The 1 RCT evaluating the technology in individuals with SUD other than OUD assessed the combined intervention of computer-based learning and a reward for abstinence. Since reward for abstinence alone has been shown to increase both abstinence and retention, the contribution of the web-based program to the overall treatment effect cannot be determined. The treatment effect on abstinence was not observed at follow-up, raising further questions about the relative effects of the rewards and the web program. While the RCT reported a positive effect on the intermediate outcome of retention, the relationship between retention and relevant health outcomes in this trial is uncertain. A retrospective secondary analyses of data from the trial reported an association between

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engagement with the app and abstinence at 9 to 12 weeks, but study design limitations preclude drawing conclusions from this study. Given these limitations, further study in well-designed trials is needed to determine the effects of prescription digital therapeutics on relevant outcomes in individuals with SUD. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Digital Health Technologies for Opioid Use Disorder

Populations

ReSET-O is indicated for adult patients with OUD who are in outpatient treatment with transmucosal buprenorphine and contingency management under the supervision of a clinician.

Interventions

ReSET-O is a prescription-based mobile device app that deliver behavioral therapy in a series of interactive therapy lessons. The lessons include a CBT component and skill building exercises, which may be delivered with videos, animations, and graphics. The app is modeled on the CRA. The mobile app provides a way for patients to self-report cravings, triggers, and buprenorphine use. The module sequence and progress with the lesson modules can be selected and viewed by the treating clinician.

ReSET-O is intended to be used as an adjunct to outpatient treatment that includes transmucosal buprenorphine and contingency management for patients 18 years or older who are currently under the supervision of a clinician.

Comparators

The comparator is treatment as usual in a clinician supervised outpatient program with contingency management. In the pivotal studies described below, treatment as usual for SUD consisted of group or individual therapy sessions for 4 to 6 hours per week and urine drug testing. Treatment as usual for OUD included 3 times per week sublingual buprenorphine administration and urine drug testing with contingency management, and in person meetings with a clinician every other week.

Outcomes

The outcome which is most frequently cited as the most important outcome for patients is abstinence from the substance of abuse.[11,] This primary outcome should be measured during therapy, at the end of therapy, and at longer-term (e.g., 3-, 6-, and 12- month) follow-up to assess the durability of the treatment.

Other outcomes that have been reported as important to patients are drug craving, employment, and stable relationships. A semi-structured assessment of 7 potential problem areas in substance-abusing patients is the Addiction Severity Index.[12,] The domains are medical status, employment and support, drug use, alcohol use, legal status, family/social status, and psychiatric status. The Addiction Severity Index provides severity ratings of the client's need for treatment and composite scores which measure problem severity during the prior 30 days.

The Maudsley Addiction Profile is a brief standardized interview that assesses treatment outcomes in domains of substance abuse, health risk behavior, physical and psychological health, and personal social functioning.[13,]

Retention in a treatment program is commonly used in addiction research but is an indirect measure of treatment success. Observational data from the Drug Abuse Treatment Outcome Studies suggest that most addicted individuals need at least 3 months in treatment to significantly reduce or stop their drug use and that the best outcomes occur in patients who participate in longer treatment.[14,21,] Although retention is necessary, it is not sufficient to assess effectiveness and additional outcome measures are needed.

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Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse effects, single-arm studies that capture longer periods of follow-up and/or larger populations were sought;
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

A number of studies were excluded from this evidence review because they did not report relevant outcomes (e.g., they measured cost savings or healthcare resource utilization).[22,-,26,]

Randomized Controlled Trial

In the pivotal study reported by Christensen et al (2014), CCRA was added to treatment as usual in individuals who had opioids as the primary substance of abuse (Tables 5 and 6).[27,28,] Treatment as usual included clinic visits 3 times per week with a reward for a negative urine drug screen (maximum of $997.50), sublingual buprenorphine/naloxone, and a clinician visit every 2 weeks. Participants who did not show up for any of the thrice weekly clinic visits were considered to have a positive drug screen, and were considered drop-outs if they missed 3 visits in a row. The primary outcomes were the longest continuous abstinence and total abstinence. The study was powered to detect a 3 week difference between groups in mean weeks of continuous abstinence. In the 84 day treatment program there were 9.7 more days of abstinence in the CCRA group (67.1 days) than in the control group (57.4 days; p=.01), but the trial did not meet 1 of the primary outcomes of a significant difference between the 2 groups in the longest abstinence (5.5 days; p=.214). The group using the computerized therapy had an increase in medication Addiction Severity Index scores (p=.04), but did not show a significant improvement on the overall Addiction Severity Index (p>.16). The data on abstinence and Addiction Severity Index was not reported in the 510(K) summary for the U.S. FDA.[28,]

Table 5. Summary of Key Randomized Controlled Trial Characteristics

Study; Trial	Countries	Sites	Participants	Interventions	
				Active[a]	*Comparator*
Christensen et al (2014); FDA Submission K173681 [27,28,]	U.S.	1	170 opioid-dependent adults	12 weeks of CCRA (69 modules on a desktop in the clinic) + contingency management + buprenorphine/ naloxone (n=92)	12 weeks of contingency management + buprenorphine/ naloxone (n=78)

CCRA: computer-based community reinforcement approach.
[a]CCRA consisted of 20 to 30 min multimedia computer modules. Patients completed a mean of 36.6 (standard deviation, 18.1) out of 62 total CCRA modules in the study by Campbell et al. There were a total of 69 CCRA modules in the study by Christensen et al.

Table 6. Summary of Key Randomized Controlled Trial Results

Study	Abstinence	Total Abstinence	Retention	Dropping Out of Treatment	ASI overall	ASI Medication Subscale
Christensen et al (2014); FDA Submission K173681 [27,28,]	Longest Abstinence in Days (+ SD)	Total Days + SD	Treatment Completion			
CRA + contingency management	55	67.1 + 19.3	80.4%	17.6%		

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Study	Abstinence	Total Abstinence	Retention	Dropping Out of Treatment	ASI overall	ASI Medication Subscale
Contingency management	49.5	57.4 + 28.0	64.1%	31.6%		
HR/Diff/OR (95% CI)	Diff: 5.5	Diff: 9.7 (2.3 to 17.2)	OR: 2.30 (1.15 to 4.60)	HR: 0.47 (0.26 to 0.85)		
p	.214	.011		.0224	>.24	.04

ASI: Addiction Severity Index; CI: confidence interval; CRA: community reinforcement approach; Diff: difference; HR: hazard ratio; OR: odds ratio; SD: standard deviation.

The trial had a number of limitations in relevance and in design and conduct that preclude determination of the effect of the intervention on relevant health outcomes (Tables 7 and 8).

- The choice (e.g., retention) and timing (e.g., during treatment) of the outcome measures. Abstinence after a treatment program is a main objective of therapy. The main effect of the technology was on retention, and there was no follow-up after 12 weeks.
- The potential for performance bias among the volunteers in this unblinded study. There may have been greater motivation to use the new technology in patients who agreed to participate in the study. While acknowledging the difficulty of blinding with this type of intervention, providing a control intervention of similar intensity, such as computer time that is not based on CRA, is feasible.

Given these limitations, further study in well-designed trials is needed to determine the effects of the technology on addiction.

Table 7. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Christensen et al (2014); FDA Submission K173681 [27,28,]		2. Intervention was conducted in the clinic	3. Delivery was not a similar intensity as the intervention.	1. Uncertain significance of retention as an outcome.	1. The study did not extend after 12 week treatment period, limiting inferences on efficacy for abstinence.

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 8. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Christensen et al (2014); FDA Submission K173681 [27,28,]		1. Participants and investigators were not blinded to treatment assignment.				

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The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

Observational Studies

Study design and results of observational studies are shown in Tables 9 and 10.

Marichich et al (2021) performed an industry-funded analysis of reSET-O data from 3144 patients with OUD who had filled a 12 week prescription of the software.[29,] Participants were instructed to complete at least 4 modules per week with a total possible of 31 core modules and 36 supplemental modules. Analysis of the software's data showed that about half of the patients completed all 31 modules, 66% completed half of the modules, and 74% of patients actively participated through 12 weeks. Use decreased from 100% in the first week to 55% of individuals completing 4 modules in week 12. (Retention in the pivotal study by Christensen was 80% for the software compared to 64% for contingency management alone).[27,28,] Abstinence during the last 4 weeks of treatment was determined by either urine drug screening or self-report recorded on reSET-O. With a conservative estimate of missing data considered to be a positive drug screen, 66% of patients were estimated to be abstinent during the last 4 weeks of the prescription. For patients who completed 3 to 5 modules in the first week, abstinence in the final 4 weeks ranged from 83% to 89%. A limitation of this study is that patients who completed more modules in the first week may have been more motivated to remain abstinent, and cause and effect cannot be determined from this non-comparative observational study.

Marichich et al (2021) also published data from a subset of 643 individuals from the above cohort who completed the 12-week prescription and were then prescribed a second 12-week refill prescription.[30,] At the end of the second prescription period, 86.0% of the cohort were abstinent and 91.4% were retained in treatment through 24 weeks.

Table 9. Observational Study Characteristics

Study	Country	Participants	Treatment	Follow-Up
Marichich et al (2021)[29,]	U.S.	3144 patients with buprenorphine medication for OUD who were under the care of a clinician and filled a 12-week prescription for reSET-O	Four 30 min modules per week for a total of 31 core modules and 36 supplemental modules on a mobile device; total treatment time 12 weeks	12 weeks
Marichich et al (2021)[30,]	U.S.	643 individuals from the above cohort who had completed a 12-week prescription	Same as above; with a total treatment time of 24 weeks	24 weeks

OUD: opioid use disorder.

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Table 10. Summary of Observational Study Results

Study	Participants Completing all Core Modules	Participants Completing Half of Modules	Retention	Abstinence
Marichich et al (2021)[29],	49%	66%	Through 12 weeks: 74.2%	During weeks 9 to 12: 66%
Marichich et al (2021)[30],	64%	85%	Through 24 weeks: 91.4%	During weeks 21 to 24: 86%

Section Summary: Digital Health Technologies for Opioid Use Disorder

Mobile digital technology is proposed as an adjunct to outpatient treatment that includes transmucosal buprenorphine and contingency management; however, there are a number of limitations in the current evidence base that limit any conclusions regarding efficacy. The 1 RCT evaluating the technology in individuals with OUD did not meet a primary objective of longest days of abstinence. While there was a positive effect on the intermediate outcome of retention, the relationship between retention and relevant health outcomes in this trial is uncertain. Retrospective observational studies found that participants who completed more modules with the mobile app had greater abstinence during weeks 9 to 12 and, in a subgroup of individuals who received a refill prescription, during weeks 21 to 24, but the retrospective design and lack of a control group with comparable motivation limits interpretation of these results. Given these limitations, further study in well-designed trials is needed to determine the effects of prescription digital therapeutics on relevant outcomes in individuals with OUD.

Summary of Evidence

For individuals with SUD other than OUD who receive a prescription digital therapeutic, the evidence includes 1 pivotal RCT and secondary analyses of data from the trial. Relevant outcomes are symptoms, morbid events, change in disease status, quality of life, and medication use. Mobile digital technology is proposed as an adjunct to outpatient treatment; however, there are a number of limitations in the current evidence base that limit any conclusions regarding efficacy. The RCT assessed the combined intervention of computer-based learning and a reward for abstinence. Since reward for abstinence alone has been shown to increase both abstinence and retention, the contribution of the web-based program to the overall treatment effect cannot be determined. The treatment effect on abstinence was not observed at follow-up, raising further questions about the relative effects of the rewards and the web program. While the RCT reported a positive effect on the intermediate outcome of retention, the relationship between retention and relevant health outcomes in this trial is uncertain. A retrospective secondary analyses of data from the trial reported an association between engagement with the app and abstinence at 9 to 12 weeks, but study design limitations preclude drawing conclusions from this study. Given these limitations, further study in well-designed trials is needed to determine the effects of prescription digital therapeutics on relevant outcomes in individuals with SUD. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with OUD who receive a prescription digital therapeutic, the evidence includes 1 pivotal RCT and analysis of data of more than 3000 patients from the mobile app. Relevant outcomes are symptoms, morbid events, change in disease status, quality of life, and medication use. Mobile digital technology is proposed as an adjunct to outpatient treatment that includes transmucosal buprenorphine and contingency management; however, there are a number of limitations in the current evidence base that limit any conclusions regarding efficacy. The RCT did not meet a primary objective of longest days of abstinence. While there was a positive effect on the intermediate outcome of retention, the relationship between retention and relevant health outcomes in this trial is uncertain. Retrospective observational studies found that participants who completed more modules with the mobile app had greater abstinence during weeks 9 to 12 and, in a subgroup of individuals who received a refill prescription, during weeks 21 to 24, but the retrospective design and lack of a control group with comparable motivation limits interpretation of these results. Given these

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limitations, further study in well-designed trials is needed to determine the effects of prescription digital therapeutics on relevant outcomes in individuals with OUD. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Supplemental Information

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American Society of Addiction Medicine

In 2020, the American Society of Addiction Medicine (ASAM) published a focused update of their National Practice Guideline for the Treatment of Opioid Use Disorder.[31,] The guideline recommended that psychosocial treatment should be considered in conjunction with pharmacological treatment for opioid use disorder and noted, "At a minimum, the psychosocial treatment component of the overall treatment program should include assessment of psychosocial needs; individual and/or group counseling; linkages to existing support systems; and referrals to community-based services." They also noted that "psychosocial treatment may also include more intensive individual counseling and psychotherapy, contingency management, and mental health services" and, "while questions remain about which specific psychosocial therapies work best with which pharmacological treatments, there is widespread support for recommending psychosocial treatment as an important component of a patient's opioid use disorder treatment plan." The guideline did not address digital health therapies.

National Institute on Drug Abuse

The 2018 Principles of Drug Addiction and Treatment from the National Institute on Drug Abuse describes evidence-based approaches to drug addiction treatment.[21,] Behavioral therapies include cognitive-behavioral therapy (alcohol, marijuana, cocaine, methamphetamine, nicotine), contingency management (alcohol, stimulants, opioids, marijuana, nicotine), community reinforcement approach plus vouchers (alcohol, cocaine, opioids), motivational enhancement therapy (alcohol, marijuana, nicotine), the matrix model (stimulants), 12-step facilitation therapy (alcohol, stimulants, opiates) and family behavior therapy. The guidelines did not address digital health therapies for substance use disorders.

U.S. Preventive Services Task Force Recommendations

Not applicable

Medicare National Coverage

There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this review are listed in Table 11.

Table 11. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT04129580[a]	A Randomized Clinical Trial of Comprehensive Cognitive Behavioral Therapy (CBT) Via reSET-O for	200	Sep 2023

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NCT No.	Trial Name	Planned Enrollment	Completion Date
	a Hub and Spoke Medication Assisted Treatment (MAT) System of Care		
NCT04817267[a]	Pilot Study of reSET-O to Treatment-as-usual in Acute Care Settings	60	Mar 2024
NCT04542642[a]	A Randomized, Controlled, Open-Label, Decentralized Study, to Evaluate Patient Engagement With PEAR-008, a Game-Based Digital Therapeutic for the Treatment of Opioid Use Disorder	130	Aug 2022
NCT04907045	Non-randomized parallel groups pilot study to evaluate intervention delivery, data collection, and analysis procedures. Two primary care clinics will implement the reSET and reSET-O digital therapeutics for substance use disorders. There will be one clinic per arm in this pilot study. Implementation strategies will be varied across arms.	700	Jul 2024
NCT05160233	Digital Treatments for Opioids and Other Substance Use Disorders (DIGITS) in Primary Care: A Hybrid Type-III Implementation Trial	13,000	Jul 2024
NCT04927143	Encouraging Abstinence Behavior in a Drug Epidemic	600	Jun 2024

NCT: national clinical trial.
[a] Denotes industry-sponsored or cosponsored trial.

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Documentation for Clinical Review

- No records required

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms of the Policy.

The following codes are included below for informational purposes. Inclusion or exclusion of a code(s) does not constitute or imply member coverage or provider reimbursement policy. Policy Statements are intended to provide member coverage information and may include the use of some codes for clarity. The Policy Guidelines section may also provide additional information for how to interpret the Policy Statements and to provide coding guidance in some cases.

Type	Code	Description
CPT®	0702T	Remote therapeutic monitoring of a standardized online digital cognitive behavioral therapy program ordered by a physician or other qualified health care professional; supply and technical support, per 30 days ***(Deleted code effective 1/1/2023)***
	0703T	Remote therapeutic monitoring of a standardized online digital cognitive behavioral therapy program ordered by a physician or other qualified health care professional; management services by physician or other qualified health care professional, per calendar month ***(Deleted code effective 1/1/2023)***
	98978	Remote therapeutic monitoring (e.g., therapy adherence, therapy response); device(s) supply with scheduled (e.g., daily) recording(s) and/or programmed alert(s) transmission to monitor cognitive behavioral therapy, each 30 days ***(Code effective 1/1/2023)***
HCPCS	A9291	Prescription digital behavioral therapy, FDA-cleared, per course of treatment ***(Code effective 4/1/2022)***

Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

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Effective Date	Action
06/01/2022	New policy.
09/01/2022	Policy statement and literature review updated. Policy title changed from Digital Health Therapies for Substance Abuse to current one.
03/01/2023	Coding update

Definitions of Decision Determinations

Medically Necessary: Services that are Medically Necessary include only those which have been established as safe and effective, are furnished under generally accepted professional standards to treat illness, injury or medical condition, and which, as determined by Blue Shield, are: (a) consistent with Blue Shield medical policy; (b) consistent with the symptoms or diagnosis; (c) not furnished primarily for the convenience of the patient, the attending Physician or other provider; (d) furnished at the most appropriate level which can be provided safely and effectively to the patient; and (e) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the Member's illness, injury, or disease.

Investigational/Experimental: A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

Split Evaluation: Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

Prior Authorization Requirements and Feedback (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department at (800) 541-6652, or the Transplant Case Management Department at (800) 637-2066 ext. 3507708 or visit the provider portal at www.blueshieldca.com/provider.

We are interested in receiving feedback relative to developing, adopting, and reviewing criteria for medical policy. Any licensed practitioner who is contracted with Blue Shield of California or Blue Shield of California Promise Health Plan is welcome to provide comments, suggestions, or concerns. Our internal policy committees will receive and take your comments into consideration.

For utilization and medical policy feedback, please send comments to: MedPolicy@blueshieldca.com

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.

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Appendix A

POLICY STATEMENT (No Changes)	
BEFORE	**AFTER**
Digital Health Therapies for Substance Use Disorders 5.01.35 **Policy Statement:** I. Digital health therapies for individuals with substance use disorders are considered **investigational**.	**Digital Health Therapies for Substance Use Disorders 5.01.35** **Policy Statement:** I. Digital health therapies for individuals with substance use disorders are considered **investigational**.

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