Re-SET-O

Clinical Policy ID: CCP.1429

Recent review date: 10/2024

Next review date: 2/2026

Policy contains: Opioid use disorder; community reinforcement approach; re-SET-O.

AmeriHealth Caritas has developed clinical policies to assist with making coverage determinations. AmeriHealth Caritas' clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of "medically necessary," and the specific facts of the particular situation are considered, on a case by case basis, by AmeriHealth Caritas when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. AmeriHealth Caritas' clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. AmeriHealth Caritas' clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, AmeriHealth Caritas will update its clinical policies as necessary. AmeriHealth Caritas' clinical policies are not guarantees of payment.

Coverage policy

Use of re-SET-O is investigational/not clinically proven and, therefore, not medically necessary.

Limitations

No limitations were identified during the writing of this policy.

Alternative covered services

- Cognitive behavioral therapy.
- Buprenorphine (Subutex) pharmacological therapy.
- Methadone pharmacological therapy.
- Inpatient drug detoxification rehabilitation treatment.
- Opioid drug addiction support groups (Substance Abuse and Mental Health Services Administration, 2021).

Background

In the United States, drug overdoses have risen over the past several decades and remain one of the leading causes of injury death in adults. Deaths from synthetic opioids have also increased in recent years (Spencer, 2023).

A variety of interventions are used to prevent synthetic opioid overdoses. One of these is buprenorphine, approved by the U.S. Food and Drug Administration in 2002, at relatively high doses, i.e., 16 mg/day or more. The treatment failure rate for buprenorphine is 25% versus 100% for placebo (National Institute on Drug Abuse, 2021). High-dose buprenorphine suppresses illicit opioid use at rates similar to methadone, according to a Cochrane study of 5,430 subjects (Mattick, 2014).

Treatment of opioid use disorder with buprenorphine can be combined with counseling and participation in social support programs. The drug can be given in an office, community hospital, health department, or correctional facility, while methadone is limited to clinics (Substance Abuse and Mental Health Services Administration, 2024).

Drugs and behavior modification for opioid use disorder continue to evolve. On December 10, 2018, the U.S. Food and Drug Administration approved re-SET-O, which is the first prescription digital therapeutic for opioid use disorder. The patient downloads the prescription software application to a mobile device to be used along with drug treatment and contingency management (behavior modification, based on rewards) for opioid use disorder. The Administration gave full approval to market the device on May 23, 2019 (U.S. Food and Drug Administration, 2018, 2019).

Re-SET-O is not used as a substitute for opioid use disorder medication-assisted treatment. Rather, it represents an upgrade to the government-approved re-SET (a similar intervention for substance abuse disorders) (Lovett, 2020). Re-SET-O is classified as a cognitive behavioral therapy tool modeled on the Community Reinforcement Approach, and can serve as a training, monitoring, and reminder tool for health care providers and patients in maintaining an outpatient treatment program.

After installing the application, the patient can complete lessons, answer quiz questions, report medication usage, and report substance use, cravings, and triggers, making it more likely that a patient will seek treatment when needed. In January 2019, Sandoz Inc. and Pear Therapeutics Inc. made re-SET-O available by prescription for 12 weeks of treatment (Coppock, 2019).

In April 2023, Pear Therapeutics filed Chapter 11 bankruptcy. Newly created Harvest Bio, LLC (Delaware) purchased assets related to re-SET-O (Hagen, 2023).

Findings

Guidelines

No professional guidelines on treating opioid addiction address re-SET-O. The American Society of Addiction Medicine includes cognitive behavioral therapy as one treatment of the disorder, but does not mention re-SET-O or any other web-based or internet-based approach (American Society of Addiction Medicine, 2020).

A Canadian guideline on opioid addiction treatment does not mention re-SET-O, and only recommends that psychosocial therapies be routinely offered — but not viewed as mandatory — as an alternative or adjunct means of treatment (Bruneau, 2018). A guideline from the College of Family Physicians in Canada on opioid addiction stated that cognitive behavioral therapy has not demonstrated efficacy in retention, and recommends only brief psychosocial interventions such as counseling. The guideline does not mention re-SET-O or other prescription digital therapeutics (Korownyk, 2019).

Evidence review

A review of comparative clinical effectiveness and value of re-SET-O and two other digital health technologies for opioid use disorder concluded that existing evidence does not show a net health benefit. The report also calls on manufacturers to provide evidence of effectiveness of these new technologies (Institute for Clinical and Economic Review, 2020).

A trial of 507 adults in a substance abuse program randomized subjects into those receiving 12 weeks of treatment as usual (individual and group counseling) with or without two hours of weekly care with the Therapeutic Education System. The group with additional care had a lower dropout rate (hazard ratio = .72) and a higher abstinence rate (odds ratio = 1.62) (Campbell, 2014).

A trial of 170 opioid-dependent adults studied efficacy of buprenorphine plus contingency management (i.e., patients could earn up to $997.50 each during the study to reward urine tests negative for opioids). Trial subjects were randomized into groups with and without an in-clinic, internet-based community reinforcement approach. Clinic visits to administer buprenorphine and test urine for opioids occurred three times a week for 12 weeks. The group with the internet reinforcement averaged a significant 9.7 more days of abstinence ($P = .011$), and a significantly lower dropout rate from treatment (19.6% versus 35.9%, $P = .013$) (Christensen, 2014).

The findings from the Campbell and Christensen randomized trials, which used an intervention with a mechanism of action similar to re-SET-O, were the basis of the regulatory approval of re-SET-O as an adjunctive treatment for opioid addiction. The research also showed statistically significantly higher retention in the treatment program of subjects who used the desktop computer version of re-SET-O (82.4%) compared with 68.4% for those who did not (U.S. Food and Drug Administration, 2018).

A secondary analysis of the Christensen study found participants with a digital therapeutic were more likely to have opioid abstinence during weeks nine through 12 (77.3% versus 62.1%, $P = .02$), and were less likely to stop treatment (hazard ratio 0.49, 95% confidence interval 0.26 to 0.92). No significant difference in the rate of adverse events occurred ($P = .42$) (Maricich, 2021).

An analysis of 351 participants (82.6% Medicaid) with opioid use disorder treated with buprenorphine compared utilization six months before and after re-SET-O initiation. Significant decreases occurred in inpatient admissions ($P = .024$), drug tests ($P < .001$), psychiatry visits ($P = .036$), and other pathology/laboratory ($P = .039$). Insignificant decreases occurred for alcohol/substance rehabilitation visits ($P = .348$), office/other outpatient visits ($P = .302$), other rehabilitation visits ($P = .387$), emergency department visits ($P = .247$), and surgery visits ($P = .070$). Insignificant increases included behavioral rehabilitation ($P = .124$) and mental health rehabilitation ($P = .097$) (Velez, 2021).

After 12-months follow-up, when compared to the control group (n = 978), the re-SET-O group (n = 901) experienced greater use of clinician services, a 9% increase in buprenorphine adherence, and lower overall costs, which were driven by significant reductions in inpatient stays ($P = .026$), hospital readmissions ($P = .033$), and nonsignificant reductions in unique hospital encounters and emergency department visits. A greater reduction in overall costs occurred among Medicaid participants (Velez, 2022).

A retrospective analysis compared healthcare resource utilization before and after initiation of re-SET-O in 101 participants with opioid and non-opioid substance use disorders. Use of re-SET-O was associated with reductions in healthcare resource utilization and lower healthcare costs over a six month period. These reductions were attributed to significant decreases in inpatient stays ($P = .003$), partial hospitalizations ($P = .021$), emergency room visits ($P < .004$), some clinician services, and facility encounters (Shah, 2022). However, re-SET-O has not been approved for use in non-opioid substance use disorders.

In 2023, we added two manufacturer-sponsored studies. One trial updates findings presented previously with longer follow-up data (Velez, 2022 update of 2021), and the other includes participants with non-opioid substance

use disorders (Shah, 2022). Both studies compared healthcare resource utilization and cost data with and without the use of re-SET-O. The results confirm previous findings and no policy changes are warranted.

In 2024, we updated the references and found no newly published, relevant information to add to the policy. No policy changes are warranted.

References

On September 3, 2024, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were “community reinforcement approach,” “opioids,” “prescription digital therapeutic,” and “re-SET-O.” We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

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Policy updates

9/2019: initial review date and clinical policy effective date: 11/2019

10/2020: Policy references updated.

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