Protocol

Buprenorphine Implant for Treatment of Opioid Dependence

(50126)

Medical Benefit		**Effective Date**: 01/01/19	**Next Review Date**: 09/19
Preauthorization	Yes	**Review Dates**: 09/18	

Preauthorization is required.

The following protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.

Populations	Interventions	Comparators	Outcomes
Individuals: • Who are addicted to opioids but stable on low-to-moderate doses of transmucosal buprenorphine	Interventions of interest are: • Buprenorphine implants	Comparators of interest are: • Transmucosal buprenorphine	Relevant outcomes include: • Change in disease status • Morbid events • Health status measures • Medication use • Treatment-related morbidity

DESCRIPTION

Buprenorphine is a partial μ-opioid agonist used to treat patients with an opioid addiction. Administered transmucosally, buprenorphine can be used with or without naloxone, which is an opioid antagonist. Though effective, a clinical strategy of using transmucosal buprenorphine is prone to nonadherence, diversion, abuse, and accidental misuse. To lower these risks and improve adherence, Braeburn Pharmaceuticals has developed a buprenorphine (Probuphine), implant to provide sustained delivery of buprenorphine for up to six months via four subdermally inserted rods. Probuphine is intended as a maintenance treatment for a select subgroup of opioid-dependent patients who are clinically stable on a low dose of transmucosal buprenorphine (≤ 8 mg/d). These implants are inappropriate for new treatment recipients and those who do not have sustained and prolonged clinical stability while being maintained on a generic equivalent of buprenorphine.

SUMMARY OF EVIDENCE

For individuals who are addicted to opioids but stable on low-to-moderate doses of transmucosal buprenorphine who receive buprenorphine implants, the evidence includes a randomized controlled trial. Relevant outcomes are change in disease status, morbid events, health status measures, medication use, and treatment-related morbidity. In the pivotal trial, the proportion of patients who reported for no more than two out of six months any evidence of illicit opioid use was similar between the buprenorphine implant arm (63%) and the sublingual buprenorphine arm (64%). The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

POLICY

Buprenorphine subdermal implants may be considered **medically necessary** when all four of the following criteria have been met:

1. The individual has been diagnosed with opioid dependence; and
2. The individual has been treated with a stable transmucosal buprenorphine dose (eight mg or less per day of a sublingual Subutex or Suboxone tablet or its transmucosal buprenorphine product equivalent) for three months or more without any need for supplemental dosing or adjustments; and
3. The individual is currently on a maintenance dose* of eight mg or less per day of a sublingual Subutex or Suboxone tablet or its transmucosal buprenorphine product equivalent to achieve sustained prolonged clinical stability on transmucosal buprenorphine; and
4. Buprenorphine implants are used as part of a comprehensive substance use disorder treatment program that includes counseling and psychosocial support.

*Food and Drug Administration indications specify that maintenance doses should not be tapered to a lower dose for the sole purpose of transitioning to buprenorphine implants (https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/204442s006lbl.pdf).

Buprenorphine implants are considered **investigational** for all other indications, including but not limited to:

1. When the medically necessary criteria above have not been met;
2. For new entrants to treatment;
3. For individuals who have not achieved and sustained prolonged clinical stability while being maintained on buprenorphine eight mg or less per day of a Subutex or Suboxone sublingual tablet or generic equivalent;
4. For individuals not enrolled in a comprehensive substance use disorder treatment program;
5. Treatment for longer than 12 months.

Individuals can be transitioned back to transmucosal buprenorphine-containing medications for continued treatment after 12 months as needed. Retreatment with buprenorphine implant after a prior 12-month treatment period is considered **investigational** under all circumstances.

POLICY GUIDELINES

Inserting up to four buprenorphine implants once in each arm at an interval of six months may be considered medically necessary.

The prescribing information also provides guidance on acceptable doses of transmucosal buprenorphine that demonstrating stable maintenance dosing (https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/204442s006lbl.pdf):

- Buprenorphine (Subutex) sublingual tablet (generic equivalent) eight mg or less per day;
- Buprenorphine and naloxone (Suboxone) sublingual tablet (generic equivalent) eight mg/two mg or less per day;
- Buprenorphine and naloxone (Bunavail™) buccal film 4.2 mg/0.7 mg or less per day;
- Buprenorphine and naloxone (Zubsolv®) sublingual tablets 5.7 mg/1.4 mg or less per day.

Additionally, the prescribing information includes the following factors in determining clinical stability and suitability for Probuphine treatment (https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/204442s006lbl.pdf):

Period free from illicit opioid drug use;

- Stability of living environment;
- Participation in a structured activity/job;
- Consistent participation in recommended behavioral therapy/peer support program;
- Consistent compliance with clinic visit requirements;
- Minimal to no desire or need to use illicit opioids;
- Period without episodes of hospitalizations (addiction or mental health issues), emergency room visits, or crisis interventions;
- Social support system.

BACKGROUND

OPIOID MISUSE

It has been estimated that over 200,000 deaths in the United States between 1999 and 2016 have been attributed to prescription opioid overdoses.[1]

Treatment

Buprenorphine is among the main options in a medication-assisted treatment strategy for opioid dependence. Transmucosal buprenorphine products have a potential for diversion to an illicit drug market and have resulted in accidental poisonings of small children.[2] To minimize the misuse, Braeburn Pharmaceuticals developed Probuphine, an implantable buprenorphine that would be difficult to divert or abuse, and therefore would less likely be accidentally ingested by children. Further, as an implant, it would maximize adherence passively for six or 12 months.

The initial new drug application, submitted by Braeburn in October 2012, sought approval of buprenorphine implants for initial treatment of patients with opioid dependence after just a few days of titration on a transmucosal formulation. The Food and Drug Administration issued a complete response letter for this new drug application, stating that, although the two six month trials met the prespecified end points, the dose provided by the implant "was too low to provide effective treatment for patients new to buprenorphine treatment."[3] However, data from a subset of patients revealed that four buprenorphine implants yielded buprenorphine concentrations similar to those observed with sublingual buprenorphine (anywhere from four to eight mg based on average exposure [e.g., mean area under the receiver operating characteristic curve values] or concentration). Thus, a subset of patients stabilized on sublingual buprenorphine eight mg or less could benefit from buprenorphine implants, which is the current target population for which these implants are approved.

REGULATORY STATUS

On May 26, 2016, buprenorphine implant (Probuphine®; Braeburn Pharmaceuticals) was approved by the U.S. Food and Drug Administration through the new drug application process for the maintenance treatment of opioid dependence in patients who have achieved and sustained prolonged clinical stability on low-to-moderate doses of an agent containing transmucosal buprenorphine (i.e., doses of eight mg/d of Subutex® or Suboxone® [Indivior] sublingual tablet or generic equivalent).

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

REFERENCES

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

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13. Kampman K, Jarvis M. American Society of Addiction Medicine (ASAM) national practice guideline for the use of medications in the treatment of addiction involving opioid use. J Addict Med. Sep-Oct 2015;9(5):358-367. PMID 26406300