BlueCross BlueShield of Arizona
An Independent Licensee of the Blue Cross and Blue Shield Association

MEDICAL COVERAGE GUIDELINES
SECTION: DRUGS

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BUPRENORPHINE IMPLANT FOR TREATMENT OF OPIOID DEPENDENCE

- **Probuphine®**

Non-Discrimination Statement and Multi-Language Interpreter Services information are located at the end of this document.

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Medical Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Medical Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Medical Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Medical Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

BUPRENORPHINE IMPLANT FOR TREATMENT OF OPIOID DEPENDENCE (cont.)

Description:

Probuphine (buprenorphine) implant is indicated for the maintenance treatment of opioid dependence in individuals who have achieved and sustained prolonged clinical stability on low-to-moderate doses of a transmucosal buprenorphine-containing product (i.e., doses of no more than 8 mg per day of Subutex or Suboxone sublingual tablet or generic equivalent). The implants are inserted into the upper portion of one arm and left in place for 6 months of treatment and then removed at the end of the sixth month. Use of Probuphine (buprenorphine) implants should not be given for additional treatment cycles after one insertion in each upper arm. There is no clinical experience with insertion of the implants beyond insertion in each arm or insertion into other sites other than the upper arm.

Probuphine (buprenorphine) implant should be used as part of a complete treatment program to include counseling and psychosocial support.

Prescription use of this product is limited under the Drug Addiction Treatment Act where the provider meets certain requirements and who have notified the secretary of Health and Human Services of their intent to prescribe or dispense the product for the treatment of opioid dependence and have been assigned a unique identification number to be included on every prescription.

Probuphine (buprenorphine) implant is not appropriate for new entrants to treatment and individuals who have not achieved and sustained prolonged clinical stability, while being maintained on buprenorphine 8 mg per day or less of a Subutex or Suboxone sublingual tablet equivalent or generic equivalent.

Probuphine (buprenorphine) implant is available only through a restricted program called the PROBUPHINE REMS Program.

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. To minimize the misuse, Probuphine is an implantable buprenorphine that would be difficult to divert or abuse, and would less likely be accidentally ingested by children. Further, it would maximize adherence passively for 6 or 12 month.

BUPRENORPHINE IMPLANT FOR TREATMENT OF OPIOID DEPENDENCE (cont.)

Definitions:

Adult: Age 18 years and older.

Doses of transmucosal buprenorphine that demonstrating stable maintenance dosing:
- Subutex sublingual tablet (generic equivalent) 8 mg or less per day for 3 months or more
- Suboxone sublingual tablet (generic equivalent) 8 mg/2 mg or less per day for 3 months or more
- Bunavail buccal film 4.2 mg/0.7 mg or less per day for 3 months or more
- Zubsolv sublingual tablets 5.7 mg/1.4 mg or less per day for 3 months or more

Risk Evaluation and Mitigation Strategies (REMS):
Use of Probuphine is subject to a Risk Evaluation and Mitigation Strategies (REMS) program that requires provider, patient, and dispensing pharmacy be enrolled into the program. Only providers and Pharmacies enrolled into the REMS may prescribe and dispense the drug, respectively, to individuals who are also in the program. A REMS program attempts to manage known or potentially serious risks associated with a drug product and is required by the Food and Drug Administration (FDA) for some drugs to ensure that the benefits of a drug outweigh its risks.

BUPRENORPHINE IMPLANT FOR TREATMENT OF OPIOID DEPENDENCE (cont.)

Criteria:

PROBUPHINE IS AVAILABLE ONLY THROUGH RESTRICTED DISTRIBUTION UNDER A RISK EVALUATION AND MITIGATION STRATEGY (REMS) PROGRAM CALLED PROBUPHINE REMS PROGRAM.

See Resources section for FDA-approved dosage.

- Probuphine (buprenorphine subdermal implants) are considered ***medically necessary*** for insertion of up to 4 implants once in each arm at an interval of 6 months with documentation of **ALL** of the following:

  1. Diagnosis of opioid dependence
  2. Has been treated with a stable transmucosal buprenorphine dose (≤ 8 mg/d of a sublingual Subutex or Suboxone tablet or its transmucosal buprenorphine product equivalent) for 3 months or more without any need for supplemental dosing or adjustments
  3. Currently on a maintenance dose of 8 mg per day or less of a sublingual Subutex or Suboxone tablet or its transmucosal buprenorphine product equivalent to achieve sustained prolonged clinical stability on transmucosal buprenorphine
  4. Used as part of a comprehensive substance use disorder treatment program that includes counseling and psychosocial support
  5. Absence of hypersensitivity to buprenorphine or any other ingredients in Probuphine (e.g., ethylene vinyl acetate)
  6. There is no pre-existing moderate to severe hepatic impairment (Child-Pugh Class B to C)
  7. Individual is not using MAOI or within 14 days of stopping an MAOI
  8. Clinical stability and suitability for Probuphine treatment is demonstrated with documentation of **ALL** of the following:

     - 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 (addition or mental health issues), emergency room visits, or crisis interventions
     - Social support system

BUPRENORPHINE IMPLANT FOR TREATMENT OF OPIOID DEPENDENCE (cont.)

Criteria: (cont.)

- Probuphine (buprenorphine subdermal implants) for retreatment after a prior 12 month treatment period is considered ***not medically necessary*** and ***experimental or investigational*** based upon:

  1. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
  2. Insufficient evidence to support improvement of the net health outcome, and
  3. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives.

- Probuphine (buprenorphine subdermal implants) for all other indications not previously listed or if above criteria not met is considered ***experimental or investigational*** based upon:

  1. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
  2. Insufficient evidence to support improvement of the net health outcome, and
  3. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives.

  These indications include, *but are not limited to:*

  - New entrants to treatment
  - For use in individuals who have not achieved and sustained prolonged clinical stability while being maintained on buprenorphine 8 mg per day or less of a Subutex or Suboxone sublingual tablet or generic equivalent
  - For use in individuals not enrolled in a comprehensive substance use disorder treatment program
  - Treatment for longer than 12 months
  - Treatment with dosing or frequency outside the FDA-approved dosing and frequency.

BUPRENORPHINE IMPLANT FOR TREATMENT OF OPIOID DEPENDENCE (cont.)

Resources:

Literature reviewed 08/27/18. We do not include marketing materials, poster boards and non-published literature in our review.

The BCBS Association Medical Policy Reference Manual (MPRM) policy is included in our guideline review. References cited in the MPRM policy are not duplicated on this guideline.

1. 5.01.26 BCBS Association Medical Policy Reference Manual. Buprenorphine Implant for Treatment of Opioid Dependence. Re-issue date 08/09/2018, issue date 10/13/2016.

Probuphine Package Insert:

- FDA-approved indication and dosage:

Indication	Recommended Dose
Contains buprenorphine, a partial opioid agonist. Indicated for the maintenance treatment of opioid dependence in patients who have achieved and sustained prolonged clinical stability on low-to-moderate doses of a transmucosal buprenorphine-containing product (i.e., doses of no more than 8 mg per day of Subutex or Suboxone sublingual tablet or generic equivalent). Should not be used as part of a complete treatment program to include counseling and psychological support Not appropriate for new entrants to treatment and patients who have not achieved and sustained prolonged clinical stability, while being maintained on buprenorphine 8 mg per day or less of a Subutex or Suboxone sublingual tablet or generic equivalent.	Prescription use of this product is limited under the Drug Addiction Treatment Act. Four Probuphine implants are inserted subdermally in the upper arm for 6 months of treatment and are removed by the end of the sixth month. Probuphine implants should not be used for additional treatment cycles after one insertion in each upper arm. Probuphine implants must be inserted and removed by trained Healthcare Providers only. Probuphine implants should be administered in patients who have achieved and sustained prolonged clinical stability on transmucosal buprenorphine. Examine the insertion site one week following insertion of Probuphine implants for signs of infection or other problems.

Approval Duration:
12 months

No renewal or continuation beyond implantation of 2 cycles of 6 months per arm

Individual to be transitioned back to transmucosal buprenorphine-containing medications for continued treatment after 12 months of implant treatment, as needed

BUPRENORPHINE IMPLANT FOR TREATMENT OF OPIOID DEPENDENCE (cont.)

Non-Discrimination Statement:

Blue Cross Blue Shield of Arizona (BCBSAZ) complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability or sex. BCBSAZ provides appropriate free aids and services, such as qualified interpreters and written information in other formats, to people with disabilities to communicate effectively with us. BCBSAZ also provides free language services to people whose primary language is not English, such as qualified interpreters and information written in other languages. If you need these services, call (602) 864-4884 for Spanish and (877) 475-4799 for all other languages and other aids and services.

If you believe that BCBSAZ has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability or sex, you can file a grievance with: BCBSAZ's Civil Rights Coordinator, Attn: Civil Rights Coordinator, Blue Cross Blue Shield of Arizona, P.O. Box 13466, Phoenix, AZ 85002-3466, (602) 864-2288, TTY/TDD (602) 864-4823, crc@azblue.com. You can file a grievance in person or by mail or email. If you need help filing a grievance BCBSAZ's Civil Rights Coordinator is available to help you. You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at: U.S. Department of Health and Human Services, 200 Independence Avenue SW., Room 509F, HHH Building, Washington, DC 20201, 1–800–368–1019, 800–537–7697 (TDD). Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html

Multi-Language Interpreter Services:

Spanish: Si usted, o alguien a quien usted está ayudando, tiene preguntas acerca de Blue Cross Blue Shield of Arizona, tiene derecho a obtener ayuda e información en su idioma sin costo alguno. Para hablar con un intérprete, llame al 602-864-4884.

Navajo: Díí kwe'é atah nílínigíí Blue Cross Blue Shield of Arizona haada yit'éego bína'ídíłkidgo éí doodago Háida bíjá anilyeedígíí t'áadoo le'é yína'ídíłkidgo beehaz'áanii hóló díí t'áá hazaadk'ehjí háká a'doowołgo bee haz'ą doo bąąh íłínígóó. Ata' halne'ígíí kojį' bich'į' hodíilnih 877-475-4799.

Chinese: 如果您，或是您正在協助的對象，有關於插入項目的名稱 Blue Cross Blue Shield of Arizona 方面的問題，您有權利免費以您的母語得到幫助和訊息。洽詢一位翻譯員，請撥電話 在此插入數字 877-475-4799。

Vietnamese: Nếu quý vị, hay người mà quý vị đang giúp đỡ, có câu hỏi về Blue Cross Blue Shield of Arizona quý vị sẽ có quyền được giúp và có thêm thông tin bằng ngôn ngữ của mình miễn phí. Để nói chuyện với một thông dịch viên, xin gọi 877-475-4799.

Arabic:
إن كان لديك أو لدى شخص تساعده أسئلة بخصوص Blue Cross Blue Shield of Arizona، فلديك الحق في الحصول على المساعدة والمعلومات الضرورية بلغتك من دون اية تكلفة. للتحدث مع مترجم اتصل ب 877-475-4799.

BUPRENORPHINE IMPLANT FOR TREATMENT OF OPIOID DEPENDENCE (cont.)

Multi-Language Interpreter Services: (cont.)

Tagalog: Kung ikaw, o ang iyong tinutulangan, ay may mga katanungan tungkol sa Blue Cross Blue Shield of Arizona, may karapatan ka na makakuha ng tulong at impormasyon sa iyong wika ng walang gastos. Upang makausap ang isang tagasalin, tumawag sa 877-475-4799.

Korean: 만약 귀하 또는 귀하가 돕고 있는 어떤 사람이 Blue Cross Blue Shield of Arizona 에 관해서 질문이 있다면 귀하는 그러한 도움과 정보를 귀하의 언어로 비용 부담없이 얻을 수 있는 권리가 있습니다. 그렇게 통역사와 얘기하기 위해서는 877-475-4799 로 전화하십시오.

French: Si vous, ou quelqu'un que vous êtes en train d'aider, a des questions à propos de Blue Cross Blue Shield of Arizona, vous avez le droit d'obtenir de l'aide et l'information dans votre langue à aucun coût. Pour parler à un interprète, appelez 877-475-4799.

German: Falls Sie oder jemand, dem Sie helfen, Fragen zum Blue Cross Blue Shield of Arizona haben, haben Sie das Recht, kostenlose Hilfe und Informationen in Ihrer Sprache zu erhalten. Um mit einem Dolmetscher zu sprechen, rufen Sie bitte die Nummer 877-475-4799 an.

Russian: Если у вас или лица, которому вы помогаете, имеются вопросы по поводу Blue Cross Blue Shield of Arizona, то вы имеете право на бесплатное получение помощи и информации на вашем языке. Для разговора с переводчиком позвоните по телефону 877-475-4799.

Japanese: ご本人様、またはお客様の身の回りの方でも、Blue Cross Blue Shield of Arizona についてご質問がございましたら、ご希望の言語でサポートを受けたり、情報を入手したりすることができます。料金はかかりません。通訳とお話される場合、877-475-4799 までお電話ください。

Farsi:
اگر شما، یا کسی که شما به او کمک میکنید ، سوال در مورد Blue Cross Blue Shield of Arizona ، داشته باشید حق این را دارید که کمک و اطلاعات به زبان خود را به طور رایگان دریافت نمایید 877-475-4799
.[تماس حاصل نمایید.

Assyrian:
Blue Cross Blue Shield of Arizona، ...
.877-475-4799

Serbo-Croatian: Ukoliko Vi ili neko kome Vi pomažete ima pitanje o Blue Cross Blue Shield of Arizona, imate pravo da besplatno dobijete pomoć i informacije na Vašem jeziku. Da biste razgovarali sa prevodiocem, nazovite 877-475-4799.

Thai: หากคณ หรอคนทคณกาลงชวยเหลอมคาถามเกยวกบ Blue Cross Blue Shield of Arizona
คณมสทธทจะไดรบความชวยเหลอและขอมลในภาษา ของคณไดโดยไมมคาใชจาย พดคยกบลาม โทร 877-475-4799