

Buprenorphine / Naloxone Buccal Film (BUNAVAIL) C-III

National PBM Abbreviated Drug Review

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VHA Pharmacy Benefits Management Services,
Medical Advisory Panel, and VISN Pharmacist Executives

The PBM prepares abbreviated reviews to compile information relevant to making formulary decisions. The manufacturer's labeling should be consulted for detailed drug information. VA clinical experts may provide input on the content. Wider field review is not sought. Documents no longer current will be placed in the Archive section of www.pbm.va.gov.

Executive Summary:

- Buprenorphine / naloxone buccal film (BUNAVAIL, by BioDelivery Sciences) was approved on 6 June 2014 by the Food and Drug Administration (FDA) for the maintenance treatment of opioid dependence, and should be used as part of a complete treatment plan to include counseling and psychosocial support.
- The main difference between buprenorphine / naloxone buccal film and sublingual tablets is a two-fold greater bioavailability due to greater absorption.

Conclusions: Buprenorphine / naloxone buccal film produces buprenorphine bioavailabilities (systemic exposures) similar to those of SUBOXONE (buprenorphine / naloxone) sublingual tablets at approximately half the dose of buprenorphine. The more efficient absorption is achieved by using a trademarked BioErodible MucoAdhesive (BEMA[®]) technology. The manufacturer claims that the lower buprenorphine doses may “help to reduce the potential for misuse and diversion and potentially lessen the incidence of certain side effects” and that the buccal film may potentially overcome some of the challenges associated with sublingual administration. However, no clinical studies have been performed to support these claims. Potential clinical concerns with the buccal film include dosing and administration confusion when switching between the sublingual formulations and the buccal film, as well as look-alike, sound-alike name confusion with other buprenorphine-containing products. The buccal film may be considered in the rare patients who are unable to use SL tablets. The criteria for use of buprenorphine sublingual products also apply to the buccal film.

Introduction

Buprenorphine / naloxone buccal film (BUNAVAIL, by BioDelivery Sciences) was approved on 6 June 2014 by the Food and Drug Administration (FDA) for the maintenance treatment of opioid dependence, and should be used as part of a complete treatment plan to include counseling and psychosocial support. The buccal film uses BioErodible MucoAdhesive (BEMA[®]) technology and is the first formulation of buprenorphine / naloxone intended for administration on the inside of the cheek.

The purposes of this abbreviated monograph are to (1) evaluate the available evidence of safety, tolerability, efficacy, cost, and other pharmaceutical issues that would be relevant to evaluating buprenorphine / naloxone buccal film for possible addition to the VA National Formulary; (2) define its role in therapy; and (3) identify parameters for its rational use in the VA.

Pharmacokinetics

The main difference between buprenorphine / naloxone buccal film and sublingual tablets is a two-fold greater bioavailability due to greater absorption. There was wide intersubject variability but low intrasubject variability in buccal absorption of buprenorphine and naloxone in doses ranging from 0.875 to 6.3 mg. The buccal film is not bioequivalent to buprenorphine / naloxone sublingual tablets (SUBOXONE).

Relative to without liquids, co-administration of liquids with BUNAVAIL buccal film reduces systemic exposure up to 59% for buprenorphine and up to 76% for naloxone, depending on the pH of the liquid.

Doses that provide equivalent exposure of buprenorphine are one BUNAVAIL 4.2 mg/0.7 mg buccal film to one SUBOXONE 8 mg/2 mg sublingual tablet. The naloxone exposure was 33% lower with BUNAVAIL buccal film than with SUBOXONE sublingual tablets.

FDA Approved Indication(s) and Off-label Uses

Buprenorphine / naloxone buccal film, C-III buccal film is indicated for the maintenance treatment of opioid dependence and should be used as part of a complete treatment plan to include counseling and psychosocial support.

Like the sublingual tablet ZUBSOLV (by Orexo US, Inc.), BUNAVAIL is indicated for only maintenance treatment of opioid dependence following induction using the SUBOXONE-equivalent generic SL tablets or SUBOXONE film (Reckitt-Benckiser). BUNAVAIL is not approved for induction therapy.

Under the Drug Addiction Treatment Act (DATA) codified at 21 U.S.C. 823(g), prescription use of this product in the treatment of opioid dependence is limited to physicians who meet certain qualifying requirements, and who have notified the Secretary of Health and Human Services (HHS) of their intent to prescribe this product for the treatment of opioid dependence and have been assigned a unique identification number that must be included on every prescription.

Current VA National Formulary Alternatives

Buprenorphine sublingual tablets (AB-rated generics by Barr, Ethypharm, Roxane)

Buprenorphine / naloxone sublingual tablets (Actavis Elizabeth, Amneal Pharms, Roxane)

Nonformulary Alternatives

Buprenorphine / naloxone sublingual film (SUBOXONE, Reckitt-Benckiser)

Buprenorphine / naloxone sublingual tablets (ZUBSOLV, Orexo US, Inc.)

Dosage and Administration

Physicians prescribing buprenorphine/naloxone buccal film should refer to the product information for further details. There is potential for dosing confusion because the strengths of buccal film are different from the strengths available for the sublingual tablets and film.

Bioequivalence of Sublingual and Buccal Buprenorphine Doses

To provide approximately equivalent exposure to buprenorphine, the dosage unit strength of the buccal film is about one half of that for the sublingual tablets, or 4.2/0.7 mg buccal film provides equivalent buprenorphine exposure to 8/2 mg sublingual tablets.

No recommendations for bioequivalence are given for the buccal film relative to sublingual film. Table 1 shows the bioequivalence relationships between the SUBOXONE sublingual tablets and the SUBOXONE sublingual film, ZUBSOLV sublingual tablets and BUNAVAIL buccal film; the bioequivalence relationship between sublingual film and buccal film are inferred from that between the SUBOXONE sublingual tablets and SUBOXONE sublingual film.

Table 1 Dosage Strengths Corresponding to SUBOXONE SL Tablets (Buprenorphine Exposure)

SUBOXONE SL TABLET	SUBOXONE SL FILM	ZUBSOLV SL TABLET	BUNAVAIL BUCCAL FILM
2 mg / 0.5 mg	2 mg / 0.5 mg	1.4 mg / 0.36 mg	—
4 mg / 1 mg	4 mg / 1 mg	—	2.1 mg / 0.3 mg
8 mg / 2 mg	8 mg / 2 mg*	5.7 mg/1.4 mg	4.2 mg / 0.7 mg
12 mg / 3 mg	8 mg / 2 mg + two of 2 mg / 0.5 mg*	—	6.3 mg / 1 mg

Dosage strengths are shown for buprenorphine / naloxone. * See text for further explanation.

Induction Therapy

Similar to the sublingual film, the buccal film is indicated for maintenance therapy of opioid dependence. Induction with buprenorphine/naloxone should be done with the sublingual tablets.

Maintenance Therapy

Doses should be given as a single daily dose.

Dosage should be adjusted using increments/decrements of 2.1/0.3 mg buprenorphine/naloxone buccal film units.

The recommended target dose for maintenance therapy is 8.4/1.4 mg per day of buprenorphine/naloxone. Maintenance doses range from 2.1/0.3 mg to 12.6/2.1 mg buprenorphine/naloxone per day. Doses above this range have not been shown to provide a clinical advantage.

Method of Buccal Administration

Patients require training and education on proper administration technique.

The patient should:

- use the tongue to wet the inside of the cheek or rinse the mouth with water to moisten the area immediately before placement of buccal film;
- open the individually sealed, child-resistant foil package immediately prior to use as indicated by the instructions;
- hold the buccal film with clean, dry fingers with the text (BN2, BN4, or BN6) facing up;

- place the side of the film with the text (BN2, BN4, or BN6) against the inside of the cheek;
- press and hold the film in place for 5 seconds.

When two films are required for one dose, the patient should place one film on the inside of one cheek and the other film on the inside of the other cheek. For doses requiring multiple films, no more than two films should be applied to the inside of one cheek at a time.

The patient should be instructed to avoid manipulating the film(s) with the tongue or finger(s) and avoid drinking or eating food until the film(s) dissolves. The buccal film should not be chewed or swallowed as this may result in lower peak concentrations and lower bioavailability. Drinking liquids at the time of buccal film application can reduce the bioavailability of buprenorphine by up to 59% and naloxone by up to 76%, depending on the pH of the liquid, relative to not drinking liquids.

The buccal film should not be cut or torn.

Efficacy and Safety

No clinical efficacy and safety studies were performed for buprenorphine / naloxone buccal film. Product information regarding contraindications, warnings, precautions, adverse events and drug interactions were based on clinical studies involving SUBOXONE (buprenorphine / naloxone) sublingual tablets.

Sentinel Events

None

Look-alike / Sound-alike (LA / SA) Error Risk Potential

As part of a JCAHO standard, LASA names are assessed during the formulary selection of drugs. Based on clinical judgment and an evaluation of LASA information from four data sources (Lexi-Comp, USP Online LASA Finder, First Databank, and ISMP Confused Drug Name List), the following drug names may cause LASA confusion:

NME Drug Name	Lexi-Comp	First DataBank	ISMP	Clinical Judgment
Buprenorphine/naloxone buccal film	None	None	None	Sublingual dosage forms and various strengths of the same combination Buprenorphine Bupropion Pentazocine/naloxone
BUNAVAIL	None	None	None	Boniva Oruvail Acuvail

Conclusions

Buprenorphine / naloxone buccal film produces buprenorphine bioavailabilities (systemic exposures) similar to those of SUBOXONE (buprenorphine / naloxone) sublingual tablets at approximately half the dose of buprenorphine. The more efficient absorption is achieved by using

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References:

BUNAVAIL (buprenorphine and naloxone) buccal film, CIII [prescribing information online]. BioDelivery BioDelivery Sciences International, Inc. (BDSI), Raleigh, NC. Jun 2014. Available at: <http://www.bdsi.com/siteres.aspx?resid=5a738443-a797-41cd-a39a-a8deb2a4a585> . Accessed: 23 Jun 2014.

Prepared Sep 2014. Contact person: Francine Goodman, PharmD, BCPS, National Clinical Pharmacy Program Manager, Pharmacy Benefits Management Services (10P4P)
