

BUNAVAIL[®] (Buprenorphine/naloxone) buccal film, CIII

Pronunciation: (BEWN-a-vale)

Indication and Description: On June 6, 2014, the FDA approved BUNAVAIL[®] for the maintenance treatment of opioid dependence, as part of a complete treatment plan to include counseling and psychosocial support. BUNAVAIL[®] is the first and only buccal film approved for maintenance treatment of opioid dependence.

BUNAVAIL[®] is powered by BEMA (BioErodable MucoAdhesive) technology and efficiently delivers buprenorphine with twice the bioavailability of Suboxone Sublingual Tablets.¹ Pharmacokinetic studies demonstrate exposure to buprenorphine from BUNAVAIL[®] 4.2/0.7mg and Suboxone sublingual tablets 8/2mg was equivalent. Mean circulating levels of norbuprenorphine, the primary metabolite of buprenorphine, were approximately 40% less compared to Suboxone.¹

The advanced technology of the BEMA film allows BUNAVAIL[®] to adhere to the buccal mucosa, the mucous membrane of the cheek, upon contact, where it dissolves and delivers buprenorphine and naloxone directly to the bloodstream. BEMA technology is a unique two-layer film: the mucoadhesive layer is designed to adhere upon contact with the buccal mucosa, and the backing layer promotes unidirectional flow of the medication, and prevents drug accumulation in the mouth.

Efficacy: Data from multiple studies, including a 12-week, open-label clinical study of 249 opioid-dependent patients stabilized on Suboxone sublingual tablets or film, demonstrated the safety and efficacy of BUNAVAIL[®]. In this phase III safety and tolerability trial, patients were switched from their current therapy, Suboxone sublingual film (N=144) or Suboxone sublingual tablets (N=105) to a proportional dose of BUNAVAIL[®] and maintained for 12 weeks. The mean dose of BUNAVAIL[®] at the end of the open-label period was 8.0/1.4mg, which was half the Suboxone (buprenorphine) dose at baseline. This 50% reduction in buprenorphine dose after conversion from Suboxone is consistent with data seen in PK studies and reflects the increased bioavailability of BUNAVAIL[®], as previously referenced.

- Additionally, BUNAVAIL[®] was associated with low use of non-prescribed opioids. 7.6% of patients had a positive urine test for a non-prescribed opioid.²
- Among patients with a baseline Clinical Opiate Withdrawal Scale (COWS) scores ranging from 10-25 (N=34) after discontinuation of Suboxone, initiation of BUNAVAIL[®] resulted in a decline in mean scores from >13 to ≤ 1.1 in 3 hours.²
- BUNAVAIL[®] was associated with a high rate of patient retention. 79.1% of patients remained on treatment over 12 weeks.²

Safety/Tolerability: Constipation incidence was reduced during BUNAVAIL[®] treatment in the 186 subjects who completed a symptom checklist at baseline and end of study. The incidence of constipation was 40.9% at baseline on Suboxone, and was reduced to 12.9% after 12 weeks on BUNAVAIL[®]. This represents an overall reduction of 68% of those subjects who reported having this symptom upon entering the trial on Suboxone. Treatment-emergent constipation was reported by 2.8% (7/249) of patients.²

Changes in the oral mucosa were carefully followed throughout the study. Systematic assessments were performed at screening, baseline, and at 5 periodic follow up exams. Prior to treatment with BUNAVAIL[®], oral mucosal abnormalities were identified in 5% (25/498) of the systematic oral exams. During treatment with BUNAVAIL[®], abnormalities were seen in 0.6% (6/1073) of the oral exams.²

Treatment-emergent adverse events were generally mild to moderate and ameliorated over the course of 12 weeks.² In patients switched from Suboxone to BUNAVAIL[®] in the same study, the only adverse reactions reported by at least 5% of patients were drug withdrawal syndrome, lethargy and headache.³ Adverse reactions reported by >1% but less than 5% of patients receiving BUNAVAIL[®] were: fatigue, chills, somnolence, drug dependence, insomnia, constipation, oral mucosal erythema, rhinorrhea, hyperhidrosis.³

Contraindications: Hypersensitivity to buprenorphine or naloxone. (Please refer to the full [prescribing information](#) and [medication guide](#) for safety information about buprenorphine/naloxone combinations).

Dosage/Administration: Apply BUNAVAIL[®] as a single daily dose. The recommended daily dose for maintenance is 8.4mg/1.4mg. Buccal film BUNAVAIL[®] 2.1 mg buprenorphine/0.3 mg naloxone; BUNAVAIL[®] 4.2 mg buprenorphine/0.7 mg naloxone; BUNAVAIL[®] 6.3 mg buprenorphine/ 1.0 mg naloxone.

¹ Vasisht N, Stark J, Bai SA, Finn A. Buprenorphine/naloxone buccal film has a relative buprenorphine bioavailability twice that of buprenorphine/naloxone sublingual tablets. Poster presented at: 45th Annual American Society of Addiction Medicine (ASAM); April 10-13, 2014; Orlando, FL

² Sullivan JG, Webster L. Novel Buccal Film Formulation of Buprenorphine-Naloxone for the Maintenance Treatment of Opioid Dependence: A 12-week Conversion Study. [Clin Ther.](#) 2015 Mar 29. pii: S0149-2918(15)00112-5. doi: 10.1016/j.clinthera.2015.02.027. [Epub ahead of print]

³ BUNAVAIL[®] [Prescribing Information]. Raleigh, NC; BioDelivery Sciences International.

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