Risk Evaluation and Mitigation Strategy (REMS) Document

BRIXADI (buprenorphine) extended-release REMS

I. Administrative Information

Risk: Serious harm or death that could result from intravenous self-administration
Application Number: NDA 210136
Application Holder: Braeburn Inc.
Initial REMS Approval: 05/2023
Most Recent REMS Update: 08/2025

II. REMS Goal

The goal of the BRIXADI REMS is to mitigate the risk of serious harm or death that could result from intravenous self-administration by:

- Ensuring healthcare settings and pharmacies are certified and only dispense BRIXADI directly to a healthcare provider for administration by a healthcare provider.

III. REMS Requirements

Braeburn Inc. must ensure that healthcare settings, pharmacies, and wholesalers-distributors comply with the following requirements:

1. Healthcare settings and pharmacies that dispense BRIXADI must:

To become certified to dispense	1. Designate an authorized representative to carry out the certification process and oversee implementation and compliance with the REMS on behalf of the healthcare setting or pharmacy. 2. Have the authorized representative enroll in the REMS by completing the Healthcare Setting and Pharmacy Enrollment Form and submitting it to the REMS. 3. Train all relevant staff involved in dispensing that the drug must be dispensed directly to a healthcare provider for administration by a healthcare provider, and the drug must not be dispensed to the patient. 4. Establish processes and procedures to verify BRIXADI is dispensed directly to a healthcare provider and the drug is not dispensed to the patient. 5. Establish processes and procedures to notify the healthcare provider not to dispense the drug directly to patients.
Before dispensing	6. Verify that BRIXADI is dispensed directly to a healthcare provider and the drug is not dispensed to the patient. 7. Notify the healthcare provider not to dispense the drug directly to patients.

To maintain certification to dispense	8. Have a new authorized representative enroll in the REMS by completing and submitting the Healthcare Setting and Pharmacy Enrollment Form, if the authorized representative changes.
At all times	9. Not distribute, transfer, loan or sell BRIXADI. 10. Maintain records of all processes and procedures including compliance with those processes and procedures. 11. Comply with audits by Braeburn Inc. or a third party acting on behalf of Braeburn Inc. to ensure that all processes and procedures are in place and are being followed.

2. Wholesalers-Distributors that distribute BRIXADI must:

To be able to distribute	1. Establish processes and procedures to ensure that the drug is distributed only to certified healthcare settings and pharmacies. 2. Train all relevant staff involved in distributing BRIXADI on the process and procedures to verify the healthcare settings and pharmacies are certified.
At all times	3. Distribute only to certified healthcare settings and pharmacies. 4. Maintain and submit records of all shipments of BRIXADI to Braeburn Inc. 5. Comply with audits carried out by Braeburn Inc. or a third party acting on behalf of Braeburn Inc. to ensure that all processes and procedures are in place and are being followed.

To inform healthcare providers about the REMS and the risks and safe use of BRIXADI, Braeburn Inc. must disseminate REMS communication materials according to the table below:

Target Audience	Communication Materials & Dissemination Plans
All healthcare providers who prescribe buprenorphine for the treatment of opioid use disorder; all pharmacies authorized by DEA to handle schedule III controlled substances; all Opioid Treatment Programs certified under 42 CFR 8	REMS Letter: Healthcare Provider REMS Letter with attachment: Fact Sheet: How to Obtain BRIXADI. 1. Mail within 60 calendar days of the date of the approval of the REMS and again 6 months later, or 2. eMail within 60 calendar days of the date of the approval of the REMS and again 6 months later. 3. Make available via a link from the BRIXADI REMS Website. 4. Disseminate within 60 calendar days of the date of the approval of the REMS through professional societies and request the content be provided to their members. a. The professional societies are identified in Appendix A. 5. Disseminate at Professional Meetings where Braeburn Inc. has a presence for 1 year from the date of the approval of the REMS.
All new healthcare providers who prescribe buprenorphine	REMS Letter: Healthcare Provider REMS Letter with attachment: Fact Sheet: How to Obtain BRIXADI

Target Audience	Communication Materials & Dissemination Plans
for the treatment of opioid use disorder since the last dissemination; all pharmacies authorized by DEA to handle schedule III controlled substances since the last dissemination; all Opioid Treatment Programs certified under 42 CFR 8 since the last dissemination	6. Mail annually from the date of the approval of the REMS, or 7. eMail annually from the date of the approval of the REMS.

To support REMS operations, Braeburn Inc. must:

1. Establish and maintain a REMS website, www.BRIXADIREMS.com. The REMS website must include the capability to complete healthcare setting and pharmacy certification online, the option to print the Prescribing Information, Medication Guide, and REMS materials. All product websites for consumers and healthcare providers must include prominent REMS-specific links to the REMS website. The REMS website must not link back to the promotional product website.

2. Make the REMS website fully operational and all REMS materials available through website and call center by the date BRIXADI is first commercially distributed.

3. Establish and maintain a REMS call center for REMS participants at 1-866-492-9624.

4. Establish and maintain a validated, secure database of all REMS participants who are enrolled and/or certified in the BRIXADI REMS.

5. Ensure healthcare settings and pharmacies are able to enroll by fax, email, and online.

6. Provide Healthcare Provider REMS Letter, Fact Sheet: How to Obtain BRIXADI, Healthcare Setting and Pharmacy Enrollment Form and the Prescribing Information to REMS participants who (1) attempt to dispense BRIXADI and are not yet certified or (2) inquire about how to become certified.

7. Notify healthcare settings and pharmacies, confirming certification, within 7 calendar days after they become certified in the REMS.

8. Provide wholesalers-distributors access to the database of certified healthcare settings and pharmacies.

To ensure REMS participants' compliance with the REMS, Braeburn Inc. must:

9. Verify annually that the authorized representative's name and contact information correspond to those of the current designated authorized representative for the certified healthcare setting or pharmacy. If different, the healthcare setting and pharmacy must be required to re-certify with a new authorized representative.

10. Maintain adequate records to demonstrate that REMS requirements have been met, including, but not limited to records of: BRIXADI distribution and dispensing; certification of pharmacies and healthcare settings; and audits of REMS participants.

11. Establish and maintain a plan for addressing non-compliance with REMS requirements.

12. Monitor healthcare settings, pharmacies, and wholesalers-distributors on an ongoing basis to ensure the requirements of the REMS are being met. Take corrective action if non-compliance is identified, including de-certification.

13. Audit a representative sample of healthcare settings no later than 90 calendar days after the healthcare setting is certified and receives its first shipment of BRIXADI, and audit a representative sample annually thereafter, to ensure that all REMS processes and procedures are in place, functioning, and support the REMS requirements.

14. Audit all pharmacies no later than 90 calendar days after the pharmacy is certified and receives its first shipment of BRIXADI, and audit a representative sample annually thereafter, to ensure that all REMS processes and procedures are in place, functioning, and support the REMS requirements.

15. Audit all wholesalers-distributors no later than 90 calendar days after they become authorized, and audit all wholesalers-distributors annually thereafter, to ensure that all REMS processes and procedures are in place, functioning, and support the REMS requirements.

16. Take reasonable steps to improve operations of and compliance with the requirements in the BRIXADI REMS based on monitoring and evaluation of the BRIXADI REMS.

IV. REMS Assessment Timetable

Braeburn Inc. must submit REMS Assessments at 6 months, 12 months, and annually thereafter from the date of the initial approval of the REMS (05/23/2023). To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 calendar days before the submission date for that assessment. Braeburn Inc. must submit each assessment so that it will be received by the FDA on or before the due date.

V. REMS Materials

The following materials are part of the BRIXADI REMS and are appended**:**

Enrollment Forms:

Healthcare Setting and Pharmacy:

1. Healthcare Setting and Pharmacy Enrollment Form

Communication Materials

2. Healthcare Provider REMS Letter
3. Fact Sheet: How to Obtain BRIXADI

Other Materials

4. REMS Website

VI. Statutory Elements

This REMS is required under section 505-1 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355-1) and consists of the following elements:

1. Elements to Assure Safe Use (ETASU):
    - Pharmacies and health care settings that dispense BRIXADI are specially certified under 505-1(f)(3)(B)

2. Implementation System
3. Timetable for Submission of Assessments

Appendix A: List of Professional Societies

- AATOD – American Association of the Treatment of Opioid Dependence
- ASAM – American Society of Addiction Medicine
- AAAP - American Association of Addiction Psychiatry
- ABAM – American Board of Addiction Medicine
- FSMB – Federation of State Medical Boards
- ACEP – American College of Emergency Physicians
- NCPA – National Community of Pharmacists Association
- ASHP – American Society of Health-System Pharmacists
- AOAAM – American Osteopathic Academy of Addiction Medicine
- AANP – American Association of Nurse Practitioners
- AAPA – American Association of Physician Assistants
- AphA – American Pharmacists Association