

Initial REMS Approval: 05/2016

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NDA 204442 Probuphine<sup>®</sup> (buprenorphine) Implant CIII

Opioid Partial Agonist

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## **RISK EVALUATION AND MITIGATION STRATEGY (REMS)**

### **I. GOALS:**

The goal of the Probuphine REMS is to mitigate the risk of complications of migration, protrusion, expulsion and nerve damage associated with the insertion and removal of Probuphine and the risks of accidental overdose, misuse and abuse by:

- a) Ensuring that healthcare providers are educated on the following:
  - proper insertion and removal of Probuphine
  - risk of complications of migration, protrusion, expulsion and nerve damage associated with the insertion and removal of Probuphine
  - risks of accidental overdose, misuse and abuse if an implant comes out or protrudes from the skin
- b) Informing patients about the risks of complications of migration, protrusion, expulsion and nerve damage associated with insertion and removal, as well as the risks of accidental overdose, misuse and abuse if an implant comes out or protrudes from the skin.

### **II. REMS ELEMENTS:**

#### **A. Medication Guide**

A Medication Guide will be dispensed with each Probuphine prescription in accordance with 21 CFR 208.24.

#### **B. Elements to Assure Safe Use**

1. Health care providers who prescribe Probuphine must be specially certified.
  - a. To become specially certified to prescribe Probuphine in the Probuphine REMS Program, healthcare providers must:
    - i. Review the Prescribing Information for Probuphine.

- ii. Complete the *Probuphine REMS Program Live Training: Lecture and Practicum*, and successfully complete the *Probuphine REMS Program Knowledge Assessment*.
  - iii. Enroll in the Probuphine REMS Program by completing the *Probuphine REMS Program Prescriber Enrollment Form*.
- b. As a condition of certification, prescribers must:
- i. Review the *What You Need to Know about Probuphine: A Patient's Guide* with each patient to counsel regarding the risks of insertion and removal, accidental overdose, misuse and abuse and the importance of appropriate wound care and provide the patient a copy.
  - ii. Maintain documentation of insertion and removal of Probuphine in each patient's medical record using the *Probuphine REMS Program Insertion/Removal Log* or by using another method/system (e.g., electronic health record) specific to the healthcare provider's practice.
- c. Braeburn Pharmaceuticals, Inc (Braeburn) must:
- i. Ensure that healthcare providers who prescribe Probuphine are specially certified, in accordance with the requirements described above.
  - ii. Provide live training for prescribers to ensure that healthcare providers can complete the certification process for the Probuphine REMS Program.
  - iii. Ensure that healthcare providers are notified when they have been certified by the Probuphine REMS Program.
  - iv. Maintain a validated, secure database of healthcare providers who are certified to prescribe Probuphine in the Probuphine REMS Program.
  - v. Ensure that healthcare providers meet the REMS certification requirements and de-certify non-compliant healthcare providers who do not maintain compliance with certification requirements.
  - vi. Ensure that certified prescribers are provided access to the database of healthcare providers who are certified to insert Probuphine.
  - vii. Provide the *Probuphine REMS Program Prescriber Enrollment Form* and the Prescribing Information to healthcare providers who (1) attempt to order Probuphine and are not yet certified, or (2) inquire about how to become certified.

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

- *Probuphine REMS Program Prescriber Enrollment Form*
- *Probuphine REMS Program What You Need to Know about Probuphine: A Patient's Guide*
- *Probuphine REMS Program Slides for Live Training: Lecture and Practicum*
- *Probuphine REMS Program Knowledge Assessment*
- *Probuphine REMS Program Insertion/Removal Log*
- *Probuphine REMS Program website, [www. PROBUPHINEREMS.com](http://www.PROBUPHINEREMS.com)*

2. Healthcare providers who insert<sup>1</sup> Probuphine must be specially certified.

- a. To become specially certified to insert Probuphine in the Probuphine REMS Program, healthcare providers must:
  - i. Review the Prescribing Information for Probuphine.
  - ii. Attest to performing a surgical procedure in the three months immediately preceding enrollment in the Probuphine REMS Program.
  - iii. Complete the *Probuphine REMS Program Live Training: Lecture and Practicum*, which includes training on the proper removal procedure for Probuphine.
  - iv. Successfully complete the *Probuphine REMS Program Knowledge Assessment* and meet the *Probuphine REMS Program Criteria for Procedural Competency*.
  - v. Enroll in the Probuphine REMS Program by completing the *Probuphine REMS Program Healthcare Provider who Performs Probuphine Surgical Procedures Enrollment Form* or *Probuphine REMS Program Healthcare Provider Dual Enrollment Form*.
- b. As a condition of certification, healthcare providers who insert Probuphine must:
  - i. Agree to insert/remove Probuphine in a healthcare setting in which a prescriber certified in the Probuphine REMS Program is also practicing.
  - ii. Ensure that the facility where the procedure is being conducted has the appropriate equipment to perform insertions and removals of Probuphine.
  - iii. Review the Medication Guide with each patient to counsel them regarding the risks of insertion and removal; accidental overdose, misuse, and abuse;

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<sup>1</sup> For the purpose of this REMS, the term insert refers to the dispensing of medication.

and the importance of appropriate wound care, and provide the patient a copy.

- iv. Document the insertion of Probuphine, including the date, serial number, number of implants inserted, name of healthcare provider performing the procedure, and location of implants for each patient by using the *Probuphine REMS Program Insertion/Removal Log* or by using another method/system (e.g., electronic health record) specific to the healthcare provider's practice.
- v. Recertify in the Probuphine REMS Program annually.

c. Braeburn must:

- i. Maintain a process to ensure that healthcare providers who inquire about becoming certified to insert Probuphine attest to performing a surgical procedure in the three (3) months immediately preceding enrollment in the Probuphine REMS Program.
- ii. Ensure that healthcare providers who insert Probuphine are specially certified, in accordance with the requirements described above.
- iii. Provide live training and competency evaluation for healthcare providers who insert Probuphine to ensure that healthcare providers can complete the certification process for the Probuphine REMS Program.
- iv. Ensure that healthcare providers are notified when they have been certified as a healthcare provider who inserts Probuphine by the Probuphine REMS Program.
- v. Maintain a validated, secure database of healthcare providers who are certified to perform insertions in the Probuphine REMS Program.
- vi. Ensure that healthcare providers meet the REMS certification requirements and de-certify non-compliant healthcare providers who do not maintain compliance with the REMS requirements.
- vii. Ensure that healthcare providers who insert Probuphine have access to a database of certified prescribers.
- viii. Provide the *Probuphine REMS Program Healthcare Provider Who Performs Probuphine Surgical Procedures Enrollment Form* and the

Prescribing Information to healthcare providers who inquire about how to become certified to insert Probuphine.

- ix. Notify healthcare providers who insert Probuphine before their certification is due to expire of the need to recertify in the Probuphine REMS Program and provide the *Probuphine REMS Program Healthcare Provider who Performs Probuphine Surgical Procedures Recertification Form*.
- x. Make available the *Probuphine REMS Program Surgical Procedures Recertification Video* by September 30, 2016. The video must be consistent with the *Probuphine REMS Program Surgical Procedures Recertification Video* transcript.

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

- *Probuphine REMS Program Healthcare Provider Who Performs Probuphine Surgical Procedures Enrollment Form*
- *Probuphine REMS Program Healthcare Provider Dual Enrollment Form*
- *Probuphine REMS Program Criteria for Procedural Competency*
- *Probuphine REMS Program Procedure Record for Recertification*
- *Probuphine REMS Program Healthcare Provider Who Performs Probuphine Surgical Procedures Recertification Form*
- *Probuphine REMS Program Surgical Procedures Recertification Video transcript*

3. Each patient is subject to certain monitoring **for removal** of Probuphine.
  - a. Patients having Probuphine removed must be monitored to ensure that removal is performed by a healthcare provider who is certified to insert. Healthcare providers certified to insert Probuphine are trained in removal procedures as well.<sup>2</sup>
  - b. Healthcare providers who remove Probuphine must document the removal of Probuphine, including, the date, serial number, number of implants removed, name of healthcare provider performing the procedure, and location of implants for each patient by using the *Probuphine REMS Program Insertion/Removal Log* or by using another method/system (e.g., electronic health record) specific to the healthcare provider's practice.
  - c. Braeburn must ensure that the *Probuphine REMS Program Insertion/Removal Log* is available to healthcare providers for patient monitoring.

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<sup>2</sup> Healthcare providers removing Probuphine in emergency situations, or as a result of a complicated removal requiring the involvement of a surgical specialist, are exempt from the certification requirement.

4. Probuphine must be inserted only in healthcare settings in which a certified prescriber is practicing.

Braeburn must ensure that Probuphine will only be inserted in healthcare settings in which a certified prescriber is practicing.

### C. Implementation System

1. Braeburn must ensure that Probuphine is only distributed to healthcare settings in which a certified prescriber is practicing by:
  - a. Ensuring that wholesalers/distributors who distribute Probuphine comply with the program requirements for wholesalers/distributors. The wholesaler/distributor must:
    - i. Put processes and procedures in place to verify, prior to distributing Probuphine, that the healthcare providers who prescribe Probuphine are certified.
    - ii. Comply with requests to be audited by Braeburn, FDA, or a third party acting on behalf of Braeburn or FDA to ensure that all processes and procedures are in place and are being followed for the Probuphine REMS Program. In addition, wholesalers/distributors must maintain appropriate documentation and make it available for audits.
    - iii. Provide distribution data to Braeburn.
  - b. Ensuring that wholesalers/distributors maintain distribution records of all shipments of Probuphine and provide the data to Braeburn.
2. Braeburn must monitor distribution data.
3. Braeburn must audit the wholesalers/distributors within 60 calendar days after the wholesaler/distributor is authorized to ensure that all processes and procedures are in place and functioning to support the requirements of the Probuphine REMS Program. Corrective action must be instituted by Braeburn if noncompliance is identified.
4. Braeburn must maintain and make available to wholesalers/distributors a validated, secure database of healthcare providers who are certified to prescribe in the Probuphine REMS Program.
5. Braeburn must maintain records of Probuphine distribution and dispensing, certified prescribers, certified inserters, and wholesalers/distributors to meet REMS requirements.
6. Braeburn must maintain a Probuphine REMS Program Call Center (1-866-397-8939) and Probuphine REMS Program website ([www.PROBUPHINEREMS.com](http://www.PROBUPHINEREMS.com)). The REMS Program website will include the option to print the Prescribing Information, Medication Guide and Probuphine REMS materials. The *Probuphine REMS Program Surgical Procedures Recertification Video* must be available for viewing September 30, 2016. The Probuphine product website will include a prominent REMS-specific link to the Probuphine REMS Program Website.

7. Braeburn must ensure that within 5 calendar days of REMS approval the Probuphine REMS Program website is fully operational (with the exception of the *Probuphine REMS Program Surgical Procedures Recertification Video*) and the REMS materials listed in or appended to the Probuphine REMS document are available through the Probuphine REMS Program website or by calling the Probuphine REMS Program Call Center.
8. Braeburn must continuously monitor the certified prescribers and healthcare providers who are certified to insert Probuphine to ensure the requirements of the Probuphine REMS Program are being met. Braeburn must institute corrective action if noncompliance is identified.
9. Annually, Braeburn must audit 10% (or a total of 15; whichever is greater) of the inserters who recertify within 90 calendar days of recertification to ensure that all processes and procedures are in place and functioning to support the requirements of the Probuphine REMS Program. The certified inserters must also be included in Braeburn's ongoing annual audit plan. Braeburn must institute corrective action if noncompliance is identified.
10. Braeburn must take reasonable steps to improve implementation of and compliance with the requirements in the Probuphine REMS Program based on monitoring and evaluation of the Probuphine REMS Program.

#### **D. Timetable for Submission of Assessments**

Braeburn must submit REMS Assessments for Probuphine to the FDA at 6 months and 1 year from the date of the REMS approval and then annually thereafter. 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 must submit each assessment so that it will be received by the FDA on or before the due date.