

Initial REMS approval: 07/2012
Most recent modification: 09/2014

NDA 22580

QSYMIA (phentermine and topiramate extended-release) Capsules
[Category: anorectic and antiepileptic]

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RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOAL

To inform prescribers and females of reproductive potential about:

- the increased risk of congenital malformations, specifically orofacial clefts, in infants exposed to Qsymia during the first trimester of pregnancy
- the importance of pregnancy prevention for females of reproductive potential receiving Qsymia
- the need to discontinue Qsymia immediately if pregnancy occurs.

II. REMS ELEMENTS

A. Medication Guide

The Medication Guide will be dispensed with each Qsymia prescription in accordance with 21 CFR 208.24.

The Medication Guide is part of the REMS and is appended.

B. Elements to Assure Safe Use

1. Training will be provided to healthcare providers who prescribe Qsymia

- a. VIVUS will ensure that training is made available to healthcare providers (HCPs) who prescribe Qsymia. VIVUS will ensure that the following training is available:
 - i. Online training available at the Qsymia REMS website
 - ii. Electronic training modules available from VIVUS medical liaisons during prescriber visits, at professional society meetings, and at medical educational venues
 - iii. Print training modules available at the Qsymia REMS website, from VIVUS medical liaisons during prescriber visits, at professional society

meetings, at medical educational venues, or by calling VIVUS Medical Information

- b. VIVUS will maintain a database of all HCPs (using a unique identifying number) who have completed the training. Completion of the training will be defined as:
 - i. For online training completed independently by the HCP, viewing of all module training screens and completion of the HCP registration form and post-training knowledge assessment questions
 - ii. For electronic or print training modules delivered in person by VIVUS medical liaisons, viewing of all module training materials and completion and submission (either electronically or by fax) to VIVUS of the HCP registration form and post-training knowledge assessment questions by the HCP
 - iii. For print training modules completed independently by the HCP, viewing of all module training materials and completion and submission by fax to VIVUS of the HCP registration form and post-training knowledge assessment questions.
 - iv. For print training modules completed independently by HCPs in integrated healthcare delivery systems, viewing of all module training materials and completion and submission to the integrated healthcare delivery system of the HCP registration form and post-training knowledge assessment questions. The integrated healthcare system will then forward the HCP registration forms and post-training knowledge assessment questions to VIVUS.
- c. On a monthly basis, VIVUS will compare the database of trained HCPs with the list of prescribers provided to VIVUS by certified pharmacies and by the pharmacy management systems to identify those Qsymia prescribers who have not yet completed the training, and will contact the identified prescribers to complete training. Ninety-five percent of untrained prescribers will be contacted and provided training materials or access to such materials within 30 days of identification.
- d. VIVUS will inform HCPs who have prescribed Qsymia of any substantial changes to the Qsymia REMS program, including
 - i. significant changes to the operation of the program, or
 - ii. changes to the Prescribing Information and Medication Guide that affect the risk-benefit profile of Qsymia.
- e. VIVUS will ensure that, as part of training, the following additional appended training materials that are part of the REMS are available to prescribers:
 - i. *Risk of Birth Defects with Qsymia* patient brochure
 - ii. *Healthcare Provider Counseling Tool for Females of Reproductive Potential*
 - iii. *Prescriber Dosing and Management Checklist*

- f. The following appended training materials are part of the REMS:
 - i. Online Qsymia REMS training
 - ii. Print Qsymia REMS training

- g. In order to facilitate prescriber training and education, **A Dear Healthcare Provider (DHCP) letter** will be sent within 60 days of product approval and again at 12 and 24 months after product approval. The initial DHCP letter will be sent to HCPs who are likely to prescribe Qsymia or have written a prescription for an obesity medical treatment within the prior 12 month period. This includes, but is not limited to, general practitioners, family practitioners, internists, gynecologists, endocrinologists, cardiologists, and nurse practitioners/physician assistants. Subsequent DHCP letters will be sent to HCPs who are likely to prescribe Qsymia (as described above), HCPs who have written a prescription for an obesity medical treatment in the prior 12 months, and any HCP who has prescribed Qsymia within the prior 12 month period.
 - i. VIVUS will distribute the DHCP letters via electronic mail, through the mail, or via facsimile. The DHCP letter will include a link or URL for the Qsymia REMS website landing page.
 - ii. In order to further facilitate prescriber training and education, within 60 days of product approval, and again at 12 and 24 months after product approval, VIVUS will send a Dear Medical Society letter to the following professional organizations, and will request that the DHCP letter be provided to the members of the professional organizations:

- American Academy of Family Physicians (AAFP)
- American Academy of Nurse Practitioners (AANP)
- American Academy of Physicians Assistants (AAPA)
- American Association of Clinical Endocrinologists (AAACE)
- American Association of Diabetic Educators (AADE)
- American Board of Physician Nutrition Specialists (ABPNS)
- American College of Cardiology (ACC)
- American College of Obstetricians and Gynecologists (ACOG)
- American College of Physicians (ACP)
- American College of Preventive Medicine (ACPM)
- American Diabetes Association (ADA)
- American Gastroenterological Association (AGA)
- American Heart Association (AHA)
- American Medical Association (AMA)
- American Osteopathic Association (AOA)
- American Pharmacists Association (APhA)
- American Society for Metabolic and Bariatric Surgery (ASMBS)
- American Society for Preventive Cardiology (ASPC)
- American Society of Bariatric Physicians (ASBP)
- The Endocrine Society (ENDO)
- The Obesity Society (TOS)

- iii. The Dear Healthcare Provider and Dear Medical Society letters are part of the REMS and are appended.
- h. VIVUS will make the prescriber training materials, the DHCP and Dear Medical Society letters, the *Risk of Birth Defects with Qsymia* patient brochure, the *Healthcare Provider Counseling Tool for Females of Reproductive Potential*, the *Prescriber Dosing and Management Checklist*, and professional labeling (including the Medication Guide) available via a dedicated REMS-specific link from the Qsymia website as well as through VIVUS Medical Information.

The Qsymia REMS website is part of the REMS; the landing page screen shot is appended

- i. VIVUS will maintain a REMS Support Center within VIVUS Medical Information to support prescribers and patients in interfacing with the REMS. VIVUS will ensure that all materials listed in or appended to the Qsymia REMS will be available on the Qsymia REMS website www.QsymiaREMS.com or by calling VIVUS Medical Information at 1-888-998-4887.

2. Pharmacies that dispense Qsymia will be specially certified

- a. VIVUS will ensure that Qsymia will only be dispensed by certified pharmacies.
- b. To become certified, each pharmacy, including each pharmacy chain, each independent retail pharmacy, and each mail order pharmacy, must designate an Authorized Representative to internally coordinate and oversee the Qsymia REMS program. The Authorized Representative must complete the Qsymia REMS Pharmacy Training Program, knowledge assessment questions and sign an enrollment form acknowledging the following:
 - i. the REMS requirement to provide a Medication Guide and the *Risk of Birth Defects with Qsymia* patient brochure to each patient each time Qsymia is dispensed
 - ii. a pharmacy management system is in place, and has been validated, to systematically direct that the Qsymia Medication Guide and the *Risk of Birth Defects with Qsymia* patient brochure be provided to each patient each time Qsymia is dispensed
 - iii. the pharmacy will refrain from reselling or transferring Qsymia to another pharmacy or distributor
 - iv. that pharmacists and staff involved with the dispensing of Qsymia will be trained before dispensing Qsymia about the risks associated with Qsymia and the REMS requirement to provide a Medication Guide and the *Risk of Birth Defects with Qsymia* patient brochure to each patient each time Qsymia is dispensed
 - v. that all Qsymia retail prescriptions, regardless of the method of payment, will be processed through the pharmacy management system

- vi. that the pharmacy and pharmacy personnel will cooperate with pharmacy survey and audit requirements
- vii. that the pharmacy will provide quarterly Qsymia REMS compliance reports to VIVUS as described in the REMS supporting document
- viii. that the pharmacy will provide a list of Qsymia prescribers to VIVUS as described in the REMS supporting document

The following appended materials are part of the REMS:

- Pharmacy Enrollment Form, Independent Pharmacy
- Pharmacy Enrollment Form, Corporate Entity of Retail Chain Pharmacy
- Pharmacy Enrollment Form, Mail Order Pharmacy
- Online Qsymia REMS Pharmacy Training module
- Print Qsymia REMS Pharmacy Training module

C. Implementation System

An implementation system will be established for the Qsymia REMS program to monitor and evaluate whether the Elements to Assure Safe Use are meeting the program's goals.

1. VIVUS will ensure that pharmacies dispensing Qsymia are specially certified using the criteria described above.
2. VIVUS will maintain a database (Certified Pharmacy Database) of all pharmacies [using a unique identification number] that are certified.
3. This database will also be accessible by pharmacy management systems and contract distributors as needed to implement the REMS.
4. A "Certified Pharmacy Locator" tool will be available on the Qsymia REMS website to assist patients and providers in locating certified pharmacies.
5. Pharmacy certification will be verified by the contract distributor(s) using the Certified Pharmacy Database prior to shipping Qsymia.
6. VIVUS will ensure that the pharmacy management system is configured to:
 - i. reject all prescriptions from non-certified pharmacies
 - ii. notify non-certified pharmacies that pharmacy certification is required to dispense Qsymia, and how to become certified
 - iii. notify the pharmacy if REMS-required prescriber data is missing, and to enter and submit such data prior to dispense
 - iv. direct the pharmacy to provide a Medication Guide and *Risk of Birth Defects with Qsymia* patient brochure with every Qsymia dispense.
7. VIVUS will ensure that a Qsymia REMS Pharmacy Support Center is maintained to support the pharmacy certification procedures and address any stakeholder questions from the pharmacies or distributors. The Qsymia REMS Pharmacy Support Center is available at 1-855-302-6698.
8. VIVUS will monitor distribution data and prescription dispensing data to ensure that only contract distributors are distributing Qsymia, and only certified pharmacies are dispensing Qsymia. Corrective action will be initiated

by VIVUS for distributors and pharmacies found non-compliant with the REMS.

9. VIVUS will conduct surveys and audits of certified pharmacies to ensure that Qsymia is being dispensed according to the REMS requirements. The pharmacies will submit REMS quarterly compliance reports to VIVUS as described in the REMS supporting document. If a certified pharmacy is found to be non-compliant, VIVUS will institute corrective action.
10. VIVUS will ensure that the online and print Qsymia REMS Pharmacy Training modules, Pharmacy Enrollment Forms, and Qsymia REMS Pharmacy Support Center contact information are available on the REMS Program website (www.QsymiaREMS.com) as well as by calling the Qsymia REMS Pharmacy Support Center (1-855-302-6698) or VIVUS Medical Information (1-888-998-4887).
 - i. VIVUS will ensure that the Qsymia REMS Pharmacy Training and Pharmacy Enrollment Forms can be completed online or in paper form and submitted to the Qsymia REMS Pharmacy Support Center by fax (1-855-302-6699).
 - ii. VIVUS will ensure that pharmacies that submit Pharmacy Enrollment Forms are notified within 48 hours of receipt of the enrollment form and advised of next steps to complete the certification. Processing of enrollment forms and pharmacy management systems verification will be required to complete the certification.
11. If there are substantive changes to the Qsymia REMS or REMS program, VIVUS will update all affected materials and notify certified pharmacies. Substantive changes are defined as:
 - i. significant changes to the operation of the Qsymia REMS or REMS Program, or
 - ii. changes to the Prescribing Information and Medication Guide that affect the risk-benefit profile of Qsymia

Based on monitoring and evaluation of these elements to assure safe use, VIVUS will take reasonable steps to improve implementation of these elements to meet the goals of the REMS.

D. Timetable for Submission of Assessments

VIVUS will submit REMS Assessments to FDA at 6 months and 12 months from the date of initial approval of the REMS, and 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 days before the submission date for that assessment. VIVUS will submit each assessment so that it will be received by the FDA on or before the due date.

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