

Initial REMS approval: 07/2012
Most recent modification: 07/2017

NDA 22580

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

VIVUS, Inc.
900 E. Hamilton Avenue, Suite 550
Campbell, CA 95008
1-650-934-5200

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.

RE-03-001-03

MEDICATION GUIDE
QSYMIA® (Kyoo sim ee' uh)
(phentermine and topiramate extended-release)
Capsules CIV

Read this Medication Guide before you start taking Qsymia and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or treatment. If you have any questions about Qsymia, talk to your healthcare provider or pharmacist.

What is the most important information I should know about Qsymia?

(For other side effects, also see [“What are the possible side effects of Qsymia?”](#))

Qsymia can cause serious side effects, including:

- **Birth defects (cleft lip/cleft palate).** If you take Qsymia during pregnancy, your baby has a higher risk for birth defects called cleft lip and cleft palate. These defects can begin early in pregnancy, even before you know you are pregnant.

Women who are pregnant must not take Qsymia.

Women who can become pregnant should:

1. Have a negative pregnancy test before taking Qsymia and every month while taking Qsymia.
2. Use effective birth control (contraception) consistently while taking Qsymia. Talk to your healthcare provider about how to prevent pregnancy.

If you become pregnant while taking Qsymia, stop taking Qsymia immediately, and tell your healthcare provider right away. Healthcare providers and patients should report all cases of pregnancy to:

- FDA MedWatch at 1-800-FDA-1088, and
 - The Qsymia Pregnancy Surveillance Program at 1-888-998-4887
- **Increases in heart rate.** Qsymia can increase your heart rate at rest. Your healthcare provider should check your heart rate while you take Qsymia. Tell your healthcare provider if you experience, while at rest, a racing or pounding feeling in your chest lasting several minutes when taking Qsymia.
 - **Suicidal thoughts or actions.** Topiramate, an ingredient in Qsymia, may cause you to have suicidal thoughts or actions.

Call your healthcare provider right away if you have any of these symptoms, especially if they are new, worse, or worry you:

- thoughts about suicide or dying
 - attempts to commit suicide
 - new or worse depression
 - new or worse anxiety
 - feeling agitated or restless
 - panic attacks
 - trouble sleeping (insomnia)
 - new or worse irritability
 - acting aggressive, being angry, or violent
 - acting on dangerous impulses
 - an extreme increase in activity and talking (mania)
 - other unusual changes in behavior or mood
- **Serious eye problems** which include:
 - any sudden decrease in vision, with or without eye pain and redness,
 - a blockage of fluid in the eye causing increased pressure in the eye (secondary angle closure glaucoma).

These problems can lead to permanent vision loss if not treated. Tell your healthcare provider right away if you have any new eye symptoms.

What is Qsymia?

Qsymia is a prescription medicine that contains phentermine and topiramate extended-release that may help some obese adults or some overweight adults who also have weight-related medical problems lose weight and keep the weight off.

Qsymia should be used with a reduced calorie diet and increased physical activity.

It is not known if Qsymia changes your risk of heart problems or stroke or of death due to heart problems or stroke.

It is not known if Qsymia is safe and effective when taken with other prescription, over-the-counter, or herbal weight loss products.

It is not known if Qsymia is safe and effective in children under 18 years old.

Qsymia is a federally controlled substance (CIV) because it contains phentermine and can be abused or lead to drug dependence. Keep Qsymia in a safe place, to protect it from theft. Never give your Qsymia to anyone else, because it may cause death or harm them. Selling or giving away this medicine is against the law.

Who should not take Qsymia?

Do not take Qsymia if you:

- are pregnant, planning to become pregnant, or become pregnant during Qsymia treatment.
- have glaucoma
- have thyroid problems (hyperthyroidism)
- are taking certain medicines called monoamine oxidase inhibitors (MAOIs) or have taken MAOIs in the past 14 days.
- are allergic to topiramate, sympathomimetic amines such as phentermine, or any of the ingredients in Qsymia. See the end of this Medication Guide for a complete list of ingredients in Qsymia.

What should I tell my healthcare provider before taking Qsymia?

Tell your healthcare provider if you:

- are pregnant or planning to become pregnant
- have had a heart attack or stroke
- have or have had an abnormal heart rhythm
- have or have had depression, mood problems, or suicidal thoughts or behavior
- have eye problems, especially glaucoma
- have a history of metabolic acidosis (too much acid in the blood) or a condition that puts you at higher risk for metabolic acidosis such as
 - chronic diarrhea, surgery, a diet high in fat and low in carbohydrates (ketogenic diet), weak, brittle, or soft bones (osteomalacia, osteoporosis, osteopenia), or decreased bone density
- have kidney problems, have kidney stones, or are getting kidney dialysis
- have liver problems
- have seizures or convulsions (epilepsy)
- are breastfeeding. It is not known if Qsymia passes into your breast milk. You and your healthcare provider should decide if you will take Qsymia or breastfeed. You should not do both.

Tell your healthcare provider about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements. Qsymia taken with other medicines may affect how each medicine works and may cause side effects.

Especially tell your healthcare provider if you take:

- **Birth control pills.** Tell your healthcare provider if your menstrual bleeding changes while you are taking birth control pills and Qsymia.

- **Water pills** (diuretics) such as hydrochlorothiazide (HCTZ)
- **Any medicines that impair or decrease your thinking, concentration, or muscle coordination**
- **Carbonic anhydrase inhibitors** [such as ZONEGRAN[®] (zonisamide), DIAMOX[®] (acetazolamide) or NEPTAZANE[®] (methazolamide)]
- **Seizure medicines** such as Valproic acid (DEPAKENE[®] or DEPAKOTE[®])

Ask your healthcare provider or pharmacist for a list of these medicines, if you are not sure.

Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist each time you get a new medicine. Do not start a new medicine without talking to your healthcare provider.

How should I take Qsymia?

- Your healthcare provider should start you on a diet and exercise program when you start taking Qsymia. Stay on this program while you are taking Qsymia.
- **Do not** change your dose without talking to your healthcare provider.
- Qsymia can be taken with or without food.
- If you miss a dose of Qsymia, wait until the next morning to take your usual dose of Qsymia. **Do not** double your dose.
- **To start treatment with Qsymia**
 - Take one Qsymia 3.75 mg/23 mg capsule (Figure A) once each morning for the first 14 days
 - After taking Qsymia 3.75 mg/23 mg capsule for 14 days, then take one Qsymia 7.5 mg/46 mg capsule (Figure B) once each morning
- **After taking Qsymia for 12 weeks**
 - Your healthcare provider should either (1) tell you to stop taking Qsymia or (2) increase your dose of Qsymia if you do not lose a certain amount of weight within the first 12 weeks of treatment at the recommended dose.
- **If your healthcare provider increases the dose of Qsymia**
 - Take one Qsymia 11.25 mg/69 mg capsule (Figure C) once each morning for 14 days
 - After taking 14 days of Qsymia 11.25 mg/69 mg capsule, then take one Qsymia 15 mg/92 mg capsule (Figure D) once each morning
- **Stopping Qsymia treatment**

Your healthcare provider should tell you to stop taking Qsymia if you have not lost a certain amount of weight after an additional 12 weeks of treatment on the higher dose.

Do not stop taking Qsymia without talking to your healthcare provider. Stopping Qsymia suddenly can cause serious problems, such as seizures. Your healthcare provider will tell you how to stop taking Qsymia slowly.



Figure A

Qsymia (3.75 mg/23 mg)
Cap and body are purple
with white printing



Figure B

Qsymia (7.5 mg/46 mg)
Cap is purple with white
printing and the body is
yellow with black
printing



Figure C

Qsymia (11.25 mg/69 mg)
Cap and body are yellow
with black printing

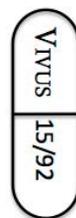


Figure D

Qsymia (15 mg/92 mg)
Cap is yellow with black
printing and the body is
white with black printing

If you take too much Qsymia, call your healthcare provider or go to the nearest emergency room right away.

What should I avoid while taking Qsymia?

- **Do not get pregnant while taking Qsymia.** See [“What is the most important information I should know about Qsymia.”](#)
- **Do not drink alcohol while taking Qsymia.** Qsymia and alcohol can affect each other causing side effects such as sleepiness or dizziness.
- **Do not drive a car or operate heavy machinery, or do other dangerous activities until you know how Qsymia affects you.** Qsymia can slow your thinking and motor skills, and may affect vision.

What are the possible side effects of Qsymia?

- See [“What is the most important information I should know about Qsymia?”](#) at the beginning of this Medication Guide
- **Mood changes and trouble sleeping.** Qsymia may cause depression or mood problems, and trouble sleeping. Tell your healthcare provider if symptoms occur.
- **Concentration, memory, and speech difficulties.** Qsymia may affect how you think and cause confusion, problems with concentration, attention, memory, or speech. Tell your healthcare provider if symptoms occur.
- **Increases of acid in bloodstream (metabolic acidosis).** If left untreated, metabolic acidosis can cause brittle or soft bones (osteoporosis, osteomalacia, osteopenia), kidney stones, can slow the rate of growth in children, and may possibly harm your baby if you are pregnant. Metabolic acidosis can happen with or without symptoms. Sometimes people with metabolic acidosis will:
 - feel tired
 - not feel hungry (loss of appetite)
 - feel changes in heartbeat

have trouble thinking clearly

Your healthcare provider should do a blood test to measure the level of acid in your blood before and during your treatment with Qsymia.

- **Low blood sugar (hypoglycemia) in people with type 2 diabetes mellitus who also take medicines used to treat type 2 diabetes mellitus.** Weight loss can cause low blood sugar in people with type 2 diabetes mellitus who also take medicines used to treat type 2 diabetes mellitus (such as insulin or sulfonylureas). You should check your blood sugar before you start taking Qsymia and while you take Qsymia.
- **Possible seizures if you stop taking Qsymia too fast.** Seizures may happen in people who may or may not have had seizures in the past if you stop Qsymia too fast. Your healthcare provider will tell you how to stop taking Qsymia slowly.
- **Kidney stones.** Drinking plenty of fluids when taking Qsymia to help decrease your chances of getting kidney stones. If you get severe side or back pain, and/or blood in your urine, call your healthcare provider
- **Decreased sweating and increased body temperature (fever).** People should be watched for signs of decreased sweating and fever, especially in hot temperatures. Some people may need to be hospitalized for this condition.

Common side effects of Qsymia include:

- numbness or tingling in the hands, arms, feet, or face (paraesthesia)
- dizziness
- change in the way foods taste or loss of taste (dysgeusia)
- trouble sleeping (insomnia)
- constipation
- dry mouth

Tell your healthcare provider if you have any side effect that bothers you or does not go away.

These are not all of the possible side effects of Qsymia. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to VIVUS at 1-888-998-4887 or FDA at 1-800-FDA-1088.

How should I store Qsymia?

- Store Qsymia at room temperature between 59°F to 77°F (15°C to 25°C).

Keep Qsymia and all medicines out of the reach of children.

General Information about Qsymia

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use Qsymia for a condition for which it was not

prescribed. Do not give Qsymia to other people, even if they have the same symptoms you have. It may harm them.

This Medication Guide summarizes important information about Qsymia. If you would like more information, talk with your healthcare provider. You can ask your pharmacist or healthcare provider for information about Qsymia that is written for healthcare professionals.

For more information, go to www.QsymiaREMS.com or call 1-888-998-4887.

What are the ingredients in Qsymia?

Active Ingredient: phentermine hydrochloride and topiramate extended-release

Inactive Ingredients: methylcellulose, sucrose, starch, microcrystalline cellulose, ethylcellulose, povidone, gelatin, talc, titanium dioxide, FD&C Blue #1, FD&C Red #3, FD&C Yellow #5 and #6, and pharmaceutical black and white inks.

This Medication Guide has been approved by the U.S. Food and Drug Administration.



Copyright © 2012-2017 VIVUS, Inc. All rights reserved.

VIVUS, Inc
900 E. Hamilton Avenue, Suite 550
Campbell, CA 95008 USA

US Patent Numbers: 7,056,890; 7,553,818; 7,659,256; 7,674,776; 8,580,298;
8,580,299; 8,895,057; 8,895,058; 9,011,905; and 9,011,906

Qsymia is a registered trademark of VIVUS, Inc.

ME-03-001-05



Risk of Birth Defects with Qsymia® **(phentermine and topiramate extended-release) capsules CIV**

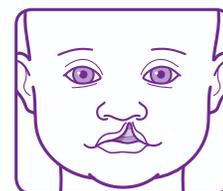
Please read the following important safety information about the use of Qsymia in females who can become pregnant.

You are considered a female who can become pregnant if this applies to you:

- You have never had a hysterectomy (uterus removed), surgical sterilization (tubes tied), or both ovaries removed and
- You have not gone through menopause. Menopause should be confirmed by your healthcare provider

1) Qsymia can increase the risk of a birth defect called cleft lip or cleft palate (as shown in the picture)

- These defects happen early in pregnancy, sometimes even before you know you are pregnant



cleft lip

2) You should have a pregnancy test taken BEFORE starting treatment with Qsymia and EVERY MONTH after that while on treatment

- Talk with your healthcare provider about when and where to have your pregnancy testing performed
- If you have a positive pregnancy test, or you miss a period, or you think you might be pregnant, you must not start Qsymia, or if you are already taking Qsymia, you should stop it immediately and tell your healthcare provider right away

3) While you are on Qsymia therapy, you should use effective birth control methods every time you have sex with a male

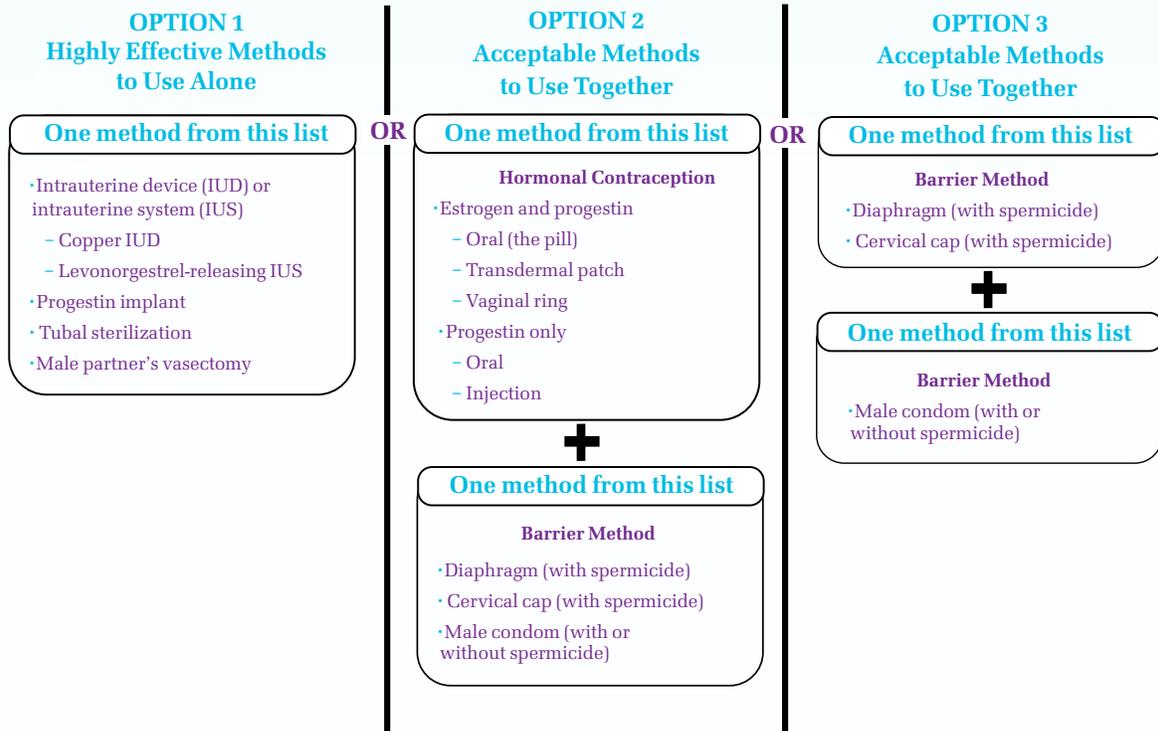
- Certain birth control methods are effective when used alone. Other birth control methods are not as effective by themselves, so you should use a second method of birth control

Talk to your healthcare provider to help decide what birth control options are best for you.

Please see the chart on the back to review birth control options.



Your Birth Control Options



Keep in mind, even the most effective birth control methods can fail. But your chances of getting pregnant are lowest if the methods you choose are always used correctly and every time you have sex.

Please read the accompanying Qsymia® Medication Guide as it contains additional important safety information about your treatment. This information does not take the place of talking to your healthcare provider about your medical condition or treatment. If you have any questions about Qsymia, talk to your healthcare provider or pharmacist, contact VIVUS Medical Information at 1-888-998-4887, or visit the Web site www.QsymiaREMS.com.





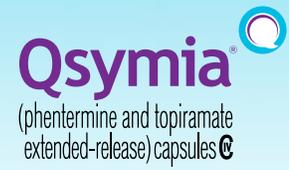
Healthcare Provider Counseling Tool for Females of Reproductive Potential

Use this counseling tool to discuss the increased risk of teratogenicity associated with the use of Qsymia® with your patients, and the important steps that should be taken to minimize the risk of fetal exposure.

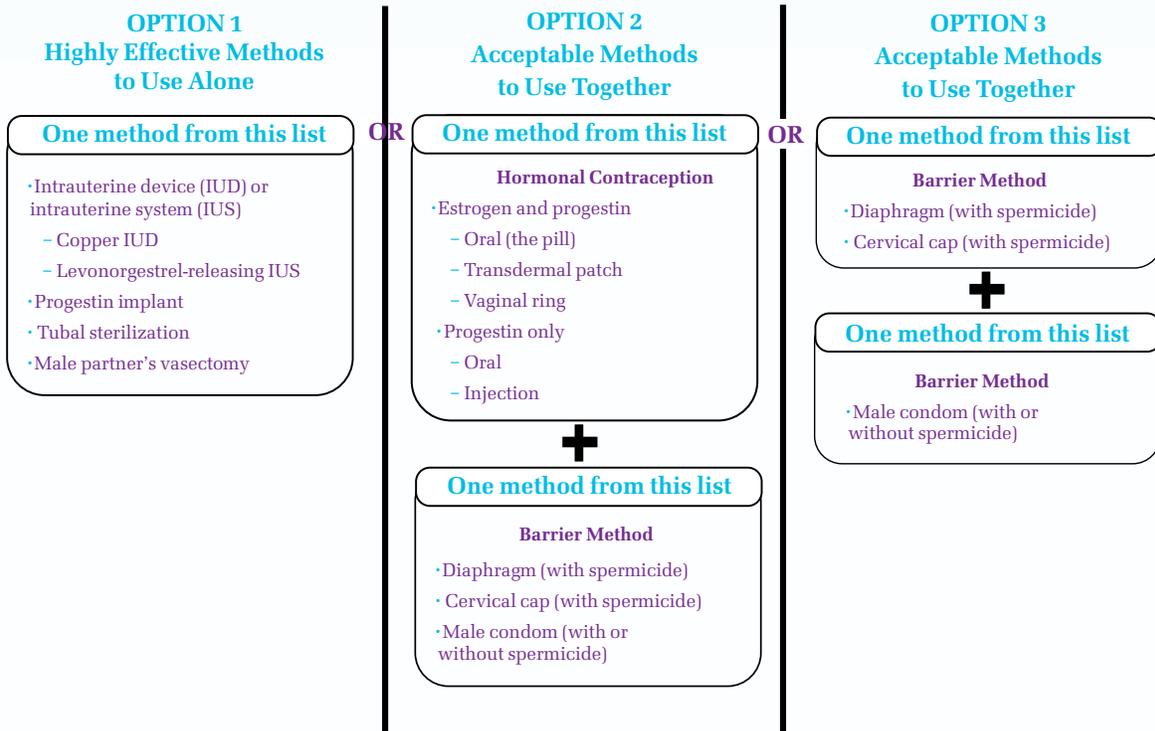
Females of reproductive potential are women who have NOT had a hysterectomy, bilateral oophorectomy, or medically documented spontaneous ovarian failure, and have not gone through menopause. Menopause should be clinically confirmed by an individual's healthcare provider.

The following points should be reviewed and discussed with all females of reproductive potential:

- **Qsymia can increase the risk of congenital malformations, specifically orofacial clefts**
 - Advise patients that orofacial clefts (cleft lip and cleft palate) occur early in pregnancy, at ~5 to 6 weeks gestation (post-conception), which may be before a patient realizes she is pregnant
- **Effective methods of contraception should be used consistently during treatment with Qsymia**
 - Advise patients that they should consistently use effective methods of contraception while taking Qsymia
 - The table on the back provides effective methods of contraception to review and discuss with your patient
 - Consider referral to a gynecologist if additional counseling or contraceptive selection is required
- **Pregnancy testing is recommended before initiating treatment with Qsymia and monthly during treatment**
 - Advise patients to undergo pregnancy testing before starting Qsymia and monthly thereafter. Discuss with patients whether pregnancy testing should be performed in the office or with a home pregnancy test
 - Advise patients that if they have a positive pregnancy test initially, they will not be prescribed Qsymia, and if they are already taking Qsymia and realize they are pregnant, they must stop it immediately and report the pregnancy to you
- **Review the *Risk of Birth Defects with Qsymia* patient brochure and the *Qsymia Medication Guide* with your patient. Provide these documents to your patient**



Acceptable Contraception Methods for Females of Reproductive Potential





Prescriber Dosing and Management Checklist

Qsymia* is indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adult patients with an initial body mass index (BMI) of:

- 30 kg/m² or greater (obese) or
- 27 kg/m² or greater (overweight) in the presence of at least one weight-related comorbidity such as hypertension, type 2 diabetes mellitus, or dyslipidemia

Limitations of Use:

- The effect of Qsymia on cardiovascular morbidity and mortality has not been established
- The safety and effectiveness of Qsymia in combination with other products intended for weight loss, including prescription and over-the-counter drugs, and herbal preparations, have not been established

Identify Appropriate Patients

- BMI* 30 or greater (obese) or BMI 27 or greater (overweight) with at least one weight-related comorbidity such as hypertension, type 2 diabetes mellitus, or dyslipidemia
- Must NOT be pregnant, trying to get pregnant, or unable/unwilling to comply with contraceptive guidance
- Must not have glaucoma
- Must not have hyperthyroidism
- Must not be using monoamine oxidase inhibitors (MAOIs) or have used them within 14 days
- Must not have known hypersensitivity or idiosyncrasy to the sympathomimetic amines

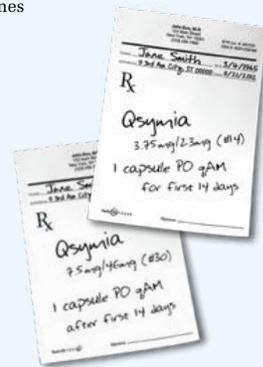
Start

Write 2 prescriptions:

- Qsymia 3.75 mg/23 mg (starting dose) for the first 14 days
- Qsymia 7.5 mg/46 mg (recommended dose) after the first 14 days
- Once daily, in the morning, with or without food
- Moderate hepatic impairment or moderate/severe renal impairment: dose should not exceed 7.5 mg/46 mg
- Suggested follow-up: 2-8 weeks

Instruct patients to begin Qsymia treatment as follows:

1. Take only one 3.75 mg/23 mg[†] capsule each morning for the first 14 days of treatment. 
2. AFTER the first 14 days of 3.75 mg/23 mg treatment is complete, take one 7.5 mg/46 mg[†] capsule each morning. 
3. Do NOT take 3.75 mg/23 mg and 7.5 mg/46 mg at the same time.



Counsel Patients

Counsel patients at each visit to:

- Consistently use contraception to avoid pregnancy because of the increased risk of teratogenicity, if she is a female of reproductive potential. Refer these patients to the *Risk of Birth Defects with Qsymia*[®] patient brochure
- Modify their lifestyle, eat properly, and engage in regular physical activity
- Not share Qsymia with anyone else
- Report any symptoms of concern

Monitor Patients

Monitor all patients at each visit for:

- Weight, status of comorbidities, and achievement of goals
- Adjustments/modifications to concomitant medications
- Use of effective contraception, if applicable. Test for pregnancy on a monthly basis if patient is a female of reproductive potential
- Heart rate: discontinue for sustained elevations
- Emergent/worsening depression, suicidal thoughts or behaviors
- Important side effects (e.g., cognitive dysfunction, glaucoma, metabolic acidosis, kidney stones)
 - Consider lowering dose or discontinuing medication for patients who experience important side effects

After 12 weeks at recommended dose of 7.5 mg/46 mg[†]:

- If weight loss less than 3%, discontinue Qsymia or escalate the dose
- To escalate dose, write 2 prescriptions:
 - Qsymia 11.25 mg/69 mg (titration dose) for 14 days
 - Qsymia 15 mg/92 mg after 14 days
- Qsymia 3.75 mg/23 mg and Qsymia 11.25 mg/69 mg are for titration purposes only
- Instruct patients to escalate the Qsymia dose as follows:
 1. Take only one 11.25 mg/69 mg[†] capsule each morning for 14 days of dose escalation. 
 2. AFTER the 14 days of dose escalation with 11.25 mg/69 mg is complete, take only one 15 mg/92 mg[†] capsule each morning. 
 3. Do NOT take 11.25 mg/69 mg and 15 mg/92 mg at the same time.

After additional 12 weeks following dose escalation to 15 mg/92 mg:

- If weight loss less than 5% after 12 weeks, discontinue treatment
- Discontinue Qsymia 15 mg/92 mg gradually by taking a dose every other day for at least 1 week prior to stopping altogether, due to the possibility of precipitating a seizure with abrupt cessation of the drug

*BMI is measured in kg/m².
[†]Pills not shown as actual size.

Important Safety Information

Qsymia® is contraindicated in pregnancy; in patients with glaucoma; in hyperthyroidism; in patients receiving treatment or within 14 days following treatment with monoamine oxidase inhibitors (MAOIs); or in patients with hypersensitivity or idiosyncrasy to sympathomimetic amines, topiramate, or any of the inactive ingredients in Qsymia.

Qsymia can cause fetal harm. Females of reproductive potential should have a negative pregnancy test before treatment and monthly thereafter and use effective contraception consistently during Qsymia therapy. If a patient becomes pregnant while taking Qsymia, treatment should be discontinued immediately, and the patient should be informed of the potential hazard to the fetus.

Qsymia can cause an increase in resting heart rate. Regular measurement of resting heart rate is recommended for all patients taking Qsymia, especially patients with cardiac or cerebrovascular disease or when initiating or increasing the dose of Qsymia. Qsymia has not been studied in patients with recent or unstable cardiac or cerebrovascular disease and therefore use is not recommended.

Topiramate, a component of Qsymia, increases the risk of suicidal thoughts or behavior in patients taking these drugs for any indication. Patients should be monitored for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior. Discontinue Qsymia in patients who experience suicidal thoughts or behaviors. Qsymia is not recommended in patients with a history of suicidal attempts or active suicidal ideation.

Acute angle closure glaucoma has been reported in patients treated with topiramate, a component of Qsymia. Symptoms include acute onset of decreased visual acuity and/or eye pain. Symptoms typically occur within 1 month of initiating treatment with topiramate but may occur at any time during therapy. The primary treatment to reverse symptoms is immediate discontinuation of Qsymia.

Qsymia can cause mood disorders, including depression, and anxiety, as well as insomnia. Qsymia can cause cognitive dysfunction (e.g., impairment of concentration/attention, difficulty with memory, and speech or language problems, particularly word-finding difficulties). Since Qsymia has the potential to impair cognitive function, patients should be cautioned about operating hazardous machinery, including automobiles.

Hyperchloremic, non-anion gap, metabolic acidosis has been reported in patients treated with Qsymia. If metabolic acidosis develops and persists, consideration should be given to reducing the dose or discontinuing Qsymia.

Qsymia can cause an increase in serum creatinine. If persistent elevations in creatinine occur while taking Qsymia, reduce the dose or discontinue Qsymia.

Weight loss may increase the risk of hypoglycemia in patients with type 2 diabetes mellitus treated with insulin and/or insulin secretagogues (e.g., sulfonylureas). Qsymia has not been studied in combination with insulin. A reduction in the dose of antidiabetic medications which are non-glucose-dependent should be considered to mitigate the risk of hypoglycemia.

The most commonly observed side effects in controlled clinical studies, ≥5% and at least 1.5 times placebo, include paraesthesia, dizziness, dysgeusia, insomnia, constipation, and dry mouth.

To report negative side effects, contact VIVUS Inc., at 1-888-998-4887 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Important Safety Information

Full Prescribing Information

Medication Guide

Welcome to the

Qsymia® (phentermine and topiramate extended-release) capsules CIV Healthcare Provider Training Program

Overview

FDA has required a Risk Evaluation and Mitigation Strategy (REMS) for Qsymia so that healthcare providers can be informed about the increased risk of teratogenicity associated with Qsymia therapy.

Purpose

The purpose of the REMS is to inform prescribers and females of reproductive potential (FRP) about the:

- Increased risk of congenital malformations, specifically orofacial clefts, in infants exposed to Qsymia during the first trimester of pregnancy
- Importance of pregnancy prevention for FRP
- Need to discontinue Qsymia immediately if pregnancy occurs

This is an audio program. You will hear its entire contents via voice-over narration.

This program should take approximately 20 minutes of your time to complete.



← Back

Next →

Screen 1 of 30

www.QsymiaREMS.com

© 2012-2014 VIVUS Inc. All rights reserved. 09/2014
RE-03-004-02

Important Safety Information

Full Prescribing Information

Medication Guide

Before you consider prescribing Qsymia, it is important to be aware of the increased risk of teratogenicity associated with Qsymia therapy.

The information presented in this Training Program does not include a complete list of all risks and safety information on Qsymia.

Before prescribing Qsymia, please read the Qsymia Prescribing Information and Qsymia Medication Guide available within this presentation.

Further information is also available on the Web site www.QsymiaREMS.com



← Back

Screen 2 of 30



www.QsymiaREMS.com

© 2012-2014 VIVUS Inc. All rights reserved. 08/2014
RE-03-004-02

Important Safety Information

Full Prescribing Information

Medication Guide

Complete the Qsymia Healthcare Provider Training Program in 3 easy steps:

Register

Register for the program
(which includes providing your
NPI or DEA # for validation)

Read

Read through the REMS
information for Qsymia

Review

Review your knowledge by answering
some true or false questions



◀ Back

Next ▶

Screen 3 of 30



www.QsymiaREMS.com

© 2012-2014 VIVUS Inc. All rights reserved. 08/2014
RE-03-004-02

Important Safety Information

Full Prescribing Information

Medication Guide

Once you complete the program, you will have the opportunity to print out all the Qsymia materials, including:

- Healthcare Provider Counseling Tool for Females of Reproductive Potential
- Prescriber Dosing and Management Checklist
- *Risk of Birth Defects with Qsymia* patient brochure
- Dear Healthcare Provider Letter
- Qsymia Prescribing Information
- Qsymia Medication Guide
- Certificate of Completion



◀ Back

Next ▶

Screen 4 of 30



www.QsymiaREMS.com

© 2012-2014 VIVUS Inc. All rights reserved. 08/2014
RE-03-004-02

[Important Safety Information](#)

[Full Prescribing Information](#)

[Medication Guide](#)

Complete the registration form below

First Name	<input type="text"/>	NPI #	<input type="text"/>		
Last Name	<input type="text"/>	DEA #	<input type="text"/>		
Are you a:	MD <input type="radio"/>	DO <input type="radio"/>	PA <input type="radio"/> NP <input type="radio"/>	I am a Kaiser Permanente Healthcare Provider:	<input type="checkbox"/>
Date of Birth	<input type="text"/>	MM/DD/YYYY	Telephone (Optional)	<input type="text"/>	
E-Mail	<input type="text"/>	Confirm E-Mail	<input type="text"/>		

Why do we need this information?

As part of the Qsymia REMS, it is important to ensure that physicians who are prescribing Qsymia have received training on the teratogenic risks associated with Qsymia.



[← Back](#)

Screen 5 of 30



www.QsymiaREMS.com

© 2012-2014 VIVUS Inc. All rights reserved. 08/2014
RE-03-004-02

Important Safety Information

Full Prescribing Information

Medication Guide

Please provide your address to complete your registration

Address 1	<input type="text"/>	State	<input type="text"/>
Address 2	<input type="text"/>	ZIP	<input type="text"/>
City	<input type="text"/>		



← Back

Next →

Screen 6 of 30



www.QsymiaREMS.com

© 2012-2014 VIVUS Inc. All rights reserved. 08/2014
RE-03-004-02

Important Safety Information

Full Prescribing Information

Medication Guide

Indication and Patient Selection

Qsymia is indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adult patients with an initial body mass index (BMI) of:

- 30 kg/m² or greater (obese), or
- 27 kg/m² or greater (overweight) in the presence of at least one weight-related comorbidity such as hypertension, type 2 diabetes mellitus, or dyslipidemia

Limitations of use:

- The effect of Qsymia on cardiovascular morbidity and mortality has not been established
- The safety and effectiveness of Qsymia in combination with other products intended for weight loss, including prescription and over-the-counter drugs, and herbal preparations, have not been established



← Back

Next →

Screen 7 of 30

www.QsymiaREMS.com

© 2012-2014 VIVUS Inc. All rights reserved. 08/2014
RE-03-004-02

Important Safety Information

Full Prescribing Information

Medication Guide

Increased Risk of Teratogenicity

Qsymia is classified as **Pregnancy Category X**

- Qsymia is contraindicated in pregnant women because the use of Qsymia can cause fetal harm. Available data indicate an increase in oral clefts (cleft lip with or without cleft palate) in infants exposed to topiramate, one of the components of Qsymia, during the first trimester of pregnancy.

Qsymia[®]
(phentermine and topiramate
extended-release) capsules

← Back

Next →

Screen 8 of 30



www.QsymiaREMS.com

© 2012-2014 VIVUS Inc. All rights reserved. 08/2014
RE-03-004-02

Important Safety Information

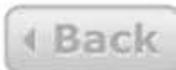
Full Prescribing Information

Medication Guide

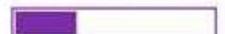
Increased Risk of Teratogenicity (con't)

Studies evaluating the risk of major congenital malformations and/or oral clefts with exposure to topiramate, a component of Qsymia, during pregnancy include the following:

- The North American Anti-Epileptic Drug (NAAED) Pregnancy Registry (2010) analysis
- A retrospective evaluation of a Wolters Kluwer claims database (January 2003-December 2010 from the United States)
- A retrospective observational study using 4 U.S. electronic healthcare databases (FORTRESS)
- A case-control study using data from the Slone Epidemiology Center Birth Defects Study (BDS, 1997-2009) and the Centers for Disease Control's (CDC's) National Birth Defects Prevention Study (NBDPS, 1996-2007)



Screen 9 of 30



www.QsymiaREMS.com

© 2012-2014 VIVUS Inc. All rights reserved. 08/2014
RE-03-004-02

Important Safety Information

Full Prescribing Information

Medication Guide

Increased Risk of Teratogenicity (con't)

The NAAED Pregnancy Registry reports an estimated increase in risk for oral clefts of 9.60 (95% CI 3.60-25.70).

An increase in oral clefts was observed with all dose strengths of topiramate.

SUMMARY OF STUDIES EVALUATING THE ASSOCIATION OF TOPIRAMATE IN UTERO EXPOSURE AND ORAL CLEFTS

EPIDEMIOLOGY STUDY	ORAL CLEFTS		MAJOR CONGENITAL MALFORMATIONS	
	PREVALENCE/ODDS RATIO	95% CI	ESTIMATED INCREASE IN RISK	95% CI
WOLTERS KLUWER*	1.47	0.36-6.06	1.12	0.81-1.55
FORTRESS*	2.22	0.78-6.36	1.21	0.99-1.47
SLONE/CDC	5.36	1.49-20.07	1.01	0.37-3.22

*Sponsored by the maker of Qsymia® (phentermine and topiramate extended-release) capsules CIV.

CI=confidence interval.

These data show that exposure to topiramate, a component of Qsymia, in pregnancy is associated with a 2- to 5-fold increase in risk of oral clefts.

Other data sources confirm the increased risk of oral clefts with topiramate exposure during pregnancy (ie, animal studies and Adverse Event Reporting System data).



← Back

Next →

Screen 10 of 30



www.QsymiaREMS.com

© 2012-2014 VIVUS Inc. All rights reserved. 08/2014
RE-03-004-02

Important Safety Information

Full Prescribing Information

Medication Guide

Counseling for Females of Reproductive Potential*

Qsymia can cause fetal harm.

Advise females of reproductive potential that you recommend:

- Pregnancy testing prior to beginning Qsymia and monthly during therapy
- Use of effective contraception consistently during Qsymia therapy; even females who believe they cannot become pregnant should use effective contraception while taking Qsymia
- If you become pregnant while taking Qsymia, stop Qsymia immediately and notify your healthcare provider

*Females of reproductive potential are women who have NOT had a hysterectomy, bilateral oophorectomy, or medically documented spontaneous ovarian failure, and have not gone through menopause. Menopause should be clinically confirmed by an individual's healthcare provider.

Advise nursing mothers not to use Qsymia. Qsymia may be present in human milk because topiramate and amphetamines (phentermine has pharmacologic activity and a chemical structure similar to amphetamines) are excreted in human milk.



Screen 11 of 30



www.QsymiaREMS.com

© 2012-2014 VIVUS Inc. All rights reserved. 08/2014
RE-03-004-02

Important Safety Information

Full Prescribing Information

Medication Guide

Counseling for Females of Reproductive Potential (con't)

Acceptable Contraception Methods for Females of Reproductive Potential

Option 1 Highly Effective Methods to Use Alone	Option 2 Acceptable Methods to Use Together	Option 3 Acceptable Methods to Use Together
One method from this list <ul style="list-style-type: none">• Intrauterine device (IUD) or intrauterine system (IUS)<ul style="list-style-type: none">- Copper IUD- Levonorgestrel-releasing IUS• Progestin implant• Tubal sterilization• Male partner's vasectomy	One method from this list <p>Hormonal Contraception</p> <ul style="list-style-type: none">• Estrogen and progestin<ul style="list-style-type: none">- Oral (the pill)- Transdermal patch- Vaginal ring• Progestin only<ul style="list-style-type: none">- Oral- Injection <p>+</p> One method from this list <p>Barrier Method</p> <ul style="list-style-type: none">• Diaphragm (with spermicide)• Cervical cap (with spermicide)• Male condom (with or without spermicide)	One method from this list <p>Barrier Method</p> <ul style="list-style-type: none">• Diaphragm (with spermicide)• Cervical cap (with spermicide) <p>+</p> One method from this list <p>Barrier Method</p> <ul style="list-style-type: none">• Male condom (with or without spermicide)



← Back

Screen 12 of 30



www.QsymiaREMS.com

© 2012-2014 VIVUS Inc. All rights reserved. 08/2014
RE-03-004-02

Important Safety Information

Full Prescribing Information

Medication Guide

Dispensed to Patients Through Certified Pharmacies

Qsymia is available only through certified pharmacies that provide a Qsymia Medication Guide and *Risk of Birth Defects with Qsymia* patient brochure with every prescription and refill as required by the REMS.

Please note that Qsymia is not available outside this network of certified pharmacies. (A full listing of certified pharmacies can be accessed at the end of this presentation.)

Qsymia[®]
(phentermine and topiramate
extended-release) capsules 

◀ Back

Next ▶

Screen 13 of 30



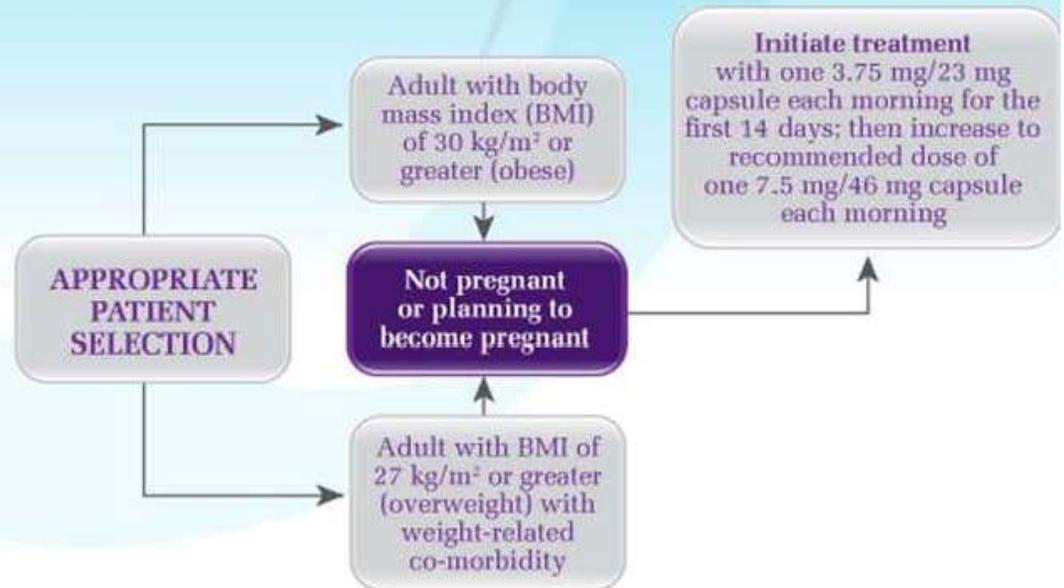
www.QsymiaREMS.com

© 2012-2014 VIVUS Inc. All rights reserved. 08/2014
RE-03-004-02

Dosage and Administration

Initiation of Treatment

- Qsymia should be taken in the morning, with or without food
- Avoid dosing with Qsymia in the evening due to the possibility of insomnia
- For patients with moderate hepatic impairment or moderate/severe renal impairment, the Qsymia dose should not exceed the recommended dose of Qsymia 7.5 mg/46 mg (phentermine 7.5 mg/topiramate 46 mg extended-release)
- The suggested follow-up after administration of initial treatment is 2 to 8 weeks
- To initiate treatment: Start with one Qsymia 3.75 mg/23 mg (phentermine 3.75 mg/topiramate 23 mg extended-release) capsule each morning for the first 14 days; then increase to recommended dose of one Qsymia 7.5 mg/46 mg capsule each morning



← Back

Screen 14 of 30



www.QsymiaREMS.com

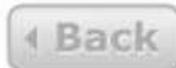
© 2012-2014 VIVUS Inc. All rights reserved. 08/2014
RE-03-004-02

Dosage and Administration (con't)

Evaluate weight loss with the recommended dose of Qsymia, 7.5 mg/46 mg, at week 12 of treatment

If a patient has not lost at least 3% of baseline body weight on the recommended dose of Qsymia, 7.5 mg/46 mg, discontinue Qsymia or escalate the dose as directed, as it is unlikely that the patient will achieve and sustain clinically meaningful weight loss at the Qsymia 7.5 mg/46 mg dose.

To escalate the dose: Increase to one Qsymia 11.25 mg/69 mg (phentermine 11.25 mg/topiramate 69 mg extended-release) capsule each morning for 14 days, followed by dosing one Qsymia 15 mg/92 mg (phentermine 15 mg/topiramate 92 mg extended-release) capsule each morning.



Important Safety Information

Full Prescribing Information

Medication Guide

Dosage and Administration (con't)

Evaluate weight loss following dose escalation to Qsymia 15 mg/92 mg after 12 weeks of treatment

If a patient has not lost at least 5% of baseline body weight on Qsymia 15 mg/92 mg, discontinue Qsymia, as it is unlikely that the patient will achieve and sustain clinically meaningful weight loss with continued treatment.

To discontinue Qsymia 15 mg/92 mg, have the patient take a dose every other day for at least 1 week prior to stopping treatment altogether, due to the possibility of precipitating a seizure with abrupt cessation of dosing.



← Back

Screen 16 of 30



www.QsymiaREMS.com

© 2012-2014 VIVUS Inc. All rights reserved. 08/2014
RE-03-004-02

Important Safety Information

Full Prescribing Information

Medication Guide

Please complete your certification by taking the following brief quiz.



← Back

Screen 17 of 30



www.QsymiaREMS.com

© 2012-2014 VIVUS Inc. All rights reserved. 08/2014
RE-03-004-02

Important Safety Information

Full Prescribing Information

Medication Guide

1 of 5

True or False: The major risk for females of reproductive potential (FRP) being treated with Qsymia is that of teratogenicity (birth defects), specifically the risk of cleft lip with or without cleft palate.



True



False

Qsymia[®]
(phenelzine and topiramate
extended-release) capsules

← Back

Screen 18 of 30



www.QsymiaREMS.com

© 2012-2014 VIVUS Inc. All rights reserved. 03/2014
RE-03-004-02

Important Safety Information

Full Prescribing Information

Medication Guide

1 of 5

True or False: The major risk for females of reproductive potential (FRP) being treated with Qsymia is that of teratogenicity (birth defects), specifically the risk of cleft lip with or without cleft palate.



True



False

The correct answer is TRUE.

Topiramate, a component of Qsymia, has been associated with an increased risk of cleft lip with or without cleft palate in infants exposed to topiramate during the first trimester of pregnancy.



← Back

Screen 19 of 30



www.QsymiaREMS.com

© 2012-2014 VIVUS Inc. All rights reserved. 08/2014
RE-03-004-02

Important Safety Information

Full Prescribing Information

Medication Guide

2 of 5

True or False: If a patient hasn't achieved 3% weight loss following 12 weeks of treatment on the recommended dose of Qsymia 7.5 mg/46 mg (phentermine 7.5 mg/topiramate 46 mg extended-release), discontinuation of therapy or dose escalation should be considered.



True



False

Qsymia[®]
(phentermine and topiramate
extended-release) capsules 

← Back

Screen 20 of 30



www.QsymiaREMS.com

© 2012-2014 VIVUS Inc. All rights reserved. 08/2014
RE-03-004-02

Important Safety Information

Full Prescribing Information

Medication Guide

2 of 5

True or False: If a patient hasn't achieved 3% weight loss following 12 weeks of treatment on the recommended dose of Qsymia 7.5 mg/46 mg (phentermine 7.5 mg/topiramate 46 mg extended-release), discontinuation of therapy or dose escalation should be considered.



True



False

The correct answer is **TRUE**.

If a patient has not lost at least 3% of baseline body weight on Qsymia 7.5 mg/46 mg, discontinue Qsymia or escalate the dose as directed, as it is unlikely that the patient will achieve and sustain clinically meaningful weight loss at the Qsymia 7.5 mg/46 mg dose.

Qsymia[®]
(phentermine and topiramate
extended-release) capsules 6

← Back

Screen 21 of 30



www.QsymiaREMS.com

© 2012-2014 VIVUS Inc. All rights reserved. 08/2014
RE-03-004-02

Important Safety Information

Full Prescribing Information

Medication Guide

3 of 5

True or False: Women taking Qsymia should use contraception unless they have had infertility or trouble getting pregnant in the past.



True



False

Qsymia[®]
(phenflermine and topiramate
extended-release) capsules 

← Back

Screen 22 of 30



www.QsymiaREMS.com

© 2012-2014 VIVUS Inc. All rights reserved. 08/2014
RE-03-004-02

Important Safety Information

Full Prescribing Information

Medication Guide

3 of 5

True or False: Women taking Qsymia should use contraception unless they have had infertility or trouble getting pregnant in the past.



True



False

The correct answer is **FALSE**.

ALL women, except those who have gone through menopause or undergone surgical sterilization, should be advised to consistently use effective contraception, even women who have had difficulty getting pregnant in the past.

Qsymia[®]
(phentermine and topiramate
extended-release) capsules

← Back

Screen 23 of 30



www.QsymiaREMS.com

© 2012-2014 VIVUS Inc. All rights reserved. 08/2014
RE-03-004-02

Important Safety Information

Full Prescribing Information

Medication Guide

4 of 5

True or False: If I don't think a patient is at risk for pregnancy, I don't need to discuss contraception.

True

False

Qsymia[®]
(phenelzine and topiramate
extended-release) capsules

← Back

Screen 24 of 30



www.QsymiaREMS.com

© 2012-2014 VIVUS Inc. All rights reserved. 08/2014
RE-03-004-02

Important Safety Information

Full Prescribing Information

Medication Guide

4 of 5

True or False: If I don't think a patient is at risk for pregnancy, I don't need to discuss contraception.



True



False

The correct answer is FALSE.

It is important to have this conversation with all patients. It is important to know whether a patient is:

- Trying to get pregnant and not using contraception, in which case do not prescribe Qsymia
- Sexually active and what contraception she is using, in which case reinforce the importance of consistent use of effective contraception
- Surgically sterilized or has gone through menopause that has been clinically confirmed, in which case no contraception is required

It is important to have this conversation with all patients, so that if there is a female of reproductive potential in the house, the patient knows to keep Qsymia in a secure location and not share it with anyone else.



← Back

Screen 25 of 30



www.QsymiaREMS.com

© 2012-2014 VIVUS Inc. All rights reserved. 08/2014
RE-03-004-02

Important Safety Information

Full Prescribing Information

Medication Guide

5 of 5

True or False: If a woman thinks she is pregnant, she should continue taking Qsymia until the pregnancy is confirmed.



True



False

Qsymia[®]
(pherfermine and topiramate
extended-release) capsules

← Back

Screen 26 of 30



www.QsymiaREMS.com

© 2012-2014 VIVUS Inc. All rights reserved. 08/2014
RE-03-004-02

Important Safety Information

Full Prescribing Information

Medication Guide

5 of 5

True or False: If a woman thinks she is pregnant, she should continue taking Qsymia until the pregnancy is confirmed.



True



False

The correct answer is FALSE.

If a woman believes she might be pregnant, she should stop taking Qsymia immediately and contact her healthcare provider.

Qsymia[®]
(phentermine and topiramate
extended-release) capsules **6**

← Back

Screen 27 of 30



www.QsymiaREMS.com

© 2012-2014 VIVUS Inc. All rights reserved. 08/2014
RE-03-004-02

Important Safety Information Full Prescribing Information Medication Guide

5 of 5 True taking

The correct answer is...
If a woman believes she...
contact her healthcare...

she should continue...
a immediately and...

Please review the Qsymia Prescribing Information and Qsymia Medication Guide before prescribing.

Qsymia[®]
(phenelzine and lisdexamfetamine extended-release) capsules

← Back Next →

Screen 28 of 30

www.QsymiaREMS.com

© 2012-2014 VIVUS Inc. All rights reserved. 08/2014
RE-03-004-02

[Important Safety Information](#)

[Full Prescribing Information](#)

[Medication Guide](#)

Congratulations!

You have completed the Qsymia Healthcare Provider Training Program. Take this opportunity to review printable versions of the Qsymia REMS materials by clicking on the links below or learn more about Qsymia by going to www.QsymiaREMS.com.

- [Healthcare Provider Counseling Tool for Females of Reproductive Potential](#)
- [Prescriber Dosing and Management Checklist](#)
- [Risk of Birth Defects with Qsymia patient brochure](#)
- [Dear Healthcare Provider Letter](#)
- [Qsymia Prescribing Information](#)
- [Qsymia Medication Guide](#)
- [Certificate of Completion](#)
- [Certified Pharmacy Locator on \[www.QsymiaREMS.com\]\(http://www.QsymiaREMS.com\)](#)



[← Back](#)

Screen 29 of 30

www.QsymiaREMS.com

© 2012-2014 VIVUS Inc. All rights reserved. 08/2014
RE-03-004-02

Important Safety Information

Full Prescribing Information

Medication Guide

Close

Congratu

You have comp
printable versio
going to www.

- [Healthcare of Reprodu](#)
- [Prescriber](#)
- [Risk of Bir](#)
- [Dear Healt](#)

to review
about Qsymia by

Qsymia[®] (phentermine and topiramate extended-release) capsules CIV Healthcare Provider Training Program

Name: **John Q. Sample**

Date: **August 18, 2014**

This certificate confirms that you have completed the Qsymia
Healthcare Provider Training Program.

Qsymia[®]
(phentermine and topiramate
extended-release) capsules 6

VIVUS[®]

Print

Qsymia[®]
(phentermine and topiramate
extended-release) capsules 6

Screen 29 of 30

VIVUS Inc. All rights reserved. 03/2014
RE-03-004-02

Important Safety Information

Full Prescribing Information

Medication Guide

For more information, contact VIVUS Medical Information
at 1-888-998-4887 or visit
www.QsymiaREMS.com

Qsymia[®]
(phenelzine and topiramate
extended-release) capsules

◀ Back

Next ▶

Screen 30 of 30

www.QsymiaREMS.com

© 2012-2014 VIVUS Inc. All rights reserved. 08/2014
RE-03-004-02

Important Safety Information

Qsymia® is contraindicated in pregnancy; in patients with glaucoma; in hyperthyroidism; in patients receiving treatment or within 14 days following treatment with monoamine oxidase inhibitors (MAOIs); or in patients with hypersensitivity or idiosyncrasy to sympathomimetic amines, topiramate, or any of the inactive ingredients in Qsymia.

Qsymia can cause fetal harm. Females of reproductive potential should have a negative pregnancy test before treatment and monthly thereafter and use effective contraception consistently during Qsymia therapy. If a patient becomes pregnant while taking Qsymia, treatment should be discontinued immediately, and the patient should be informed of the potential hazard to the fetus.

Qsymia can cause an increase in resting heart rate. Regular measurement of resting heart rate is recommended for all patients taking Qsymia, especially patients with cardiac or cerebrovascular disease or when initiating or increasing the dose of Qsymia. Qsymia has not been studied in patients with recent or unstable cardiac or cerebrovascular disease and therefore use is not recommended.

Topiramate, a component of Qsymia, increases the risk of suicidal thoughts or behavior in patients taking these drugs for any indication. Patients should be monitored for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior. Discontinue Qsymia in patients who experience suicidal thoughts or behaviors. Qsymia is not recommended in patients with a history of suicidal attempts or active suicidal ideation.

Acute angle closure glaucoma has been reported in patients treated with topiramate, a component of Qsymia. Symptoms include acute onset of decreased visual acuity and/or eye pain. Symptoms typically occur within 1 month of initiating treatment with topiramate but may occur at any time during therapy. The primary treatment to reverse symptoms is immediate discontinuation of Qsymia.

Qsymia can cause mood disorders, including depression, and anxiety, as well as insomnia. Qsymia can cause cognitive dysfunction (e.g., impairment of concentration/attention, difficulty with memory, and speech or language problems, particularly word-finding difficulties). Since Qsymia has the potential to impair cognitive function, patients should be cautioned about operating hazardous machinery, including automobiles.

Hyperchloremic, non-anion gap, metabolic acidosis has been reported in patients treated with Qsymia. If metabolic acidosis develops and persists, consideration should be given to reducing the dose or discontinuing Qsymia.

Qsymia can cause an increase in serum creatinine. If persistent elevations in creatinine occur while taking Qsymia, reduce the dose or discontinue Qsymia.

This information comes from a link to [QsymiaREMS.com](https://www.vivus.com/REMS)

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use QSYMIA® safely and effectively. See full prescribing information for QSYMIA.

QSYMIA (phentermine and topiramate extended-release) capsules, for oral use, CIV
Initial U.S. Approval: 2012

-----**INDICATIONS AND USAGE**-----

Qsymia is a combination of phentermine, a sympathomimetic amine anorectic, and topiramate extended-release, an antiepileptic drug, indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adults with an initial body mass index (BMI) of:

- 30 kg/m² or greater (obese) (1) or
- 27 kg/m² or greater (overweight) in the presence of at least one weight-related comorbidity such as hypertension, type 2 diabetes mellitus, or dyslipidemia (1)

Limitations of Use:

- The effect of Qsymia on cardiovascular morbidity and mortality has not been established (1).
- The safety and effectiveness of Qsymia in combination with other products intended for weight loss, including prescription and over-the-counter drugs, and herbal preparations, have not been established (1).

-----**DOSAGE AND ADMINISTRATION**-----

- Take once daily in morning. Avoid evening dose to prevent insomnia (2.1).
- Recommended dose: Qsymia 3.75 mg/23 mg (phentermine 3.75 mg/topiramate 23 mg extended-release) daily for 14 days; then increase to 7.5 mg/46 mg daily (2.1).
- Discontinue or escalate dose (as described) if 3% weight loss is not achieved after 12 weeks on 7.5 mg/46 mg dose (2.1).
- Discontinue Qsymia if 5% weight loss is not achieved after 12 weeks on maximum daily dose of 15 mg/92 mg (2.1).
- Discontinue 15 mg/92 mg dose gradually (as described) to prevent possible seizure (2.1).
- Do not exceed 7.5 mg/46 mg dose for patients with moderate or severe renal impairment or patients with moderate hepatic impairment (2.2, 2.3).

-----**DOSAGE FORMS AND STRENGTHS**-----

Capsules: (phentermine mg/topiramate mg extended-release)

- 3.75 mg/23 mg (3)

- Known hypersensitivity or idiosyncrasy to sympathomimetic amines (4)

-----**WARNINGS AND PRECAUTIONS**-----

- **Fetal Toxicity:** Females of reproductive potential: Obtain negative pregnancy test before treatment and monthly thereafter; use effective contraception. Qsymia is available through a limited program under a Risk Evaluation and Mitigation Strategy (REMS) (5.1).
- **Increase in Heart Rate:** Monitor heart rate in all patients, especially those with cardiac or cerebrovascular disease (5.2).
- **Suicidal Behavior and Ideation:** Monitor for depression or suicidal thoughts. Discontinue Qsymia if symptoms develop (5.3).
- **Acute Myopia and Secondary Angle Closure Glaucoma:** Discontinue Qsymia (5.4).
- **Mood and Sleep Disorders:** Consider dose reduction or withdrawal for clinically significant or persistent symptoms (5.5).
- **Cognitive Impairment:** May cause disturbances in attention or memory. Caution patients about operating automobiles or hazardous machinery when starting treatment (5.6).
- **Metabolic Acidosis:** Measure electrolytes before/during treatment (5.7).
- **Elevated Creatinine:** Measure creatinine before/during treatment (5.8).
- **Use of Antidiabetic Medications:** Weight loss may cause hypoglycemia. Measure serum glucose before/during treatment (5.9).

-----**ADVERSE REACTIONS**-----

Most common adverse reactions (incidence greater than or equal to 5% and at a rate at least 1.5 times placebo) are: paraesthesia, dizziness, dysgeusia, insomnia, constipation, and dry mouth (6.1).

To report SUSPECTED ADVERSE REACTIONS, contact VIVUS Inc., at 1-888-998-4887 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

-----**DRUG INTERACTIONS**-----

- **Oral contraceptives:** Altered exposure may cause irregular bleeding but not increased risk of pregnancy. Advise patients not to discontinue oral contraceptives if spotting occurs (7.2).
- **CNS depressants including alcohol:** Potentiate CNS depressant effects. Avoid concomitant use of alcohol (7.3).
- **Non-potassium sparing diuretics:** May potentiate hypokalemia. Measure potassium before/during treatment (7.4).

This information comes from a link to QsymiaREMS.com

MEDICATION GUIDE
QSYMIA® (Kyoo sim ee' uh)
(phentermine and topiramate extended-release)
Capsules CIV

Read this Medication Guide before you start taking Qsymia and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or treatment. If you have any questions about Qsymia, talk to your healthcare provider or pharmacist.

What is the most important information I should know about Qsymia?

(For other side effects, also see **“What are the possible side effects of Qsymia?”**)

Qsymia can cause serious side effects, including:

- **Birth defects (cleft lip/cleft palate).** If you take Qsymia during pregnancy, your baby has a higher risk for birth defects called cleft lip and cleft palate. These defects can begin early in pregnancy, even before you know you are pregnant.

Women who are pregnant must not take Qsymia.

Women who can become pregnant should:

1. Have a negative pregnancy test before taking Qsymia and every month while taking Qsymia.
2. Use effective birth control (contraception) consistently while taking Qsymia. Talk to your healthcare provider about how to prevent pregnancy.

If you become pregnant while taking Qsymia, stop taking Qsymia immediately, and tell your healthcare provider right away. Healthcare providers and patients should report all cases of pregnancy to:

- FDA MedWatch at 1-800-FDA-1088, and
- The Qsymia Pregnancy Surveillance Program at 1-888-998-4887

- **Increases in heart rate.** Qsymia can increase your heart rate at rest. Your

This information comes from a link to [QsymiaREMS.com](https://www.QsymiaREMS.com)

Qsymia® (phentermine and topiramate extended-release) capsules CIV Healthcare Provider Training Program

Overview

FDA has required a Risk Evaluation and Mitigation Strategy (REMS) for Qsymia so that healthcare providers can be informed about the increased risk of teratogenicity associated with Qsymia therapy.

Purpose

The purpose of the REMS is to inform prescribers and females of reproductive potential (FRP) about the:

- Increased risk of congenital malformations, specifically orofacial clefts, in infants exposed to Qsymia during the first trimester of pregnancy
- Importance of pregnancy prevention for FRP
- Need to discontinue Qsymia immediately if pregnancy occurs

Complete the Qsymia Healthcare Provider Training Program in 2 easy steps:

1. Read through the entirety of this program.
2. Confirm you've read through and understand the program's content by faxing your completed assessment and registration information to VIVUS at 1-877-205-5098.

Step 1: Read through the entirety of the program

Before you consider prescribing Qsymia, it is important to be aware of the increased risk of teratogenicity associated with Qsymia therapy.

The information presented in this Training Program does not include a complete list of all risks and safety information on Qsymia.

Before prescribing Qsymia, please read the accompanying Qsymia Prescribing Information and Qsymia Medication Guide.

Further information is also available on the Web site www.QsymiaREMS.com.

Indication and Patient Selection

Qsymia is indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adult patients with an initial body mass index (BMI) of:

- 30 kg/m² or greater (obese), or
- 27 kg/m² or greater (overweight) in the presence of at least one weight-related comorbidity such as hypertension, type 2 diabetes mellitus, or dyslipidemia

Limitations of use:

- The effect of Qsymia on cardiovascular morbidity and mortality has not been established
- The safety and effectiveness of Qsymia in combination with other products intended for weight loss, including prescription and over-the-counter drugs, and herbal preparations, have not been established

www.QsymiaREMS.com

Qsymia[®]
(phentermine and topiramate extended-release) capsules ©

Increased Risk of Teratogenicity

Qsymia is classified as **Pregnancy Category X**

- Qsymia is contraindicated in pregnant women because the use of Qsymia can cause fetal harm. Available data indicate an increase in oral clefts (cleft lip with or without cleft palate) in infants exposed to topiramate, one of the components of Qsymia, during the first trimester of pregnancy.

Studies evaluating the risk of major congenital malformations and/or oral clefts with exposure to topiramate, a component of Qsymia, during pregnancy include the following:

- The North American Anti-Epileptic Drug (NAAED) Pregnancy Registry (2010) analysis
- A retrospective evaluation of a Wolters Kluwer claims database (January 2003-December 2010 from the United States)
- A retrospective observational study using 4 U.S. electronic healthcare databases (FORTRESS)
- A case-control study using data from the Slone Epidemiology Center Birth Defects Study (BDS, 1997-2009) and the Centers for Disease Control's (CDC's) National Birth Defects Prevention Study (NBDPS, 1996-2007)

The NAAED Pregnancy Registry reports an estimated increase in risk for oral clefts of 9.60 (95% CI 3.60-25.70).

An increase in oral clefts was observed with all dose strengths of topiramate.

SUMMARY OF STUDIES EVALUATING THE ASSOCIATION OF TOPIRAMATE IN UTERO EXPOSURE AND ORAL CLEFTS

EPIDEMIOLOGY STUDY	ORAL CLEFTS		MAJOR CONGENITAL MALFORMATIONS	
	PREVALENCE/ODDS RATIO	95% CI	ESTIMATED INCREASE IN RISK	95% CI
WOLTERS KLUWER ^a	1.47	0.36-6.06	1.12	0.81-1.55
FORTRESS ^a	2.22	0.78-6.36	1.21	0.99-1.47
SLONE/CDC	5.36	1.49-20.07	1.01	0.37-3.22

^aSponsored by the maker of Qsymia® (phentermine and topiramate extended-release) capsules CIV.

CI=confidence interval.

These data show that exposure to topiramate, a component of Qsymia, in pregnancy is associated with a 2- to 5-fold increase in risk of oral clefts.

Other data sources confirm the increased risk of oral clefts with topiramate exposure during pregnancy (ie, animal studies and Adverse Event Reporting System data).

www.QsymiaREMS.com



© 2012-2017 VIVUS Inc. All rights reserved. RE-03-003-04 08/2014 VMI-573



Counseling for Females of Reproductive Potential*

Qsymia can cause fetal harm.

Advise females of reproductive potential that you recommend:

- Pregnancy testing prior to beginning Qsymia and monthly during therapy
- Use of effective contraception consistently during Qsymia therapy; even females who believe they cannot become pregnant should use effective contraception while taking Qsymia
- If you become pregnant while taking Qsymia, stop Qsymia immediately and notify your healthcare provider

*Females of reproductive potential are women who have NOT had a hysterectomy, bilateral oophorectomy, or medically documented spontaneous ovarian failure, and have not gone through menopause. Menopause should be clinically confirmed by an individual's healthcare provider.

Acceptable Contraception Methods for Females of Reproductive Potential

Option 1 - Highly Effective Methods to Use Alone

One method from this list

• Intrauterine device (IUD) or intrauterine system (IUS) - Copper IUD - Levonorgestrel-releasing IUS	• Progestin implant • Tubal sterilization • Male partner's vasectomy
--	--

OR

Option 2 - Acceptable Methods to Use Together

One method from this list

Hormonal Contraception

- Estrogen and progestin
- Oral (the pill)
- Transdermal patch
- Vaginal ring
- Progestin only
- Oral
- Injection

+

One method from this list

Barrier Method

- Diaphragm (with spermicide)
- Cervical cap (with spermicide)
- Male condom (with or without spermicide)

OR

Option 3 - Acceptable Methods to Use Together

One method from this list

Barrier Method

- Diaphragm (with spermicide)
- Cervical cap (with spermicide)

+

One method from this list

Barrier Method

- Male condom (with or without spermicide)

Advise nursing mothers not to use Qsymia. Qsymia may be present in human milk because topiramate and amphetamines (phentermine has pharmacologic activity and a chemical structure similar to amphetamines) are excreted in human milk.

Find patient education and other support tools at www.QsymiaREMS.com.

Dispensed to Patients Through Certified Pharmacies

Qsymia is available only through certified pharmacies that provide a Qsymia Medication Guide and *Risk of Birth Defects with Qsymia* patient brochure with every prescription and refill as required by the REMS. Please note that Qsymia is not available outside this network of certified pharmacies.

A full listing of the certified pharmacies can be found at: www.QsymiaREMS.com.

www.QsymiaREMS.com

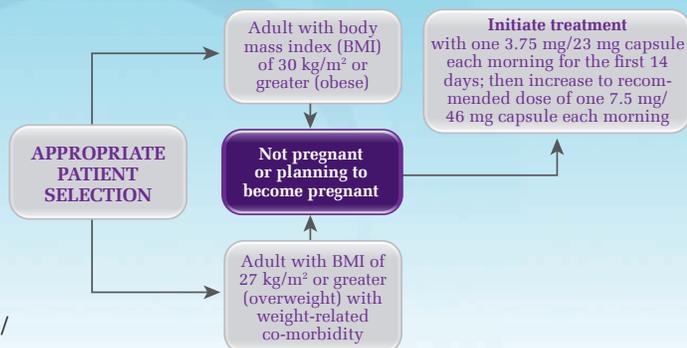
NDA 022580 / Sequence No. 0495

56 of 116

CONFIDENTIAL

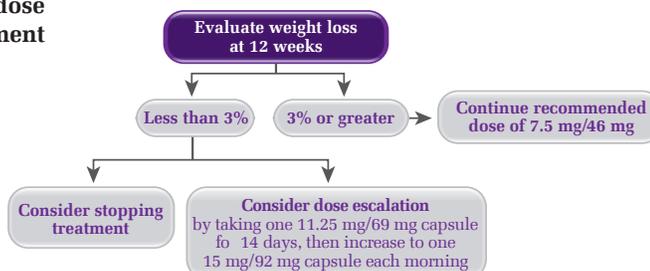
Dosage and Administration

- Qsymia should be taken in the morning, with or without food
- Avoid dosing with Qsymia in the evening due to the possibility of insomnia
- For patients with moderate hepatic impairment or moderate/severe renal impairment, the Qsymia dose should not exceed the recommended dose of Qsymia 7.5 mg/46 mg (phentermine 7.5 mg/topiramate 46 mg extended-release)
- The suggested follow-up after administration of initial treatment is 2 to 8 weeks
- To initiate treatment: Start with one Qsymia 3.75 mg/23 mg (phentermine 3.75 mg/topiramate 23 mg extended-release) capsule each morning for the first 14 days; then increase to recommended dose of one Qsymia 7.5 mg/46 mg capsule each morning



Evaluate weight loss with the recommended dose of Qsymia, 7.5 mg/46 mg, at week 12 of treatment

If a patient has not lost at least 3% of baseline body weight on the recommended dose of Qsymia, 7.5 mg/46 mg, discontinue Qsymia or escalate the dose as directed, as it is unlikely that the patient will achieve and sustain clinically meaningful weight loss at the Qsymia 7.5 mg/46 mg dose.



To escalate the dose: Increase to one Qsymia 11.25 mg/69 mg (phentermine 11.25 mg/topiramate 69 mg extended-release) capsule each morning for 14 days, followed by dosing one Qsymia 15 mg/92 mg (phentermine 15 mg/topiramate 92 mg extended-release) capsule each morning.

Evaluate weight loss following dose escalation to Qsymia 15 mg/92 mg after 12 weeks of treatment

If a patient has not lost at least 5% of baseline body weight on Qsymia 15 mg/92 mg, discontinue Qsymia, as it is unlikely that the patient will achieve and sustain clinically meaningful weight loss with continued treatment.

To discontinue Qsymia 15 mg/92 mg, have the patient take a dose every other day for at least 1 week prior to stopping treatment altogether, due to the possibility of precipitating a seizure with abrupt cessation of dosing.



www.QsymiaREMS.com



© 2012-2017 VIVUS Inc. All rights reserved. RE-03-003-04 08/2014 VMI-573



Step 2: Confirm you've read through and understand the Qsymia REMS by answering 5 assessment questions found on the next page.

Fax your completed assessment and registration information to VIVUS at 1-877-205-5098.

Additional information and tools can be found at www.QsymiaREMS.com.

- **Healthcare Provider Counseling Tool for Females of Reproductive Potential**
- **Prescriber Dosing and Management Checklist**
- ***Risk of Birth Defects with Qsymia* patient brochure**
- **Dear Healthcare Provider Letter**
- **Qsymia Prescribing Information**
- **Qsymia Medication Guide Certified**
- **Certified Pharmacy Locator on www.QsymiaREMS.com**

For more information, contact VIVUS Medical Information at 1-888-998-4887 or visit www.QsymiaREMS.com.

www.QsymiaREMS.com

Qsymia[®]
(phentermine hydrochloride)
extended-release capsules

5

Important Safety Information

Qsymia® is contraindicated in pregnancy; in patients with glaucoma; in hyperthyroidism; in patients receiving treatment or within 14 days following treatment with monoamine oxidase inhibitors (MAOIs); or in patients with hypersensitivity or idiosyncrasy to sympathomimetic amines, topiramate, or any of the inactive ingredients in Qsymia.

Qsymia can cause fetal harm. Females of reproductive potential should have a negative pregnancy test before treatment and monthly thereafter and use effective contraception consistently during Qsymia therapy. If a patient becomes pregnant while taking Qsymia, treatment should be discontinued immediately, and the patient should be informed of the potential hazard to the fetus.

Qsymia can cause an increase in resting heart rate. Regular measurement of resting heart rate is recommended for all patients taking Qsymia, especially patients with cardiac or cerebrovascular disease or when initiating or increasing the dose of Qsymia. Qsymia has not been studied in patients with recent or unstable cardiac or cerebrovascular disease and therefore use is not recommended.

Topiramate, a component of Qsymia, increases the risk of suicidal thoughts or behavior in patients taking these drugs for any indication. Patients should be monitored for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior. Discontinue Qsymia in patients who experience suicidal thoughts or behaviors. Qsymia is not recommended in patients with a history of suicidal attempts or active suicidal ideation.

Acute angle closure glaucoma has been reported in patients treated with topiramate, a component of Qsymia. Symptoms include acute onset of decreased visual acuity and/or eye pain. Symptoms typically occur within 1 month of initiating treatment with topiramate but may occur at any time during therapy. The primary treatment to reverse symptoms is immediate discontinuation of Qsymia.

Qsymia can cause mood disorders, including depression and anxiety, as well as insomnia. Qsymia can cause cognitive dysfunction (e.g., impairment of concentration/attention, difficulty with memory, and speech or language problems, particularly word-finding difficulties). Since Qsymia has the potential to impair cognitive function, patients should be cautioned about operating hazardous machinery, including automobiles.

Hyperchloremic, non-anion gap, metabolic acidosis has been reported in patients treated with Qsymia. If metabolic acidosis develops and persists, consideration should be given to reducing the dose or discontinuing Qsymia.

Qsymia can cause an increase in serum creatinine. If persistent elevations in creatinine occur while taking Qsymia, reduce the dose or discontinue Qsymia.

Weight loss may increase the risk of hypoglycemia in patients with type 2 diabetes mellitus treated with insulin and/or insulin secretagogues (e.g., sulfonylureas). Qsymia has not been studied in combination with insulin. A reduction in the dose of antidiabetic medications which are non-glucose-dependent should be considered to mitigate the risk of hypoglycemia.

The most commonly observed side effects in controlled clinical studies, 5% or greater and at least 1.5 times placebo, include paraesthesia, dizziness, dysgeusia, insomnia, constipation, and dry mouth.

To report negative side effects, contact VIVUS, Inc. at 1-888-998-4887 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

www.QsymiaREMS.com



© 2012-2017 VIVUS Inc. All rights reserved. RE-03-003-04 08/2014 VMI-573



Assessment Answers

1 of 5

True or False: The major risk for females of reproductive potential (FRP) being treated with Qsymia is that of teratogenicity (birth defects), specifically the risk of cleft lip with or without cleft palate.

The correct answer is TRUE.

Topiramate, a component of Qsymia, has been associated with an increased risk of cleft lip with or without cleft palate in infants exposed to topiramate during the first trimester of pregnancy.

2 of 5

True or False: If a patient hasn't achieved 3% weight loss following 12 weeks of treatment on the recommended dose of Qsymia, 7.5 mg/46 mg (phentermine 7.5 mg/topiramate 46 mg extended-release), discontinuation of therapy or dose escalation should be considered.

The correct answer is TRUE.

If a patient has not lost at least 3% of baseline body weight on Qsymia 7.5 mg/46 mg, discontinue Qsymia or escalate the dose as directed, as it is unlikely that the patient will achieve and sustain clinically meaningful weight loss at the Qsymia 7.5 mg/46 mg dose.

3 of 5

True or False: Women taking Qsymia should use contraception unless they have had infertility or trouble getting pregnant in the past.

The correct answer is FALSE.

ALL women, except those who have gone through menopause or undergone surgical sterilization, should be advised to consistently use effective contraception, even women who have had difficulty getting pregnant in the past.

4 of 5

True or False: If I don't think a patient is at risk for pregnancy, I don't need to discuss contraception.

The correct answer is FALSE.

It is important to have this conversation with all patients. It is important to know whether a patient is:

- Trying to get pregnant and not using contraception, in which case do not prescribe Qsymia
- Sexually active and what contraception she is using, in which case reinforce the importance of consistent use of effective contraception
- Surgically sterilized or has gone through menopause that has been clinically confirmed, in which case no contraception is required

It is important to have this conversation with all patients, so that if there is a female of reproductive potential in the house, the patient knows to keep Qsymia in a secure location and not share it with anyone else.

5 of 5

True or False: If a woman thinks she is pregnant, she should continue taking Qsymia until the pregnancy is confirmed.

The correct answer is FALSE.

If a woman believes she might be pregnant, she should stop taking Qsymia immediately and contact her healthcare provider.



www.QsymiaREMS.com

© 2012-2017 VIVUS Inc. All rights reserved. RE-03-003-04 08/2014 VMI-573





**IMPORTANT DRUG WARNING –
REMS required for Qsymia® (phentermine and topiramate extended-release) capsules CIV**

Subject: Risk of Teratogenicity with Qsymia
FDA-Required Risk Evaluation and Mitigation Strategy (REMS)

Date

Dear Healthcare Provider:

VIVUS would like to inform you of the increased risk of teratogenicity with Qsymia in order to ensure its safe and appropriate use. This letter does not describe all the risks associated with Qsymia.

Qsymia is a schedule IV controlled substance (C-IV).

Qsymia is indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adult patients with an initial body mass index (BMI) of:

- 30 kg/m² or greater (obese), or
- 27 kg/m² or greater (overweight) in the presence of at least one weight-related comorbidity such as hypertension, type 2 diabetes mellitus, or dyslipidemia

Limitations of Use:

- The effect of Qsymia on cardiovascular morbidity and mortality has not been established
- The safety and effectiveness of Qsymia in combination with other products intended for weight loss, including prescription and over-the-counter drugs and herbal preparations have not been established

The Food and Drug Administration (FDA) determined a Risk Evaluation and Mitigation Strategy is necessary to ensure the benefits of Qsymia outweigh the increased risk of teratogenicity.

Risk of Teratogenicity associated with Qsymia therapy

- Qsymia can cause fetal harm. A fetus exposed to topiramate, a component of Qsymia, in the first trimester of pregnancy has an increased risk of oral clefts (cleft lip with or without cleft palate) according to data from pregnancy registries and epidemiology studies
- Qsymia is contraindicated in pregnancy (Pregnancy Category X)

Please continue to following page



Recommendations to mitigate the risk of teratogenicity in females of reproductive potential taking Qsymia®

- Females of reproductive potential should have a negative pregnancy test before starting Qsymia and monthly thereafter during Qsymia therapy
- Females of reproductive potential should use effective contraception consistently during Qsymia therapy
- If a patient becomes pregnant while taking Qsymia, treatment should be discontinued immediately, and the patient should be apprised of the potential hazard to the fetus

Patient counseling regarding the risk of teratogenicity associated with Qsymia therapy

- Advise females of reproductive potential to use effective contraception consistently while taking Qsymia because Qsymia can cause certain kinds of birth defects (oral clefts). Even females who believe they cannot become pregnant should use effective contraception consistently while taking Qsymia
- Inform patients who become pregnant while taking Qsymia to discontinue Qsymia immediately, and contact you for further follow-up

Qsymia Healthcare Provider Training Program

Training, support, and additional information about the increased teratogenic risk are available for prescribers. Visit www.QsymiaREMS.com to take the prescriber training program.

Dispensing by certified pharmacies

Qsymia is available only through certified pharmacies that provide a Qsymia Medication Guide and *Risk of Birth Defects with Qsymia* patient brochure with every prescription and refill as required by the REMS. Qsymia is now available through certified retail pharmacies in addition to certified mail order pharmacies. The list of certified pharmacies can be found at www.QsymiaREMS.com.

Reporting adverse events

Healthcare providers should report all suspected adverse events associated with the use of Qsymia. If you become aware of a patient experiencing an adverse event while taking Qsymia, please contact VIVUS Medical Information at 1-888-998-4887 or the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see the accompanying Qsymia Prescribing Information, Qsymia Medication Guide and *Risk of Birth Defects with Qsymia* patient brochure. For more information, visit www.QsymiaREMS.com or call VIVUS Medical Information at 1-888-998-4887.

Sincerely,

Santosh T. Varghese, MD
Vice President, Medical & Regulatory Affairs, Pharmacovigilance, and QA
VIVUS, Inc.



© 2012-2014 VIVUS, Inc. All rights reserved. 08/2014 RE 03 008 02



**IMPORTANT DRUG WARNING –
REMS required for Qsymia® (phentermine and topiramate extended-release) capsules CIV**

Subject: Risk of Teratogenicity with Qsymia
FDA-Required Risk Evaluation and Mitigation Strategy (REMS)

Date

Dear Medical Society:

VIVUS would like to inform you of the increased risk of teratogenicity with Qsymia in order to ensure its safe and appropriate use. This letter does not describe all the risks associated with Qsymia.

Qsymia is a schedule IV controlled substance (C-IV).

Qsymia is indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adult patients with an initial body mass index (BMI) of:

- 30 kg/m² or greater (obese), or
- 27 kg/m² or greater (overweight) in the presence of at least one weight-related comorbidity such as hypertension, type 2 diabetes mellitus, or dyslipidemia

Limitations of Use:

- The effect of Qsymia on cardiovascular morbidity and mortality has not been established
- The safety and effectiveness of Qsymia in combination with other products intended for weight loss, including prescription and over-the-counter drugs and herbal preparations have not been established

The Food and Drug Administration (FDA) determined a Risk Evaluation and Mitigation Strategy is necessary to ensure the benefits of Qsymia outweigh the increased risk of teratogenicity.

Risk of Teratogenicity associated with Qsymia therapy

- Qsymia can cause fetal harm. A fetus exposed to topiramate, a component of Qsymia, in the first trimester of pregnancy has an increased risk of oral clefts (cleft lip with or without cleft palate) according to data from pregnancy registries and epidemiology studies
- Qsymia is contraindicated in pregnancy (Pregnancy Category X)

Please continue to following page



Recommendations to mitigate the risk of teratogenicity in females of reproductive potential taking Qsymia®

- Females of reproductive potential should have a negative pregnancy test before starting Qsymia and monthly thereafter during Qsymia therapy
- Females of reproductive potential should use effective contraception consistently during Qsymia therapy
- If a patient becomes pregnant while taking Qsymia, treatment should be discontinued immediately, and the patient should be apprised of the potential hazard to the fetus

Patient counseling regarding the risk of teratogenicity associated with Qsymia therapy

- Advise females of reproductive potential to use effective contraception consistently while taking Qsymia because Qsymia can cause certain kinds of birth defects (oral clefts). Even females who believe they cannot become pregnant should use effective contraception consistently while taking Qsymia
- Inform patients who become pregnant while taking Qsymia to discontinue Qsymia immediately, and contact you for further follow-up

Qsymia Healthcare Provider Training Program

Training, support, and additional information about the increased teratogenic risk are available for prescribers. Visit www.QsymiaREMS.com to take the prescriber training program.

Dispensing by certified pharmacies

Qsymia is available only through certified pharmacies that provide a Qsymia Medication Guide and *Risk of Birth Defects with Qsymia* patient brochure with every prescription and refill as required by the REMS. Qsymia is now available through certified retail pharmacies in addition to certified mail order pharmacies. The list of certified pharmacies can be found at www.QsymiaREMS.com.

Reporting adverse events

Healthcare providers should report all suspected adverse events associated with the use of Qsymia. If you become aware of a patient experiencing an adverse event while taking Qsymia, please contact VIVUS Medical Information at 1-888-998-4887 or the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see the accompanying Qsymia Prescribing Information, Qsymia Medication Guide, Risk of Birth Defects with Qsymia patient brochure, and Dear Healthcare Provider Letter. For more information, visit www.QsymiaREMS.com or call VIVUS Medical Information at 1-888-998-4887.

Sincerely,

Santosh T. Varghese, MD
Vice President, Medical & Regulatory Affairs, Pharmacovigilance, and QA
VIVUS, Inc.



© 2012-2014 VIVUS, Inc. All rights reserved 08/2014 RE 03 009 02

[Important Safety Information](#) | [Full Prescribing Information](#) | [Medication Guide](#)

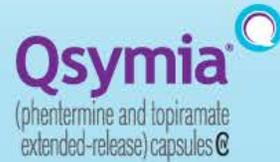
[Healthcare Provider
Training Program](#)

[Pharmacy
Training Program](#)

[Information for
Pharmacists](#)

[Qsymia Certified
Pharmacy Network](#)

[Risk of Birth Defects
Patient Brochure](#)



Risk Evaluation and Mitigation Strategy (REMS)

A Risk Evaluation and Mitigation Strategy (REMS) is a strategy to manage known or potential serious risks associated with a drug product and is required by the Food and Drug Administration (FDA) to ensure that the benefits of a drug outweigh its risks. The FDA has required a REMS for Qsymia.

The purpose of the Qsymia REMS is to inform prescribers and females of reproductive potential about the:

- Increased risk of congenital malformation, specifically orofacial clefts, in infants exposed to Qsymia during the first trimester of pregnancy
- Importance of pregnancy prevention for females of reproductive potential receiving Qsymia
- Need to discontinue Qsymia immediately if pregnancy occurs

Healthcare Provider Training Program

The Qsymia REMS includes a healthcare provider training program.

Complete the Qsymia Healthcare
Provider Training Program

START

Counseling Females on Risk of Birth Defects with Qsymia

- Counsel females of reproductive potential at initial and all follow-up visits on the increased risk of orofacial clefts in infants exposed to Qsymia during the first trimester of pregnancy
- Counsel females of reproductive potential to have a pregnancy test before starting Qsymia and monthly thereafter during therapy
- Discuss the need for consistent use of effective contraception during therapy
- Make use of the REMS tools supporting patient education that are available on this Web site

Dispensed to Patients Through Certified Pharmacies

Qsymia is available only through certified pharmacies. [Click Here](#) to learn more.

[Privacy Policy](#) :: [Terms of Use](#)

©2012-2014 VIVUS Inc. All rights reserved.

RE-03-010-02 08/2014

Materials for Healthcare Providers

[Healthcare Provider Counseling Tool
for Females of Reproductive Potential](#)
[Prescriber Dosing and Management Checklist](#)
[Healthcare Provider Training Program](#)
[Dear Healthcare Provider Letter](#)
[Full Prescribing Information](#)

Materials for Patients

[Risk of Birth Defects with Qsymia patient brochure](#)
[Medication Guide](#)

These materials can be downloaded and printed.

For additional information, please contact VIVUS Medical
Information at 1-888-998-4887.



Qsymia[®] Risk Evaluation and Mitigation Strategy (REMS)

Pharmacy Enrollment Form - Independent Pharmacy

Because of the teratogenic risk associated with Qsymia therapy, Qsymia is available through a limited program under the REMS. Under the Qsymia REMS, only certified pharmacies may distribute Qsymia. I understand that my independent pharmacy dispensing location must comply with the program requirements for certified pharmacies and the terms of the agreement contained in this form. As the designated Authorized Pharmacy Representative, I acknowledge that:

1. I have reviewed and successfully completed the Qsymia Pharmacy Training Program and the knowledge assessment questions.
2. I understand the risks associated with Qsymia.
3. I understand and agree to comply with the requirements of the Qsymia REMS program for pharmacies.
 - a. The pharmacy management system configuration and/or updates will be in place and verified with the Qsymia REMS Pharmacy Administrator to ensure that Qsymia prescription claims are submitted in accordance with the program requirements.
 - b. The pharmacy management system will be in place to systematically direct that certified independent pharmacy dispensing locations provide a Medication Guide and the *Risk of Birth Defects with Qsymia* patient brochure to each patient each time Qsymia is dispensed.
 - c. My certified pharmacy will refrain from reselling or transferring Qsymia to another pharmacy or distributor.
 - d. Pharmacy training of pharmacists and staff involved with the dispensing of Qsymia has been completed and documented including the need to provide a Medication Guide and the *Risk of Birth Defects with Qsymia* patient brochure each time Qsymia is dispensed in order to comply with the REMS requirements.
 - e. All Qsymia prescription claims, regardless of the method of payment, must be processed through my pharmacy management system, claims routing switch, or through pharmacy software system for Qsymia REMS verification.
 - f. My certified pharmacy is subject to, and must comply with, survey requirements to ensure that the REMS requirements are being following to maintain pharmacy certification under the Qsymia REMS. Failure to comply may result in decertification.





4. I will oversee compliance with the Qsymia REMS program requirements.
5. I acknowledge, that prior to Qsymia REMS pharmacy certification, the Qsymia REMS Pharmacy Support Center will contact me if an agreement is needed to permit the switch provider to use prescription data from this pharmacy to conduct the REMS.

Authorized Pharmacy Representative to complete (all fields required):

First Name _____ **Last Name** _____

Phone Number _____ **Fax** _____

Email _____

Address _____ **City** _____

State _____ **Zip Code** _____

Pharmacy Name _____

Pharmacy DEA# _____ **Pharmacy NCPDP ID** _____

Pharmacy NPI _____ **Pharmacy Store # (optional)** _____

Signature _____ **Date** _____

Authorized Pharmacy Representative

Please fax completed form to the Qsymia REMS Pharmacy Support Center (855-302-6699).

Once this form is successfully processed, you will receive a fax or e-mail with instructions on how to submit test transaction(s) to the Qsymia REMS program to ensure that your pharmacy management system has been successfully configured/updated to communicate with the Qsymia REMS program. Upon successful verification of connectivity, you will be provided with the Terms & Conditions to become certified. Once this process is complete your pharmacy will receive a confirmation from the Qsymia REMS Pharmacy Support Center and you will be considered certified and permitted to order, receive, and dispense Qsymia.

If you have any questions or require additional information, please contact the Qsymia REMS Pharmacy Support Center at 1-855-302-6698.





Qsymia[®] Risk Evaluation and Mitigation Strategy (REMS)

Pharmacy Enrollment Form - Corporate Entity of Retail Chain Pharmacy

Because of the teratogenic risk associated with Qsymia therapy, Qsymia is available through a limited program under the REMS. Under the Qsymia REMS, only certified pharmacies may distribute Qsymia. I understand that my certified retail pharmacy dispensing locations must comply with the program requirements for certified pharmacies and the terms contained in this form. As the Authorized Corporate Pharmacy Representative, I acknowledge that:

1. I have reviewed and successfully completed the Qsymia Pharmacy Training Program and the knowledge assessment questions.
2. I understand the risks associated with Qsymia.
3. I understand and agree to comply with the requirements of the Qsymia REMS program for pharmacies.
 - a. The pharmacy management system configuration and/or updates will be in place and verified with the Qsymia REMS Pharmacy Support Center to ensure that Qsymia prescription claims are submitted in accordance with the program requirements.
 - b. The pharmacy management system will be in place to systematically direct that all certified retail pharmacy dispensing locations provide a Medication Guide and the *Risk of Birth Defects with Qsymia* patient brochure to each patient each time Qsymia is dispensed.
 - c. All certified retail pharmacy dispensing locations will refrain from reselling or transferring Qsymia to another pharmacy or distributor.
 - d. All certified retail pharmacy dispensing locations will complete training of pharmacists and staff involved with the dispensing of Qsymia and will comply with the REMS requirement to provide a Medication Guide and the *Risk of Birth Defects with Qsymia* patient brochure each time Qsymia is dispensed.
 - e. I will maintain all records of certified retail pharmacy dispensing location training and acknowledgement forms.
 - f. All certified retail pharmacy dispensing locations will be made aware that all Qsymia prescription claims, regardless of the method of payment, must be processed through our pharmacy management system and "pharmacy claims routing switch" for Qsymia REMS verification.





- g. I will ensure proper authorization or provision of data rights to my switch provider are in place to meet Qsymia REMS program requirements.
 - h. All certified retail pharmacy dispensing locations are subject to, and must comply with, surveys to assess compliance with the REMS requirements in order to maintain pharmacy certification.
 - i. Each corporate entity of a certified retail chain pharmacy is subject to, and must comply with, audit requirements to ensure that the REMS requirements are being followed to maintain their pharmacy certification under the Qsymia REMS.
4. I will oversee compliance with the Qsymia REMS program requirements and will provide quarterly compliance reports back to VIVUS to assess effectiveness and comply with all audit requirements.

Authorized Corporate Pharmacy Representative to complete (all fields required):

First Name _____ **Last Name** _____

Phone Number _____ **Fax** _____

Email _____

Corporate Pharmacy Name _____

Address _____ **City** _____

State _____ **Zip Code** _____

Signature _____ **Date** _____

Authorized Corporate Pharmacy Representative

Please fax completed form to the Qsymia REMS Pharmacy Support Center (855-302-6699).

Once this form is successfully processed, you will receive a fax or e-mail with instructions on how to submit test transaction(s) to the Qsymia REMS program to ensure that your pharmacy management system has been successfully configured/updated to communicate with the Qsymia REMS program.

After successful completion of the test transaction(s) you will receive a corporate pharmacy enrollment confirmation via fax and/or email from the Qsymia REMS Pharmacy Support Center. Your corporate entity will be considered certified and your retail chain dispensing locations will be eligible to complete their certification procedures.





The Qsymia Pharmacy Training Program for your pharmacy dispensing locations will be made available through the Qsymia REMS Pharmacy Support Center. Once the training program and knowledge assessment are completed at a pharmacy dispensing location within your organization, it is your responsibility to capture the pharmacy dispensing location information noted below and provide to the Qsymia REMS Pharmacy Support Center. Once the Qsymia REMS Pharmacy Support Center receives, processes and confirms the required pharmacy dispensing location information from you, this pharmacy dispensing location will be considered certified and permitted to order, receive, and dispense Qsymia.

The following required pharmacy dispensing location fields must be provided to the Authorized Corporate Pharmacy Representative for each trained pharmacy dispensing location: Responsible Pharmacist first and last name, dispensing pharmacy address with zip code, phone and fax numbers, pharmacy DEA, NCPDP ID and NPI numbers; and pharmacy store # (optional).

If you have any questions or require additional information, please contact the Qsymia REMS Pharmacy Support Center at 1-855-302-6698.





Qsymia[®] Risk Evaluation and Mitigation Strategy (REMS)

Pharmacy Enrollment Form - Mail Order Pharmacy

Because of the teratogenic risk associated with Qsymia therapy, Qsymia is available through a limited program under the REMS. Under the Qsymia REMS, only certified pharmacies may distribute Qsymia. I understand that my certified mail order pharmacy must comply with the program requirements for certified pharmacies and the terms contained in this form. As the Authorized Pharmacy Representative, I acknowledge that:

1. I have reviewed and successfully completed the Qsymia Pharmacy Training Program and the knowledge assessment questions.
2. I understand the risks associated with Qsymia.
3. I understand and agree to comply with the requirements of the Qsymia REMS program for pharmacies.
 - a. The pharmacy management system is in place, and has been validated, to systematically direct that a Medication Guide and the *Risk of Birth Defects with Qsymia* patient brochure be provided to each patient each time Qsymia is dispensed.
 - b. The pharmacy will refrain from reselling or transferring Qsymia to another pharmacy or distributor.
 - c. The 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 each time Qsymia is dispensed.
 - d. The pharmacy and pharmacy personnel will cooperate with pharmacy audit requirements in order to maintain pharmacy certification.
 - e. The pharmacy will maintain a list of Qsymia prescribers that will be provided to VIVUS monthly.
4. I will oversee compliance with the Qsymia REMS program requirements and will provide quarterly compliance reports back to VIVUS to assess effectiveness and comply with all audit requirements.





Authorized Pharmacy Representative to complete (all fields required):

First Name _____ **Last Name** _____

Phone Number _____ **Fax** _____

Email _____

Mail Order Pharmacy Name _____

Address _____ **City** _____

State _____ **Zip Code** _____

Signature _____ **Date** _____

Authorized Pharmacy Representative

Please fax this completed form to the Qsymia REMS Pharmacy Support Center at 1-855-302-6699.

If you have any questions or require additional information, please contact the Qsymia REMS Pharmacy Support Center at 1-855-302-6698.



Qsymia® (phentermine and topiramate extended-release) capsules CIV Pharmacy Training Program

Overview

The Food and Drug Administration (FDA) has required a Risk Evaluation and Mitigation Strategy (REMS) for Qsymia to ensure the benefits of Qsymia outweigh the increased risk of teratogenicity.

Purpose

The purpose of the REMS is to inform prescribers, pharmacies, and females of reproductive potential (FRP) about the:

- Increased risk of congenital malformations, specifically orofacial clefts, in infants exposed to Qsymia during the first trimester of pregnancy
- Importance of pregnancy prevention for FRP
- Need to discontinue Qsymia immediately if pregnancy occurs



The Qsymia Pharmacy Training Program

Complete the Qsymia Pharmacy Certification in 3 easy steps:

1. Read through the entirety of this Pharmacy Training Program and confirm you understand the program's content by completing the knowledge assessment questions.
 - For mail order pharmacies, your knowledge assessment may be completed by the Authorized Pharmacy Representative (AR) and faxed to the Qsymia REMS Pharmacy Support Center at 1-855-302-6699
 - For chain pharmacies, your knowledge assessment responses may be managed by your Authorized Pharmacy Representative. Please contact your corporate Authorized Pharmacy Representative for instructions on completing your knowledge assessment
 - For independent pharmacies, your knowledge assessment may be completed and faxed to the Qsymia REMS Pharmacy Support Center at 1-855-302-6699
2. Complete Pharmacy Enrollment Form and fax to the Qsymia REMS Pharmacy Support Center at 1-855-302-6699.
 - For chain pharmacies, a Pharmacy Enrollment Form must be completed by the Authorized Representative for the corporate chain organization
 - For chain pharmacy dispensing locations, a Pharmacy Enrollment Form must be completed by the Responsible Pharmacist, and can be obtained from the Authorized Representative for the corporate chain organization
 - For independent pharmacies, a Pharmacy Enrollment Form is required for the Authorized Pharmacy Representative for the dispensing pharmacy location
 - For mail order pharmacies, an Enrollment Form must be completed by the Authorized Representative for the mail order pharmacy organization
3. Complete the vendor verification/validation process. Upon successful completion of your training program, knowledge assessment and enrollment form, you will receive instructions on how to complete the vendor verification steps to verify your pharmacy management system is successfully connected to the Qsymia REMS network for all Qsymia claims and dispenses. (This does not apply to Mail Order pharmacies.)



The Qsymia Pharmacy Training Program

Step 1: Complete Pharmacy Training Program, Including Knowledge Assessment

These training materials are being provided to assist pharmacists with understanding the risks of Qsymia and the pharmacy requirements under the REMS. Before you are eligible to dispense Qsymia, it is important to be aware of the increased risk of teratogenicity associated with Qsymia therapy.

The information presented in this Training Program does not include a complete list of all risks and safety information on Qsymia. Before dispensing Qsymia, please read the accompanying Qsymia Prescribing Information and the *Risk of Birth Defects with Qsymia* patient brochure.

Further information is also available on the Web site, www.QsymiaREMS.com or by calling the Qsymia REMS Pharmacy Support Center at 1-855-302-6698.



Indication and Patient Selection

Qsymia is indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adult patients with an initial body mass index (BMI) of:

- 30 kg/m² or greater (obese), or
- 27 kg/m² or greater (overweight) in the presence of at least one weight-related comorbidity such as hypertension, type 2 diabetes mellitus, or dyslipidemia

Limitations of use:

- The effect of Qsymia on cardiovascular morbidity and mortality has not been established
- The safety and effectiveness of Qsymia in combination with other products intended for weight loss, including prescription and over-the-counter drugs, and herbal preparations, have not been established



Increased Risk of Teratogenicity

Qsymia is classified as **Pregnancy Category X**

- Qsymia is contraindicated in pregnant women because the use of Qsymia can cause fetal harm. Available data indicate an increase in oral clefts (cleft lip with or without cleft palate) in infants exposed to topiramate, one of the components of Qsymia, during the first trimester of pregnancy

Qsymia[®]
(phentermine and topiramate
extended-release) capsules 

© 2012-2014 VIVUS Inc. All rights reserved. RE-03-017-01 08/2014

5

Increased Risk of Teratogenicity

Studies evaluating the risk of major congenital malformations and/or oral clefts with exposure to topiramate, a component of Qsymia, during pregnancy include the following:

- The North American Anti-Epileptic Drug (NAAED) Pregnancy Registry (2010) analysis
- A retrospective evaluation of a Wolters Kluwer claims database (January 2003-December 2010 from the United States)
- A retrospective observational study using 4 U.S. electronic healthcare database (FORTRESS)
- A case-control study using data from the Slone Epidemiology Center Birth Defects Study (BDS, 1997-2009) and the Centers for Disease Control's (CDC's) National Birth Defects Prevention Study (NBDPS, 1996-2007)

The NAAED Pregnancy Registry suggested an estimated increase in risk for oral clefts of 9.60 (95% CI 3.60 – 25.70).

An increase in oral clefts was observed with all dose strengths of topiramate.



Summary of Data on Teratogenicity Risk

SUMMARY OF STUDIES EVALUATING THE ASSOCIATION OF TOPIRAMATE IN UTERO EXPOSURE AND ORAL CLEFTS

EPIDEMIOLOGY STUDY	ORAL CLEFTS		MAJOR CONGENITAL MALFORMATIONS	
	PREVALENCE/ODDS RATIO	95% CI	ESTIMATED INCREASE IN RISK	95% CI
WOLTERS KLUWER ^a	1.47	0.36-6.06	1.12	0.81-1.55
FORTRESS ^a	2.22	0.78-6.36	1.21	0.99-1.47
SLONE/CDC	5.36	1.49-20.07	1.01	0.37-3.22

^aSponsored by the maker of Qsymia[®] (phentermine and topiramate extended-release) capsules CIV.

CI=confidence interval.

These data show that exposure to topiramate, a component of Qsymia, in pregnancy is associated with a 2- to 5-fold increase in risk of oral clefts.

Other data sources confirm the increased risk of oral clefts with topiramate exposure during pregnancy (ie, animal studies and Adverse Event Reporting System data).



Counseling Provided by HCPs for Females of Reproductive Potential*

Qsymia can cause fetal harm.

Advise females of reproductive potential that labeling recommends:

- Pregnancy testing prior to beginning Qsymia and monthly during therapy. Specific documentation of the result is not required at the pharmacy level
- Use of effective contraception consistently during Qsymia therapy because Qsymia can cause certain kinds of birth defects (oral clefts). Even females who believe they cannot become pregnant should use effective contraception while taking Qsymia due to the potential for increased fertility associated with weight loss
- If a patient becomes pregnant while taking Qsymia, Qsymia should be discontinued immediately and the patient advised to notify their healthcare provider

*Females of reproductive potential are women who have NOT had a hysterectomy, bilateral oophorectomy, or medically documented spontaneous ovarian failure, and have not gone through menopause. Menopause should be clinically confirmed by an individual's healthcare provider.

Advise nursing mothers not to use Qsymia. Qsymia may be present in human milk because topiramate and amphetamines (phentermine has pharmacologic activity and a chemical structure similar to amphetamines) are excreted in human milk.



Acceptable Contraceptive Methods for Females of Reproductive Potential (con't)

Acceptable Contraception Methods for Females of Reproductive Potential

Option 1 Highly Effective Methods to Use Alone	Option 2 Acceptable Methods to Use Together	Option 3 Acceptable Methods to Use Together
<p>One method from this list</p> <ul style="list-style-type: none">• Intrauterine device (IUD) or intrauterine system (IUS)<ul style="list-style-type: none">- Copper IUD- Levonorgestrel-releasing IUS• Progestin implant• Tubal sterilization• Male partner's vasectomy	<p>One method from this list</p> <p>Hormonal Contraception</p> <ul style="list-style-type: none">• Estrogen and progestin<ul style="list-style-type: none">- Oral (the pill)- Transdermal patch- Vaginal ring• Progestin only<ul style="list-style-type: none">- Oral- Injection <p>+</p> <p>One method from this list</p> <p>Barrier Method</p> <ul style="list-style-type: none">• Diaphragm (with spermicide)• Cervical cap (with spermicide)• Male condom (with or without spermicide)	<p>One method from this list</p> <p>Barrier Method</p> <ul style="list-style-type: none">• Diaphragm (with spermicide)• Cervical cap (with spermicide) <p>+</p> <p>One method from this list</p> <p>Barrier Method</p> <ul style="list-style-type: none">• Male condom (with or without spermicide)

Patient education and other support tools are available at
www.QsymiaREMS.com



Qsymia Is Only Dispensed Through Certified Pharmacies

Under the REMS, Qsymia is only available through certified pharmacies. To become a certified pharmacy, an authorized or responsible pharmacy representative must agree to:

1. Refrain from reselling or transferring Qsymia to another pharmacy or distributor
2. Train pharmacists and staff involved with the dispensing of Qsymia about the risks associated with Qsymia and the REMS requirement to provide a Medication Guide and *Risk of Birth Defects with Qsymia* patient brochure each time Qsymia is dispensed
3. To be subject to and comply with surveys or audits (as applicable) to evaluate understanding of the risks associated with the use of Qsymia, and compliance with the requirements of the REMS

The list of certified pharmacies will be updated within 1-2 business days after a new pharmacy is certified and eligible to dispense. Prescribers and patients will be able to use a “Certified Pharmacy Locator” tool to identify certified pharmacies in their area, which can be found at www.QsymiaREMS.com.

Please note that Qsymia is not available outside this network of certified pharmacies.



Dispensing Conditions

All Qsymia retail prescription claims, regardless of the method of payment, will be processed through the pharmacy management system:

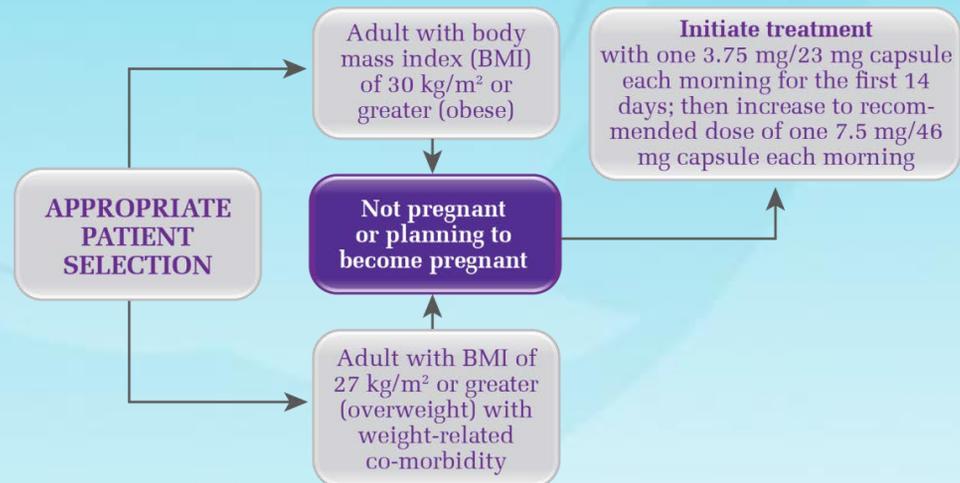
- i. For claims that are rejected, Qsymia cannot be dispensed.
- ii. For claims that are approved, Qsymia must be dispensed with a Medication Guide and the *Risk of Birth Defects with Qsymia* patient brochure each time Qsymia is dispensed.

Please note that Qsymia is not available outside this network of certified pharmacies.



Prescriber Dosing and Management Algorithm

- Prescriber needs to initiate treatment by providing **two** prescriptions
 - one for 3.75 mg/23 mg 1 po qAM #14 (no refills) and
 - a second for 7.5 mg/46 mg 1 po qAM #30 (with refills potentially)



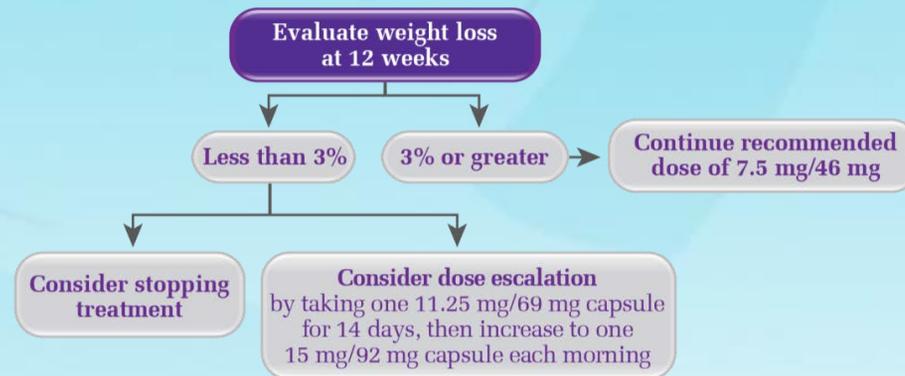
Only one Qsymia capsule to be taken daily, using sequence for dose escalations noted above.

Please see Qsymia Prescribing Information.



Prescriber Dosing and Management Algorithm (con't)

- Prescriber needs to escalate dose by providing **two** prescriptions
 - one for 11.25 mg/69 mg 1 po qAM #14 (no refills) and
 - a second for 15 mg/92 mg 1 po qAM #30 (with refills potentially)



Only one Qsymia capsule to be taken daily, using sequence for dose escalations noted above.

Please see Qsymia Prescribing Information.



Patient Counseling

1. The Medication Guide and patient brochure contain important information that patients should read and become familiar with.
2. Qsymia should be taken in the morning, with or without food.
3. Avoid taking Qsymia in the evening due to the possibility of insomnia.
4. Advise patients to start treatment with Qsymia as follows:
 - Take one Qsymia 3.75 mg/23 mg capsule once each morning for the first 14 days
 - After the first 14 days is complete, take one Qsymia 7.5 mg/46 mg capsule once each morning
 - Do not take Qsymia 3.75 mg/23 mg and Qsymia 7.5/46 mg capsules together
5. If an increase in Qsymia dose is prescribed after medical evaluation, advise patients to increase the dose of Qsymia as follows:
 - Take one Qsymia 11.25 mg/69 mg capsule once each morning for 14 days
 - After the 14 days is complete, take one Qsymia 15 mg/92 mg capsule once each morning
 - Do not take Qsymia 11.25/69 mg and Qsymia 15 mg/92 mg capsules together
6. Advise patients NOT to stop Qsymia without talking with their HCP as serious side effects such as seizures may occur.



Important Safety Information

Qsymia® is contraindicated in pregnancy; in patients with glaucoma; in hyperthyroidism; in patients receiving treatment or within 14 days following treatment with monoamine oxidase inhibitors (MAOIs); or in patients with hypersensitivity or idiosyncrasy to sympathomimetic amines, topiramate, or any of the inactive ingredients in Qsymia.

Qsymia can cause fetal harm. Females of reproductive potential should have a negative pregnancy test before treatment and monthly thereafter and use effective contraception consistently during Qsymia therapy. If a patient becomes pregnant while taking Qsymia, treatment should be discontinued immediately, and the patient should be informed of the potential hazard to the fetus.

Qsymia can cause an increase in resting heart rate. Regular measurement of resting heart rate is recommended for all patients taking Qsymia, especially patients with cardiac or cerebrovascular disease or when initiating or increasing the dose of Qsymia. Qsymia has not been studied in patients with recent or unstable cardiac or cerebrovascular disease and therefore use is not recommended.

Topiramate, a component of Qsymia, increases the risk of suicidal thoughts or behavior in patients taking these drugs for any indication. Patients should be monitored for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior. Discontinue Qsymia in patients who experience suicidal thoughts or behaviors. Qsymia is not recommended in patients with a history of suicidal attempts or active suicidal ideation.

Acute angle closure glaucoma has been reported in patients treated with topiramate, a component of Qsymia. Symptoms include acute onset of decreased visual acuity and/or eye pain. Symptoms typically occur within 1 month of initiating treatment with topiramate but may occur at any time during therapy. The primary treatment to reverse symptoms is immediate discontinuation of Qsymia.



Important Safety Information (con't)

Qsymia can cause mood disorders, including depression and anxiety, as well as insomnia. Qsymia can cause cognitive dysfunction (e.g., impairment of concentration/attention, difficulty with memory, and speech or language problems, particularly word-finding difficulties). Since Qsymia has the potential to impair cognitive function, patients should be cautioned about operating hazardous machinery, including automobiles.

Hyperchloremic, non-anion gap, metabolic acidosis has been reported in patients treated with Qsymia. If metabolic acidosis develops and persists, consideration should be given to reducing the dose or discontinuing Qsymia.

Qsymia can cause an increase in serum creatinine. If persistent elevations in creatinine occur while taking Qsymia, reduce the dose or discontinue Qsymia.

Weight loss may increase the risk of hypoglycemia in patients with type 2 diabetes mellitus treated with insulin and/or insulin secretagogues (e.g., sulfonylureas). Qsymia has not been studied in combination with insulin. A reduction in the dose of antidiabetic medications which are non-glucose-dependent should be considered to mitigate the risk of hypoglycemia.

The most commonly observed side effects in controlled clinical studies, 5% or greater and at least 1.5 times placebo, include paraesthesia, dizziness, dysgeusia, insomnia, constipation, and dry mouth.

To report negative side effects, contact VIVUS Inc., at 1-888-998-4887 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.



Additional Information and Tools

Additional information and tools can be found at www.QsymiaREMS.com.

- Healthcare Provider Counseling Tool for Females of Reproductive Potential
- Provider Dosing and Management Checklist
- *Risk of Birth Defects with Qsymia* patient brochure
- Dear Healthcare Provider Letter
- Qsymia Prescribing Information
- Qsymia Medication Guide

For more information on Qsymia or the Qsymia REMS Program, contact VIVUS Medical Information at 1-888-998-4887 or visit www.QsymiaREMS.com.

For more information on Pharmacy Certification, contact the Qsymia REMS Pharmacy Support Center at 1-855-302-6698.



Completing the Program

Step 2: Confirm Understanding Through Knowledge Assessment

Confirm that you've read through and understand the Qsymia Pharmacy Training Program by completing the knowledge assessment questions and the required pharmacy enrollment form.

Knowledge assessment questions: (choose True or False)

	True	False
1. The major risk for females of reproductive potential (FRP) is that of teratogenicity (birth defects), specifically the risk of cleft lip with or without cleft palate.	<input type="checkbox"/>	<input type="checkbox"/>
2. If a woman thinks she is pregnant, she should continue taking Qsymia until the pregnancy is confirmed.	<input type="checkbox"/>	<input type="checkbox"/>
3. The Qsymia REMS specifically prohibits certified pharmacies from reselling or redistributing Qsymia to another pharmacy or distributor.	<input type="checkbox"/>	<input type="checkbox"/>
4. The Medication Guide and patient brochure <i>Risk of Birth Defects with Qsymia</i> should be dispensed only with new prescriptions.	<input type="checkbox"/>	<input type="checkbox"/>
5. All Qsymia prescription claims, regardless of the method of payment, must be processed through the pharmacy management system.	<input type="checkbox"/>	<input type="checkbox"/>
6. For claims that are rejected, Qsymia can still be dispensed if the patient pays by cash.	<input type="checkbox"/>	<input type="checkbox"/>
7. Qsymia is not available outside the network of certified pharmacies.	<input type="checkbox"/>	<input type="checkbox"/>



Pharmacy Knowledge Assessment

1 of 7

True or False:

The major risk for females of reproductive potential (FRP) is that of teratogenicity (birth defects), specifically the risk of cleft lip with or without cleft palate.

Qsymia[®]
(phentermine and topiramate
extended-release) capsules

Pharmacy Knowledge Assessment (con't)

1 of 7

True or False:

The major risk for females of reproductive potential (FRP) is that of teratogenicity (birth defects), specifically the risk of cleft lip with or without cleft palate.

The correct answer is TRUE.

Topiramate, a component of Qsymia[®] (phentermine and topiramate extended-release) capsules CIV, has been associated with an increased risk of cleft lip with or without cleft palate in infants exposed to topiramate during the first trimester of pregnancy.

Qsymia[®]
(phentermine and topiramate
extended-release) capsules

Pharmacy Knowledge Assessment (con't)

2 of 7

True or False:

If a woman thinks she is pregnant, she should continue taking Qsymia until the pregnancy is confirmed.



Pharmacy Knowledge Assessment (con't)

2 of 7

True or False:

If a woman thinks she is pregnant, she should continue taking Qsymia until the pregnancy is confirmed.

The correct answer is FALSE.

If a woman believes she might be pregnant, she should stop taking Qsymia immediately and contact her healthcare provider.



Pharmacy Knowledge Assessment (con't)

3 of 7

True or False:

The Qsymia REMS specifically prohibits certified pharmacies from reselling or redistributing Qsymia to another pharmacy or distributor.

Qsymia[®]
(phentermine and topiramate
extended-release) capsules 

Pharmacy Knowledge Assessment (con't)

3 of 7

True or False:

The Qsymia REMS specifically prohibits certified pharmacies from reselling or redistributing Qsymia to another pharmacy or distributor.

The correct answer is TRUE.

To be eligible for initial certification, and to maintain ongoing certification, pharmacies must agree and abide by the requirement that they not resell or redistribute Qsymia to any other pharmacy, distributor, physician's office, or any other location. Qsymia is only available through the network of certified pharmacies.



Pharmacy Knowledge Assessment (con't)

4 of 7

True or False:

The Medication Guide and patient brochure *Risk of Birth Defects with Qsymia* should be dispensed only with new prescriptions.



Pharmacy Knowledge Assessment (con't)

4 of 7

True or False:

The Medication Guide and patient brochure *Risk of Birth Defects with Qsymia* should be dispensed only with new prescriptions.

The correct answer is FALSE.

A Medication Guide and patient brochure *Risk of Birth Defects with Qsymia* must be provided to the patient each time Qsymia is dispensed, whether the prescription being filled is a new prescription or a refill. This is a condition of certification, and systems must be in place to remind the pharmacist of this requirement each time they dispense a prescription for Qsymia.



Pharmacy Knowledge Assessment (con't)

5 of 7

True or False:

All Qsymia prescription claims, regardless of the method of payment, must be processed through the pharmacy management system.

Qsymia[®]
(phentermine and topiramate
extended-release) capsules

Pharmacy Knowledge Assessment (con't)

5 of 7

True or False:

All Qsymia prescription claims, regardless of the method of payment, must be processed through the pharmacy management system.

The correct answer is TRUE.

In order to become a certified pharmacy, pharmacies must agree that all Qsymia prescription claims must be processed through the pharmacy management system, regardless of payment method.



Pharmacy Knowledge Assessment (con't)

6 of 7

True or False:

For claims that are rejected, Qsymia can still be dispensed if the patient pays by cash.

Qsymia[®]
(phentermine and topiramate
extended-release) capsules

Pharmacy Knowledge Assessment (con't)

6 of 7

True or False:

For claims that are rejected, Qsymia can still be dispensed if the patient pays by cash.

The correct answer is FALSE.

For claims that are rejected, Qsymia cannot be dispensed, regardless of payment method.



Pharmacy Knowledge Assessment (con't)

7 of 7

True or False:

Qsymia is not available outside the network of certified pharmacies.



Pharmacy Knowledge Assessment (con't)

7 of 7

True or False:

Qsymia is not available outside the network of certified pharmacies.

The correct answer is TRUE.

Qsymia is only available through the network of certified pharmacies.



Qsymia® (phentermine and topiramate extended-release) capsules CIV Pharmacy Training Program

Overview

The Food and Drug Administration (FDA) has required a Risk Evaluation and Mitigation Strategy (REMS) for Qsymia to ensure the benefits of Qsymia outweigh the increased risk of teratogenicity.

Purpose

The purpose of the REMS is to inform prescribers, pharmacies, and females of reproductive potential (FRP) about the:

- Increased risk of congenital malformations, specifically orofacial clefts, in infants exposed to Qsymia during the first trimester of pregnancy
- Importance of pregnancy prevention for FRP
- Need to discontinue Qsymia immediately if pregnancy occurs

Complete the Qsymia Pharmacy Certification in 3 easy steps:

1. Read through the entirety of this Pharmacy Training Program and confirm you understand the program's content by completing the knowledge assessment questions.
 - For mail order pharmacies, your knowledge assessment may be completed by the Authorized Pharmacy Representative (AR) and faxed to the Qsymia REMS Pharmacy Support Center at 1-855-302-6699
 - For chain pharmacies, your knowledge assessment responses may be managed by your Authorized Pharmacy Representative. Please contact your corporate Authorized Pharmacy Representative for instructions on completing your knowledge assessment
 - For independent pharmacies, your knowledge assessment may be completed and faxed to the Qsymia REMS Pharmacy Support Center at 1-855-302-6699
2. Complete Pharmacy Enrollment Form and provide to the Qsymia REMS Pharmacy Support Center at 1-855-302-6699.
 - For chain pharmacies, a Pharmacy Enrollment Form must be completed by the Authorized Representative for the corporate chain organization
 - For chain pharmacy dispensing locations, a Pharmacy Enrollment Form must be completed by the Responsible Pharmacist, and can be obtained from the Authorized Representative for the corporate chain organization
 - For independent pharmacies, a Pharmacy Enrollment Form is required for the Authorized Pharmacy Representative for the dispensing pharmacy location
 - For mail order pharmacies, an Enrollment Form must be completed by the Authorized Representative for the mail order pharmacy organization
3. Complete the vendor verification/validation process. Upon successful completion of your program training, knowledge assessment and certification form, you will receive instructions on how to complete the vendor verification steps to verify your pharmacy management system is successfully connected to the Qsymia REMS network for all Qsymia claims and dispenses. (This does not apply to Mail Order pharmacies.)

www.QsymiaREMS.com

Qsymia[®]
(phentermine and topiramate extended-release) capsules CIV

Step 1: Complete Pharmacy Training Program Including Knowledge Assessment

These training materials are being provided to assist pharmacists with understanding the risks of Qsymia and the pharmacy requirements under the REMS. Before you are eligible to dispense Qsymia, it is important to be aware of the increased risk of teratogenicity associated with Qsymia therapy.

The information presented in this Training Program does not include a complete list of all risks and safety information on Qsymia. Before dispensing Qsymia, please read the accompanying Qsymia Prescribing Information, Qsymia Medication Guide, and the *Risk of Birth Defects with Qsymia* patient brochure.

Further information is also available on the Web site, www.QsymiaREMS.com or by calling Qsymia REMS Pharmacy Support Center at 1-855-302-6698.

Indication and Patient Selection

Qsymia is indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adult patients with an initial body mass index (BMI) of:

- 30 kg/m² or greater (obese), or
- 27 kg/m² or greater (overweight) in the presence of at least one weight-related comorbidity such as hypertension, type 2 diabetes mellitus, or dyslipidemia

Limitations of use:

- The effect of Qsymia on cardiovascular morbidity and mortality has not been established
- The safety and effectiveness of Qsymia in combination with other products intended for weight loss, including prescription and over-the-counter drugs, and herbal preparations, have not been established

www.QsymiaREMS.com



© 2013-2014 VIVUS Inc. All rights reserved. RE-03-018-01 08/2014



Increased Risk of Teratogenicity

Qsymia is classified as **Pregnancy Category X**

- Qsymia is contraindicated in pregnant women because the use of Qsymia can cause fetal harm. Available data indicate an increase in oral clefts (cleft lip with or without cleft palate) in infants exposed to topiramate, one of the components of Qsymia, during the first trimester of pregnancy

Studies evaluating the risk of major congenital malformations and/or oral clefts with exposure to topiramate, a component of Qsymia, during pregnancy include the following:

- The North American Anti-Epileptic Drug (NAAED) Pregnancy Registry (2010) analysis
- A retrospective evaluation of a Wolters Kluwer claims database (January 2003-December 2010 from the United States)
- A retrospective observational study using 4 U.S. electronic healthcare databases (FORTRESS)
- A case-control study using data from the Slone Epidemiology Center Birth Defects Study (BDS, 1997-2009) and the Centers for Disease Control's (CDC's) National Birth Defects Prevention Study (NBDPS, 1996-2007)

The NAAED Pregnancy Registry suggested an estimated increase in risk for oral clefts of 9.60 (95% CI 3.60 – 25.70).

An increase in oral clefts was observed with all dose strengths of topiramate.

SUMMARY OF STUDIES EVALUATING THE ASSOCIATION OF TOPIRAMATE IN UTERO EXPOSURE AND ORAL CLEFTS

EPIDEMIOLOGY STUDY	ORAL CLEFTS		MAJOR CONGENITAL MALFORMATIONS	
	PREVALENCE/ ODDS RATIO	95% CI	ESTIMATED INCREASE IN RISK	95% CI
WOLTERS KLUWER ^a	1.47	0.36-6.06	1.12	0.81-1.55
FORTRESS ^a	2.22	0.78-6.36	1.21	0.99-1.47
SLONE/CDC	5.36	1.49-20.07	1.01	0.37-3.22

^aSponsored by the maker of Qsymia® (phentermine and topiramate extended-release) capsules CIV.

CI=confidence interval.

These data show that exposure to topiramate, a component of Qsymia, in pregnancy is associated with a 2- to 5-fold increase in risk of oral clefts.

Other data sources confirm the increased risk of oral clefts with topiramate exposure during pregnancy (ie, animal studies and Adverse Event Reporting System data).

www.QsymiaREMS.com



Counseling Provided by HCPs for Females of Reproductive Potential*

Qsymia can cause fetal harm.

Advise females of reproductive potential that labeling recommends:

- Pregnancy testing prior to beginning Qsymia and monthly during therapy. Specific documentation of the result is not required at the pharmacy level
- Use of effective contraception consistently during Qsymia therapy because Qsymia can cause certain kinds of birth defects (oral clefts). Even females who believe they cannot become pregnant should use effective contraception while taking Qsymia due to the potential for increased fertility associated with weight loss
- If a patient becomes pregnant while taking Qsymia, Qsymia should be discontinued immediately and the patient advised to notify their healthcare provider

Acceptable Contraception Methods for Females of Reproductive Potential

Option 1 - Highly Effective Methods to Use Alone

One method from this list

<ul style="list-style-type: none">• Intrauterine device (IUD) or intrauterine system (IUS)- Copper IUD- Levonorgestrel-releasing IUS	<ul style="list-style-type: none">• Progestin implant• Tubal sterilization• Male partner's vasectomy
--	--

OR

Option 2 - Acceptable Methods to Use Together

<div style="border: 1px solid #4a4a8a; padding: 5px;">One method from this list Hormonal Contraception<ul style="list-style-type: none">• Estrogen and progestin<ul style="list-style-type: none">- Oral (the pill)- Transdermal patch- Vaginal ring• Progestin only<ul style="list-style-type: none">- Oral- Injection</div>	<div style="font-size: 2em; color: #4a4a8a;">+</div>	<div style="border: 1px solid #4a4a8a; padding: 5px;">One method from this list Barrier Method<ul style="list-style-type: none">• Diaphragm (with spermicide)• Cervical cap (with spermicide)• Male condom (with or without spermicide)</div>
---	--	---

OR

Option 3 - Acceptable Methods to Use Together

<div style="border: 1px solid #4a4a8a; padding: 5px;">One method from this list Barrier Method<ul style="list-style-type: none">• Diaphragm (with spermicide)• Cervical cap (with spermicide)</div>	<div style="font-size: 2em; color: #4a4a8a;">+</div>	<div style="border: 1px solid #4a4a8a; padding: 5px;">One method from this list Barrier Method<ul style="list-style-type: none">• Male condom (with or without spermicide)</div>
--	--	--

*Females of reproductive potential are women who have NOT had a hysterectomy, bilateral oophorectomy, or medically documented spontaneous ovarian failure, and have not gone through menopause. Menopause should be clinically confirmed by an individual's healthcare provider.

Advise nursing mothers not to use Qsymia. Qsymia may be present in human milk because topiramate and amphetamines (phentermine has pharmacologic activity and a chemical structure similar to amphetamines) are excreted in human milk.

www.QsymiaREMS.com



© 2013-2014 VIVUS Inc. All rights reserved. RE-03-018-01 08/2014



Qsymia is only dispensed through Certified Pharmacies

Under the REMS, Qsymia is only available through certified pharmacies. To become a certified pharmacy, an authorized or responsible pharmacy representative must agree to:

- 1) Refrain from reselling or transferring Qsymia to another pharmacy or distributor.
- 2) Train pharmacists and staff involved with the dispensing of Qsymia about the risks associated with Qsymia and the REMS requirement to provide a Medication Guide and *Risk of Birth Defects with Qsymia* patient brochure each time Qsymia is dispensed.
- 3) To be subject to and comply with surveys or audits (as applicable) to evaluate understanding of the risks associated with the use of Qsymia, and compliance with the requirements of the REMS.

The list of certified pharmacies will be updated within 1-2 business days after a new pharmacy is certified and eligible to dispense. Prescribers and patients will be able to use a “Certified Pharmacy Locator” tool to identify certified pharmacies in their area and can be found at www.QsymiaREMS.com.

Please note that Qsymia is not available outside this network of certified pharmacies.

www.QsymiaREMS.com

Qsymia[®]
(phentermine hydrochloride)
extended-release capsules

5

Dispensing Conditions

All Qsymia retail prescription claims, regardless of the method of payment, will be processed through the pharmacy management system

- i. For claims that are rejected, Qsymia cannot be dispensed.
- ii. For claims that are approved, Qsymia must be dispensed with a Medication Guide and the *Risk of Birth Defects with Qsymia* patient brochure each time Qsymia is dispensed.

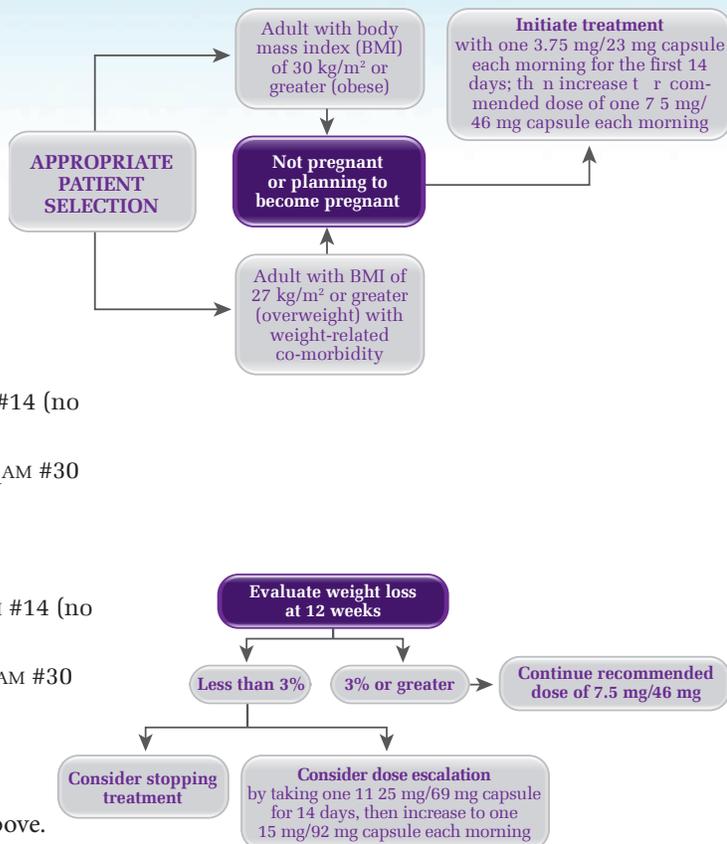
Please note that Qsymia is not available outside this network of certified pharmacies.

Prescriber Dosing and Management Algorithm

- Prescriber needs to initiate treatment by providing **two** prescriptions
 - one for 3.75 mg/23 mg 1 po qAM #14 (no refills) and
 - a second for 7.5 mg/46 mg 1 po qAM #30 (with refills potentially)
- Prescriber needs to escalate dose by providing **two** prescriptions
 - one for 11.25 mg/69 mg 1 po qAM #14 (no refills) and
 - a second for 15 mg/92 mg 1 po qAM #30 (with refills potentially)

Only one Qsymia capsule to be taken daily, using sequence for dose escalations noted above.

Please see Qsymia Prescribing Information.



www.QsymiaREMS.com



© 2013-2014 VIVUS Inc. All rights reserved. RE-03-018-01 08/2014



Patient Counseling

1. The Medication Guide and patient brochure contain important information that patients should read become familiar with.
2. Qsymia should be taken in the morning, with or without food.
3. Avoid taking Qsymia in the evening due to the possibility of insomnia.
4. Advise patients to start treatment with Qsymia as follows:
 - Take one Qsymia 3.75 mg/23 mg capsule once each morning for the first 14 days
 - After the first 14 days is complete, take one Qsymia 7.5 mg/46 mg capsule once each morning
 - Do not take Qsymia 3.75 mg/23 mg and Qsymia 7.5/46 mg capsules together
5. If an increase in Qsymia dose is prescribed after medical evaluation, advise patients to increase the dose of Qsymia as follows:
 - Take one Qsymia 11.25 mg/69 mg capsule once each morning for 14 days
 - After the 14 days is complete, take one Qsymia 15 mg/92 mg capsule once each morning
 - Do not take Qsymia 11.25/69 mg and Qsymia 15 mg/92 mg capsules together
6. Advise patients NOT to stop Qsymia without talking with their HCP as serious side effects such as seizures may occur.

Important Safety Information

Qsymia® is contraindicated in pregnancy; in patients with glaucoma; in hyperthyroidism; in patients receiving treatment or within 14 days following treatment with monoamine oxidase inhibitors (MAOIs); or in patients with hypersensitivity or idiosyncrasy to sympathomimetic amines, topiramate, or any of the inactive ingredients in Qsymia.

Qsymia can cause fetal harm. Females of reproductive potential should have a negative pregnancy test before treatment and monthly thereafter and use effective contraception consistently during Qsymia therapy. If a patient becomes pregnant while taking Qsymia, treatment should be discontinued immediately, and the patient should be informed of the potential hazard to the fetus.

Qsymia can cause an increase in resting heart rate. Regular measurement of resting heart rate is recommended for all patients taking Qsymia, especially patients with cardiac or cerebrovascular disease or when initiating or increasing the dose of Qsymia. Qsymia has not been studied in patients with recent or unstable cardiac or cerebrovascular disease and therefore use is not recommended.

Topiramate, a component of Qsymia, increases the risk of suicidal thoughts or behavior in patients taking these drugs for any indication. Patients should be monitored for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior. Discontinue Qsymia in patients who experience suicidal thoughts or behaviors. Qsymia is not recommended in patients with a history of suicidal attempts or active suicidal ideation.

Acute angle closure glaucoma has been reported in patients treated with topiramate, a component of Qsymia. Symptoms include acute onset of decreased visual acuity and/or eye pain. Symptoms typically occur within 1 month of initiating treatment with topiramate but may occur at any time during therapy. The primary treatment to reverse symptoms is immediate discontinuation of Qsymia.

Qsymia can cause mood disorders, including depression and anxiety, as well as insomnia. Qsymia can cause cognitive dysfunction (e.g., impairment of concentration/attention, difficulty with memory, and speech or language problems, particularly word-finding difficulties). Since Qsymia has the potential to impair cognitive function, patients should be cautioned about operating hazardous machinery, including automobiles.

Hyperchloremic, non-anion gap, metabolic acidosis has been reported in patients treated with Qsymia. If metabolic acidosis develops and persists, consideration should be given to reducing the dose or discontinuing Qsymia.

Qsymia can cause an increase in serum creatinine. If persistent elevations in creatinine occur while taking Qsymia, reduce the dose or discontinue Qsymia.

Weight loss may increase the risk of hypoglycemia in patients with type 2 diabetes mellitus treated with insulin and/or insulin secretagogues (e.g., sulfonylureas). Qsymia has not been studied in combination with insulin. A reduction in the dose of antidiabetic medications which are non-glucose-dependent should be considered to mitigate the risk of hypoglycemia.

The most commonly observed side effects in controlled clinical studies, 5% or greater and at least 1.5 times placebo, include paraesthesia, dizziness, dysgeusia, insomnia, constipation, and dry mouth.

To report negative side effects, contact VIVUS, Inc. at 1-888-998-4887 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

www.QsymiaREMS.com

Qsymia[®]
(phentermine
topiramate) capsules

7

Additional Information and Tools

Additional information and tools can be found at www.QsymiaREMS

- Healthcare Provider Counseling Tool for Females of Reproductive Potential
- Provider Dosing and Management Checklist
- *Risk of Birth Defects with Qsymia* patient brochure
- Dear Healthcare Provider Letter
- Qsymia Prescribing Information
- Qsymia Medication Guide

For more information on Qsymia or the Qsymia REMS Program, contact VIVUS Medical Information at 1-888-998-4887 or visit www.QsymiaREMS.com.

For more information on Pharmacy Certification, contact the Qsymia REMS Pharmacy Support Center at 1-855-302-6698.

www.QsymiaREMS.com



© 2013-2014 VIVUS Inc. All rights reserved. RE-03-018-01 08/2014



Step 2: Confirm Understanding Through Knowledge Assessment

Completing the Program

Confirm that you've read through and understand the Qsymia Pharmacy Training Program by completing the knowledge assessment questions and all required pharmacy enrollment form.

Knowledge assessment questions (choose True or False):

	True	False
1 The major risk for females of reproductive potential (FRP) is that of teratogenicity (birth defects), specifically the risk of cleft lip with or without cleft palate.	<input type="checkbox"/>	<input type="checkbox"/>
2 If a woman thinks she is pregnant, she should continue taking Qsymia until the pregnancy is confirmed.	<input type="checkbox"/>	<input type="checkbox"/>
3 The Qsymia REMS specifically prohibits certified pharmacies from reselling or redistributing Qsymia to another pharmacy or distributor.	<input type="checkbox"/>	<input type="checkbox"/>
4 The Medication Guide and patient brochure <i>Risk of Birth Defects with Qsymia</i> should be dispensed only with new prescriptions.	<input type="checkbox"/>	<input type="checkbox"/>
5 All Qsymia prescription claims, regardless of the method of payment, must be processed through the pharmacy management system.	<input type="checkbox"/>	<input type="checkbox"/>
6 For claims that are rejected, Qsymia can still be dispensed if the patient pays by cash.	<input type="checkbox"/>	<input type="checkbox"/>
7 Qsymia is not available outside the network of certified pharmacies.	<input type="checkbox"/>	<input type="checkbox"/>

www.QsymiaREMS.com

Qsymia[®]
(phentermine hydrochloride)
extended-release capsules

Pharmacy Knowledge Assessment

1 of 7

True or False: The major risk for females of reproductive potential (FRP) is that of teratogenicity (birth defects), specifically the risk of cleft lip with or without cleft palate.

The correct answer is TRUE.

Topiramate, a component of Qsymia® (phentermine and topiramate extended-release) capsules CIV, has been associated with an increased risk of cleft lip with or without cleft palate in infants exposed to topiramate during the first trimester of pregnancy.

2 of 7

True or False: If a woman thinks she is pregnant, she should continue taking Qsymia until the pregnancy is confirmed.

The correct answer is FALSE.

If a woman believes she might be pregnant, she should stop taking Qsymia immediately and contact her healthcare provider.

3 of 7

True or False: The Qsymia REMS specifically prohibits certified pharmacies from reselling or redistributing Qsymia to another pharmacy or distributor.

The correct answer is TRUE.

To be eligible for initial certification, and to maintain ongoing certification, pharmacies must agree and abide by the requirement that they not resell or redistribute Qsymia to any other pharmacy, distributor, physician's office, or any other location. Qsymia is only available through the network of certified pharmacies.

4 of 7

True or False: The Medication Guide and patient brochure *Risk of Birth Defects with Qsymia* should be dispensed only with new prescriptions.

The correct answer is FALSE.

A Medication Guide and patient brochure *Risk of Birth Defects with Qsymia* must be provided to the patient each time Qsymia is dispensed, whether the prescription being filled is a new prescription or a refill. This is a condition of certification, and systems must be in place to remind the pharmacist of this requirement each time they dispense a prescription for Qsymia.

www.QsymiaREMS.com



© 2013-2014 VIVUS Inc. All rights reserved. RE-03-018-01 08/2014



10

Pharmacy Knowledge Assessment (Continued)

5 of 7

True or False: All Qsymia prescription claims, regardless of the method of payment, must be processed through the pharmacy management system.

The correct answer is TRUE.

In order to become a certified pharmacy, pharmacies must agree that all Qsymia prescription claims must be processed through the pharmacy management system, regardless of payment method.

6 of 7

True or False: For claims that are rejected, Qsymia can still be dispensed if the patient pays by cash.

The correct answer is FALSE.

For claims that are rejected, Qsymia cannot be dispensed, regardless of payment method.

7 of 7

True or False: Qsymia is not available outside the network of certified pharmacies.

The correct answer is TRUE.

Qsymia is only available through the network of certified pharmacies.