

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
22580Orig1s000

REMS

Initial REMS approval 07/2012

NDA 22580

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

VIVUS, Inc.

Contact: VIVUS Medical Information

Phone: 1-888-998-4887

Fax: 1-855-298-9012

RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOAL

To inform prescribers and female patients 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 or printed training modules available from VIVUS medical liaisons during prescriber visits, at professional society meetings, and at medical educational venues.

- b. VIVUS will maintain a database of all prescribers (using a unique identifying number) who have completed the training. Completion of the training will be defined as:
- i. For electronic training completed independently by the HCP, viewing of all module training screens and completion of post-training knowledge assessment questions,
 - ii. For training modules delivered in person by VIVUS medical liaison, a statement from the medical liaison that all training materials were reviewed and the post-training knowledge assessment questions were completed
 - iii. For print training modules completed independently by the HCP, mailing or faxing a tear-off statement to VIVUS acknowledging full review of materials and completion of the post-training knowledge assessment questions
- c. On a monthly basis, VIVUS will compare the database of trained healthcare providers with the list of prescribers maintained by certified pharmacies 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. patient brochure entitled *Risk of Birth Defects with Qsymia*
 - 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 healthcare providers 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 healthcare providers who are likely to prescribe Qsymia (as described above), healthcare providers who have written a prescription for an obesity medical treatment in the prior 12 months, and any healthcare provider 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 to 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 appended.

iv. The Dear Medical Society letter and Dear Healthcare Provider letter will be provided to MedWatch at the same time they are provided to the professional organizations and healthcare professionals.

h. VIVUS will make the REMS, the training materials, the DHCP and Dear Medical Society letters, the patient brochure entitled *Risk of Birth Defects with Qsymia*, 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 department.

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

i. VIVUS will maintain a Program Coordinating Center with a Call Center 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 through the REMS Program website www.QsymiaREMS.com or by calling the Call Center at 1-888-998-4887.

2. Pharmacies that dispense Qsymia will be specially certified

a. VIVUS will contract with and certify pharmacies to dispense Qsymia. To become certified, the pharmacy must agree to the following:

- i. To provide a Medication Guide and patient brochure entitled *Risk of Birth Defects with Qsymia* each time Qsymia is dispensed
- ii. To refrain from reselling or transferring Qsymia to another pharmacy or distributor.
- iii. To train all pharmacists and staff involved with the dispensing of Qsymia to provide a Medication Guide and a patient brochure entitled *Risk of Birth Defects with Qsymia* each time Qsymia is dispensed
- iv. To maintain a list of Qsymia prescribers that will be made available to VIVUS upon request.

b. VIVUS will maintain a link to the list of certified pharmacies on www.QsymiaREMS.com.

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 ensure that Qsymia is distributed only to pharmacies certified in the Qsymia REMS program.
3. VIVUS will monitor distribution data and prescription data to ensure that only certified pharmacies are dispensing Qsymia.
4. VIVUS will monitor and audit the dispensing systems to check that all processes and procedures are in place and functioning to support the requirements of the

Qsymia REMS; that is, to ensure that the Medication Guide and patient brochure entitled *Risk of Birth Defects with Qsymia* are being dispensed with each prescription, that Qsymia is not being resold or transferred to another pharmacy or distributor, that all pharmacists and other staff involved with dispensing are trained, and that a list of prescribers is maintained and made available to VIVUS upon request.

5. VIVUS will receive regular reports and conduct audits of certified pharmacies to ensure that Qsymia is being dispensed according to the specified REMS requirements. All pharmacies will be audited in year one and every two years thereafter. If a certified pharmacy is found to be non-compliant, VIVUS will institute corrective action.
6. 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 this 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-03-001-00

Risk of Birth Defects with Qsymia Patient Brochure

Risk of Birth Defects with Qsymia[™]
(phentermine and topiramate extended-release) capsules CIV

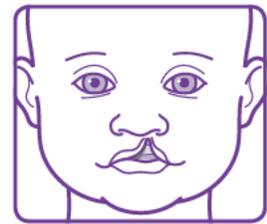
Please read the following important safety information about the use of Qsymia in females who can become pregnant.

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

OPTION 1 - Highly Effective Methods to Use Alone

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

OPTION 2 - Acceptable Methods to Use Together

Choose first method

Hormonal Contraception

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

and

Choose second method

Barrier Method

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

OPTION 3 - Acceptable Methods to Use Together

Choose first method

Barrier Method

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

and

Choose second method

Barrier Method

- Male condom (with or without spermicide)

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

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 to Qsymia.

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, 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 receiving treatment with Qsymia
 - The table on the back provides effective methods of contraception to review and discuss with your patient
 - Consider referral to a gynecologist if appropriate
- **Pregnancy testing is recommended before initiating treatment with Qsymia and monthly during treatment**
 - Advise patients to undergo pregnancy testing before starting treatment with 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, they will not be prescribed Qsymia, and if they are already receiving Qsymia, 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**

OPTION 1 - Highly Effective Methods to Use Alone

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

OPTION 2 - Acceptable Methods to Use In Combination

Choose first method	Choose second method
Hormonal Contraception <ul style="list-style-type: none"> • Estrogen and progestin <ul style="list-style-type: none"> - Oral contraceptives - Transdermal patch - Vaginal ring • Progestin only <ul style="list-style-type: none"> - Oral - Injection 	Barrier Method <ul style="list-style-type: none"> • Diaphragm (with spermicide) • Cervical cap (with spermicide) • Male condom (with or without spermicide)

and

OPTION 3 - Acceptable Methods to Use In Combination

Choose first method	Choose second method
Barrier Method <ul style="list-style-type: none"> • Diaphragm (with spermicide) • Cervical cap (with spermicide) 	Barrier Method <ul style="list-style-type: none"> • Male condom (with or without spermicide)

and

Prescriber Dosing and Management Checklist

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

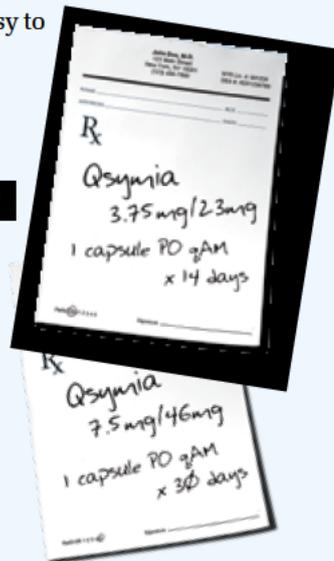
Identify Appropriate Patients

- 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
- No glaucoma
- No hyperthyroidism
- Not using monoamine oxidase inhibitors (MAOIs) or have not used within 14 days
- No known hypersensitivity or idiosyncrasy to the sympathomimetic amines

Start

Write 2 prescriptions:

- 14 days on Qsymia 3.75 mg/23 mg[†] 
- 30 days on recommended dose of Qsymia 7.5 mg/46 mg[†] 
- 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



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

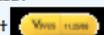
Monitor Patients

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
- Emergence/worsening depression, suicidal thoughts or behaviors
- Important side effects (eg, 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:
 - 14 days on Qsymia 11.25 mg/69 mg[†] 
 - 30 days on Qsymia 15 mg/92 mg[†] 
- Qsymia 3.75 mg/23 mg and Qsymia 11.25 mg/69 mg are for titration purposes only

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[™] (phentermine and topiramate extended-release) capsules CIV 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 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.

Online Qsymia REMS Training

Welcome to the

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

Important Safety Information

Full Prescribing Information

Medication Guide

Click below to begin the presentation

Begin ▶

//This screen will only show when the interaction is viewed through a mobile device//



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Welcome to the

Important Safety Information

Full Prescribing Information

Medication Guide

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.



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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 Full Prescribing Information and Qsymia Medication Guide available within this presentation.

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

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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



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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 Full Prescribing Information
- Qsymia Medication Guide
- Certificate of Completion

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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.

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Complete the registration form below

First Name NPI #

Last Name DEA #

Are you a: MD DC Other Healthcare Provider:

Date of Birth

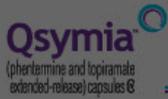
E-Mail

Enter a valid NPI #

Close

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.



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Complete the registration form below

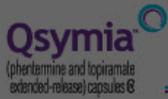
First Name	<input type="text"/>	NPI #	<input type="text"/>
Last Name	<input type="text"/>	DEA #	<input type="text"/>
Are you a:	MD <input type="radio"/>	DO <input type="radio"/>	Healthcare Provider: <input type="checkbox"/>
Date of Birth	<input type="text"/>		
E-Mail	<input type="text"/>		

Enter a valid DEA #

Close

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.



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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"/>		



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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

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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.

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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)

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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	
	PREVALENCE/ ODDS RATIO	95% CI
WOLTERS KLUWER ^a	1.47	0.36-6.06
FORTRESS ^a	2.00	0.71-5.68
SLONE/CDC	5.36	1.49-20.07

^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).


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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

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.

*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.



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Counseling for Females of Reproductive Potential (con't)

Highly effective methods to use alone

Acceptable Contraception Methods for Females of Reproductive Potential

OPTION 1

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

Counseling for Females of Reproductive Potential (con't)

Acceptable methods to use in combination

Acceptable Contraception Methods for Females of Reproductive Potential

OPTION 2

OPTION 3

Choose first method	Choose second method	Choose first method	Choose second method
Hormonal Contraception <ul style="list-style-type: none"> • Estrogen and progestin <ul style="list-style-type: none"> – Oral contraceptives – Transdermal patch – Vaginal ring • Progestin only <ul style="list-style-type: none"> – Oral – Injection 	and	Barrier Method <ul style="list-style-type: none"> • Diaphragm (with spermicide) • Cervical cap (with spermicide) • Male condom (with or without spermicide) 	and
		Barrier Method <ul style="list-style-type: none"> • Diaphragm (with spermicide) • Cervical cap (with spermicide) 	Barrier Method <ul style="list-style-type: none"> • Male condom (with or without spermicide)


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Dispensed to Patients Through Certified Mail Order Pharmacies

Qsymia is available only through certified mail order 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 mail order pharmacies. (A full listing of certified mail order pharmacies can be accessed at the end of this presentation.)

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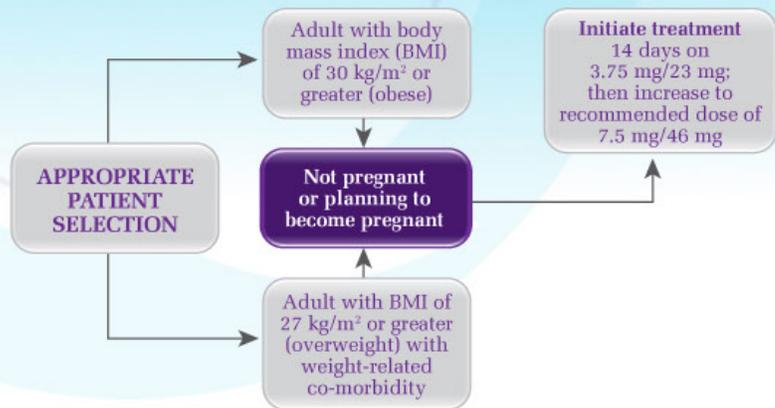
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Dosage and Administration

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
- The suggested follow-up after administration of initial treatment is 2 to 8 weeks


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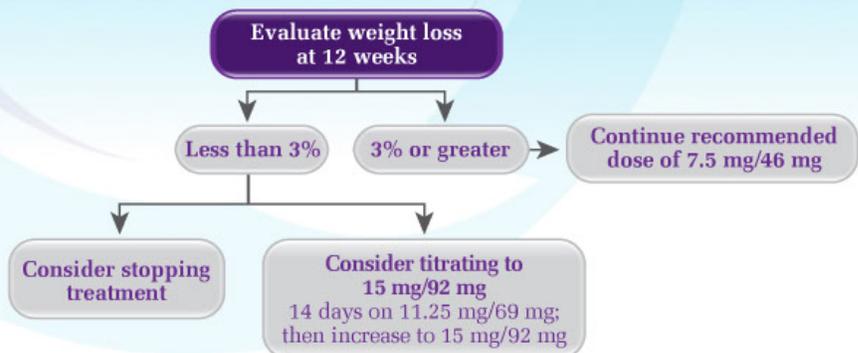
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Dosage and Administration (con't)

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 Qsymia 11.25 mg/69 mg (phentermine 11.25 mg/topiramate 69 mg extended-release) daily for 14 days, followed by dosing Qsymia 15 mg/92 mg (phentermine 15 mg/topiramate 92 mg extended-release) daily.



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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.

Evaluate weight loss after
12 weeks on 15 mg/92 mg



Less than 5% of baseline



Discontinue treatment
To discontinue 15 mg/92 mg, take dose
every other day for at least 1 week
to avoid precipitating a seizure



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Please complete your certification by taking the following brief quiz.



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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



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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.

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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 should be considered.

**True****False**

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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 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.

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



True



False

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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.

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



True



False



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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.

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



True



False



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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.



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Important Safety Information

Full Prescribing Information

Medication Guide

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True
taking

should continue

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

Close

The correct answer is I

If a woman believes she
contact her healthcare provider.

immediately and

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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 Full Prescribing Information](#)
- [Qsymia Medication Guide](#)
- [Certificate of Completion](#)
- [Certified Mail Order Pharmacy Listing on \[www.QsymiaREMS.com\]\(http://www.QsymiaREMS.com\)](#)

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Close

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

Name **Dr. Howard Green**

Date **July 25, 2012**

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



Print



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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

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//PDF of ISI will launch upon "click" of the Important Safety Information tab and is accessible on all screens//

Important Safety Information

Qsymia™ (phentermine and topiramate extended-release) capsules CIV 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 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.

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Print Qsymia REMS Training

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 to 1-973-746-7960.

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 Full 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

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	
	PREVALENCE/ ODDS RATIO	95% CI
WOLTERS KLUWER ^a	1.47	0.36-6.06
FORTRESS ^a	2.00	0.71-5.68
SLONE/CDC	5.36	1.49-20.07

^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 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

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 Contraception Methods for Females of Reproductive Potential

OPTION 1 - Highly Effective Methods to Use Alone

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

OPTION 2 - Acceptable Methods to Use In Combination

Choose first method

Hormonal Contraception

- Estrogen and progestin
 - Oral contraceptives
 - Transdermal patch
 - Vaginal ring
- Progestin only
 - Oral
 - Injection

Choose second method

Barrier Method

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

and

OPTION 3 - Acceptable Methods to Use In Combination

Choose first method

Barrier Method

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

Choose second method

Barrier Method

- Male condom (with or without spermicide)

and

*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.

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

Dispensed to Patients Through Certified Mail Order Pharmacies

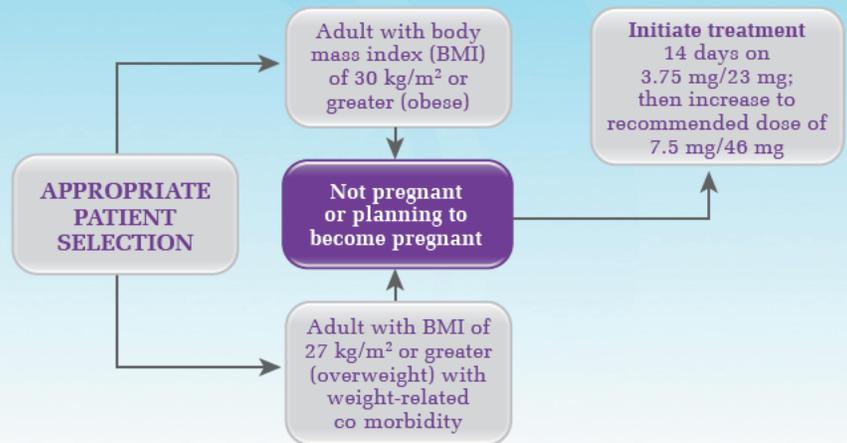
Qsymia is available only through certified mail order pharmacies that provide a Qsymia Medication Guide and *Risk of Birth Defects with Qsymia* patient brochure with every prescription and refill as required by the REMS.

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

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

Dosage and Administration

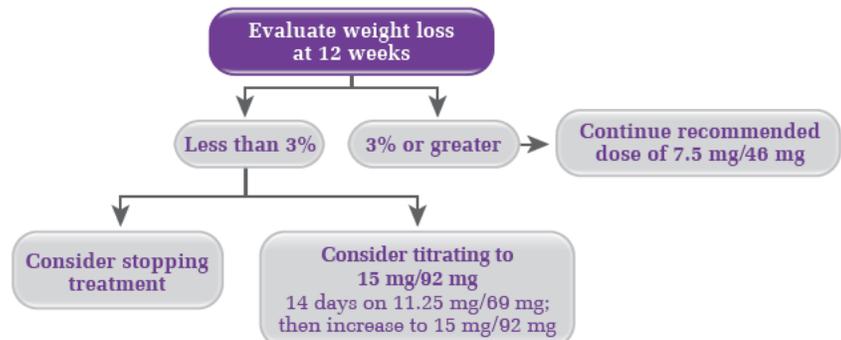
- Qsymia should be taken in the morning, with or without food
- Avoid dosing with Qsymia in the evening due to the possibility of insomnia
- For patients with moderate hepatic impairment or moderate/severe renal impairment, the Qsymia dose should not exceed the recommended dose of Qsymia, 7.5 mg/46 mg
- The suggested follow-up after administration of initial treatment is 2 to 8 weeks



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.

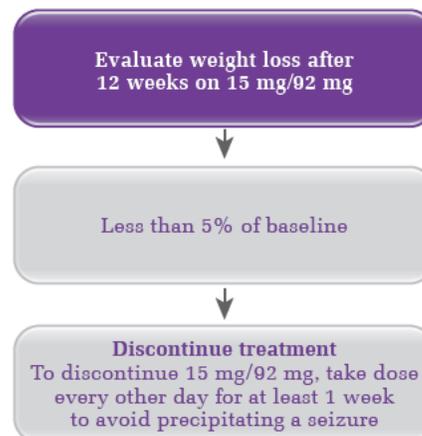
To escalate the dose: Increase to Qsymia 11.25 mg/69 mg (phentermine 11.25 mg/topiramate 69 mg extended-release) daily for 14 days, followed by dosing Qsymia 15 mg/92 mg (phentermine 15 mg/topiramate 92 mg extended-release) daily.



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

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 1-973-746-7960.

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 Full Prescribing Information**
- **Qsymia Medication Guide**

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

Important Safety Information

Qsymia™ (phentermine and topiramate extended-release) capsules CIV 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 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

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 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

Dear Healthcare Provider Letter

**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 mail order pharmacies

Qsymia is available only through certified mail order 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. The list of certified mail order 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 Full Prescribing Information and Qsymia Medication Guide. For more information, visit www.QsymiaREMS.com or call VIVUS Medical Information at 1-888-998-4887.

Sincerely,

Barbara Troupin, MD, MBA
Vice President, Scientific Communication and Risk Management
VIVUS, Inc.



Dear Medical Society Letter

**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:

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- 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

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Patient counseling regarding the risk of teratogenicity associated with Qsymia therapy

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Please see the accompanying Qsymia Full Prescribing Information and Qsymia Medication Guide. For more information, visit www.QsymiaREMS.com or call VIVUS Medical Information at 1-888-998-4887.

Sincerely,

Barbara Troupin, MD, MBA
Vice President, Scientific Communication and Risk Management
VIVUS, Inc.

Qsymia REMS Website screen shot



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 Patients 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 Mail Order Pharmacies

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

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

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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.

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

ERIC C COLMAN
07/17/2012