Print Qsymia REMS Pharmacy Training Module

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

1

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/m^2 or greater (obese), or
- 27 kg/m^2 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

VIVUS

© 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

[a]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).

www.QsymiaREMS.com

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

3

Reference ID: 3634966

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

- 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 + **One method from this list**

Hormonal Contraception

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

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 + **One method from this list**

Barrier Method

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

Barrier Method

- Male condom (with or without spermicide)

*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

VIVUS

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

Qsymia (phentermine and topiramate extended-release) capsules ®

4

Reference ID: 3634966

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 and topiramate extended-release) capsules ®

Reference ID: 3634966

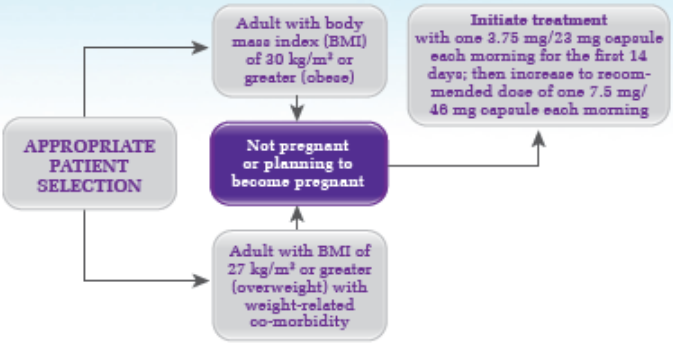
Dispensing Conditions

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.

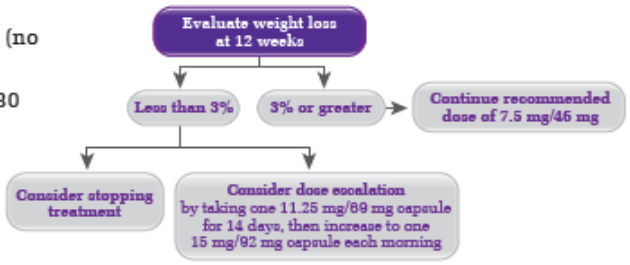
ii. For claims that are approved, Qsymia must be dispensed with a Medication Guide and the *Risk of Birth Defects with Qsymia* patient brochure each time Qsymia is dispensed.

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

VIVUS

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

Qsymia (phentermine and topiramate extended-release) capsules ®

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 and topiramate extended-release) capsules ®

7

Reference ID: 3634966

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

VIVUS

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

Qsymia
(phentermine and topiramate extended-release) capsules ®

8

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.	☐	☐
2	If a woman thinks she is pregnant, she should continue taking Qsymia until the pregnancy is confirmed.	☐	☐
3	The Qsymia REMS specifically prohibits certified pharmacies from reselling or redistributing Qsymia to another pharmacy or distributor.	☐	☐
4	The Medication Guide and patient brochure *Risk of Birth Defects with Qsymia* should be dispensed only with new prescriptions.	☐	☐
5	All Qsymia prescription claims, regardless of the method of payment, must be processed through the pharmacy management system.	☐	☐
6	For claims that are rejected, Qsymia can still be dispensed if the patient pays by cash.	☐	☐
7	Qsymia is not available outside the network of certified pharmacies.	☐	☐

www.QsymiaREMS.com

Qsymia (phentermine and topiramate extended-release) capsules ®

Reference ID: 3634966

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

VIVUS

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

Qsymia (phentermine and topiramate extended-release) capsules CIV

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.

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