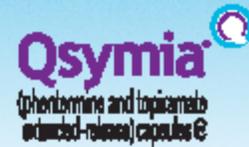


- Qsymia Dear Healthcare Provider letter



**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 pharmacies

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

Reporting adverse events

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

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

Sincerely,

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



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- Eliquis Dear Healthcare Provider Letter

[Insert Month DD, YEAR]

IMPORTANT DRUG WARNING

ELIQUIS[®] (apixaban) tablets

Subject: Discontinuing ELIQUIS without introducing an adequate alternative anticoagulant places nonvalvular atrial fibrillation patients at an increased risk of thrombotic events, including stroke

Dear Healthcare Professional:

The purpose of this letter is to inform you of important safety information for ELIQUIS (apixaban). ELIQUIS is an oral, reversible factor Xa inhibitor indicated to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation.

The FDA has determined that a Risk Evaluation and Mitigation Strategy (REMS) is necessary to ensure that the benefits of ELIQUIS outweigh the potential risks in patients with nonvalvular atrial fibrillation including:

- Increased risk of thrombotic events, including stroke, when discontinuing ELIQUIS without an adequate alternative anticoagulant

Please read the recommendations in the US Prescribing Information (USPI) on how to convert patients with nonvalvular atrial fibrillation from ELIQUIS to warfarin or other anticoagulants.

The ELIQUIS[®] labeling includes a **BOXED WARNING** to highlight the safety issue of increased risk of thrombotic events following discontinuation of ELIQUIS[®].

WARNING: DISCONTINUING ELIQUIS IN PATIENTS WITHOUT ADEQUATE CONTINUOUS ANTICOAGULATION INCREASES RISK OF STROKE

Discontinuing ELIQUIS places patients at an increased risk of thrombotic events. An increased rate of stroke was observed following discontinuation of ELIQUIS in clinical trials in patients with nonvalvular atrial fibrillation. If anticoagulation with ELIQUIS must be discontinued for a reason other than pathological bleeding, coverage with another anticoagulant should be strongly considered.

Increased Risk of Stroke with Discontinuation of ELIQUIS

ELIQUIS has an apparent half-life of 12 hours during repeat dosing, therefore, the anticoagulant effect of ELIQUIS is present when the drug is taken and for at least a day after discontinuation. Discontinuing ELIQUIS in the absence of adequate alternative anticoagulation increases the risk of thrombotic events. An increased rate of stroke was observed during the transition from ELIQUIS to warfarin in clinical trials in patients with nonvalvular atrial fibrillation. If ELIQUIS must be discontinued for a reason other than pathological bleeding, consider coverage with another anticoagulant.

Patient Counseling

Advise patients to take ELIQUIS only as directed and not to discontinue ELIQUIS without first speaking to you.

Medication Guide

The Medication Guide contains information to support patient counseling regarding the risks and benefits of treatment with ELIQUIS. Additional copies of the ELIQUIS Medication Guide may be obtained from:

- Bristol-Myers Squibb toll-free line at 1-855-354-7847
- the ELIQUIS REMS website at <http://www.ELIQUISREMS.com>

Reporting Adverse Events

To report all suspected adverse events associated with the use of ELIQUIS, please contact:

- Bristol-Myers Squibb at 1-800-721-5072 and/or
- FDA Medwatch Program at 1-800-FDA-1088 or www.fda.gov/medwatch.

For more information regarding ELIQUIS, please contact the Medical Information department at 1-800-321-1335 or visit the website at www.ELIQUIS.com.

This letter is not intended as a comprehensive description of risks associated with the use of ELIQUIS. Please read the accompanying USPI, including Medication Guide, for a complete description of these risks.

Sincerely,

[Click here to enter names of signatories]

Enclosure: ELIQUIS USPI with Medication Guide

[BMS Corporate logo] [Pfizer Inc logo]

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- Caprelsa Dear Professional Society Letter



IMPORTANT DRUG WARNING

SUBJECT: Serious Risks of QT prolongation, Torsades de pointes and Sudden death for Caprelsa® (vandetanib); FDA required restricted distribution program.

DATE

Dear (Medical Society):

AstraZeneca Pharmaceuticals LP would like to inform you and your membership of the approval of CAPRELSA (vandetanib), a new kinase inhibitor that has been approved by the Food and Drug Administration (FDA) for the treatment of symptomatic or progressive medullary thyroid cancer in patients with unresectable locally advanced or metastatic disease. Use of CAPRELSA in patients with indolent, asymptomatic or slowly progressing disease should be carefully considered because of the treatment related risks of CAPRELSA.

CAPRELSA can prolong the QT interval and cases of Torsades de pointes and sudden death were reported in clinical trials. Because of these risks, CAPRELSA is available only through a restricted distribution program called CAPRELSA REMS Program. **Under the CAPRELSA REMS Program, only prescribers and pharmacies enrolled in the program can prescribe and dispense CAPRELSA.**

In order to prescribe CAPRELSA, prescribers must:

- Read the Healthcare Provider (HCP) Letter, review HCP Education Pamphlet or HCP REMS Education Slide Set; and the CAPRELSA full Prescribing Information
- Complete the Prescriber Training Program (online or by phone)
- Complete the Prescriber Enrollment Form

To ENROLL, visit www.caprelsarems.com or call 1-800-236-9933.

To increase awareness of QT prolongation, Torsades de pointes and sudden death and the requirement for prescribers to enroll, please share this communication with the members of your society. We would ask that you also provide a link to the CAPRELSA REMS website at www.CAPRELSArem.com when disseminating this information to your members.

Please see the enclosed HCP Education Pamphlet that outlines the risk of QT prolongation, Torsades de pointes and sudden death associated with CAPRELSA.

This is not a complete list of all the Warnings and Precautions of CAPRELSA. Please see the enclosed full Prescribing Information for CAPRELSA.

Sincerely,

James W. Blasetto, M.D., MPH
Vice President, US Strategic Development
AstraZeneca LP
1800 Concord Pike, P.O. Box 8355
Wilmington, DE 19803-8355

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