

Risk Minimization Action Plan (RiskMAP)

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RiskMAP Overview

- Identified Risk
- Intervention
- Assessments

RiskMAP – Identified Risks

- Past history of depressive disorders and/or suicidality or patients with a diagnosis of depressive disorders or current anti-depressant therapy
- Treatment with anti-epileptic therapy
- Short-term (cosmetic) use

RiskMAP – Interventions

Healthcare Professionals

- Routine Measures
 - Continuing Medical Education
 - Product-focused Education
 - Awareness Campaign
- Enhanced Measures
 - Physician Check-List
 - Medication Guide
 - Patient Access Program
 - Physician/Patient Treatment Plan

Patient/Family

- Routine Measures
 - Product-focused Education
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RiskMAP – Assessments

Starts with Patient Access Program

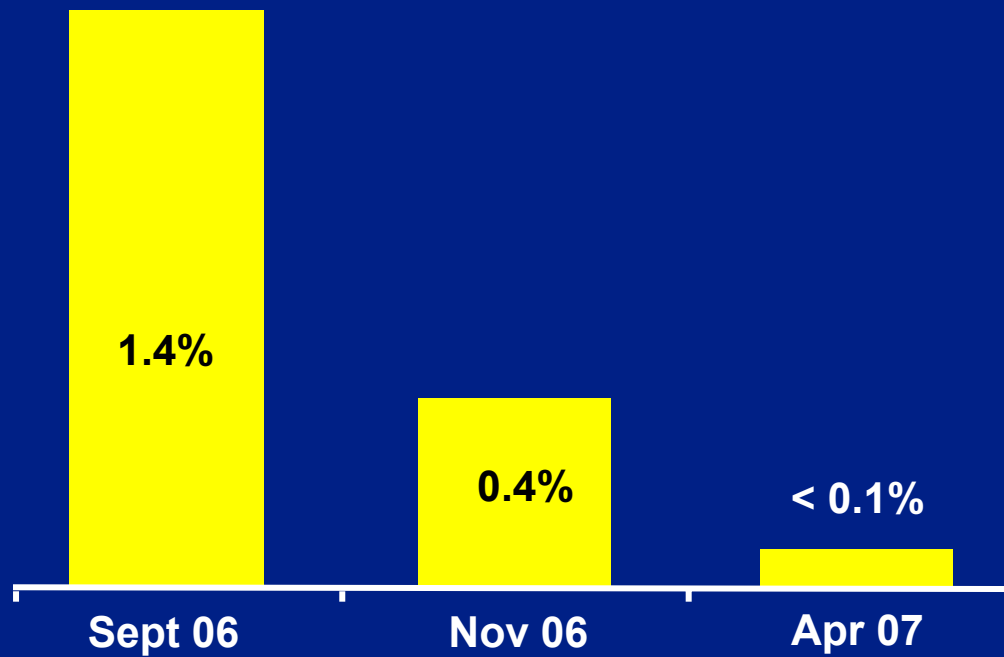
- Enhanced pharmacovigilance
 - detailed specific forms for depression and seizures
- Physician and patient survey

Start after Commercial Launch

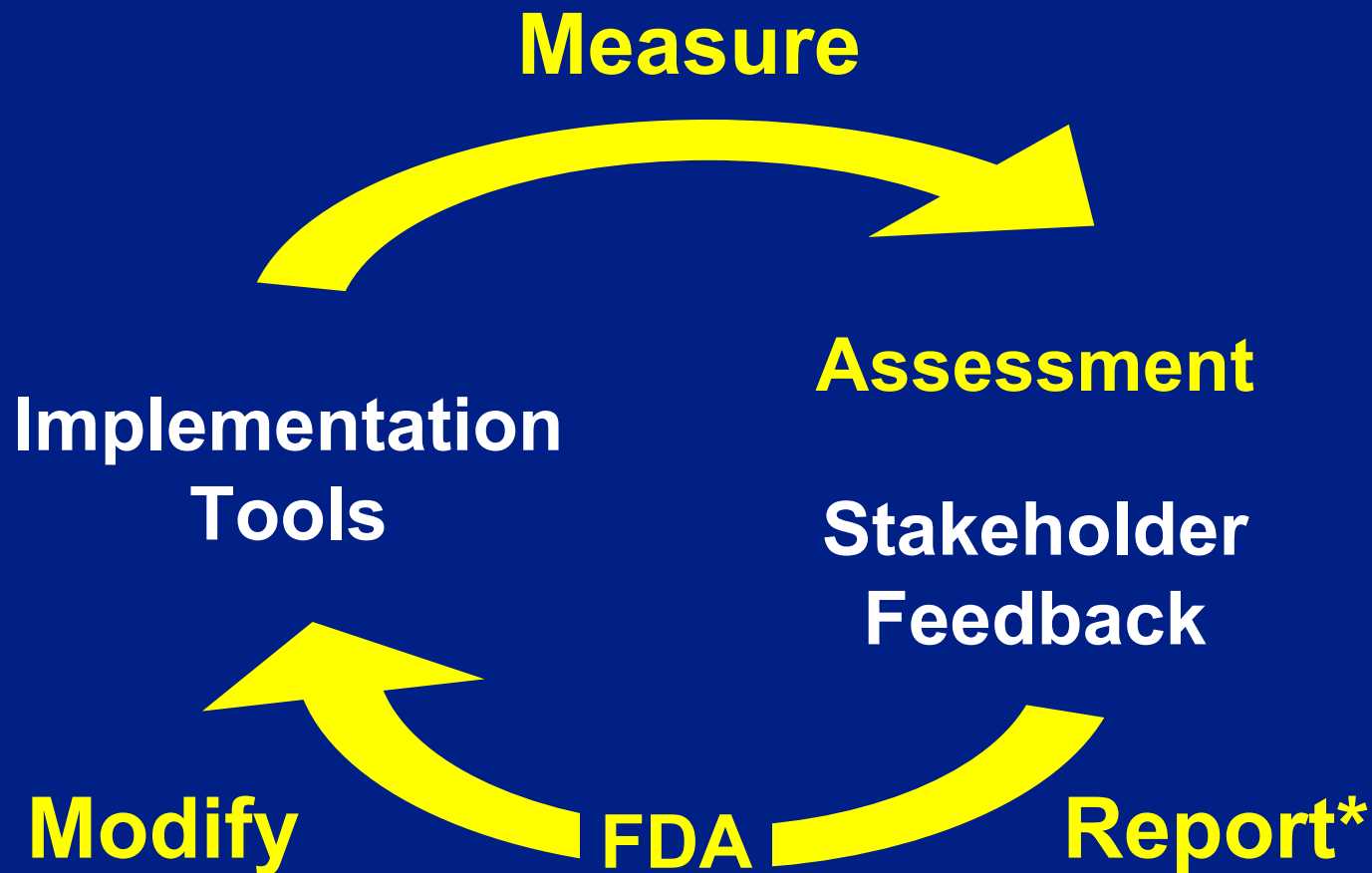
- Prescription survey
- Health insurance claims databases
- Automatic medical record databases
- Disease registry in collaboration with American College of Cardiology

UK Prescription Survey

- Percent of patients with severe depression



RiskMAP Iterative Operating Principles



* Periodic RiskMAP Progress Report

MM-139

Key Messages

General Disease Awareness

- Obesity is a chronic disease requiring long-term comprehensive treatment (including diet and exercise)
- Treating obesity is associated with both positive and negative mood changes
- Obesity is associated with several co-morbidities including depressive disorders
- Depressive disorders and their consequences should be recognized, diagnosed and treated appropriately

Key Messages

Treatment with Rimonabant

- At time of prescription, screen patients for:
 - past history of depressive disorders and/or suicidality
 - diagnosis of depressive disorders
 - current anti-depressant and/or anti-epileptic therapy
 - other elements of the prescribing information
- Discuss with patient treatment goals and expectations
- Reassess patients at 1, 3, 6, 9 and 12 months during the first year
- Depression has been observed with rimonabant treatment which could lead to suicidal thoughts
- When depressive disorders and/or suicidality are suspected, health care professionals should consider appropriate therapeutic action

Physician Check List

• Front

Patients most likely to benefit from Rimonabant are xxxxx xxxxx xxxxx xxxxx xxxxx xxxxx xxxxx xxxxx xxxxxxxxxxxx xxxxxxxxxxxx xxxxxxxxxxxx xxxxxxxxxxxx xxxxxxxxxxxx xxxxx xxxxx xxxxx xxxxx.

Before prescribing Rimonabant, please check the following items:

				If yes:
Is your patient age	below 18 ?	No <input type="checkbox"/>	Yes <input type="checkbox"/>	→Not recommended
	above 75 ?	No <input type="checkbox"/>	Yes <input type="checkbox"/>	→Use with caution
Is your patient a woman, if yes is she:	lactating	No <input type="checkbox"/>	Yes <input type="checkbox"/>	→ Contra-indicated
	pregnant	No <input type="checkbox"/>	Yes <input type="checkbox"/>	→Not recommended
Is your patient BMI	< or = 26.9 ?	No <input type="checkbox"/>	Yes <input type="checkbox"/>	→Not indicated
	Between 27and 29.9, with no other cardiovascular risk factor ?	No <input type="checkbox"/>	Yes <input type="checkbox"/>	→Not indicated
Is your patient suffering from uncontrolled psychiatric illness, e.g. major depression?		No <input type="checkbox"/>	Yes <input type="checkbox"/>	
Is your patient currently receiving an antidepressive treatment		No <input type="checkbox"/>	Yes <input type="checkbox"/>	
Is your patient treated for epilepsy?		No <input type="checkbox"/>	Yes <input type="checkbox"/>	→Use with caution
Is your patient currently receiving a treatment with a potent CYP3A4 inhibitor?		No <input type="checkbox"/>	Yes <input type="checkbox"/>	→Use with caution
Is your patient known as having hypersensitivity to one of the constituents of Rimonabant ?		No <input type="checkbox"/>	Yes <input type="checkbox"/>	→Contra-indicated
Is your patient suffering from severe renal failure ?		No <input type="checkbox"/>	Yes <input type="checkbox"/>	→Should not be used
Is your patient suffering from hepatic failure ?	yes, moderate	No <input type="checkbox"/>	Yes <input type="checkbox"/>	→Use with caution
	yes, severe	No <input type="checkbox"/>	Yes <input type="checkbox"/>	→Should not be used
Is your patient committed only to short term cosmetic use ?		No <input type="checkbox"/>	Yes <input type="checkbox"/>	→Not recommended

- Does your patient have a history of depressive disorders or suicidality
- Is your patient currently suffering from depressive disorders
- Is your patient currently treated with antidepressants or anti-epileptics

Medication Guide

Based on 21 CFR 208.20

Medication Guide
ZIMULTI® Tablets
(Rimonabant)

Read the Medication Guide that comes with ZIMULTI before you start taking it. Talk to your doctor if you have any questions about ZIMULTI. This Medication Guide does not take the place of talking with your doctor about your medical condition or treatment.

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

A statement describing the particular safety concerns associated with the drug product. The statement should describe specifically what the patient should know about the drug product, such as, weighing particular risks against the benefits of the drug, avoiding particular behaviors (e.g., activities, drugs), observing certain events (e.g., symptoms, signs) that could prevent or mitigate a serious adverse effect, or engaging in particular behaviors (e.g., adhering to the dosing regimen).

What is ZIMULTI?

A section that identifies a drug product's name, its uses, and its risks.

Who should not take ZIMULTI?

Information on circumstances under which the drug product should not be used. The Medication Guide shall contain directions regarding what to do if any of these circumstances occur, such as contacting the licensed practitioner, discontinuing use of the drug product, or seeking medical attention.

How should I take ZIMULTI?

Information on the proper use of the drug product.

What should I avoid while taking ZIMULTI?

A statement or statements of specific, important precautions patients should take to ensure proper use of the drug.

What are the possible or reasonably likely side effects of ZIMULTI?

A statement of the adverse reactions reasonably likely to be caused by the drug product that are serious or occur frequently.

A statement of the risk, if there is one, of patients' developing dependence on the drug product.

General Information about ZIMULTI:

General information about the safe and effective use of prescription drug products.

Rx Only

- **Most important information**

- In some patients Rimonabant use has been associated with an increase in depression, anxiety and suicidal thoughts
- Depression is one of the most important causes of suicidal thoughts and actions. Some people may have a higher risk of having depression and/or suicidal thoughts. These include a previous history of depression/suicidal thoughts

- **How can I watch for and try to prevent depression/suicidal thoughts and actions**

- Pay close attention to any changes in mood, behavior, thoughts, ...
- Call your doctor right away if you or your family member has any of these symptoms
 - List symptoms
- Keep all follow-up visits with your doctor as scheduled

Disease Awareness Campaign



- No Direct-To-Consumer (DTC) ads for rimonobant for at least one year

WHAT:

Excess mid section weight is a condition that many people struggle with throughout their lifetime. More and more evidence shows mid section weight is more than a cosmetic concern, it can contribute to type 2 diabetes and even an unhealthy cholesterol profile. Diet, exercise and life style changes are the most effective way of dealing with this condition

There are treatment options available but in some cases, these options may contribute to changes in mood and depression.

For more information please call: 1 800 xxx xxxx

Visit our website: www.xxx.com

How:

- In-office discussions
- Print
- Internet

Physician/Patient Treatment Plan

- Participants

- Physicians
- Allied Health Professionals
- Patients and their family
- Pharmacists

- Tool Kits

- Physician Tool Kit
- Patient/Family Tool Kit
- Allied Health Professional Tool Kit
- Internet
- Pharmacy

- Materials

- language appropriate for physician or patient
- suggested dialogue for each physician/patient return visit

- Feedback

- Track comprehension, acceptance and utilization of tools
- monthly physician survey
- monthly patient survey

Physician/Patient Treatment Plan

- **Physician tool kit**

- Disease awareness
- US package insert
- Physician check list
- Most frequently prescribed anti-depressants and anti-epileptics
- Depressive disorders and suicidality screening tools
- Reminder of other adverse events

- **Patient tool kit**

- Disease awareness
- Medication guide
- Most frequently prescribed anti-depressants and anti-epileptics
- Depression-self assessment tool
- Return visit schedule
- Treatment diary

Physician/Patient Treatment Plan



Physician/Patient Treatment Plan

Physician Dialogue:

Talk to your patients about

- **Benefit:** measure weight, waist circumference, adjust diet and exercise prescription and concomitant therapy (eg, antidiabetic medication)
- **Adverse events**

**Months
1, 3, 6, 9, 12**

Scripted dialogue

Patient Dialogue:

Talk to your doctor about

- **Benefit:** Chart your progress toward agreed upon therapy goals
- **Changes in your mood, dizziness, sleeping, feeling anxious**



Patient Access Program

- Evaluate the appropriateness of the RMP tools
- A 'controlled launch' to fine tune the elements of the RMP
- Physicians provided with education material educated on disease and benefit-risk profile
- Lessons learned to be introduced into full commercial launch

Patient Access Program

- Participants
 - Geographically diverse
 - Specialists/generalists
 - 20,000 Physicians and 20,000 Allied Health
 - 10 patients/physician
- Assessment
 - Monthly message recall
 - materials (eg, checklist, educational material, etc.)
 - benefit/risk profile
 - appropriate patient profile
 - Physician/patient follow-up tracking
 - Patient diary

Prescription Survey

- Methodology
- Design
 - Retrospective survey of physicians
- Sample
 - A total of 2,400 patients
 - 800 patients at each sample
 - 3 most recent patients prescribed Rimonabant, per physician
- Data Collection
 - 3 data collection points spaced 4 months apart
 - Data collection to start 1 month after launch of Rimonabant

RiskMAP Summary

- Identified Risk
- Intervention
- Assessments

Who is the Appropriate Patient?

- NOT Everyone
- Appropriate
 - patients with a BMI > 27 kg/m² with at least one cardiovascular risk factor or a BMI ≥ 30 kg/m²
 - chronic indication intended for long-term use
- Not Appropriate
 - past history of depressive disorders and/or suicidality or patients with a diagnosis of depressive disorders or current anti-depressant therapy
 - treatment with anti-epileptic therapy

Conclusion

- The sponsor is committed to working with FDA and other stakeholder groups in the US to implement a RiskMAP that addresses the serious and growing problem of obesity and the related co-morbidities while assuring a rigorously positive benefit-risk equation for rimonabant