

1 Problem

What When	Problem(s)	Increased risk of heart attacks, stroke death	
	Date	See timeline	
	Different, unusual, unique	Two thirds of diabetics die of heart problems; Drug originally licensed with warning about risks for patients with heart failure	
Where	Unit, area, equipment	Worldwide	
	Task being performed	Rosiglitazone (found in Avandia, Avandamet and Avaglim)	
		Second-line treatment for Type 2 Diabetes (after metformin)	
Impact to the Goals	Patient Safety	Increased occurrence of heart attack, stroke, death	
	Employee Impact	?	
	Compliance	Delay in publishing test data	
	Organization	Reduced sales (\$2.5 billion in 2006, ~\$408 million in 2009 in US)	>\$2 billion
	Patient Services	Lawsuits against manufacturer	>\$1 billion
	Environmental	N/A	
	Property, Equip, Mts	N/A	
	Labor, Time	?	
Frequency	Heart problems in 66,000 to 200,000 people (One person suffers heart problems for every 60 taking the drug)	This incident ~\$3 billion Annualized Cost ?	

ROSIGLITAZONE

Cause Map

Masked test results increase risk of heart disease

Making medical decisions is difficult - even with all the information. When information about health risks determined during clinical trials is kept from the public, the impact can cost patient lives.

"Patients trust drug companies with their health and their lives."
-Senator Max Baucus

Since rosiglitazone was approved for use in controlling blood sugar in Type 2 diabetics who did not have success with front line treatments in 1999, studies have shown that users of this drug (included in trade name drugs Avandia, Avandamet and Avaglim) increases the risk of heart disease in users. This is of particular concern because most Type 2 diabetics die from heart disease. It is estimated that 60,000 to 200,000 people have suffered from heart disease due to these drugs.

A black box warning was placed on these drugs, but not until November 2007. The European Medicines Agency recommended that the drug be suspended from European markets in 2010, and the drug was withdrawn from New Zealand markets in 2011. What took so long?

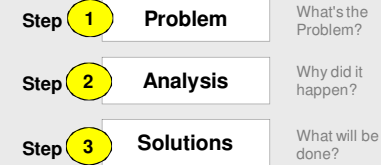
The patient safety goal is impacted because of the increased occurrence of stroke, heart attack, and death. The compliance goal is impacted because - according to the Senate Finance Committee - trial results that would have indicated the increased risk for cardiovascular disease were not publicly released in a timely manner. Reduced sales as a result of the risk are estimated to be more than \$2 billion (an impact to the organizational goal) and lawsuits (an impact to the patient services goal) are projected to cost more than \$1 billion.

Although the actual mechanism that is causing the increased risk of cardiovascular disease is unknown, the cause of the increased occurrence of heart attack, stroke and death is due to the prescribing of the drug rosiglitazone. Although rosiglitazone has been found to be an effective second-line treatment for Type 2 diabetes, it is unlikely that doctors would have prescribed it as readily had they known about the increased risk of heart disease. Instead, they were likely swayed by a multi-million dollar advertising campaign, while test results that showed increased cardiovascular risk were allegedly covered up.

Cause Mapping is a Root Cause Analysis method that captures basic cause-and-effect relationships supported with evidence.

CAUSE MAPPING

Problem Solving • Incident Investigation • Root Cause Analysis

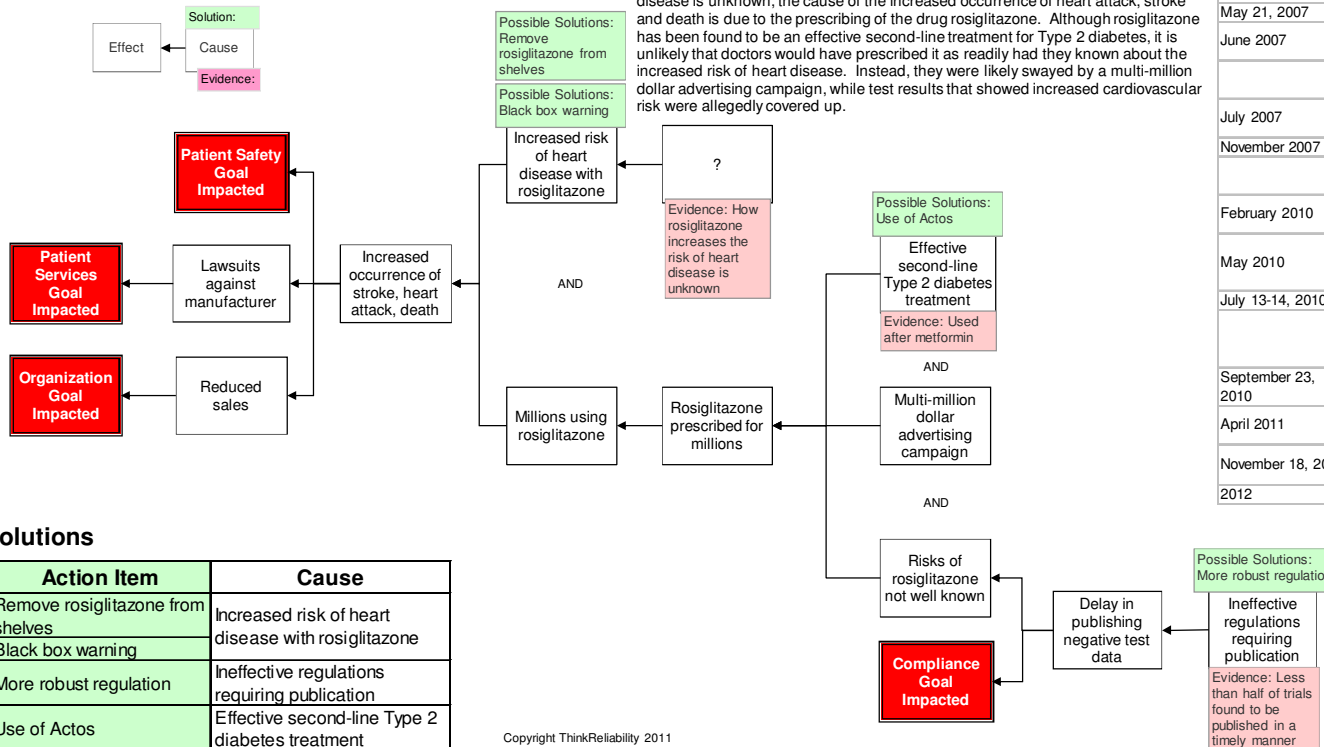


Timeline

Date	Time	Description
1999		FDA approves Avandia for controlling diabetes
November 2003		Manufacturer study reveals heart problems
January 2004		World Health Organization alert
2005		Manufacturer releases meta-analysis to the FDA
Fall 2006		Lancet study shows Avandia can prevent diabetes
May 2007		New England Journal of Medicine publishes analysis showing drug increases risk of heart attacks by 43%
May 21, 2007		FDA releases safety alert on Avandia
June 2007		NEJM publishes study by manufacturer showing drug does not cause heart problems
		House of Representatives meets to consider whether the FDA should continue to allow Avandia to be sold
July 2007		FDA advisory committee concludes increased risk of heart disease but that drug should remain on market
November 2007		Black box warning placed on drug at request of FDA
		British Medical Journal study released discussing adverse cardiovascular events
February 2010		Senate Finance Committee accuses manufacturer of holding back data showing problems
May 2010		Studies in Journal of the American Medical Association and Archives of Internal Medicine show that drug increases risk of cardiovascular problems
July 13-14, 2010		FDA convenes another advisory committee meeting vote
		Senate Finance Committee releases findings that manufacturer failed to publish studies that found serious health risks in a timely manner
September 23, 2010		European Medicines Agency recommended that the drug be suspended from the European market
April 2011		Drug withdrawn from New Zealand market after Medsafe concluded that the risks outweigh the benefits
November 18, 2011		Avandia may only be sold with a prescription from a certified doctor through mail order to specified pharmacies in U.S.
2012		Patent expires

2 Analysis

Cause Map - Add detail as information becomes available.



3 Solutions

No.	Action Item	Cause
1	Remove rosiglitazone from shelves	Increased risk of heart disease with rosiglitazone
2	Black box warning	Ineffective regulations requiring publication
3	More robust regulation	Effective second-line Type 2 diabetes treatment
4	Use of Actos	

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