

**Rezulin<sup>®</sup>**  
**(Troglitazone) Tablets**

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Presentation to the  
Endocrinologic and Metabolic Drugs  
Advisory Committee

Parke-Davis Pharmaceutical Research  
March 26, 1999

## **Introduction**

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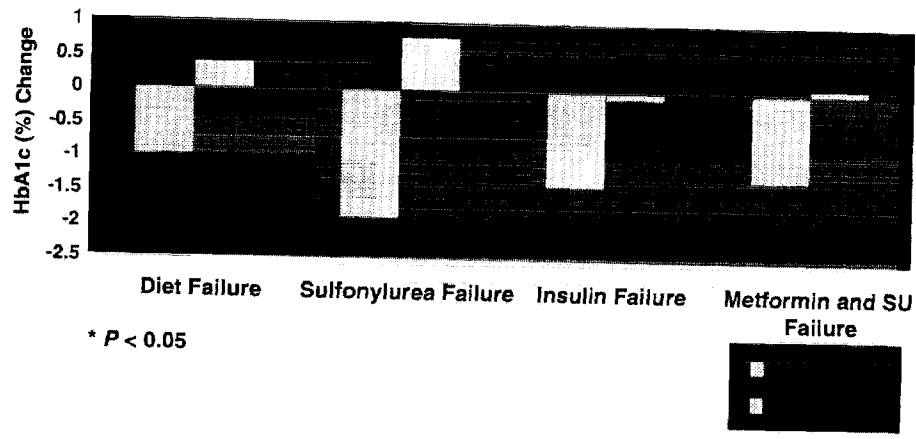
Robert Zerbe, MD  
Sr. Vice-President, Clinical Research  
and Development  
Parke-Davis

## **Rezulin® Timeline**

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- July 1996 Initial NDA Submission (Insulin Combination)
- January 1997 Initial Approval
- February 1997 SNDA Submission (Sulfonylurea Combination, Monotherapy)
- August 1997 SNDA Approval
- November 1998 SNDA Submission (Triple Therapy)

# Efficacy of Rezulin



## **Labeling Changes Related to Hepatic Failure**

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### **October/December 1997**

- Boxed Warning
- Routine Monitoring Added
- No therapy if ALT > 3X ULN

### **July 1998**

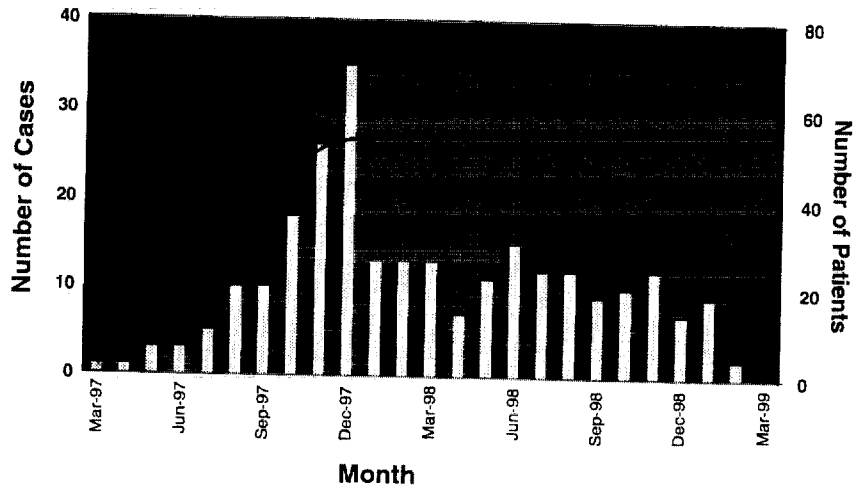
- Monitoring Extended
- Intensive Follow-up for Mild Elevations
- No therapy if ALT > 1.5 X ULN
- Discontinue monotherapy if no response in two months

## **Parke-Davis Initiatives**

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- Better understanding of mechanism and epidemiology
- Better definition of patients who can gain greatest benefit
- Professional education regarding the importance of monitoring

# Reports of Jaundice



## **Agenda**

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**Introduction**

**Robert Zerbe, MD**

**Hepatic Events**

**Paul Watkins, MD  
Univ. of Michigan  
Professor of Medicine and  
Professor of Pharmacology**

**Incidence of Serious  
Liver Events**

**Mark Pierce, MD, PhD  
V.P., Clinical Research**

**Gerald Faich, MD, MPH  
President, Pharmaceutical  
Safety Assessment, Inc.**

**Comparative Safety of  
Alternative Therapies**

**Philip Home, DM, DPhil  
Univ. of Newcastle, UK  
Professor of Diabetes  
Medicine**

**Lunch**



## **Agenda (Cont'd.)**

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**Benefits of Rezulin Therapy**

**Randall Whitcomb, MD  
V.P., Clinical Research**

**Risk-Benefit Summary**

**Robert Zerbe, MD**

## **Key Points**

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- The risk of liver related death and transplant with Rezulin is low and declining
- The risk compares favorably to the risk of serious events associated with other available treatments
- Physicians have a high awareness of the risk and the need for monitoring
- Rezulin, through it's unique mechanism, provides marked benefit in combination and as monotherapy to hundreds of thousands of patients