

Summary of Risk - Benefit Assessment

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Questions for Consideration

1. Does Rezulin play a causative role in cases of severe hepatotoxicity?
2. What is the risk of such events?
3. How does this risk compare to that of other therapies?
4. What are the benefits of Rezulin?
5. Is the risk:benefit ratio for Rezulin favorable?
6. What additional steps can be taken to further improve both safety and efficacy of Rezulin?

1. Does Rezulin Play a Causative Role in Cases of Severe Hepatotoxicity?

- The data indicate that Rezulin is associated with rare cases of idiosyncratic liver failure

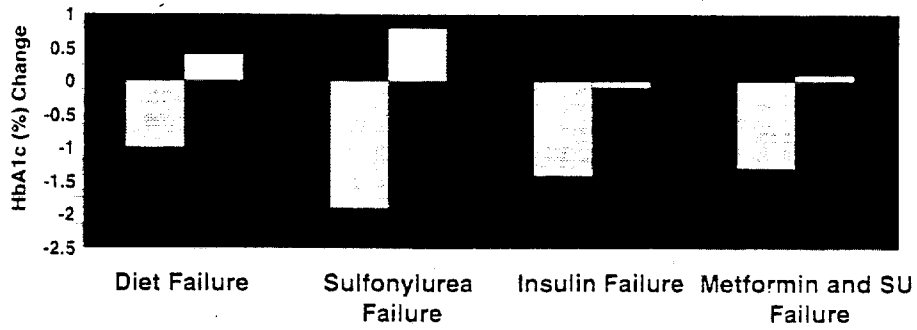
2. What Is the Risk of Such Events?

- The risk is low, and has decreased since monitoring was implemented

3. How Does the Risk Compare to That of Other Therapies?

- Though the pathologies differ from drug to drug, all of the available treatments for type 2 diabetes, including Rezulin, carry a similar, albeit small, risk of death

Efficacy of Rezulin



* $P < 0.05$



4. What Are the Benefits of Rezulin?

- Efficacy has been demonstrated in a spectrum of combinations as well as monotherapy. It's unique mechanism of action is complementary and appears to be preserving endogenous pancreatic function, which translates into better and longer lasting control.

5. Is the Risk:Benefit Ratio for Rezulin Favorable?

- Risk is low and comparable to alternative therapies
- Benefit is complementary and unique, adding significantly to the therapeutic armamentarium in a life threatening disease
- Risk:benefit is surely acceptable given this uniqueness of benefit

6. What Additional Steps can be Taken to Further Improve Both Safety and Efficacy of Rezulin?

- Warn against the use in patients with pre-existing liver disease
- Refine trial period and patient definition for monotherapy
- Patient package insert
- Expand education program
- Clinical Studies to identify greatest benefit