

## Thiazolidinedione (Glitazone) Recommendations

- 1) Consider *Avandia*® (rosiglitazone) or *Actos*® (pioglitazone) for initial monotherapy in the *non-obese* ± insulin or for combination therapy with metformin in the obese or metformin secondary failure population.
  - I) Consider *Actos*® (pioglitazone) if LDL-cholesterol is elevated AND no other drugs metabolized by the p-450 3A4, CYP2C8 system are used.
  - II) Use *Actos*® (pioglitazone) with caution in combination with statins as CPK elevations and/or myositis and/or rhabdomyolysis have been reported
  - III) *Actos*® (pioglitazone) may have innate PPAR-alpha activity similar to the fibric acid derivatives
  - IV) Consider *Avandia*® (rosiglitazone) and add an HMG-coA Reductase Inhibitor if LDL-cholesterol is elevated.
  - V) Effect on P450: troglitazone > pioglitazone > rosiglitazone
- (3) Follow FDA guidelines. Monitor LFTs as well as CPK if indicated periodically.
- (4) Do *not* use thiazolidinediones in the presence of heart failure.
- (5) Discontinue if edema, heart failure, anemia, CPK elevation, myositis, transaminase elevation, or weight gain (>3%) occurs.
- (6) The frequency of HF is 2.5 fold higher with insulin and glitazones
- (7) hepatotoxicity: 0.17/3505 patients
- (8) Very slow onset (4 to 6 weeks), if no response after 3-4 months, considers another agent.

### Comparison Chart of Glitazones

	Rosiglitazone (Avandia®)	Pioglitazone (Actos®)
Edema	++	++
Anemia	+	+
Wt gain	++	++
LDL increase	++ (p<0.05)	± (n.s.)
HDL increase	± (n.s.)	+/-
Triglyceride decrease	±(n.s.)	++ (p<0.05)
Drug interactions	+	++
Use in Heart Failure	Avoid	Avoid
Cardiomegaly (CXR)	[data requested]	0.197% (p<0.1)
Dosing Interval	4 to 8 mg once or b.i.d	15 to 45 mg daily
Costs	\$ 75.90	\$ 88.20

## Summary

### Mean Changes in Study Endpoints

	Pioglitazone	Rosiglitazone	P Value*
Triglycerides, mg/dL	-55.2 <sup>†</sup>	-13.3 <sup>†</sup>	<0.001
Total cholesterol, mg/dL	-8.5 <sup>†</sup>	+4.8 <sup>†</sup>	<0.001
HDL-C, mg/dL	+2.7 <sup>†</sup>	-0.1	0.064
LDL-C, mg/dL	-5.1 <sup>†</sup>	+3.6 <sup>†</sup>	<0.001
HbA <sub>1c</sub> , %	-1.04 <sup>†</sup>	-1.18 <sup>†</sup>	0.589
Weight gain, lb	+2.0 <sup>†</sup>	+1.6 <sup>†</sup>	0.558

\*Pioglitazone vs rosiglitazone, †P<0.05 vs baseline.