June 2003 - Comparison data for Sucanon (Diab II), Avandia and Actos

Clinical measure	**Sucanon (V-411)**	**Avandia (rosiglitazone)**	**Actos (pioglitazone)**
Fasting Blood Glucose reduction	2.95 mmol/L (2 mg b.i.d.) *6 vs. glibenclamide 1.48 mmol/L **Note: FBG reduction with Sucanon is equal to the reductions seen with the maximum dose of rosiglitazone (3.0 mmol/L for 4 mg 2 x per day) and pioglitazone (3.11 mmol/L for 45 mg daily)**	2.1 mmol/L – 2 mg b.i.d. - *1 3.0 mmol/L – 4 mg b.i.d. - *1 1.4 mmol/L – 4 mg once daily -*1 1.9 mmol/L twice daily -* 2.3 mmol/L – 8 mg once daily - *1 3.0 mmol/L – 4 mg b.i.d.- *2 2.3 mmol/L – 4 mg twice daily *2 1.4 mmol/L – 2 mg twice daily - *2 vs. glibenclamide 1.72 mmol/L	1.66 mmol/L – 15 mg daily - *3 1.78 mmol/L – 30 mg daily - *3 3.11 mmol/L – 45 mg daily - *3 [Note: in same series of studies, pioglitazone 7.5 mg daily had no effect on FBG]
Effects on lipids	"Elevated cholesterol and triglyceride levels…were reduced to normal levels….The level of reduction in cholesterol and triglyceride was clinically and statistically significant." **Note: LDL cholesterol increase (14% - 18%) that is seen with rosigliatzone does not occur with Sucanon – instead (Table 3) V-411 is associated with improvements in blood lipid levels (total cholesterol reduction of 11% and triglyceride reduction of 17%) ***	Rosiglitazone monotherapy was associated with increases in LDL-cholesterol,14.1% (4 mg per day) and 18.6% (8 mg per day) "Increases in LDL occurred primarily during the first two months and levels remained elevated throughout the trial."	"Pioglitazone may have a slightly more favorable effect on lipid profile [than rosiglitazone]. Mean decreases in triglycerides, and increases in HDL-cholesterol were noted."*4
Effect on weight	V-411 (Sucanon) was associated with maintenance or moderate loss of weight	"Over 26 weeks, the mean weight gain with rosiglitazone monotherapy was 1.2 kg at a dose of 4 mg/day and 3.5 kg at a dose of 8 mg/day." *4	"Thiazolidinediones, like sulphonylureas and insulin, are associated with weight gain." *4

Clinical Measure	**SUCANON** **Note: the strong tendency of thiazolidinediones (rosiglitazone and pioglitazone) to produce weight gain is a significant negative of their use for Type II diabetes therapy.**	**AVANDIA** "In the comparison with glibenclamide, patients treated with 4 mg and 8 mg of rosiglitazone daily gained a mean of 1.75 kg and 2.95 kg respectively versus a 1.9 kg gain in the glibenclamide group."*2 "Rosiglitazone was associated with a gain in mean body weight over time due to increased body fat […..and there may also have been a contribution from fluid retention.] Among patients treated with rosiglitazone monotherapy for at least 12 months, approximately 35% gained >5% in body weight and 11% gained >10%."*5 [in short, 46% gained at 5% to 10%, or more, in body weight] "The body weight is a safetyconcern especially due to the fact that a large proportion of type 2 diabetics patients are overweight. The cardiovascular consequences of both obesity and type 2 diabetes are an issue of conrern, taking into consideration also the LDL increase induced by rosiglitazone."	**ACTOS** "Pioglitazone appears to be associated with a similar pattern of weight gain [as rosiglitazone]]; on average 2.8 kg after 26 weeks." *4
Liver (hepatic) involvement	V-411 is not in TZD class; no risk of liver involvement **Note: No risk of hepatic involvement; no need for the expense of monitoring liver enzymes prior to or during therapy**	Label recommends that liver enzymes be checked prior to initiation; treatment should not be initiated if levels are raised.*2 Liver enzymes are monitored every two months for the first year and periodically thereafter.	Label recommends checking of liver enzymes prior to initiation of therapy.
Other clinical symptoms and side effects	"…loss of, or reduction in, disease-related symptoms which included polyuria, polydipsia, polyphagia and fatigue…" *6	"Oedema has been reported in patients taking thiazolidinediones. In trials, oedema was reported in 4.8% of patients treated with rosiglitazone and 3.6% of patients	"The most commonly reported adverse events in patients receiving monotherapy were: upper respiratory tract infection,

Clinical measure	SUCANON	AVANDIA	ACTOS
	No reported edema in patients taking V-411; no reports of upper respiratory tract infection and injury	treated with pioglitazone." *2 "Adverse events reported for > 5% of patients on rosiglitazone monotherapy therapy were upper respiratory tract infection and injury." *5	headache, sinusitis, myalgia, tooth disorder and pharyngitis."*4
Response rate	"A response analysis was done by the study coordinator in China and it was stated to be highly significant…overall response rate of 87%." "Very high level of patient acceptability." **Note: The response rate to V-411 is > 80% (*6) while response rate to rosiglitazone and pioglitatazone is <60%.**	Response rates up to 54% "The response rate was 28-54% in the rosiglitazone treatment groups." *5	[response rates under 60%]

*1 Lebovitz HE, Patel J et al. Rosiglitazone once or twice daily improves glycaemic control in type 2 diabetic patients. Diabetologica 1998; 41 (Suppl 1): A238, Abs.922

*2 Avandia – SmithKline Beecham Pharmaceuticals, Philadelphia, PA 19101. Available from www.fda.gov/cder/foi/label/1999/2107

*3 Schneider R, Lessem J, Lekich R. Pioglitazone is effective in the treatment of patients with Type 2 Diabetes.

*4 South Thames Drug Information Service, published by Guy's Hospital, London SE1 9RT, Therapeutic Update October 1999

*5 European Agency for Evaluation of Medicinal Products [EMEA], EMEA 2003, CPMP/1043/00

*6 "Profile of V-411" – BIO-97-0002-03/09/07