

Pargluva (muraglitazar) tablets

NDA 21-865

Draft questions for advisory committee meeting on September 9, 2005

1. Do the efficacy findings with Pargluva 2.5 and 5 mg daily support use for the proposed indications in the treatment of type 2 diabetes as:
 - a. Monotherapy
 - b. Combination therapy in patients not adequately controlled on metformin or sulfonylurea alone
2. Is there adequate evidence (either direct or by extrapolation) that Pargluva 1.5 mg daily is effective for the proposed indications?
3. Do the preclinical (pharmacology/toxicology) findings in conjunction with the results of the clinical trials with Pargluva 2.5 and 5 mg permit adequate understanding of the risks associated with use, with specific regard to the following issues?
 - a. Fluid retention/edema/CHF as:
 - i. Monotherapy
 - ii. Combination therapy
 - b. Hepatic effects
 - c. Muscle effects
4. Comment on concerns about adverse effects (e.g., cardiovascular) of Pargluva beyond those expected based on its putative mechanism(s) of action (i.e., compared to pioglitazone).
5. Are there patients for whom treatment with Pargluva 2.5 and 5 mg daily poses particular safety concerns?
6. Are there patients for whom a lower dose (starting and/or maximum) of Pargluva should be considered?
7. Comment on the discussions regarding the rodent carcinogenicity of Pargluva.
8. Should Pargluva be approved for the proposed indications?
 - a. Monotherapy
 - b. Combination therapy in patients not adequately controlled on metformin or sulfonylurea alone
9. If yes, comment on doses and special populations.
10. 10. If no, what additional information is needed?