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Abstract - Master Thesis Project, the Pharmacy Programme

Pharmacodynamic modeling and simulation of oral antidiabetic treatment to facilitate market positioning of drugs under evaluation

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Objective: To describe and quantitate the response to various oral antidiabetic therapies/placebo over time using pharmacodynamic models.

Methods: Clinical trial data, including fasting plasma glucose (FPG) and HbA1c response over time and dosing information, were collected in the literature and gathered in a database. An indirect pharmacodynamic response model, describing the interplay between FPG, HbA1c and the natural progression of disease was fitted to the observed data in the NONMEM software. Drugs were assumed to either effect the production or elimination of glucose. Eventually the model was used to investigate the difference in treatment outcome between glipizide and sitagliptin containing regimens. Simulations were carried out at varying dose levels and study durations.

Results: The model was predicting both FPG and HbA1c data reasonably well for five classes of drugs. Some random variability between studies and populations were observed due to differences in drug effects and in the rate of disease progression. Glipizide was observed to have a higher magnitude of effect but the effect duration was shorter as compared to sitagliptin.

Conclusion: Type 2 diabetes is a fast growing disease which today affect about 5% of all adults worldwide. It is of interest to evaluate and develop new antidiabetic drugs since none of the current drugs available on the market can provide optimal treatment for diabetes patients. By fitting pharmacodynamic models to literature data new drug candidates early can be put under evaluation relative to the competitive landscape and the number of costly long-term clinical studies may be reduced.