Executive summary

This descriptive study aimed to describe temporal trends in prescription patterns of pioglitazone in diabetic patients according to the European Summary of Product Characteristics, and to evaluate the implementation of different risk minimization measures regarding bladder cancer, heart failure (HF), and the need for regular monitoring of therapy benefits, introduced in July 2011 in clinical practice within the UK. We identified 32,947 patients with pioglitazone use, of which 57.9% were male, and most patients were between 50 and 79 years of age. A diagnosis for hypertension was recorded in approximately 60% of the study population, ischemic heart disease in 16% of patients, and mild chronic kidney disease (CKD) in almost half of all pioglitazone users. HF was prevalent in 2.6% of patients before treatment initiation with pioglitazone, whereby the relative frequency decreased over time; there was a decrease in the number of patients with prevalent HF initiating pioglitazone therapy from 3.8% of all new pioglitazone users prior to August 2007 to 1.6% post July 2011. In total, 37.5% of all pioglitazone users who developed incident bladder cancer, and 22.4% with incident macroscopic hematuria after the label change in July 2011, were withdrawn from the drug right after diagnosis (6/16 for bladder cancer and 15/67 for macroscopic hematuria), whereas the remainder had an ongoing pioglitazone therapy of at least one prescription. In case of an unacceptably high HbA1c value of ≥9% after 2011, 25.2% of patients were taken off the drug immediately. The majority of current pioglitazone users with prevalent bladder cancer before July 2011 were not taken off the drug after the label change in July 2011. GPs complied with second line-status of pioglitazone in 86.7% of patients, with metformin being by far the most frequently used antidiabetic drug before (71.8%) pioglitazone treatment initiation. In total, we observed 16.4% of pioglitazone users with a co-prescription for insulin, and despite its off-label status, the proportion of co-prescription was highest before August 2007 (18.3%)

and declined thereafter to 7.1% after July 2011. Overall, we observed a lower incidence rate (IR) of incident HF in pioglitazone users (5.77/1000 py) than previously reported (30.9/1000 py), which might be due to heterogeneity of the two study populations, due to differences in co-medication, or due to disease duration. We observed 2 to 4.5 fold increased IRs of HF when comparing patients who were co-prescribed insulin compared to patients on pioglitazone without insulin, but the total number of patients with a combined therapy with insulin and pioglitazone decreased over time.