

Clinical Study Synopsis for Public Disclosure

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2. ABSTRACT

Name of company: Boehringer Ingelheim			
Name of finished medicinal product: TRAJENTA			
Name of active ingredient: Linagliptin			
Report date: 11 Jun 2015	Study number: 1218.161	Version/Revision: 1.0	Version/Revision date:
Title of study:	A description of oral and non-insulin injected glucose-lowering therapy utilization patterns including initiation, switching, and discontinuation Phase 2 of the BIDM study program Final Report 1		
Keywords:	Linagliptin, DPP-4 inhibitors, utilization, cohort, oral and non-insulin injected hypoglycaemic agents.		
Rationale and background:	Dipeptidyl peptidase-4 (DPP-4) inhibitors, including linagliptin, saxagliptin, and sitagliptin, are new class of oral glucose-lowering agents approved in the United States. Understanding the utilization patterns of these agents will aid in identifying potential sources of bias and imbalances in comorbidities between users of DPP-4 and other agents that need to be accounted for in future comparative effectiveness and safety studies		
Research question and objectives:	This study is for a series of descriptive analyses conducted within a cohort of patients using linagliptin, other DPP-4 inhibitors, and other oral and non-insulin injected glucose-lowering medications in May 2011 through June 2012. Understanding 1) the existing utilization patterns for linagliptin, sitagliptin, saxagliptin, and other oral and non-insulin injected glucose-lowering agents and (2) the differences in utilization patterns between these agents will help with the design, analysis and interpretation of comparative effectiveness and safety studies of linagliptin, other DPP-4 inhibitors, and other agents. The objectives of the study are to: • Provide an overview of existing utilization patterns for linagliptin, other DPP-4 inhibitors, and other oral and non-insulin injected glucose-lowering agents, in order to detect potential selective prescribing patterns that might lead to channeling bias. • Examine utilization patterns by patient characteristics. • Examine treatment initiation, switching and discontinuation.		

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Study design:	Observational cohort study		
Setting:	US health insurance databases: United Healthcare May 2011 through June 2012 MarketScan May 2011 through June 2012		
Subjects and study size, including dropouts:	Among 319,920 new initiators of a non-insulin glucose-lowering agent from May 2011 through Dec 2012 who were at least 18 years of age and enrolled for a minimum of 6 months in United Healthcare before treatment initiation, 49,742 had no recorded diagnosis of T2DM prior to index date, 46,446 had a diagnosis of T1DM or secondary diabetes, 53 received ≥ 2 drugs within the same class on the index date and 17 had evidence of ambiguous age and were excluded, leaving a total of 223,662 patients. Restricting this population to the study period of May 2011 – June 2012 left a total of 155,345 in the final cohort (2,820 linagliptin, 18,491 sitagliptin, 8,100 saxagliptin 72,694 metformin, 33,868 sulfonylurea, 7,203 glitazone, 1,184 meglitinides, 495 AGIs and 10,490 GLP-1). Among 908,900 new initiators of a non-insulin glucose-lowering agent between May 2011 and Dec 2012 who were at least 18 years of age and enrolled for a minimum of 6 months in MarketScan before treatment initiation, 144,862 had no recorded diagnosis of T2DM prior to index date, 114,581 had a diagnosis of T1DM or secondary diabetes, 150 received ≥ 2 drugs within the same class on the index date and 10 had evidence of ambiguous age, leaving a total of 649,297 patients. Restricting this population to the study period of May 2011 – June 2012 left a total of 459,722 in the final cohort (7,708 linagliptin, 58,769 sitagliptin, 24,550 saxagliptin, 205,213 metformin, 104,422 sulfonylurea, 22,310 glitazones, 5,412 meglitinides, 1,918 AGIs, and 29,420 GLP-1s). Within each database, we also performed propensity score (PS) matching of linagliptin initiators to each of the other exposure groups.		
Variables and data sources:	Data for this study come from United Healthcare (a large national commercial health insurer in the US), and MarketScan (claims database from commercial employer-sponsored health plans in the US).		

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		Patient baseline characteristics including demographics, clinical conditions, and health service use were identified from medical and prescription claims and enrollment files. Utilization measures were derived from United Healthcare and MarketScan prescription claims data. Utilization measures included: • Treatment initiation on specific diabetes medications • Treatment sequencing (before and after entering in the cohort) • Time until treatment discontinuation • Time until treatment switch • Time until treatment augmentation • Adherence measures (e.g., medication possession ratio) Patients were censored at drug discontinuation, end of continuous health plan enrollment, death, or end of the study period, whichever came first.	
Results:		In the period May 2011 – June 2012, we identified 155,345 (United Healthcare) and 459,722 (MarketScan) new initiators of glucose-lowering agents that met the cohort inclusion criteria. Of these, metformin represented the most frequently initiated agent (46.8% in United Healthcare and 44.6% in MarketScan), followed by sulfonylureas (21.8% and 22.7%), and sitagliptin (11.9% and 12.8%). Linagliptin was initiated by 2,820 patients (1.8%) in United Healthcare and by 7,708 (1.7%) in MarketScan. The mean age of linagliptin users (55.9 y (years) in United Healthcare and 58.7y in MarketScan) was higher than other DPP-4s (54.2y and 58.0y), metformin (52.6y and 55.9y), sulfonylureas (53.7y and 57.9y) and glitazones (53.7y and 57.4y). A greater proportion of patients initiated linagliptin in year 2012 (57.2%) compared to year 2011 (42.8%) whereas for every other agent, there were more initiators in year 2011 compared to 2012, consistent with the longer duration of follow-up in 2011 and the fact that linagliptin was the only agent included during its launch phase. Linagliptin initiators along with meglitinide initiators had the greatest burden of comorbidities as indicated by Charlson comorbidity score (1.68 and 1.79 respectively in United Healthcare and 1.71 and 1.90 in MarketScan). Overall, linagliptin initiators (along with initiators of meglitinides) had the highest prevalences of renal dysfunction,	

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		hypertension, hyperlipidemia, and malignant neoplasms. These patterns were consistently observed across initiation subgroups (with the exception of initiators of dual therapy with metformin and treatment-naïve new users. However, these latter subgroups include few patients. Burden of comorbidities and specific co-morbid conditions were well balanced after Propensity score (PS)-matching in both data sources. The proportion of days covered (PDC) among linagliptin new users was 77.5% in United Healthcare and 78.6% in MarketScan, and was the highest observed PDC among compared treatment groups, followed by the PDC observed among saxagliptin new users (75.8% in United Healthcare and 78.1% in MarketScan). Similarly, patients initiated on linagliptin or saxagliptin were the individuals that less frequently filled only one dispensing of their medication (15.0% and 15.7%, respectively in United Healthcare, 16.4% and 15.9% in MarketScan). They also had greater persistence of therapy at 3, 6, and 12 months (51.5% and 49.8% at 12 months in United Healthcare, 50.3% and 50.1% in MarketScan), and, in United Healthcare data, less likely experienced treatment discontinuation (Incidence rate[IR] = 267.4 and IR = 264.2 per 1000 py). Results were consistent after PS-matching.	
Discussion:		Our results suggest an increase in linagliptin utilization over the study timeframe. These linagliptin initiators (along with initiators of meglitinides) exhibit a higher burden of comorbidities at baseline as indicated by Charlson comorbidity score and higher prevalence of renal dysfunction, hypertension, hyperlipidemia, and malignant neoplasms. Burden of comorbidities and specific co-morbid conditions were well balanced after PS-matching in both data sources. Linagliptin and saxagliptin new users had the highest proportion of days covered (PDC). Similarly, compared to initiators of other agents, patients initiated on linagliptin or saxagliptin less frequently filled only one dispensing of their medication, had greater persistence of therapy at 3, 6, and 12 months, and, within the United Healthcare database, were less likely to discontinue treatment. These findings remain consistent after PS-matching.	
Marketing Authorisation		Boehringer Ingelheim International GmbH	

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Holder(s):			
Names and affiliations of principal investigators:			