

Postmarketing Safety Evaluation of Aliskiren Hemifumarate, a New Molecular Entity.

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Purpose.

To evaluate the safety profile of aliskiren by calculating the adjusted reporting ratios of specific adverse events.

Methods.

The Food and Drug Administration's (FDA) Adverse Event Reporting System (AERS) data are utilized to conduct this retrospective pharmacovigilance study. Adverse event (AE) reports submitted to the AERS during the period of January 2007 through December 2008 are included in the analysis. Systematic Multi-item Gamma Poisson Shrinker (MGPS) data mining algorithm is applied to calculate the adjusted reporting ratios (ARR) of AE, which are estimated by the Empiric Bayes Geometric Mean (EBGM) values and their 95% confidence intervals (95% CI). EBGM values of >2.0 are considered as safety signals significant for regulatory decisions. Reports for aliskiren and other drugs affecting the Renin-Angiotensin-Aldosterone System (RAAS) are identified using the verbatim names for each individual class member. Reports for specific AE are identified by the utilized Preferred Terms of the Medical Dictionary for Regulatory Activities coding scheme (MedDRA PT) in the AERS.

Results.

During the study period, a total number of 2,154 reports for aliskiren are received by the AERS. Seventy four percent (1,592) of these reports had valid MedDRA terms, and included in the analysis. Compared to other RAAS modulators, aliskiren was associated with the highest ARR for angioedema (EBGM 3.9, 95% CI 3.2-4.7), renal dysfunction (EBGM 3.4, 95% CI 2.6-4.5), dry cough (EBGM 11.0, 95% CI 7.8-14.2), and diarrhoea (EBGM 4.3, 95% CI 3.2-5.8). Aliskiren ranked the second after aldosterone antagonists in hyperkalaemia (EBGM 7.4, 95% CI 3.4-13.0).

Conclusion.

Treatment with aliskiren may be associated with angioedema and renal dysfunction. Patients with signs and symptoms of angioedema should stop aliskiren and seek urgent medical help. Aliskiren should not be used by patients with risks of renal dysfunction. While additional longitudinal studies and clinical awareness is warranted, regulatory changes in product label and safety communications, e.g. dear-healthcare-professional letters are recommended meanwhile actions.