NATIONAL PBM BULLETIN

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VETERANS HEALTH ADMINISTRATION (VHA) PHARMACY BENEFITS MANAGEMENT SERVICES (PBM), MEDICAL ADVISORY PANEL (MAP), & CENTER FOR MEDICATION SAFETY (VA MEDSAFE)

RISK OF SEVERE HYPOGLYCEMIA WITH GLYBURIDE USE IN ELDERLY PATIENTS WITH RENAL INSUFFICIENCY

I. ISSUE

On September 4, 2007, VA MedSAFE sent out information about the increased risk of severe hypoglycemia with glyburide, especially in patients with renal insufficiency or decreased renal function due to age. Each VISN received a list of patients aged 65 years and older with an active prescription for glyburide and a serum creatinine ≥ 2 mg/dl so that appropriate intervention, such as a switch to glipizide, could be taken. While glyburide use in these patients has decreased significantly, there are still elderly patients with impaired renal function receiving the drug. In the second quarter of FY09, there were over 2000 patients 65 years or older, and not targeted in the initial intervention, with an active prescription for glyburide and a serum creatinine ≥ 2 mg/dl (To view results, see: Glyburide and Severe Hypoglycemia Risk Reduction Efforts_RESULTS [NOTE: Intranet use for internal VA employees only.]).

II. BACKGROUND

Glyburide has several metabolites that have hypoglycemic activity and that are excreted by the kidneys. Therefore, accumulation can occur in patients with renal failure, leading to an increased risk of hypoglycemia.[1,2] Studies have shown that the risk of hypoglycemia in elderly patients with renal insufficiency is higher with glyburide than with other sulfonylureas.[3-5] Because of the higher risk of hypoglycemia, the American Diabetes Association and the European Association for the Study of Diabetes recommend second generation sulfonylureas other than glyburide for the management of type II diabetes.[6]

III. PROVIDER RECOMMENDATIONS

Given the increased risk of severe hypoglycemia with glyburide, especially in patients with renal insufficiency or decreased renal function due to age, an alternative sulfonylurea (e.g., glipizide) is recommended. We specifically recommend avoiding glyburide in patients with a calculated creatinine clearance <50 ml/min. If an oral sulfonylurea is required, a 5mg dose of glipizide is approximately equivalent to 2.5-5mg of glyburide. The exact conversion will depend upon the degree of blood glucose control while on glyburide and susceptibility to hypoglycemia. Patients should continue with their normal blood glucose monitoring after the conversion.

IV. REFERENCES

1. Snyder RW, Berns JS. Use of insulin and oral hypoglycemic medications in patients with diabetes mellitus and advanced kidney disease. *Semin Dial*. 2004;17:365-70.
2. Harrower AD. Pharmacokinetics of oral antihyperglycaemic agents in patients with renal insufficiency. *Clin Pharmacokinet*. 1996;31:111-9.
3. Shorr RI, Ray WA, Daugherty JR, Griffin MR. Individual sulfonylureas and serious hypoglycemia in older people. *J Am Geriatr Soc*. 1996;44:751-5.
4. van Staa T, Abenhaim L, Monette J. Rates of hypoglycaemia in users of sulphonylureas. *J Clin Epidemiol*. 1997:50:745-41.
5. Ganji AS, Cukierman T, Gerstein HC, Goldsmith CH, Clase CM. A systematic review and meta-analysis of hypoglycemia and cardiovascular events. A comparison of glyburide with other secretagogues and with insulin. *Diabetes Care* 2007;30:389-94.
6. Nathan DM, Buse JB, Davidson MB, et al. Medical management of hyperglycemia in type 2 diabetes: a consensus algorithm for the initiation and adjustment of therapy. A consensus statement of the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetes Care* 2009;32:1-11.

ACTIONS:

- ***Facility COS and Chief Nurse Executives:*** *Forward this document to all appropriate providers who prescribe/use/handle this agent (e.g.,* ***primary care providers and endocrinology specialists****, including contract providers, etc.). In addition, forward to the Associate Chief of Staff (ACOS) for Research and Development (R&D). Forward to other VA employees as deemed appropriate.*
- ***ACOS for R&D:*** *Forward this document to Principal Investigators (PIs) who have authority to practice at the facility and to your respective Institutional Review Board (IRB).*