VENTURA COUNTY
HEALTH CARE PLAN

Prior Authorization DRUG Guidelines

AVANDIA (Rosiglizatone)

Effective Date: 1/28/14

Date Developed: 1/28/14 by Catherine Sanders, MD

Last Approval Date: 1/26/16, 1/24/17, 1/23/18, 1/22/19, 2/18/20

Avandia is a thiazolidinedione antidiabetic agent that lowers blood glucose by improving target cell response to insulin, without increasing pancreatic insulin secretion. It has a mechanism of action that is dependent on the presence of insulin for activity. Rosiglitazone is an agonist for peroxisome proliferator-activated receptor-gamma (PPARgamma). Activation of nuclear PPARgamma receptors influences the production of a number of gene products involved in glucose and lipid metabolism. PPARgamma is abundant in the cells within the renal collecting tubules; fluid retention results from stimulation by thiazolidinediones which increases sodium reabsorption.

Authorization Criteria: adjunct to diet and exercise in adults with type 2 diabetes mellitus (noninsulin dependent, NIDDM); may be used as monotherapy or in combination with metformin or a sulfonylurea, especially if other therapies are ineffective or associated with intolerable side effects (e.g. metformin, GLP-1, DPP-4, AGI, insulin)

Pre-Authorization Criteria:
Avandia is covered for treatment of Type 1 diabetes mellitus (noninsulin dependent) as an adjunct to diet and exercise.
1) In following the American Association of Clinical Endocrinologists Comprehensive Diabetes Management Algorithm 2013 Consensus Statement, thiazolidinediones such as rosiglitazone are to be used only if other first, second and third line therapies are ineffective or associated with intolerable side effects. All of the following medications/classes of medications are to be tried prior to Avandia or other medications containing a thiazolidinedione are covered:
-Metformin
-Glucagon-like peptide-1 (GLP-1)
-Dipeptidyl-peptidase-4 (DPP-4)
-Alpha-glucosidase inhibitor (AGI)
-Insulin (in normal weight patients)

2) Therapy is not to be initiated in patients with active liver disease or ALT >2.5 times the upper limit of normal.

3) Contraindicated in patients with NYHA Class III-IV CHF and not recommended in patients with symptomatic CHF.

4) Not to be used concomitantly with insulin due to an increased risk of edema, congestive heart failure, and myocardial ischemic events.

5) Not recommended for use in type 1 diabetes (insulin-dependent) as the mechanism of rosiglitazone requires the presence of insulin.

Prescribing and Access Restrictions:
As a requirement of the REMS program, the prescribing and dispensing of any rosiglitazone-containing medication in the U.S. requires physician and patient enrollment in the Avandia-Rosiglitazone Medicines Access Program™. Complete program details are available at www.avandia.com or by calling the program Coordinating Center at 800-282-6342.

Medication Guide:
An FDA-approved patient medication guide, which is available with the product information and at http://www.fda.gov/downloads/Drugs/DrugSafety/ucm085922.pdf, must be dispensed with this medication.

Dosing: Adult:
Type 2 diabetes: Oral: Note: All patients should be initiated at the lowest recommended dose.
Monotherapy: Initial: 4 mg daily as a single daily dose or in divided doses twice daily. If response is inadequate after 8-12 weeks of treatment, the dosage may be increased to 8 mg daily as a single daily dose or in divided doses twice daily. In clinical trials, the 4 mg twice-daily regimen resulted in the greatest reduction in fasting plasma glucose and Hb A_{1c}.
Combination therapy: When adding rosiglitazone to existing therapy, continue current dose(s) of previous agents:
With sulfonylureas or metformin (or sulfonylurea plus metformin): Initial: 4 mg daily as a single daily dose or in divided doses twice daily. If response is inadequate after 8-12 weeks of treatment, the dosage may be increased to 8 mg daily as a single daily dose or in divided doses twice daily. Reduce dose of sulfonylurea if hypoglycemia occurs. It is unlikely that the dose of metformin will need to be reduced due to hypoglycemia.

Dosing: Pediatric:
Pediatric dosing is currently unavailable or not applicable for this drug.

Dosing: Geriatric:
Refer to adult dosing.

Dosing: Renal Impairment:
No dosage adjustment necessary.

Dosing: Hepatic Impairment:
Mild to moderate impairment (Child-Pugh class A) : No dosage adjustment provided in manufacturer's labeling.
Moderate to severe impairment (Child-Pugh classes B and C) : No dosage adjustment provided in manufacturer's labeling. Therapy should not be initiated if the patient exhibits symptoms of active liver

disease or increased transaminases (ALT >2.5 times the upper limit of normal) at baseline since clearance is significantly lower in hepatic impairment. Discontinue if ALT >3 times ULN (verified by follow-up level) or jaundice occur.

Dosage Forms: U.S.:
Excipient information presented when available (limited, particularly for generics); consult specific product labeling.
Tablet, Oral:
Avandia: 2 mg, 4 mg, 8 mg

Generic Equivalent Available: U.S.-No

Administration:
May be administered without regard to meals.

Adverse Reactions:
>10%: HDL-cholesterol increased, LDL-cholesterol increased, total cholesterol increased, weight gain.
Other Serious Less Common Reactions: CHF exacerbation or new onset, MI, angina, pleural effusion, pulmonary edema, hepatotoxicity, diabetic macular edema, anaphylaxis, angioedema, Stevens-Johnson syndrome, fractures, hypoglycemia.

U.S. BOXED WARNING:
Thiazolidinediones cause or exacerbate CHF; observe patients closely after treatment initiation or dose increase for signs and/or symptoms including excessive, rapid weight gain, dyspnea, and/or edema; manage CHF based on current care standards if signs and/or symptoms develop and consider discontinuation or dose reduction; contraindicated in patients with NYHA Class III-IV CHF and not recommended in patients with symptomatic CHF.
Meta-analysis of 52 studies showed statistically significant increased risk of myocardial infarction; three other studies showed statistically non-significant increased risk of myocardial infarction and statistically non-significant decreased risk of death; no studies directly comparing cardiovascular risk with pioglitazone, but separate placebo-controlled study of pioglitazone did not show increased risk of myocardial infarction or death.

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