



Effective Health Care

Best Second-Line Oral Medication for Treating Type 2 Diabetes Mellitus

Nomination Summary Document

Results of Topic Selection Process & Next Steps

- Best second line oral medication for treating type 2 diabetes mellitus was found to be addressed by an in-process update of the 2007 AHRQ report titled *Comparative Effectiveness and Safety of Oral Diabetes Medications for Adults with Type 2 Diabetes*. Given that the in-process update covers this nomination, no further activity will be undertaken on this topic.
 - In-process Update: Comparative Effectiveness and Safety of Oral Diabetes Medications for Adults With Type 2 Diabetes: An Update of the 2007 Report. To view a description and status of the research review, please go to: <http://www.effectivehealthcare.ahrq.gov/index.cfm/search-for-guides-reviews-and-reports/>
 - To sign up for notification when this and other Effective Health Care (EHC) Program topics are posted, please go to <http://effectivehealthcare.ahrq.gov/index.cfm/join-the-email-list1/>

Topic Description

Nominator: Individual

Nomination Summary: The nominator wants to know the best second drug choice for treatment of type 2 diabetes.

Staff-Generated PICO:

Population(s): Patients with type 2 diabetes mellitus on metformin with HbA1c above goal; elderly, Medicare or Medicaid recipients

Intervention(s): Second-line oral medications for diabetes

Comparator(s): Second-line options; combinations of oral diabetes medications

Outcome(s): Standard glycemic control effectiveness measures (e.g., HbA1c level, serum glucose control, and hypoglycemic events), diabetes complications, mortality, cardiovascular events, hospitalizations, and cost-effectiveness

Key Questions from Nominator:

1. For type 2 diabetes mellitus, if metformin alone fails to adequately control glucose levels, what is the second-line drug or combination of choice?

Considerations

- The topic meets EHC Program appropriateness and importance criteria. (For more information, see <http://effectivehealthcare.ahrq.gov/index.cfm/submit-a-suggestion-for-research/how-are-research-topics-chosen/>.)
- This topic is of high importance due to the significant disease burden caused by type 2 diabetes mellitus in the US. Type 2 diabetes mellitus is generally a progressive disease characterized by a decline in pancreatic beta-cell function and increase in insulin resistance. With disease progression, patients may transition from one oral diabetes medication to another oral diabetes medication or a combination of oral diabetes medications or insulin. There are several options and potential combinations of oral medications that may be tried in an attempt to control glucose levels.
- This topic was found to be addressed by an in-process update to a 2007 AHRQ comparative effectiveness review titled *Comparative Effectiveness and Safety of Oral Diabetes Medications for Adults With Type 2 Diabetes*. Draft key questions from this report include:
 1. In adults age 18 or older with type 2 diabetes mellitus, what is the comparative effectiveness of treatment options* for the intermediate outcomes of glycemic control (in terms of HgbA1c), weight, or lipids?
 2. In adults age 18 or older with type 2 diabetes mellitus, what is the comparative effectiveness of treatment options* in terms of the following long-term clinical outcomes?
 - All-cause mortality
 - Cardiovascular mortality
 - Cardiovascular and cerebrovascular morbidity (e.g., myocardial infarction and stroke)
 - Retinopathy
 - Nephropathy
 - Neuropathy
 3. In adults age 18 or older with type 2 diabetes mellitus, what is the comparative safety of treatment options* in terms of the following adverse events and side effects?
 - Hypoglycemia
 - Liver injury
 - Congestive heart failure
 - Severe lactic acidosis
 - Cancer
 - Severe allergic reactions
 - Hip and non-hip fractures
 - Pancreatitis
 - Cholecystitis
 - Macular edema or decreased vision
 - Gastrointestinal (GI) side effects
 4. Do safety and effectiveness of these treatment options* differ across subgroups of adults with type 2 diabetes, in particular for adults age 65 or older, in terms of mortality, hypoglycemia, cardiovascular and cerebrovascular outcomes?

*Treatment options include:

- Biguanides (metformin)
 - Thiazolidinediones (rosiglitazone, pioglitazone)
 - Second-generation sulfonylureas (glyburide, glibenclamide, glipizide, glimepiride)
 - Dipeptidyl peptidase-4 inhibitors (sitagliptin, saxagliptin)
 - Meglitinides (repaglinide, nateglinide)
 - GLP-1 agonists (exenatide, liraglutide)
 - Combination of metformin plus a thiazolidinedione
 - Combination of metformin plus a sulfonylurea
 - Combination of metformin plus sitagliptin
 - Combination of metformin plus a meglitinide
 - Combination of metformin plus exenatide
 - Combination of metformin plus a basal insulin (insulin glargine, insulin detemir, NPH insulin)
 - Combination of metformin plus a premixed insulin (NPH/regular 50/50, NPH/regular 70/30, insulin lispro 50/50, insulin lispro 75/25, insulin aspart 70/30)
 - Combination of a thiazolidinedione and a sulfonylurea
 - Combination of a thiazolidinedione and a meglitinide
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- In addition to the above listed key questions, the in-process report will compare the effectiveness and safety of second-line therapies for adults with type 2 diabetes. It addresses both monotherapy and combination therapy for the management of type 2 diabetes in adults. It will also address the concerns about long-term data specifically addressed in Key Question 2. The nominator's concerns about results for subgroups of patients are specifically addressed in Key Question 4.