Members Present
Matthew Beatty, PA-C., Ryan Fremming, R.Ph, James MacNutt, D.O.Pierre Rioux, MD., Amy Sapola, PharmD., Allyson Schlichte, PharmD., and Abigail Stoddard, PharmD.

DHS Staff Present
Mary Beth Reinke, PharmD., Sara Drake, RPh., Dave Hoang, PharmD. Steven Wesbur, PharmD candidate on DUR rotation.

Other Attendants
Larry Dent, PharmD., Xerox

Public Comments: There was a question if opiate dependence and the use of Suboxone or buprenorphine film would be discussed tonight. The requestor was directed to the medication assisted treated (MAT) agenda item at HSAC’s meeting on March 10, 2016.

Approval of Minutes: Minutes from December 9, 2015 were approved.

Old Business: None.

New Business:
RetroDUR-population based interventions
The DUR Board was provided with a side-by-side comparison of the three chronic disease proposals: diabetes, lipids, and cardiovascular disease. The pharmacy staff reviewed these in advance and selected diabetes as it was the most clinically robust of the three.

Diabetes Mellitus Management Proposal
The purpose is to educate prescribers on opportunities for improving the quality and safety of drug therapy for recipients with diabetes mellitus based on the 2015 clinical practice recommendations published by the American Diabetes Association (ADA).

Setting and population: all recipients with a history of diabetes in the past 2 years.
DUR Board recommended age ≥ 18 years based on concern with performance indicators: 2, 5, 6, 13 and 14.

The purposed intervention was comprised of the following fourteen performance indicators.

Increased Risk of Adverse Events
Performance Indicator #1: Increased Risk of Adverse Events: Annual Dilated Eye Exams. N=2,287
Criteria:
- Recipients with a history of diabetes (submitted ICD-9 diagnosis code for diabetes or inferred from drug therapy) in the last 2 years AND
- Recipients without documentation of eye examinations by respective CPT and/or ICD-9 codes

DUR Board members expressed concerns that providers or recipients may not know Medicare covers eye exams or other relevant services. DUR Board asked for clarification that both ICD-9 and ICD-10 codes would be used as appropriate to the time period. Finally, the DUR Board recommended adding a statement to the prescriber letter as follow: Minnesota Medicaid benefits include annual dilated eye exams to screen for retinopathy and over-the-counter use of aspirin for use as an antiplatelet.

Performance Indicator #2: Increased Risk of Adverse Events: Recommended Laboratory Monitoring. N=5,675
Criteria:
- Recipients with a history of diabetes (submitted ICD-9/ICD-10 diagnosis code for diabetes or inferred from drug therapy) in the last 2 years AND
- Recipients without documentation of routine chemistries/laboratory monitoring (CPT codes) within the frequency recommended by the ADA (American Diabetes Association).

The DUR Board approved as presented noting it was good to include those inferred from drug therapy. The DUR Board decided in the prescriber letter that distinct recipients across all the lab indicators should be reported.

Performance Indicator #3: Increased Risk of Adverse Events: Laboratory Monitoring with SGLT2 Inhibitors. N=10
Criteria:
- Recipients receiving SGLT2 inhibitor therapy in the last 30 days AND
- Recipients without an eGFR, serum creatinine, or lipid panel test in the last 365 days.

The DUR Board agreed that SGLT2 monitoring should be kept separate to raise awareness for new medication classes.

Performance Indicator #4: Increased Risk of Adverse Drug Events with Diabetes Medications. N=22 under 18 years; N=528 ≥ 18 years.
Criteria:
- Recipients receiving antidiabetic agents in the last 30 days with a history of a comorbid condition in the last 2 years that places them at increased risk of a serious adverse event. Refer to Table 1. These are defined as a severity level 1 drug disease interaction by First Databank.

The DUR Board recommended the following two changes in the table.
- In table on drug-disease interactions, change liraglutide to GLP-1 agonists, due to class effect.
• In table on drug-disease interactions, change heart failure to acute or unstable heart failure. Metformin is okay in stable congestive heart failure (CHF), but not unstable CHF.

Table 1. Diabetes Drug-Disease Interactions

<table>
<thead>
<tr>
<th>Anti-diabetic Drug</th>
<th>Medical Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acarbose</td>
<td>• Cirrhosis</td>
</tr>
<tr>
<td></td>
<td>• GI disease</td>
</tr>
<tr>
<td>Miglitol</td>
<td>• GI disease</td>
</tr>
<tr>
<td>Pioglitazone and combination products</td>
<td>• Active liver disease</td>
</tr>
<tr>
<td></td>
<td>• Heart failure</td>
</tr>
<tr>
<td></td>
<td>• Macular edema</td>
</tr>
<tr>
<td>Rosiglitazone and combination products</td>
<td>• Renal disease or renal dysfunction</td>
</tr>
<tr>
<td></td>
<td>• Age ≥ 80 years</td>
</tr>
<tr>
<td></td>
<td>• Heart failure change to unstable congestive heart failure</td>
</tr>
<tr>
<td></td>
<td>• Acute or chronic metabolic acidosis</td>
</tr>
<tr>
<td></td>
<td>• Hepatic disease or hepatic impairment</td>
</tr>
<tr>
<td>Metformin and combination products</td>
<td>• Renal Impairment</td>
</tr>
<tr>
<td></td>
<td>• Pancreatitis</td>
</tr>
<tr>
<td></td>
<td>• GI Disease</td>
</tr>
<tr>
<td>Exenatide</td>
<td>• Renal Impairment</td>
</tr>
<tr>
<td></td>
<td>• Pancreatitis</td>
</tr>
<tr>
<td>Liraglutide change to GLP-1 agonists</td>
<td>• Multiple Endocrine Neoplasia Syndrome type 2</td>
</tr>
<tr>
<td></td>
<td>• Pancreatitis</td>
</tr>
<tr>
<td>SGLT2 Inhibitors and combination products</td>
<td>• Renal impairment</td>
</tr>
</tbody>
</table>

Underutilization
Performance Indicator #5: Underutilization of Angiotensin-Modulating Therapy. N=106 under 18 years; N=144 ≥ 18 years.
Criteria:
• Recipients with a diagnosis of diabetes (ICD-9 code or inferred from drug therapy) in the last 2 years AND
• Recipients who have either (1) Hypertension plus kidney disease (submitted ICD-9 code diagnosis required) or (2) Kidney disease (submitted ICD-9 code required), who do not have a documented contraindication or relative contraindication to angiotensin-modulating therapy (i.e., anuric renal failure, renal artery stenosis, pregnancy or a history of angioneurotic edema) AND are not receiving an angiotensin-modulating agent (ACE inhibitor or ARB) in the past 1 year.

Paragraph:
Potential Underutilization - No Angiotensin-Modulating Agent in a Diabetes Mellitus Recipient: According to submitted pharmacy and medical claims, it appears your recipient has diabetes and hypertension but is not receiving an angiotensin-modulating agent (either an ACE inhibitor or angiotensin receptor blocker). Use of an angiotensin-modulating agent has proven beneficial for decreasing or stabilizing albuminuria in incipient nephropathy and in slowing the rate of progression of advanced nephropathy. Please review your recipient's current therapy and determine whether use of an angiotensin-modulating agent would be appropriate.

DUR Board inquired what was used as the basis for creating this indicator to ensure that it was not the obsolete CMS measure. Response was that is based on new ADA guidelines.
Performance Indicator #6: Underutilization of Lipid Lowering Therapy in Diabetics. N=1,139
Criteria:
- Recipients with a diagnosis or drugs indicative of diabetes in their medical and pharmacy
  claims history, ages 40-75 and have no claims for Welchol (colesevelam) in the past year,
  AND
- Recipients who did not receive an HMG-CoA reductase inhibitor in the past year.

Paragraph updating was suggested by Amber, DUR Student. [Xerox Flag 6824]. Potential
Underutilization of Lipid Lowering Therapy with a History of Diabetes Mellitus paragraph:
According to submitted pharmacy and medical claims data, it appears your recipient has a
history of diabetes mellitus and is not receiving pharmacological lipid lowering statin therapy at
an appropriate dose to provide the recommended intensity. The 2013 ACA/AHA Guidelines
recommend that individuals with a diagnosis of diabetes receive moderate to high intensity statin
therapy. Please review your records to determine whether a lipid panel has been checked in the
past year and evaluate the potential need for an increase in or initiation of statin therapy.

DUR Board recommendation is to include the Statin Therapy table in the proposal in the
prescriber letter but to remove the Low-intensity Statin Therapy column of the table. The second
recommendation was to list as statin choices only those that preferred on DHS PDL (preferred
drug list) or those that do not require a prior authorization. [Note: pitavastatin (Livalo®) and all
brand name statins requires prior authorization].

Table 2. High- Moderate- and Low-Intensity Statin Therapy

<table>
<thead>
<tr>
<th>High-Intensity Statin Therapy</th>
<th>Moderate-Intensity Statin Therapy</th>
<th>Low-Intensity Statin Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily dose lowers LDL–C on average, by approximately ≥50%</td>
<td>Daily dose lowers LDL–C on average, by approximately 30% to &lt;50%</td>
<td>Daily dose lowers LDL–C on average, by &lt;30%</td>
</tr>
<tr>
<td>Atorvastatin 40–80 mg</td>
<td>Atorvastatin 10 20 mg</td>
<td>Simvastatin 10 mg</td>
</tr>
<tr>
<td>Rosuvastatin 20 40 mg</td>
<td>Rosuvastatin 5 10 mg</td>
<td>Pravastatin 10–20 mg</td>
</tr>
<tr>
<td></td>
<td>Simvastatin 20–40 mg‡</td>
<td>Lovastatin 20 mg</td>
</tr>
<tr>
<td></td>
<td>Pravastatin 40 80 mg</td>
<td>Fluvastatin 20–40 mg</td>
</tr>
<tr>
<td></td>
<td>Lovastatin 40 mg</td>
<td>Pitavastatin 1 mg</td>
</tr>
<tr>
<td></td>
<td>Fluvastatin XL 80 mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fluvastatin 40 mg bid</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pitavastatin 2–4 mg – remove PA required</td>
<td></td>
</tr>
</tbody>
</table>

‡Initiation of simvastatin 80 mg or titration to 80 mg is not recommended by the FDA due to the increased risk of myopathy,
including rhabdomyolysis.

Performance Indicator #7: Underutilization of Metformin. N=294
Criteria:
- Recipients >/= 18 years of age with type 2 diabetes without contraindications to
  metformin. Recipients who have been treated exclusively with insulins for the past year
  will be excluded AND
- Recipients who meet any of the following criteria: (1) history of an antidiabetic in the last
  90 days, but no history of metformin in the past year; (2) history of metformin therapy in
  the past year but no history of metformin therapy in the past 90 days; or (3) metformin
dose <1700 mg/day on the most recent claim.

Paragraph:
Potential Low Metformin Dose (DM Type 2): According to submitted pharmacy and medical claims, it appears your recipient has a history of type 2 diabetes and, although taking metformin, is not taking the recommended daily dose. Recipients should be titrated, as tolerated, to a dose of at least 850mg twice daily in order to realize the full benefits of metformin therapy. Please review your recipient's antidiabetic therapy and determine whether an increase in the dosage of metformin is clinically appropriate.

The DUR Board questioned the source of the 1700 mg/day minimum therapeutic threshold needed for metformin. The criteria will be changed < 1500 mg based on FDA labeling for adults which states “In general, clinically significant responses are not seen at doses below 1500 mg per day. However, a lower recommended starting dose and gradually increased dosage is advised to minimize gastrointestinal symptoms.”

Performance Indicator #8: Underutilization of Antiplatelet Therapy N=907
Criteria:
Recipients 18 years of age or older with a history of diabetes (submitted ICD-9 diagnosis code for diabetes or inferred from drug therapy) in the last 2 years who meet any of the following criteria:
- History of antiplatelet therapy in the last year, but no claim in the last 90 days.
- History of antiplatelet therapy in the last year with < 60 days of therapy in the last 90 days.
- History of CVD (diagnosis or procedure) in the last 2 years without antiplatelet therapy in the last 45 days.
- Males > 45 to 79 years or Females > 55 to 79 years of age and at least one risk factor (listed below) in the last year without antiplatelet therapy in the last 45 days.
  - Risk factors include: hypertension (diagnosis or inferred from drug therapy), hyperlipidemia (diagnosis or inferred from drug therapy), family history of CVD, albuminuria, or history of smoking.

The DUR Board recommended adding a statement to the prescriber letter as follow: Minnesota Medicaid benefits include annual dilated eye exams to screen for retinopathy and over-the-counter use of aspirin for use as an antiplatelet.

Nonadherence
Performance Indicator #9: Nonadherence with Maintenance Diabetes, Antihypertensive and Antilipemic Medications. N= 46 under 18 years; N=1,024 ≥ 18 years.
Criteria:
- Recipients with diabetes (submitted ICD-9/10 code for diabetes or inferred from drug therapy) in the last 2 years receiving chronic oral antidiabetic, antihypertensive, and/or antilipemic drug therapy who received less than a 60-day supply of the medication during a 90-day period.

The DUR Board approved as presented.

Duplicate Therapy
Performance Indicator #10: Duplicate Therapy with Diabetes Medications. N=2
Criteria:
- Recipients receiving sulfonylureas, thiazolidinediones, meglitinides, alpha-glucosidase inhibitors, DPP-4 inhibitors, GLP-1 agonists, or SGLT2 (sodium-glucose co-transporter 2 inhibitors which include canagliflozin (Invokana) and dapagliflozin (Farxiga) in the past 90 days who are receiving multiple sulfonylureas, or multiple thiazolidinediones or multiple meglitinides or multiple alpha-glucosidase inhibitors or multiple SGLT2 inhibitor or multiple DPP-4 inhibitors or multiple GLP-1 agonists in the past 60 days.

Larry Dent had proposed expanding criteria to include duplication of DPP4 antagonists and GLP1 agonists because both drugs’ primary function is on the same pathway. There were n=105 occurrences. DPP-4 inhibitors include sitagliptin (Januvia), saxagliptin (Onglyza), linagliptin (Tradjenta), and alogliptin (Nesina). GLP-1 (glucagon-like peptide-1) receptor agonists include exenatide (Byetta), exenatide XR (Bydureon), and liraglutide (Victoza).

The DUR Board approved adding duplication of DPP4 antagonists and GLP1 agonists.

Performance Indicator #11: Concomitant Use of Aliskiren and Angiotensin Modulating Agents in Diabetes. N=0
Criteria:
- Recipients with a history of diabetes (submitted ICD-9 diagnosis code for diabetes or inferred from drug therapy) in the last 2 years who are receiving >/= 7 days overlapping therapy with an aliskiren-containing product and an angiotensin-modulating containing product in the last 30 days.

DUR Board decided to remove as there were no occurrences.

Off-Label
Performance Indicator #12: Off-Label GLP-1 Receptor Agonist Use. N=5
Criteria:
- Recipients with a history of GLP-1 (glucagon-like peptide-1) receptor agonist use in the last 30 days. These drugs are also referred to as incretin mimetics. Drugs include exenatide (Byetta), exenatide XR (Bydureon), and liraglutide (Victoza) without a history of Type 2 diabetes (submitted ICD-9 diagnosis code for diabetes in the last 2 years or inferred therapy from oral antidiabetic therapy in the last year) or who are on insulin or pramlintide (Symlin) therapy with a history of type 1 diabetes in the last 2 years.

Paragraph:
GLP-1 agonist use with Type 1 Diabetes: According to submitted pharmacy and medical claims, it appears your recipient has received a GLP-1 agonist (Bydureon, Byetta, Victoza) and has a diagnosis of type 1 diabetes. Currently, GLP-1 agonists are only FDA-approved for the treatment of type 2 diabetes. Please review your recipient's medical record and, if appropriate, discontinue the GLP-1 agonist.

The two new GLP-1 agonists, dulaglutide (Trulicity), and albiglutide (Tanzeum), need to be added to the criteria and the prescriber paragraphs.

The DUR Board approved the criteria.
Performance Indicator #13: Metformin use in Pediatric Type 2 Diabetic Recipients. N= 3
Criteria:
- Recipients 10-17 years of age with a history of type 2 diabetes in the last 2 years who meet any of the following criteria:
  - History of an antidiabetic in the last 30 days, but no history of metformin in the past 2 years. Recipient with a history of renal/hepatic impairment, acidosis, heart failure or alcohol abuse are excluded.

Performance Indicator #14: SGLT2 Inhibitor or GLP-1 Agonist Use in Recipients < 18 Years of Age. N=0
Criteria:
- Recipients receiving SGLT2 (sodium-glucose linked transporter-2) Inhibitor or GLP-1 (glucagon-like peptide-1) Agonist therapy in the last 30 days who are less than 18 years of age.
DUR Board changed age criteria to be ≥ 18 years for the entire intervention. Therefore, #13 and #14 will not be included.

Overall recommendation for this intervention was to add the American Association of Clinical Endocrinologists (AACE) Clinical Practice Guidelines reference to prescriber letter.

Metabolic Monitoring of Children and Adolescents Receiving Antipsychotic Medications Proposal
This proposal is one of the biannual RetroDUR interventions specific to the use of antipsychotic drug in children and adolescents.
Criteria:
- Recipients less than 18 years of age with a SGA (second generation antipsychotic) prescription in the last 30 days without blood glucose monitoring within the last year and those without lipid monitoring within the last two years using the corresponding procedure billing codes listed below.

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Procedure Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>82947</td>
<td>Blood Glucose</td>
</tr>
<tr>
<td>83036</td>
<td>Glycosylated Hemoglobin (Hemoglobin A1c)</td>
</tr>
<tr>
<td>80047</td>
<td>Basic Metabolic Panel with Ionized Calcium</td>
</tr>
<tr>
<td>80048</td>
<td>Basic Metabolic Panel</td>
</tr>
<tr>
<td>80053</td>
<td>Comprehensive Metabolic Panel</td>
</tr>
<tr>
<td>80050</td>
<td>General Health Panel</td>
</tr>
<tr>
<td>80061</td>
<td>Lipid Panel</td>
</tr>
</tbody>
</table>

Table 3. Lack of monitoring when receiving antipsychotic medications.

<table>
<thead>
<tr>
<th>Increased Risk of ADE – AA MONITOR KIDS</th>
<th>2,344</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lack of SGA Antipsychotic Blood Glucose Monitoring within last year</td>
<td>1,134</td>
</tr>
<tr>
<td>Lack of SGA Antipsychotic Lipid Monitoring within last two years</td>
<td>1,210</td>
</tr>
</tbody>
</table>
Dr. Reinke discussed using HEDIS measures instead of the proposed Xerox criteria. California, for instance, sends HEDIS measure results in the prescriber communication. HEDIS includes age stratification of 1-5 years, 6-11 years, and 12-17 years. HEDIS criteria requirement is at least two antipsychotic prescriptions and at least one test for blood glucose or Hemoglobin A1c during the measurement year. Likewise, at least two antipsychotic prescriptions and at least one test for LDL-C or cholesterol during the measurement year.

DUR Board recommended using the proposed criteria rather than switching to HEDIS measures.

The proposed prescriber letter was discussed in great detail. The proposed first paragraph was revised to contain a strong message that it is no longer acceptable to rationalize not doing metabolic monitoring in children.

Prescriber letter first paragraph: “Because of significant concerns about the safety risks these medications pose to children so a monitoring plan should be in place before the child starts taking an antipsychotic.”

It was decided that it was acceptable to include the paragraph about specific measures including height, weight, and BMI; and guidelines’ monitoring recommendations, though, blood glucose and lipid monitoring are the criteria reported on.

Prescriber letter paragraph: “Regularly measure beneficiary height, weight, vital signs, and blood pressure, assess abnormal involuntary movements, and order appropriate laboratory testing (e.g., tests of liver function, measures of blood glucose levels, measures of lipid levels).”

The DUR Board recommended inclusion with the prescriber letter a table of the procedure billing codes used to determine if monitoring.

The second page of the prescriber letter included the following supporting information:

- The March 2015 report published by the Department of Health and Human Services Office of Inspector General stated that “lack of monitoring was the most commonly identified quality-of-care issue” among Medicaid-enrolled children with paid claims for second-generation antipsychotic medications.
- In 2015, the National Committee for Quality Assurance (NCQA) Healthcare Effectiveness Data and Information Set (HEDIS®) added three new measures focused on the safe and judicious use of antipsychotic medications in children and adolescents.9 One of these measures, “Metabolic Monitoring for Children and Adolescents on Antipsychotics (APM)” assesses the percentage assess the percentage of children and adolescents who have ongoing use of antipsychotic medications and had metabolic testing for both glucose/HbA1C and LDL-C/cholesterol during the measurement year.
- The AACAP practice parameters regarding the appropriate metabolic monitoring for the use of atypical antipsychotic medications in children and adolescents

The DUR Board approved as presented.

**2016 meeting dates will be:**

- May 11, 2016
- August 10, 2016
- November 2, 2016