



Minnesota Department of **Human Services**

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**Drug Utilization Review (DUR) Meeting**

November 5, 2014

**Members Present**

Matthew Beatty, PA-C, Pierre Rioux, M.D, Allyson Schlichte, Pharm.D., MBA, Abigail Stoddard, Pharm.D., MBA, and Ling Xu. Pharm.D.

**DHS Staff Present**

Mary Beth Reinke, Pharm.D., Sara Drake, RPh, and Joy Flugge, Pharm.D. student.

**Other attendants**

Larry Dent, Pharm.D.

**Public Comments:** None

**Approval of Minutes:** Yes

**Old Business:** Interventions on adherence to hypertension medications were sent to 1,459 providers for 3,600 patients. Letters were sent to 619 providers concerning 507 patients regarding the daily opioid dose threshold of 120 mg morphine equivalents which is going into effect on January 5, 2015.

**New Business:**

**RetroDUR- clinical criteria**

No new criteria were presented at this meeting.

**RetroDUR – population based interventions**

**Multiple Drug Therapy Regimen Review (Polypharmacy) Proposal**

Patients taking  $\geq 5$  medications are at risk for adverse drug events including drug-drug or drug-disease interactions, duplicate or unnecessary therapy, non-adherence, and hospitalization. The impact from interventions sent out in 2011 regarding this issue was estimated to result in over \$25,000 in medical savings and an estimated \$400,000 total savings.

**Polypharmacy**

Criteria:

The base criteria are recipients who received  $\geq 10$  medications (excluding antibiotics) within a 30-day time frame. This is further separated into a number of polypharmacy regimens in the table below.

<b>Identified Polypharmacy Regimens</b>	<b># Patients</b>
20 or More Medications* with:	
Opiates from 3 or more Prescribers and Pharmacies	0
3 or more Prescribers and Pharmacies	14
3 or More Prescribers	96
2 Prescribers	17
1 Prescriber	5
Total	132
15-19 Medications* with:	
Opiates from 3 or more Prescribers and Pharmacies	5
3 or More Prescribers and Pharmacies	40
3 or More Prescribers	293
2 Prescribers	56
1 Prescriber	33
Total	427
10-14 Medications* with:	
Opiates from 3 or more Prescribers and Pharmacies	26
3 or More Prescribers and Pharmacies	106
3 or More Prescribers	936
2 Prescribers	411
1 Prescriber	198
Total	1,677
≥ 10 Medications* with a history of cancer, HIV or chronic renal insufficiency/failure	694
<b>Total Patients</b>	<b>2,371</b>

\* Antibiotics are not counted.

All patients 18 years of age and older who have had 10 or more medications (excluding antibiotics) filled within the most recent 30 days of claims activity.

In 2011, the DUR Board elected to not include the criteria involving only 1 prescriber. This time the criteria were approved for the 1 prescriber for the 15-19 and ≥ 20 medications group. Recipients with HIV will continue to be excluded.

The DUR Board recommended including two items to the cover letter: (1) accessing patient profiles either through a Health Information request from the DHS MN-ITS website and/or from SureScript and (2) since all these recipients would qualify for payment under DHS Medication Therapy Management Services (MTMS), include coverage information about these services.

### **Medication Adherence Proposal**

Nearly one in four people are non-adherent to their prescribed medication regimens for the treatment of chronic conditions. Non-adherent patients are less likely to reach treatment goals and may have higher hospitalization and mortality rates. Good adherence to drug therapy leads to positive health outcomes. DUR criteria were presented from nine different therapeutic categories for chronic conditions: anticonvulsants (N=895), antidiabetic agents (N=410), antilipemics (N=514), antiplatelet agents (N=231), asthma drugs (N=717), antihypertensives (N=1,050), antidepressant agents (N=1,910), heart failure cardiovascular medications (N=120), and thyroid medications (N=293). This proposal will likely net a negative cost savings. However, overall health expenditures could decrease with fewer emergency room visits and hospitalizations.

### Non-adherence:

#### Criteria:

- Recipients who have received medications from one of the above nine categories for chronic conditions throughout the most recent 135 days of claims activity and who received less than 60 days of selected chronic medication in the last 90 day period of claims activity.
- Asthma drugs include inhaled corticosteroids, leukotriene antagonists, or theophylline.
- Patients receiving antidepressants also must have a diagnosis of depression.

The DUR Board discussed the following:

- This indicator is already included within each of disease-based population mailings that have been mailing on recently or will be mailing in the future such as hyperlipidemia, hypertension, and diabetes mellitus which eliminates the major categories proposed.
- Clarity is needed regarding the denominator of “throughout the most recent 135 days of claims activity”.
- Recipients who receive anticonvulsant agents may be receiving them for a reason other than a seizure disorder.
- Recipients receiving their medications through an autofill process or who otherwise fill but do not take their medications would not be captured by this intervention.
- Recipients who may have switched from one medication to the other in the same therapeutic category (e.g. anticonvulsant) would be flagged for intervention when actually non-adherence is not an issue.
- The inclusion of medication categories of HIV/AIDs and/or Hepatitis C could be considered.
- Many patients remain non-adherent despite interventions made from their primary care provider offices including phone calls that go unanswered and unreturned.

The Board proposed to consider changing the denominator in the criteria to “Recipients who have had therapy for (a chronic condition) in the past 45 days as well as 90 to 135 days ago, but less than 60 days of (this type of) therapy was filled in the past 90 days.” The Board ranked this invention the lowest out of the four presented. If considered again, explore the possibility of including oral oncology, immunosuppressants drugs, and drugs to treat Hepatitis C and HIV/AIDs diseases.

### **RetroDUR – population based interventions**

#### **Nonsteroidal Anti-Inflammatory Drugs: Drug Use Evaluation**

NSAIDs are one of the most commonly prescribed classes of drugs. Gastrointestinal (GI) problems are the most common side effects associated with NSAID use; such toxicities are a significant cause of morbidity and mortality in the U.S. and have a significant economic impact. COX-2-selective NSAIDs have also been associated with increased cardiovascular risk and can exacerbate heart failure (CHF).

## Increased Risk of Adverse Events

### 1. Increased Risk of ADE: NSAIDs and GI toxicity. N=465.

#### Criteria:

Recipients receiving a non-selective NSAID in the past 90 days for at least 35 days with any of the following risk factors:

- Concurrent warfarin use
- Concurrent steroid use
- Concurrent aspirin use (>81mg)
- History of a GI event (PUD or GI bleed diagnosis)
- Age > 60 years
- High dose NSAID (>75% maximum recommended daily dose)

The DUR Board recommended research and updating risk factors for NSAID-using patients and GI toxicity. Possible inclusions may be other antiplatelets and novel oral anticoagulants (NOACs) such as rivaroxaban (Xarelto). Because of the recent increased awareness, research interaction between SSRIs and NSAIDs and if significant add to proposal (level 1).

### 2. Use of COX-2 Inhibitors in the Absence of Risk Factors for GI Toxicity. N=12.

#### Criteria:

Recipients without any of the risk factors listed in indicator #1 and without inferred rheumatoid arthritis and/or therapeutic failure of a non-selective NSAID product.

DUR Board did not approve due to the low number of recipients and that a PA process is already in place for COX-2 Inhibitors such as Celebrex.

### 3. Increased Risk of ADE: NSAID Use and Recent Myocardial Infarction. N=1.

#### Criteria:

Recipients with an MI within the past 6 months who have prescription claims for an NSAID in the past 45 days.

DUR Board approved as presented.

### 4. Increased Risk of ADE: NSAID and Bisphosphonate. N=3.

Patients at taking an NSAID and bisphosphonate are at increased risk of GI erosion.

#### Criteria:

Recipients receiving an NSAID or COX-2 inhibitor and a concurrent bisphosphonate within the past 45 days and not already on a proton pump inhibitor or misoprostol.

DUR Board approved as presented

### 5. Increased Risk of ADE: NSAID-Induced GI Toxicity in Patients with Tobacco or Alcohol Use. N=1,335.

#### Criteria:

Recipients receiving an NSAID or COX-2 inhibitor within the past 45 days with a history of tobacco or alcohol abuse in the last 180 days. Such history is inferred by a medical diagnosis or drug therapy with the following medications: nicotine replacement therapy, bupropion (Zyban®), varenicline, acamprosate, disulfiram, or naltrexone.

DUR Board wants to exclude non-legend NSAID prescriptions and pharmacy NPI numbers in order to prevent letters being sent to pharmacists that prescribe an OTC product. Additionally, OTCs are dispensed in original containers which lead to the “days supply” being larger.

The DUR Board would also want to include in the criteria that recipients have had  $\geq 2$  fills in the last 135 days to target those on chronic therapy.

The DUR Board also expressed concern with this criterion in that there few remaining options for this population given (1) acetaminophen and acetaminophen-containing drugs should be used concomitantly with caution and (2) controlled substances should not be taken with alcohol.

#### Therapeutic Duplication

6. Concurrent Use of  $>1$  NSAID. N=21.

Recipients receiving an NSAID product within the past 45 days who also received at least one NSAID product concurrently.

DUR Board approved as presented.

#### Drug-Disease Interaction and Increased Risk of Adverse Events

7. NSAID Use in Patients with Cardiovascular Risk. N=189.

Criteria:

Recipients with a documented or inferred history of cardiovascular disease who also received a NSAID or COX-2 inhibitor for more than 90 days in the last 150 days. Assessment of CVD includes patients with more than two prescriptions for nitroglycerin or pentoxifylline in the last 180 days or documentation of:

- Diabetes
- Hyperlipidemia
- Arthrosclerosis
- MI
- Peripheral vascular disease
- Cerebral atherosclerosis
- Angioplasty
- Stent placement
- CABG or
- Artherectomy.

DUR Board approved as presented.

8. NSAID Use in Patients with Congestive Heart Failure (CHF.) N=14.

Criteria:

Recipients who have received a NSAID or COX-2 inhibitor in the last 45 days and have a history of CHF in the last 730 days.

DUR Board approved with the suggestion to combine with Performance Indicators 9, 10 and 11 in order to prevent repeat letters of intervention for patients who may qualify for more than one Indicator.

9. NSAID Use in Patients with Congestive Heart Failure (CHF) Hospitalization. N=0.

Criteria:

Recipients who have received a NSAID or COX-2 inhibitor in the last 45 days with a history of CHF in the last 730 days and a hospitalization or emergency room visit with a primary diagnosis of congestive heart failure in the last 365 days.

DUR Board approved but combine indicators 9, 10, and 11.

10. NSAID Use in Patients with CHF and Hypertension (HTN.) N=50.

Criteria:

Recipients who have received a NSAID or COX-2 inhibitor in the last 45 days and have a history of both CHF and HTN in the last 730 days.

DUR Board approved but combine indicators 9,10, and 11.

11. NSAID Use in Patients with CHF and Renal Impairment. N=14.

Criteria:

Recipients who have received a NSAID or COX-2 inhibitor in the last 45 days and have a history of both CHF in the last 730 days and renal impairment in the last 365 days.

DUR Board recommended adding renal impairment/renal disease with NSAIDs as its own indicator.

### **RetroDUR – population based interventions**

#### **Anticonvulsant Drug Use Evaluation**

Anticonvulsant medications are among the most commonly prescribed classes of medications.

This class is not only prescribed for recipients for seizure control, but also other approved indications such as bipolar disorder. Unfortunately, off-label use that lacks approval or evidence is also very common. This class of medications is associated with risks for drug-drug and drug-disease interactions as well as other potential toxicities. All of these variables have an impact on the cost/benefit ratio of the use of these medications.

#### Drug-Drug Interactions

1. Potential Level 1 Drug-Drug Interactions (DDI) Involving Anticonvulsants. N=21.

Criteria:

Recipients who have received an anticonvulsant drug during the most recent 45 days and who also received an interacting drug for at least 7 of the 45 days.

Anticonvulsants and their interacting drugs are found below:

<b>ANTICONVULSANT</b>	<b>INTERACTING DRUG(S)</b>
Carbamazepine, Clobazam, Eslicarbazepine, Felbamate, Oxcarbazepine, Phenytoin, Phenobarbital, Primidone, Rufinamide (Banzel®), Topiramate (Topamax,	Oral Contraceptives: Biphasic, triphasic and progestin only. Etonogestrel implant.

<b>ANTICONVULSANT</b>	<b>INTERACTING DRUG(S)</b>
Qudexy XR®, Trokendi XR®)	Etonogestrel-Ethinyl estradiol vaginal ring
Carbamazepine, Phenytoin, Phenobarbital, Primidone	Darunavir, Delavirdine, Etravirine
Carbamazepine, Phenobarbital, Primidone	Voriconazole
Clonazepam, Diazepam rectal, Phenobarbital, Primidone	Sodium Oxybate
Carbamazepine	Monoamine oxidase inhibitors (antidepressant and antiparkinson agents), Linezolid
Phenytoin	Disopyramide, Nefazodone

DUR Board recommended including in the cover letter that the above anticonvulsant medications can decrease efficacy of the above oral contraceptives.

Increased Risk of Adverse Events (IAE)

2. IAE with Use of Anticonvulsant. N=234.

Criteria:

Recipients who have received an anticonvulsant drug during the most recent 45 days and who also have a history of a contraindicated medical condition.

Anticonvulsant and their contraindicated medical conditions are found below:

<b>ANTICONVULSANT</b>	<b>MEDICAL CONTRAINDICATION</b>
Lamotrigine	Erythema Multiforme
Carbamazepine, Felbamate	Aplastic Anemia or Agranulocytosis
Valproic Acid Analogs	Pancreatitis, Urea Cycle Disorders
Phenobarbital, Primidone	Porphyria, Sleep Apnea, Asthma (Chronic Airway Obstruction), Obstructive Bronchitis, Apnea, or Dyspnea
Clonazepam, Valproic Acid Analogs, Felbamate	Liver Impairment
Phenytoin, Carbamazepine	Cardiac conduction Disorder
Carbamazepine, Clonazepam, Lamotrigine, Phenobarbital, Phenytoin, Primidone, Valproic Acid Analogs	Pregnancy

DUR Board approved as written.

Off-Label Use

3. Use of Anticonvulsant Therapy for Unproven Off-Label. N=1911.

Criteria:

Recipients who have received an anticonvulsant drug during the most recent 45 days with no diagnosis for an established use of the identified anticonvulsant in the past two years.

Established indications for anticonvulsants are found below:

ANTICONVULSANT	ESTABLISHED INDICATIONS
Clobazam, Eslicarbamazepine (Aptiom®), Ezogabine (Potiga®), Ethosuximide, Ethotoin, Felbamate, Levetiracetam (Keppra®), Lacosamide (Vimpat®), Methsuximide, Perampanel (Fycompa®), Phenytoin, Primidone, Rufinamide (Banzel®), Tiagabine (Gabitril®), Zonisamide, Vigabatrin (Sabril)	Convulsions/Seizure Disorders
Carbamazepine, Oxcarbazepine	Convulsions/Seizure Disorders, Bipolar Disorder, Trigeminal Neuralgia, Neuropathic Pain, Aggressive/Disruptive Behaviors
Valproic Acid Analogs	Convulsions/Seizure Disorders, Bipolar Disorder, Migraine, Aggressive/Disruptive Behaviors
Gabapentin	Convulsions/Seizure Disorders, Neuropathic Pain, Migraine, Vasomotor Symptoms of Menopause, Fibromyalgia, Restless Legs Syndrome
Pregabalin (Lyrica®)	Convulsions/Seizure Disorders, Neuropathic Pain, Fibromyalgia
Lamotrigine	Convulsions/Seizure Disorders, Bipolar Disorder
Topiramate	Convulsions/Seizure Disorders, Migraine
Phenobarbital	Convulsions/Seizure Disorders, Insomnia
Mephobarbital	Convulsions/Seizure Disorders, Generalized Anxiety



The DUR Board did not accept these criteria.

Drug-Drug Interactions

4. Concomitant Use of Chemically and/or Pharmacologically Related Anticonvulsants. N=17.

Criteria:

All recipients receiving two closely-related drugs for at least seven out of the last 45 days.

Related Anticonvulsants are found below:

ANTICONVULSANT	RELATED ANTICONVULSANT
Phenobarbital	Primidone
Carbamazepine	Oxcarbazepine, Eslicarbamazepine
Gabapentin	Pregabalin

DUR Board approved as written.

Toxicity

5. Monitoring for Potential Anticonvulsant Toxicity. N=1,153.

Criteria:

All recipients receiving carbamazepine or a valproic acid analog during the most recent 45-days period of claims with no documented hepatic monitoring (carbamazepine or valproic acid analog) or platelet count (valproic acid analog) in the past 365 days.

DUR Board discussed three concerns (1) the reliability of finding lab test billing within medical claims (2) recipients in fee-for-service care may have had lab tests while in managed care but these tests would be counted/included in this FFS intervention and (3) lab tests may not be performed by providers because of the patient out-of-pocket costs.

Out of the four interventions presented, polypharmacy and NSAID were approved.

The proposed RetroDUR intervention mailing order is:

February 2015: Diabetes Mellitus Disease Management

April 2015: Exceeding 120 mg MED opioid analgesics II using an accumulation edit if receiving from multiple opioid formulations and prescriptions

August 2015: Hyperlipidemia Management

**2015 meeting dates will be:**

- March 11, 2015
- May 13, 2015
- August 12, 2015
- November 4, 2015