Kansas Drug Utilization Review Newsletter

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Welcome to the summer 2012 edition of the "Kansas Drug Utilization Review Newsletter," published by Health Information Designs, LLC (HID). This newsletter is part of a continuing effort to keep the Medicaid provider community informed of important changes in the Kansas Medical Assistance Program (KMAP).

Helpful Web Sites	Helpful Numbers		In This Issue
KMAP Web Site https://www.kmap-state-ks.us/ **KDHE-DHCF Web Site** http://www.kdheks.gov/hcf/	**KMAP PA Help Desk** 1-800-285-4978 **Xerox PA Help Desk** 1-877-475-7567 **Xerox PA Fax** 1-866-246-8512	**Provider Customer Service** 1-800-933-6593 **Beneficiary Customer Service** 1-800-766-9012 **Pharmacy Help Desk** 1-866-405-5200	KMAP Antipsychotics Utilization Antipsychotics Polypharmacy Preferred Drug List

KMAP Antipsychotics Utilization

From January through December 2011, 138,896 claims were dispensed for antipsychotic agents for the Kansas Medical Assistance Program (KMAP) fee-for-service (FFS) population. Those claims represent 14,757 beneficiaries who received at least one claim in 2011 for an antipsychotic agent.

Out of the 14,757 beneficiaries receiving an antipsychotic agent, 1,678 beneficiaries received at least 2 different antipsychotic agents concurrently for more than 90 days. It is typically recommended that cross-titration between antipsychotic agents be finished in 8 weeks or less; the concurrent use for more than 90 days likely represents longer-term polypharmacy. There were 197 beneficiaries who received 4 different antipsychotic medications concurrently for at least 90 days. Since these beneficiaries are taking multiple antipsychotic agents at the same time they are at an increased risk for negative outcomes, including increased risk for adverse drug reactions.

The table below shows the number of beneficiaries, by age, taking 2 or more different antipsychotic agents concurrently for longer than 90 days. This data excludes duplication of the same ingredient. For example, if a beneficiary was taking Seroquel® and Seroquel XR® or Zyprexa® and Zyprexa Zydis®, those claims would not be counted as different therapies because they contain the same ingredients.

Beneficiary Age as of 12/31/11	Number of Unique Beneficiaries		
	Receiving 2 Antipsychotics	Receiving 3 Antipsychotics	Receiving 4 Antipsychotics
≤ 4 years	2	0	0
5 to 9 years	54	13	10
10 to 14 years	142	48	23
15 to 19 years	192	55	26
20 to 24 years	115	35	22
25 to 29 years	78	27	23
30 to 39 years	130	46	21
40 to 49 years	146	54	29
50 to 59 years	193	53	30
60 to 69 years	63	26	12
70 to 79 years	6	2	1
80 to 82 years	1	0	0
Totals	***1,122***	***359***	***197***

Antipsychotics Polypharmacy

Even with the limited data available to support the concurrent use of multiple antipsychotic agents for an extended period of time, this practice is commonly seen. Antipsychotic polypharmacy has multiple drawbacks, including the following:

- Higher mortality
- Increased risk for drug interactions and adverse drug reactions
- Decreased medication adherence
- Greater costs

Common Reasons for Antipsychotic Polypharmacy

The following table describes the most common reasons for antipsychotic polypharmacy and provides recommendations regarding use and administration.

Reason	Use and Administration Recommendations
Switching between antipsychotic agents	When switching from one antipsychotic agent to another, it is often recommended to cross-titrate over several weeks. During cross-titration, patients receive both antipsychotic medications. Cross-titration should typically be completed within 8 weeks.
Interrupted cross-titration	Cross-titration is often interrupted because a patient appears better while taking both medications. It is likely that the second agent alone may explain the improvement and the patient should continue to titrate off of the first agent. Once the process of switching agents has been initiated, it should be completed.
Failure of antipsychotic monotherapy	The effectiveness of an antipsychotic medication can only be determined if the patient has had an adequate dose and trial duration. Before concluding that antipsychotic monotherapy “will not work” in a patient, the patient should have received adequate trials of at least three antipsychotic agents for at least six weeks each. Studies indicate that clinicians often go to antipsychotic polypharmacy without trying an adequate number of different agents at adequate doses.
Different mechanisms of action	From an efficacy perspective there is currently no rationale for combining multiple antipsychotic agents. The only mechanism of action directly linked to antipsychotic efficacy is the effect on the dopamine D-2 receptor. All antipsychotic agents have an effect on the D-2 receptor but vary in other pharmacological properties. The relationship between other pharmacological properties and side-effects is well understood; however, their relevancy to efficacy is unknown.
To enhance the effect or increase the speed of response	Little evidence is available to support the thought that combining antipsychotic agents achieves a faster response or is more efficacious than the use of single agents. With the exception of some data suggesting there is a benefit of adding a second agent to clozapine in some populations, the use of multiple agents does not increase efficacy.
To reduce the side-effects of a single agent	Data from clinical trials to evaluate the benefit of antipsychotic combinations yield mixed results, but generally suggest that the addition of a second antipsychotic agent rarely reduces side-effects or allows a dose reduction of the first agent.
Different route of administration	Transition to appropriate monotherapy is the preferred option, but targeted use of two antipsychotics with different routes of administration may occasionally be appropriate. However, its use should generally be limited in duration.
To treat comorbid conditions	A frequent justification for use of multiple antipsychotic agents is that one of the agents is being utilized for its antipsychotic effect and the second agent is targeting a comorbid condition such as insomnia or agitation. The use of a non-antipsychotic agent for the comorbid condition is recommended, for example, the use of a benzodiazepine for agitation. Typically the non-antipsychotic agent is more targeted, has fewer side effects, and is less costly.

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Preferred Drug List

Below is a list of current preferred agents. A complete list of both preferred and non-preferred agents may be found on the KDHE-DHCF Web site. The Preferred Drug List may be updated at any time; please visit the KDHE-DHCF Web site for the most recent version.
http://www.kdheks.gov/hcf/pharmacy/pharmacy_druglist.html

Analgesics

Long-Acting Opioids
Morphine Sulfate ER
-Generics Only
OxyContin® (oxycodone SR)

Muscle Relaxants (Skeletal)
Flexeril 10mg® (cyclobenzaprine)
Parafon Forte DSC® (chlorzoxazone)
Robaxin® (methocarbamol)
Robaxin-750® (methocarbamol)
Robaxisal® (methocarbamol/aspirin)

Muscle Relaxants (Spasticity)
Lioresal® (baclofen)
Zanaflex® (tizanidine)
-Tablets Only

Oral NSAIDs
Aleve® (naproxen)
Anaprox® (naproxen sodium)
Anaprox DS® (naproxen sodium)
Ansaid® (flurbiprofen)
Arthrotec® (diclofenac/misoprostol)
Cataflam® (diclofenac potassium)
Clinoril® (sulindac)
Daypro® (oxaprozin)
Feldene® (piroxicam)
-Brand Name Only
Indocin® (indomethacin)
Lodine® (etodolac)
Meclomen® (meclofenamate)
Mobic® (meloxicam)
Motrin® (ibuprofen)
Nalfon® (fenoprofen)
Naprelan® (naproxen sodium)
Orudis® (ketoprofen)
Ponstel® (mefenamic acid)
Toradol® (ketorolac)
-Limit 5 Day Supply
Tolectin 600® (tolmetin)
Voltaren® (diclofenac sodium)
Voltaren XR® (diclofenac sodium)

Ophthalmic NSAIDs
Acular® (ketorolac)
Acular LS® (ketorolac)
Acuvail® (ketorolac)
Ocufen® (flurbiprofen)
Voltaren® (diclofenac)

Triptans
Amerge® (naratriptan)
Imitrex® (sumatriptan)
-including all generic dosage forms
Relpax® (eletriptan)

Topical NSAIDs
Voltaren® (diclofenac sodium, topical)

Antihyperlipidemics

Bile Acid Sequestrants
Colestid® (colestipol)
Prevalite® (cholestyramine)
Questran® (cholestyramine)
Questran Light® (cholestyramine)

Fibric Acid Derivatives
Fenofibrate
-Generics Only
Lopid® (gemfibrozil)
TriCor® (fenofibrate)
Triglide® (fenofibrate)
Trilipix® (fenofibric acid)

Statins
Lipitor® (atorvastatin)
Zocor® (Simvastatin)

Anti-Infectives

Anti-Herpes Virus Agents
Valtrex® (valacyclovir)
Zovirax® (acyclovir)
-Oral Dosage Forms Only

Asthma, Allergy & COPD Agents

Inhaled Corticosteroids
Asmanex® (mometasone)
Flovent Diskus® (fluticasone)
Flovent HFA® (fluticasone)
Pulmicort Respules® (budesonide)
-6 & Under Only
QVAR® (beclomethasone)

Inhaled Long Acting Inhaled Beta$_2$ Agonists
Foradil® (formoterol)
Serevent® (salmeterol)

Inhaled Short Acting Inhaled Beta$_2$ Agonists
ProAir HFA® (albuterol)
Proventil® (albuterol)
Ventolin® (albuterol)
Ventolin HFA® (albuterol)

Inhaled Long Acting Inhaled Beta$_2$ Agonists/Corticosteroid Combos
Advair® (fluticasone/salmeterol)
Advair HFA® (fluticasone/salmeterol)
Dulera® (formoterol/mometasone)
Symbicort® (budesonide/formoterol)

Intranasal Antihistamines
Astelin® (azelastine)

Intranasal Corticosteroids
Flonase® (fluticasone)
Nasonex® (mometasone)
Veramyst® (fluticasone)

Non-Sedating Antihistamines
Claritin® (loratadine)
Zyrtec® (cetirizine)

Ophthalmic Antihistamine/Mast Cell Stabilizer Combos
Alaway® (ketotifen)
Refresh® (ketotifen)
Zaditor® (ketotifen)

Biologic Agents

Adult Rheumatoid Arthritis
*Clinical PA may be required
Enbrel® (etanercept)
Humira® (adalimumab)

Ankylosing Spondylitis
*Clinical PA may be required
Enbrel® (etanercept)
Humira® (adalimumab)

Crohn's Disease
*Clinical PA may be required
Humira® (adalimumab)
Remicade® (infliximab)

Juvenile Idiopathic Arthritis
*Clinical PA may be required
Enbrel® (etanercept)
Humira® (adalimumab)

Plaque Psoriasis
*Clinical PA may be required
Enbrel® (etanercept)
Humira® (adalimumab)

Psoriatic Arthritis
*Clinical PA may be required
Enbrel® (etanercept)
Humira® (adalimumab)
Remicade® (infliximab)

Ulcerative Colitis
*Clinical PA may be required
Remicade® (infliximab)

Cardiovascular Agents

ACE Inhibitors
Accupril® (quinapril)
Capoten® (captopril)
Lotensin® (benazepril)
Monopril® (fosinopril)
Prinivil® (lisinopril)
Vasotec® (enalapril)
Zestril® (lisinopril)

Cardiovascular Agents

ACE Inhibitor/CCB Combos
Lotrel® (benazepril/amlodipine)

ARBs
Cozaar® (losartan/HCTZ)
Diovan® (valsartan)
Diovan HCT® (valsartan/HCTZ)
Hyzaar® (losartan)
Micardis® (telmisartan)
Micardis HCT® (telmisartan/HCTZ)

ARB/CCB Combos
Azor® (amlodipine/olmesartan)
Exforge® (amlodipine/valsartan)

Beta-Blockers
Betapace® (sotalol)
Betapace AF® (sotalol AF)
Blocadren® (timolol)
Corgard® (nadolol)
Coreg® (carvedilol)
Coreg CR® (carvedilol CR)
Inderal® (propranolol)
InnoPran XL® (propranolol XL)
Kerlone® (betaxolol)
Lopressor® (metoprolol tartrate)
Propranolol Intensol® (propranolol)
Sectral® (acebutolol)
Tenormin® (atenolol)
Toprol XL® (metoprolol succinate)
Visken® (pindolol)

CCBs (Dihydropyridines)
Adalat CC® (nifedipine ER)
Cardene® (nicardipine IR)
DynaCirc® (isradipine IR)
DynaCirc CR® (isradipine CR)
Norvasc® (amlodipine)
Procardia XL® (nifedipine ER)

CCBs (Non-Dihydropyridines)
Calan® (verapamil IR)
Calan SR® (verapamil SR)
Cardizem® (diltiazem IR)
Covera HS® (verapamil ER)
-Brand Name Only
Diltia XT® (diltiazem SR)
-& AB Rated Generics
Isoptin SR® (verapamil SR)
Tiazac® (diltiazem)
-& AB Rated Generics
Verelan® (verapamil SR)

Central Nervous System

Adjunct Antiepileptics
Keppra® (levetiracetam)
Lyrica® (pregabalin)
Neurontin® (gabapentin)
Zonegran® (zonisamide)

Non-Benzo Sedative Hypnotics
Zolpidem
-Generics Only

Novel Sleep Agents
Rozerem® (ramelteon)

Diabetic Agents

Alphaglucosidase Inhibitors
Glyset® (miglitol)

Biguanides
Glucophage® (metformin)
Metformin ER
-Generics Only

DPP-4 Inhibitors
Januvia® (sitagliptan)
Onglyza® (saxagliptan)
Tradjenta® (linagliptan)

Incretin Mimetics
Byetta® (exenatide)

Long-Acting Insulins
Lantus® (insulin glargine)
-Vials Only

Diabetic Agents

Insulin (Delivery Systems)
All Multi-dose vials
Novolog FlexPen® (insulin aspart)
-Pens and Vials
Novolog Mix FlexPen® (insulin aspart protamine/insulin aspart)
-Pens and Vials

Meglitinides
Starlix® (nateglinide)

2nd Generation Sulfonylureas
Amaryl® (glimepiride)
DiaBeta® (glyburide)
Glucotrol® (glipizide)
Glucotrol XL® (glipizide XL)
Glucovance® (glyburide/metformin)
Glynase PresTab® (glyburide micronized)
Micronase® (glyburide)

Thiazolidinediones
Actos® (pioglitazone)
Avandamet® (rosiglitazone/metformin)
Avandaryl® (rosiglitazone/glimepiride)
Avandia® (rosiglitazone)

Gastrointestinal Agents

H_2 Antagonists
Pepcid® (famotidine)
Zantac® (ranitidine)
Zantac EFFERdose® (ranitidine)

Pancreatic Enzyme Replacements
Creon® (pancrelipase)
Zenpep® (pancrelipase)

Proton Pump Inhibitors
Prevacid® (lansoprazole)
Prevacid SoluTab® (lansoprazole)
Prilosec® (omeprazole)
Protonix® (pantoprazole)

Serotonin 5HT3 Antagonists
Zofran® (ondansetron)
Zofran ODT® (ondansetron)

Gout Agents

Xanthine Oxidase Inhibitors
Zyloprim® (allopurinol)

Injectables

Erythropoiesis Stimulating Agents
Epogen® (epoetin alfa)
Procrit® (epoetin alfa)

Growth Hormones
*Clinical PA is required for all agents
Genotropin® (somatropin)
Genotropin MiniQuick® (somatropin)
Omnitrope® (somatropin)
Saizen® (somatropin)
Tev-Tropin® (somatropin)

Ophthalmic Agents

Ophthalmic Prostaglandin Analogs
Travatan® (travoprost)
Travatan Z® (travoprost)
Xalatan® (latanoprost)

Osteoporosis Agents

Bisphosphonates
Fosamax® (alendronate)
Fosamax Plus D® (alendronate/cholecalciferol)

Urologic Agents

Anticholinergics
Detrol® (tolterodine)
Detrol LA® (tolterodine LA)
Ditropan® (oxybutynin)
Toviaz® (fesoterodine)
Vesicare® (solifenacin)

Antipsychotics Polypharmacy

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The practice of long-term concurrent use of multiple antipsychotic agents is discouraged due to the lack of evidence demonstrating the safety and efficacy. Better proven treatment strategies should be utilized before a trial of antipsychotic polypharmacy is initiated.

If a combination of antipsychotic agents is being used, its efficacy should be monitored on an ongoing basis. Based on recent data, it may be appropriate to convert patients treated with two antipsychotic agents to monotherapy, and those patients may even show improvements in adverse effects such as weight gain. Thus, conversion to monotherapy should be considered.

References:

Essock SM, Schooler NR, Stroup TS, et al. Effectiveness of Switching from Antipsychotic Polypharmacy to monotherapy. *Am. J. Psychiatry,* 2011;168:702-708

Tandon R. Antipsychotic Polypharmacy: Update and Guidelines for Practice. *USF Medicaid Drug Therapy Management Program for Behavioral Health,* 2012. Accessed July 25, 2012 at http://medicaidmentalhealth.org/files/Guidelines/Antipsychotic%20Polypharmacy%20Update%20and%20Guidelines%20for%20Practice2012011708263376.pdf

Tsutsumi C, Uchida H, Suzuki T, et al. The Evolution of Antipsychotic Switch and Polypharmacy in Natural Practice—A Longitudinal Perspective. *Schizophr. Res*. 2011;130:40-46.

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