

UPDATE ON CONCOMITANT USE OF BENZODIAZEPINES AND OPIOIDS

BACKGROUND

The Centers for Disease Control (CDC) Guidelines for Prescribing Opioids for Chronic Pain¹ were reviewed at the April 2016 DUR Board meeting. One of the CDC guideline recommendations was that *providers should avoid prescribing opioid pain medication for patients receiving benzodiazepines whenever possible*. At this meeting, the DUR Board recommended the following actions be taken by the Division of Medicaid (DOM):

- a. Concomitant use of opioids and benzodiazepines should require a manual prior authorization (PA).
- b. MS-DUR should provide an educational mailing to providers prescribing concurrent use of benzodiazepines and opioids regarding the increased safety risks and highlight the CDC recommendation to avoid concomitant use.

On August 31, 2016, the Food and Drug Administration (FDA) announced that after extensive review of the latest scientific evidence, class-wide changes to drug labeling are required. These changes include the new Boxed Warnings and revisions to the Warnings and Precautions, Drug Interactions, and Patient Counseling information sections of the labeling.² This information should help inform health care providers and patients of the serious risks associated with the combined use of certain opioid medications and benzodiazepines.

WARNING: RISKS FROM CONCOMITANT USE WITH OPIOIDS

Concomitant use of benzodiazepines and opioids may result in profound sedation, respiratory depression, coma, and death [see *Warnings and Precautions (5.1)*, *Drug Interactions (7.X)*].

- Reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate.
- Limit dosages and durations to the minimum required.
- Follow patients for signs and symptoms of respiratory depression and sedation.

DOM is in the process of implementing an electronic PA edit to prevent concomitant use of these products without a manual PA. This report provides an update on current concomitant use of benzodiazepines and opioids in the Mississippi Medicaid population. These results will serve as a benchmark for evaluating the impact of implementing the two recommendations above.

METHODS

A retrospective analysis was conducted using DOM's pharmacy claims for all programs (fee-for-service (FFS) and coordinated care organizations (CCOs)) for the period January 1, 2016 through July 31, 2016. All claims for benzodiazepines or opioids were identified. Beneficiaries were classified as on therapy for each product for the periods defined by each date of a prescription fill plus the days supply indicated on

¹ CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016.

<http://www.cdc.gov/media/modules/dpk/2016/dpk-pod/rr6501e1er-ebook.pdf>

² FDA New Release, August 31, 2016.

<http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm518697.htm>

the prescription claim. Beneficiaries were considered to be taking both medications at the same time if their days of coverage for benzodiazepines and opioids overlapped.

RESULTS

As shown in Table 1, 11,884 beneficiaries filled prescriptions for opioids and benzodiazepines during this period.

- Of these beneficiaries, 9,781 (10.8%) were classified as taking both medications concomitantly.

Table 1: Number of Beneficiaries Filling Opioid and Benzodiazepine Prescriptions <i>(January - July, 2016 -- FFS and CCOs)</i>			
		Filled Benzodiazepine Rx	
		No	Yes
Filled Opioid Rx	No	0	7,330 (8.1%)
	Yes	71,370 (78.8%)	11,884 (13.1%)
Concomitant Use		9,781 (10.8%)	

The characteristics of beneficiaries with concomitant use of benzodiazepines and opioids are shown in Table 2.

- Almost all of these beneficiaries were ages 18 – 64 years and were not in long-term care facilities.
- More than two-thirds of these beneficiaries were female.
- More than half of beneficiaries with concomitant use were being treated with both benzodiazepines and opioids for more than 31 days.

Table 2: Characteristics of Beneficiaries With Concomitant Use of Benzodiazepine and Opioid <i>(January - July, 2016 -- FFS and CCOs)</i>			
		Beneficiaries With Concomitant Use of Benzodiazepine and Opioid	
		Number	Percent
Total unique beneficiaries		9,781	100.0%
Age*	Missing	3	0.0%
	5 or less	32	0.3%
	6 - 11	57	0.6%
	12 - 17	130	1.3%
	18 - 44	4,783	48.9%
	45 - 64	4,712	48.2%
	65+	64	0.7%
Pharmacy Coverage Plan	100 - Regular Adults	9,234	94.4%
	200 - Long Term Care	210	2.2%
	400 - EPSDT (children)	317	3.2%
	901 - Dual - LTC Facility	19	0.2%
	700 - K-Baby	1	0.0%
Gender	Female	7,488	76.6%
	Male	2,290	23.4%
Number of Days on Continuous Benzodiazepine Therapy**	1 - 7 days	1,714	17.5%
	8 - 15 days	1,068	10.9%
	16 - 31 days	1,762	18.0%
	32 - 62 days	1,513	15.5%
	63-93 days	1,140	11.7%
	94 - 186 days	2,215	22.6%
	187 or more days	369	3.8%

* Age at end of July, 2016.

** Continuous therapy was calculated as date of first fill to date of last fill plus days supply for last fill, allowing for a 15 day refill gap.

Concomitant use of two products involves two prescriptions that may not always be written by the same prescriber. The prescriber of the second product has the best opportunity to detect and avoid concomitant use, due to the availability of patient-specific medication use information when accessing the Mississippi Prescription Drug Monitoring Program (MS PMP). Table 3 denotes the provider types associated with the second product prescribed resulting in concomitant use of benzodiazepines and opioids, as well as the number of beneficiaries and the number of discrete concomitant events associated with each provider type.

Table 3: Type of Prescribers for Second Prescriptions Resulting In Discrete Events* of Benzodiazepine and Opioid Use

(January - July, 2016 -- FFS and CCOs)

Provider Type	Number of Providers	Distinct Beneficiaries		Total Discrete Concomitant Events*	Last Drug Filled for Discrete Events	
		Average Per Provider	Total		Benzo	Opioid
		DDO-Dentist	192		2.35	452
HOSP-Psych	1	8.00	8	11	11	0
MD-Addiction	5	2.50	18	22	17	5
MD-Anesth	20	4.80	96	125	60	65
MD-Card	32	2.78	89	149	138	11
MD-EM	174	3.24	563	766	575	191
MD-FP/GP	498	10.06	4,918	8,156	7,358	798
MD-Gastro	15	5.07	76	120	104	16
MD-Hem/Onc	59	3.44	203	354	288	66
MD-Hospit	27	4.81	130	220	198	22
MD-ID	4	1.00	4	5	3	2
MD-IM	240	7.02	1,684	2,808	2,559	249
MD-Nephr	10	3.30	33	55	49	6
MD-Neur	70	7.06	494	795	656	139
MD-OB/GYN	102	2.95	301	454	379	75
MD-Ortho	71	2.24	159	180	81	99
MD-Pain	41	9.29	381	488	229	259
MD-Ped	55	3.84	211	324	281	43
MD-Psych	99	10.82	1,071	1,746	1,725	21
MD-Rad	10	2.20	22	31	24	7
MD-Rheum	7	2.29	16	23	20	3
MD-Sleep	5	1.40	7	12	12	0
MD-Surg	74	1.58	117	153	92	61
MD-Urol	16	2.25	36	51	33	18
NP	657	4.67	3,495	5,303	4,377	926
NP-Mental	61	13.20	805	1,323	1,323	0
Other	215	4.11	744	1,292	1,074	218
PA	45	5.87	315	487	416	71

* Discrete events were identified as each unique event of concomitant use involving the same prescribers and drugs.

Discrete events were identified as each unique period of concomitant use involving the same prescribers and drug products. A total of 26,099 discrete events of concomitant use were identified.

Table 4 shows the drug combinations for the discrete concomitant events that occurred during this time period. Combinations of acetaminophen-hydrocodone with various benzodiazepines were the most common; with acetaminophen-alprazolam accounting for almost one-third of distinct events (31%).

Table 4: Drug Combinations Occurring With Discrete Concomitant Events of Benzodiazepine and Opioid Use <i>(January - July 2016 -- FFS and CCOs)</i>			
Drug Combination	Number of Events	Drug Combination	Number of Events
hydrocodone or hydrocodone-ibuprofen / alprazolam	9	acetaminophen-tramadol / alprazolam	71
hydrocodone or hydrocodone-ibuprofen / clonazepam	4	acetaminophen-tramadol / lorazepam	20
hydrocodone-ibuprofen / lorazepam	1	acetaminophen-tramadol / chlordiazepoxide	1
hydromorphone / alprazolam	89	acetaminophen-tramadol / clonazepam	31
hydromorphone / lorazepam	24	acetaminophen-tramadol / diazepam	17
hydromorphone / clonazepam	42	acetaminophen-tramadol / temazepam	6
hydromorphone / clorazepate	1	acetaminophen-tramadol / triazolam	1
hydromorphone / diazepam	37	acetaminophen/butalbital/caffeine/codeine / alprazolam	4
hydromorphone / temazepam	7	acetaminophen/butalbital/caffeine/codeine / clonazepam	6
acetaminophen-hydrocodone / alprazolam	7,996	acetaminophen/butalbital/caffeine/codeine / diazepam	3
acetaminophen-hydrocodone / lorazepam	1,486	acetaminophen/caffeine/dihydrocodeine / alprazolam	2
acetaminophen-hydrocodone / chlordiazepoxide	27	acetaminophen/caffeine/dihydrocodeine / clonazepam	3
acetaminophen-hydrocodone / clobazam	15	acetaminophen/caffeine/dihydrocodeine / clorazepate	2
acetaminophen-hydrocodone / clonazepam	3,826	acetaminophen/caffeine/dihydrocodeine / temazepam	1
acetaminophen-hydrocodone / clorazepate	122	buprenorphine / alprazolam	89
acetaminophen-hydrocodone / diazepam	1,858	buprenorphine / lorazepam	13
acetaminophen-hydrocodone / flurazepam	4	buprenorphine / chlordiazepoxide	1
acetaminophen-hydrocodone / oxazepam	4	buprenorphine / clobazam	1
acetaminophen-hydrocodone / temazepam	617	buprenorphine / clonazepam	56
acetaminophen-hydrocodone / triazolam	3	buprenorphine / clorazepate	1
acetaminophen-codeine / alprazolam	480	buprenorphine / diazepam	15
acetaminophen-codeine / lorazepam	85	buprenorphine / temazepam	2
acetaminophen-codeine / chlordiazepoxide	5	buprenorphine-naloxone / alprazolam	220
acetaminophen-codeine / clobazam	2	buprenorphine-naloxone / lorazepam	43
acetaminophen-codeine / clonazepam	252	buprenorphine-naloxone / clobazam	2
acetaminophen-codeine / clorazepate	9	buprenorphine-naloxone / clonazepam	238
acetaminophen-codeine / diazepam	112	buprenorphine-naloxone / clorazepate	3
acetaminophen-codeine / temazepam	40	buprenorphine-naloxone / diazepam	40
acetaminophen-oxycodone / alprazolam	1,550	buprenorphine-naloxone / temazepam	14
acetaminophen-oxycodone / lorazepam	295	butorphanol / alprazolam	2
acetaminophen-oxycodone / chlordiazepoxide	6	butorphanol / lorazepam	3
acetaminophen-oxycodone / clobazam	2	butorphanol / clonazepam	1
acetaminophen-oxycodone / clonazepam	774	fantanyl / alprazolam	260
acetaminophen-oxycodone / clorazepate	25	fantanyl / lorazepam	68
acetaminophen-oxycodone / diazepam	392	fantanyl / clonazepam	80
acetaminophen-oxycodone / oxazepam	2	fantanyl / clorazepate	3
acetaminophen-oxycodone / temazepam	145	fantanyl / diazepam	42
		fantanyl / oxazepam	2
		fantanyl / temazepam	18

**Table 4: Drug Combinations Occurring
With Discrete Concomitant Events of Benzodiazepine and Opioid Use (Continued)**
(January - July 2016 -- FFS and CCOs)

Drug Combination	Number of Events	Drug Combination	Number of Events
meperidine / alprazolam	25	oxycodone / alprazolam	537
meperidine / lorazepam	4	oxycodone / lorazepam	100
meperidine / clonazepam	2	oxycodone / chlordiazepoxide	3
meperidine / clorazepate	1	oxycodone / clobazam	2
meperidine / diazepam	12	oxycodone / clonazepam	205
meperidine / temazepam	4	oxycodone / clorazepate	9
methadone / alprazolam	26	oxycodone / diazepam	109
methadone / lorazepam	2	oxycodone / temazepam	31
methadone / clobazam	3	oxymorphone / alprazolam	23
methadone / clonazepam	21	oxymorphone / lorazepam	7
methadone / diazepam	8	oxymorphone / clonazepam	19
morphine / alprazolam	314	oxymorphone / diazepam	13
morphine / lorazepam	70	tapentadol / alprazolam	4
morphine / chlordiazepoxide	1	tapentadol / clonazepam	3
morphine / clonazepam	111	tapentadol / diazepam	1
morphine / clorazepate	3	tapentadol / temazepam	2
morphine / diazepam	59	tramadol / alprazolam	1,282
morphine / temazepam	25	tramadol / lorazepam	299
morphine-naltrexone / alprazolam	44	tramadol / chlordiazepoxide	8
morphine-naltrexone / lorazepam	4	tramadol / clobazam	1
morphine-naltrexone / clonazepam	13	tramadol / clonazepam	645
morphine-naltrexone / clorazepate	3	tramadol / clorazepate	26
morphine-naltrexone / diazepam	8	tramadol / diazepam	184
morphine-naltrexone / temazepam	4	tramadol / oxazepam	2
naloxone-pentazocine / alprazolam	1	tramadol / temazepam	83

RECOMMENDATIONS AND BOARD ACTION

The information in this report is presented for informational purposes only and will serve as a baseline data reference for evaluating the impact of the electronic PA edit and an educational initiative.

No additional DUR Board action is requested at this time.