USE OF CODEINE AND TRAMADOL IN MISSISSIPPI MEDICAID

CARRIED OVER FROM JULY 2017 DUR BOARD MEETING WITH UPDATES AND APPENDIX ADDED

BACKGROUND

In April 2017, the FDA issued a notice restricting the use of codeine and tramadol medications in children.[1] Both medications are classified as opioid narcotics. Codeine is approved to treat pain and cough. It is often used in combination with other medications in both prescription and OTC cough and pain medications. Tramadol is a prescription medication approved to treat moderate to moderately severe pain. Single ingredient codeine medications and all tramadol containing medications are FDA-approved only for use in adults.

Codeine and tramadol medications have been shown to carry serious risks such as slowed or difficult breathing and death, especially in children under 12 years of age. Since 2013, the FDA has made multiple safety updates to the labeling of both codeine and tramadol containing medications in regards to their use in children and adolescents. The new FDA drug safety communication stated the following information for the labeling of these products:

- FDA's strongest warning, called a *Contraindication*, to the drug labels of codeine and tramadol alerting that codeine should not be used to treat pain or cough and tramadol should not be used to treat pain in children younger than 12 years.
- A new *Contraindication* to the tramadol label warning against its use in children younger than 18 years to treat pain after surgery to remove the tonsils and/or adenoids.
- A new *Warning* to the drug labels of codeine and tramadol to recommend against their use in adolescents between 12 and 18 years who are obese or have conditions such as obstructive sleep apnea or severe lung disease, which may increase the risk of serious breathing problems.
- A strengthened *Warning* to mothers that breastfeeding is not recommended when taking codeine or tramadol medicines due to the risk of serious adverse reactions in breastfed infants. These can include excess sleepiness, difficulty breastfeeding, or serious breathing problems that could result in death.

The Mississippi Division of Medicaid (DOM) Universal Preferred Drug List (UPDL) currently does not include any age limits for short-acting narcotics and has a minimum age limit of 18 for selected long-acting narcotics (Xartemis® XR and Zohydro® ER). The following Universal Preferred Drug List (UPDL) excerpt illustrates no current age restrictions for codeine and tramadol medications.

[1] U.S. Food and Drug Administration. FDA MedWatch Codeine and Tramadol Medicines: Drug Safety Communication Restricting Use in Children, Recommending Against Use in Breastfeeding Women. April 20, 2017.

Figure 1: Mississippi Medicaid UPDL Narcotic Analgesics[2]

PREFERRED AGENTS	NON-PREFERRED AGENTS		PA CRITERIA
ANALGESICS, NARCOTIC - SHORT ACTING			
Acetaminophen/codeine codeine dihydrocodeine/ APAP/caffeine hydrocodone/APAP hydromorphone IBUDONE (hydrocodone/ibuprofen) meperidine morphine oxycodone capsules oxycodone/APAP oxycodone/aspirin oxycodone/ibuprofen pentazocine/APAP tramadol tramadol/APAP	ABSTRAL (fentanyl) ACTIQ (fentanyl) butalbital/APAP/caffeine/codeine butalbital/ASA/caffeine/codeine butorphanol tartrate (nasal) DEMEROL (meperidine) DILAUDID (hydromorphone) fentanyl FENTORA (fentanyl) FIORICET W/ CODEINE (butalbital/APAP/caffeine/codeine) FIORINAL W/ CODEINE (butalbital/ASA/caffeine/codeine) hydrocodone/ibuprofen LAZANDA NASAL SPRAY (fentanyl) levorphanol LORCET (hydrocodone/APAP) LORTAB (hydrocodone/APAP) MAGNACET (oxycodone/APAP) NORCO (hydrocodone/APAP) NUCYNTA (tapentadol)	ONSOLIS (fentanyl) OPANA (oxymorphone) OXECTA (oxycodone) oxycodone tablets pentazocine/naloxone PERCOCET (oxycodone/APAP) PERCODAN (oxycodone/ASA) REPREXAINE (hydrocodone/ibuprofen) ROXICET (oxycodone/acetaminophen) RYBIX (tramadol) SUBSYS (fentanyl) SYNALGOS-DC (dihydrocodeine/ aspirin/caffeine) TYLENOL W/CODEINE (APAP/codeine) TYLOX (oxycodone/APAP) ULTRACET (tramadol/APAP) ULTRAM (tramadol) VICODIN (hydrocodone/APAP) VICOPROFEN (hydrocodone/ibuprofen) XODOL (hydrocodone/acetaminophen) ZAMICET (hydrocodone/APAP) ZOLVIT (hydrocodone/APAP) ZYDONE (hydrocodone/acetaminophen)	Quantity Limits Applicable quantity limit in 31 rolling days. • **62 tablets** - codeine, oxycodone/ibuprofen, meperidine, hydromorphone, fentanyl, bultalbital/codeine combinations, morphine, tapentadol, dihydrocodeine combinations, tramadol, pentazocine • **62 tablets CUMULATIVE** - hydrocodone combinations, oxycodone combinations • **124 tablets** - butalbital/APAP 750 • **145 tablets** - butalbital/APAP 650 • **186 tablets** - butalbital/APAP 325, butalbital/ASA 325 • **5mL (2 x 2.5 bottles)** - butorphanol nasal • **180 mL CUMULATIVE** - oxycodone liquids • **480 mL CUMULATIVE** - hydrocodone liquids

PREFERRED AGENTS	NON-PREFERRED AGENTS		PA CRITERIA
ANALGESICS, NARCOTIC - LONG ACTING			
BUTRANS (buprenorphine) EMBEDA (morphine/naltrexone) fentanyl patches morphine ER tablets	ARYMO ER (morphine) [NR] BELBUCA (buprenorphine) CONZIP ER (tramadol) DOLOPHINE (methadone) DURAGESIC (fentanyl) EXALGO (hydromorphone) hydromorphone ER HYSINGLA ER (hydrocodone) KADIAN (morphine) methadone MORPHABOND (morphine) [NR] morphine ER capsules MS CONTIN (morphine) NUCYNTA ER (tapentadol) OPANA ER (oxymorphone) oxycodone ER OXYCONTIN (oxycodone) oxymorphone ER RYZOLT (tramadol)	tramadol ER ULTRAM ER (tramadol) XARTEMIS XR (oxycodone/APAP) XTAMPZA (oxycodone myristate) ZOHYDRO ER (hydrocodone bitartrate)	Minimum Age Limit • 18 years - Xartemis XR, Zohydro ER Quantity Limits Applicable quantity limit per rolling days • 31 tablets/31 days - Conzip ER, Exalgo ER, Hysingla ER, Ryzolt , Ultram ER • 62 tablets/31 days - Arymo ER, Embeda, Kadian, Methadone, Morphine ER, Opana ER, oxycodone ER, Oxycontin, Xtampza ER, Zohydro ER • 10 patches/31 days – Duragesic • 4 patches/31 days – Butrans • 40 tablets/10 days - Xartemis XR Xartemis XR MANUAL PA • Have tried 2 different preferred agents in the past 30 days • Maximum duration of therapy = 20 days per calendar year

MS-DUR examined the use of prescription medications containing codeine and tramadol during 2016 to determine their prevalence of use in the Mississippi Medicaid population.

2 Mississippi Division of Medicaid. Universal Preferred Drug List. Short/Long Acting Narcotic Analgesics. Effective July 1, 2017.

METHODS

A retrospective analysis was conducted using DOM's medical and pharmacy claims for the period January 2016 – December 2016. The analysis included data from the fee-for-service (FFS) program and the coordinated care organizations (CCOs). National drug codes (NDCs) for the drugs containing codeine or tramadol listed in the FDA safety alert were identified. All claims for these drugs were extracted. Beneficiary age was calculated at the end of the observation period (December 31, 2016). Medical claims were used to identify beneficiaries with a diagnosis of sleep apnea (ICD codes 327.2, 780.57, 780.53, 786.03, R06.81, G47.3) or having a tonsillectomy/adenoidectomy (CPT codes 42820, 42821, 42825, 42826, 42830, 42831, 42835, 42836, 42960, 42961, 42962, 42970, 42971, 42972). All beneficiaries who were enrolled for at least one month during the study period were included in the analysis. Beneficiaries were classified as receiving codeine or tramadol for pain after a tonsillectomy/adenoidectomy if there was a prescription claim for these medications within 3 days of the procedure. The list of prescription codeine and tramadol medicines published by the FDA was utilized for the analysis (Figure 2)

Figure 2: FDA List of Prescription Codeine and Tramadol Medicines[1]

Medicines Containing Codeine	Medicines Containing Tramadol
Codeine Sulfate	Conzip
Butalbital, Acetaminopen, Caffeine, and Codeine phosphate	Ultracet
Fiorinal with codeine	Ultram
Soma Compound with codeine	Ultram ER
Tylenol with codeine	Generic products containing tramadol
Promethazine with codeine (cough)	
Prometh VC with codeine (cough)	
Triacin-C (cough)	
Tuxarin ER (cough)	
Tuzistra-XR (cough)	
Generic products containing codeine	
Medicines Containing Dihydrocodeine	
Synalgos-DC	

RESULTS

Codeine and Tramadol Use in Children Under 12

Across all age groups, 4.9% of beneficiaries had claims for at least one prescription for codeine and 2.2% had claims for at least one prescription for tramadol (Table 1). Use of both medications was highest in adults 18 to 44 years of age (6.8% for codeine and 5.4% for tramadol) and adolescents 12 to 17 years of age (5.9% for codeine and 1.0% for tramadol). Only 58 children under age 12 had prescriptions for tramadol. However, 16,007 children under the age of 12 had prescription claims for codeine products.

TABLE 1: Use of Codeine and Tramadol by Age Group and Selected Conditions
(FFS and CCOs for Calendar Year 2016)

		Beneficiaries				
			Filling Codeine Prescription		Filling Tramadol Prescription	
	Age Group	Total				
Overall	TOTAL	863,709	42,663	4.9%	19,254	2.2%
	0 to 5	159,809	5,997	3.8%	4	0.0%
	6 to 11	158,281	10,010	6.3%	54	0.0%
	12 to 17	132,171	7,848	5.9%	1,288	1.0%
	18 to 44	207,754	14,182	6.8%	11,206	5.4%
	45 and above	205,694	4,626	2.3%	6,702	3.3%
Beneficiaries Having Tonsillectomy or Adenoidectomy*	TOTAL	5,507	371	6.7%	1	0.0%
	0 to 5	2,593	127	4.9%	0	0.0%
	6 to 11	1,989	203	10.2%	0	0.0%
	12 to 17	641	37	5.8%	0	0.0%
	18 to 44	270	4	1.5%	1	0.4%
	45 and above	14	0	0.0%	0	0.0%
Beneficiaries With Sleep Apnea Diagnois	TOTAL	11,542	1,037	9.0%	1,069	9.3%
	0 to 5	1,673	99	5.9%	0	0.0%
	6 to 11	1,169	116	9.9%	3	0.3%
	12 to 17	622	57	9.2%	11	1.8%
	18 to 44	2,789	368	13.2%	462	16.6%
	45 and above	5,289	397	7.5%	595	11.3%

** Prescription was filled within 3 days after the procedure was completed.*

Codeine and Tramadol Use Following Tonsillectomy/Adenoidectomy

A total of 5,223 beneficiaries under the age of 18 had a tonsillectomy or adenoidectomy during 2016. Of these beneficiaries, 367 (7.0%) had prescription claims for codeine within three days of the procedure. None of these beneficiaries had claims for a tramadol prescription.

Codeine and Tramadol Use in Children/Adolescents with Sleep Apnea

Based on medical claims, 3,464 beneficiaries under age 18 were identified as having a diagnosis of sleep apnea. Of these beneficiaries, 272 (7.9%) had prescriptions for codeine products and 11 (0.3%) had prescriptions for tramadol. Other conditions listed in the FDA warning for

codeine and tramadol such as obesity and severe lung disease, or cough were not included in this analysis due to difficulties identifying these conditions using administrative claims.

(update)

Analysis was conducted of claims between May 1 and August 31, 2017 – after the FDA warning was issued. During the four months following the FDA warning, we have observed a significant decrease in the percentage of children under age 12 being prescribed codeine overall, following tonsillectomy/adenoidectomy and when patients had sleep apneia.

TABLE 2: Use of Codeine and Tramadol by Age Group and Selected Conditions
(FFS and CCOs for May - August 2017)

	Age Group	Beneficiaries				
		Total	Filling Codeine		Filling Tramadol	
Overall	TOTAL	759,600	10,448	1.4%	7,769	1.0%
	0 to 5	156,633	1,081	0.7%	2	0.0%
	6 to 11	141,095	1,839	1.3%	33	0.0%
	12 to 17	118,125	1,867	1.6%	528	0.4%
	18 to 44	156,076	4,134	2.6%	4,081	2.6%
	45 and above	187,671	1,527	0.8%	3,125	1.7%
Beneficiaries Having Tonsillectomy or Adenoidectomy*	TOTAL	1,636	99	6.1%	8	0.5%
	0 to 5	920	24	2.6%	0	0.0%
	6 to 11	553	49	8.9%	1	0.2%
	12 to 17	195	16	8.2%	2	1.0%
	18 to 44	62	10	16.1%	3	4.8%
	45 and above	5	0	0.0%	2	40.0%
Beneficiaries With Sleep Apnea Diagnois	TOTAL	5,672	212	3.7%	310	5.5%
	0 to 5	591	5	0.8%	0	0.0%
	6 to 11	370	6	1.6%	2	0.5%
	12 to 17	278	7	2.5%	0	0.0%
	18 to 44	1,531	94	6.1%	116	7.6%
	45 and above	2,902	100	3.4%	192	6.6%

** Prescription was filled within 3 days after the procedure was completed.*

CONCLUSIONS AND RECOMMENDATIONS

(update)

During the observation period prior to the updated FDA safety notice, prescribing behaviors indicated changes needed to be made in order to be compliant with the new safety warning. Tramadol use in children and adolescents was not very common, but some cases did occur that were in conflict with the FDA recommended contraindications and warnings. Codeine use in children under age 12 years and in children/adolescents with sleep apnea was fairly high. Analysis of the four months following the safety warning indicate significant improvement has been made, but further actions are needed to more fully address this safety issue.

Recommendations:

1. DOM should set a minimum age limit of 12 years for tramadol and codeine products.

2. DOM should modify the short and long-acting narcotic electronic PA rules to require the following: *(added since July meeting)*

    a. A manual PA for beneficiaries under age 18 years with diagnosis of sleep apnea prescribed codeine or tramadol.
    b. A manual PA for beneficiaries under age 18 years prescribed codeine or tramadol within 3 days of tonsillectomy or adenoidectomy.

3. MS-DUR should implement an educational initiative to notify providers of the recent (April 20, 2017) FDA recommendations and the new clinical edits being implemented.

APPENDIX

PROVIDER EDUCATIONAL SUMMARY TO BE INCLUDED IN MAILINGS