STIMULANTS AND ASSOCIATED DIAGNOSES FOR CLINICAL EDIT

BACKGROUND

The Drug Utilization Review (DUR) Board passed a recommendation during the March 1, 2018 Board Meeting that the Division of Medicaid (DOM) implement diagnosis edits for all stimulant use in both adults and children. MS-DUR was asked to evaluate stimulant prescriptions for the presence of medical claims with diagnoses that are FDA approved in labeling or classified as medically approved indications in compendia.

METHODS

A retrospective analysis was conducted using Mississippi Medicaid pharmacy and medical claims for calendar year 2017. All prescriptions for stimulants were extracted. Medical claims were examined for the beneficiaries receiving these prescriptions to determine which, if any, of the diagnosis of approved FDA indications or compendia supported diagnosis were found in the medical claims. It should be noted that the check for approved diagnoses was a search of medical claims for the entire year and not the customary 2-years back from time of prescription fill.

Under the current electronic prior authorization process (SmartPA®), the primary compendia resource for establishing medically accepted indications is Thompson Micromedex DrugDex® (Micromedex). This is one of the compendia approved by the Centers for Medicare and Medicaid Services. The criteria used for determining medically accepted indications are:

- “Strength of Recommendation” rating of at least IIB (Recommended, In Some Cases) **and**
- "Efficacy" rating of at least IIA (Evidence Favors Efficacy).*

**Indications with IIB rating in "Efficacy" are considered but would require manual prior authorization review*.

Table 1 displays the diagnoses that meet the DOM requirement for FDA approved or Thomson Micromedex DrugDex compendia supported diagnoses for each stimulant drug.

TABLE 1: MICROMEDEX Recommendations For CNS Stimulants				
Generic (Brand) Products	**FDA Indications**	**Compendia Approved Indications***	**Strength of Recommendation**	**Efficacy**
amphetamine salt combo (Adderall, Mydayis)	ADHD	None		
	Narcolepsy			
dexmethylphenidate (Focalin)	ADHD	None		
methylphenidate (Methylin, Aptensio, Quillichew, Quillivant, Ritalin, Concerta, Metadate, Cotempla, Daytrana)	ADHD	None		
	Narcolepsy			
dextroamphetamine (Procentra, Zenzedi, Dexedrine)	ADHD (P)	ADHD (A)	IIB	IIA
	Narcolepsy			
methamphetamine (Desoxyn)	ADHD	None		
	Simple Obesity			
amphetamine (Evekeo, Adzenys, Dyanavel)	ADHD	None		
	Narcolepsy			
	Simple Obesity; adjunct			
armodafinil (Nuvigil)	Narcolepsy (A)	Bipolar, depressed (A)	IIB	IIA
	Obstructive Sleep Apnea (A)			
	Shift Work Disorder (A)			
modafinil (Provigil)	Narcolepsy (A)	Narcolepsy (P)	IIB	IIA
	Obstructive Sleep Apnea (A)	ADHD	IIB	IIA
	Shift Work Disorder (A)	Depression (Unipolar /Bipolar) adjunct (A)	IIB	IIA
		Depression adjunct-fatigue (A)	IIB	IIA
		Sleep Deprivation (A)	IIA	IIA
		Steinert myotonic dystrophy syndrome (A)	IIB	IIA
lisdexamfetamine (Vyvanse)	ADHD	None		
	Binge Eating Disorder (A)			

Unless noted indication is for both pediatrics (P) and adult (A).

* *"Strength of Recommendation" rating of at least IIB and "Efficacy" rating of at least IIA are considered a "medically-accepted indication." Indications with IIB rating in "Efficacy" would require manual review.*

RESULTS

Although Medicaid uses the age of 21 years to be classified as an adult, Micromedex indications are classified as adult and/or children. Since the generally accepted age for the adult classification is 18 years of age, MS-DUR analyzed the presence of diagnoses using age 18 as the criteria for adult. Table 2 shows the number of unique beneficiaries prescribed each drug product and the number/percentage that did not have an approved diagnosis for the product in the medical claims.

TABLE 2: Presence of Approved Diagnoses by Drug Product
(FFS and CCOs - CY 2017)

	Age < 18				Age 18 +			
	Unique Beneficiaries	Approved Indication*			Unique Beneficiaries	Approved Indication*		
Drug Product		No	Yes			No	Yes	
Amphetamine-Dextroamphetamine	5,615	968	4,647	83%	1237	496	741	60%
Amphetamine-Dextroamphetamine ER	5,948	1,167	4,781	80%	610	199	411	67%
Adderall	47	7	40	85%	13	7	6	46%
Adderall XR	905	156	749	83%	103	40	63	61%
Mydayis	7	3	4	57%	0	0	0	0%
Dexmethylphenidate Hydrochloride	2,038	413	1,625	80%	45	11	34	76%
Dexmethylphenidate Hydrochloride ER	776	118	658	85%	25	6	19	76%
Focalin	74	16	58	78%	3	1	2	67%
Focalin XR	5,344	1,065	4,279	80%	151	54	97	64%
Methylphenidate Hydrochloride	2,337	442	1,895	81%	113	49	64	57%
Methylphenidate Hydrochloride CD	315	72	243	77%	9	3	6	67%
Methylphenidate Hydrochloride ER	6,863	1,512	5,351	78%	322	96	226	70%
Methylphenidate Hydrochloride SR	3	1	2	67%	0	0	0	0%
Aptensio XR	29	9	20	69%	0	0	0	0%
Concerta	96	22	74	77%	9	1	8	89%
Cotempla XR-ODT	10	1	9	90%	0	0	0	0%
Daytrana	210	48	162	77%	4	1	3	75%
Metadate CD	1,170	275	895	76%	36	10	26	72%
Metadate ER	15	4	11	73%	1	1	0	0%
Methylin	7	1	6	86%	0	0	0	0%
Ritalin	3	0	3	100%	1	0	1	100%
Ritalin LA	13	4	9	69%	0	0	0	0%
QuilliChew ER	1,950	391	1,559	80%	11	2	9	82%
Dextroamphetamine Sulfate	100	13	87	87%	8	6	2	25%
Zenzedi	6	1	5	83%	1	1	0	0%
Adzenys XR-ODT	1,723	265	1,458	85%	31	12	19	61%
Dyanavel XR	17	4	13	76%	0	0	0	0%
Evekeo	58	13	45	78%	4	3	1	25%
Armodafinil	1	1	0	0%	16	6	10	63%
Nuvigil	1	1	0	0%	6	2	4	67%
Modafinil	4	0	4	100%	46	14	32	70%
Provigil	11	5	6	55%	40	10	30	75%
Lisdexamfetamine	0	0	0	0%	0	0	0	0%
Vyvanse	18,419	3,852	14,567	79%	1154	462	692	60%
TOTAL	54,115	10,850	43,265	80%	3,999	1,493	2,506	63%

** Approved indications for each prodcut are listed in Table 1.*

It is not uncommon for providers to generalize indications across a therapeutic class or across similar products. Table 3 provides the number of cases where potential generalization of indications may have occurred for pediatric (age < 18 years) beneficiaries where a FDA approved or compendia supported diagnosis for each drug was not present in medical claims data. Since depression is a compendia accepted diagnosis for only Nuvigil and Provigil, it is reasonable to assume that this diagnosis is present due to an existing comorbidity rather than being the indication for use of the other stimulants. The results in Table 3 indicate that for children, the lack of an approved diagnosis is most likely the result of not currently requiring a diagnosis rather than class generalization of indications.

TABLE 3: Presence of Other Diagnoses by Drug
For Beneficiaries Not Having An Approved Diagnosis
Beneficiaries < 18 Years Old

	Unique Beneficiaries W/O Approved Indication	Number of Beneficiaries With Diagnoses that are FDA Indicated or Compendia Supported for Other Products *(shaded cells indicate diagnoses approved for the product itself)*								
		ADHD	NARC	OBES	DEP	INSOM	BIP-DEP	OSA	SHIFT	BINGE
Amphetamine-Dextroamphetamine	968			11	39	8	2	4	0	0
Amphetamine-Dextroamphetamine ER	1,167			9	46	10	2	1	0	1
Adderall	7			0	1	0	0	0	0	0
Adderall XR	156			0	5	3	0	1	0	0
Mydayis	3			0	0	0	0	0	0	0
Dexmethylphenidate Hydrochloride	413		0	4	28	2	2	0	0	0
Dexmethylphenidate Hydrochloride ER	118		0	0	1	0	0	0	0	0
Focalin	16		0	0	0	0	0	0	0	0
Focalin XR	1,065		0	7	49	3	5	3	0	0
Methylphenidate Hydrochloride	442			2	18	1	1	6	0	0
Methylphenidate Hydrochloride CD	72			0	2	0	0	0	0	0
Methylphenidate Hydrochloride ER	1,512			7	60	7	2	4	0	0
Methylphenidate Hydrochloride SR	1			0	0	0	0	0	0	0
Aptensio XR	9			0	0	0	0	0	0	0
Concerta	22			0	0	0	0	0	0	0
Cotempla XR-ODT	1			0	0	0	0	0	0	0
Daytrana	48			0	2	1	0	0	0	0
Metadate CD	275			3	14	0	0	1	0	0
Metadate ER	4			0	0	0	0	0	0	0
Methylin	1			0	0	0	0	0	0	0
Ritalin LA	4			0	0	0	0	0	0	0
QuilliChew ER	391			0	13	1	0	1	0	0
Dextroamphetamine Sulfate	13			0	0	0	0	0	0	0
Zenzedi	1			0	0	0	0	0	0	0
Adzenys XR-ODT	265				3	1	0	1	0	0
Dyanavel XR	4				0	0	0	0	0	0
Evekeo	13				0	1	0	0	0	0
Armodafinil	1	1	1	0	0	0	0	0	0	0
Nuvigil	1	0	1	0	1	0	0	0	0	0
Modafinil	0								0	0
Provigil	5			0	0	0	0	1	0	0
Lisdexamfetamine	0									
Vyvanse	3,852		5	33	196	20	19	12	0	3

ADHD - attention deficit/hyperactivity disorder
NARC - narcolepsy
OBES - simple obesity
DEP - depression (unipolar/bipolar) adjunct (A)
INSOM - sleep deprivation (A)
BIP-DEP - bipolar, depressed (A)
OSA - obstructive sleep apnea (A)
SHIFT - shift work disorder (A)
BINGE - binge eating disorder (A)

Table 4 provides the number of cases where potential generalization of indications may have occurred for adult (age ≥ 18 years) beneficiaries where a FDA approved or compendia supported diagnosis for each drug was not present in medical claims data. Since diagnoses are required for adults using some of the stimulants, it is not surprising that fewer adults had a lack of an approved indication. For the adults not having an approved indication, depression was again the most frequent diagnosis occurring in the medical records. As with children, the presence of depression as a comorbidity is more likely rather than the depression being the reason for prescribing the stimulant.

TABLE 4: Presence of Other Diagnoses by Drug
For Beneficiaries Not Having Approved Diagnsois
Beneficiaries 18 + Years Old

	Unique Beneficiaries W/O Approved Indication	**Number of Beneficiaries With Diagnoses that are FDA Indicated or Compendia Supported for Other Products** ***(shaded cells indicate diagnoses approved for the product itself)***								
		ADHD	NARC	OBES	DEP	INSOM	BIP-DEP	OSA	SHIFT	BINGE
Amphetamine-Dextroamphetamine	496			15	104	8	21	10	0	0
Amphetamine-Dextroamphetamine ER	199			7	36	5	6	2	1	0
Adderall	7			1	0	0	0	0	0	0
Adderall XR	40			1	7	1	2	1	0	0
Dexmethylphenidate Hydrochloride	11		0	0	1	0	0	0	0	0
Dexmethylphenidate Hydrochloride ER	6		0	0	0	0	0	0	0	0
Focalin	1		0	0	0	0	0	0	0	0
Focalin XR	54		0	1	9	1	0	0	0	0
Methylphenidate Hydrochloride	49			1	11	0	3	2	0	0
Methylphenidate Hydrochloride CD	3			0	0	0	0	0	0	0
Methylphenidate Hydrochloride ER	96			1	6	1	2	1	0	0
Concerta	1			0	0	0	0	0	0	0
Daytrana	1			0	0	0	0	0	0	0
Metadate CD	10			0	1	0	0	0	0	0
Metadate ER	1			0	0	0	0	0	0	0
QuilliChew ER	2			0	1	0	0	0	0	0
Dextroamphetamine Sulfate	6			0	1	0	0	0	0	0
Zenzedi	1			0	0	0	0	0	0	0
Adzenys XR-ODT	12				3	0	2	0	0	0
Evekeo	3				1	0	0	0	0	0
Armodafinil	6	0		0	2	0				0
Nuvigil	2	0		0	0	0				0
Modafinil	14			0						0
Provigil	10			0						0
Lisdexamfetamine	0									
Vyvanse	462		3	15	93	14	26	10	0	

ADHD - attention deficit/hyperactivity disorder
NARC - narcolepsy
OBES - simple obesity
DEP - depression (unipolar/bipolar) adjunct (A)
INSOM - sleep deprivation (A)
BIP-DEP - bipolar, depressed (A)
OSA - obstructive sleep apnea (A)
SHIFT - shift work disorder (A)
BINGE - binge eating disorder (A)

CONCLUSIONS AND RECOMMENDATIONS

- Although children have not had a diagnosis required for use of stimulants, 20% were taking stimulants without an approved diagnosis present for the product.
- In spite of having diagnosis requirements for use of some stimulants by adults, 37% of adult beneficiaries taking stimulants did not have an approved diagnosis present for the product.
- A total of 1,499 prescribers wrote initial prescriptions for stimulants when an approved diagnosis was not available in the medical claims.

TABLE 5: Number of Beneficairies and Prescribers With Outlier Cases

BENEFICIARIES WITHOUT APPROVED DIAGNOSES				
age	Pharmacy Program			
	FFS	UHC	MAG	TOTAL
< 18	4,160	3,121	3,094	10,375
18 +	327	619	587	1,533
Total	4,487	3,740	3,681	11,908

PRESCRIBERS				
Number of Beneficiaries Without Approved Diagnoses				
1	2-4	5-9	10+	TOTAL
565	420	194	320	1,499

Recommendations:

1. DOM should implement an electronic prior authorization procedure requiring the presence of at least one of the listed FDA approved or compendia supported diagnoses for each stimulant product. This diagnosis can be present in the medical claims paid within 24 months of the prescription fill or written on the prescription by the provider and submitted by the pharmacist with the prescription claim. (NOTE: The DUR Board has already approved such an edit, this is a confirmation of the approved indications that will be listed for each product.)

Prior to Implementation of the Edit:

2. MS-DUR will initiate an educational mailing to inform providers about the diagnosis requirement and will work with the Mississippi Chapter of the American Academy of Pediatrics and other state professional medical, nursing and pharmacy associations to electronically disseminate information about the upcoming edit.

3. DOM will include a notice about the upcoming edit in the upcoming Provider Bulletin(s).