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Drug Use Evaluation: Antidepressants in Children

Purpose of the Evaluation: Due to limited available evidence on use of tricyclic antidepressants (TCAs) in children and adolescents, the Pharmacy & Therapeutics committee requested an evaluation of antidepressant prescribing patterns in the Oregon Medicaid population with particular focus on evaluation of safe and medically appropriate use of TCAs for children.

Research Questions:

1) How frequently are antidepressants prescribed in children with Food and Drug Administration (FDA)-approved or guideline endorsed indications?
2) Which prescriber types and specialties are associated with antidepressant use in children?
3) Are there antidepressant classes associated with more frequent emergency department visits or hospitalizations?
4) What patient characteristics (relevant diagnoses or prior treatments) are associated with tricyclic antidepressant (TCA) therapy in children?
5) What treatment characteristics (duration of therapy and dose) are associated with TCA therapy in children?

Conclusions:

1. FDA-approved or guideline endorsed indications
    a. Over 13,000 children and adolescents were identified who had claims for an antidepressant therapy over the course of one year. In 74% of patients, prescriptions were filled for a selective serotonin reuptake inhibitor (SSRI), most commonly fluoxetine or sertraline. Paid claims for TCAs were present in 5.6% of the population (n=734), and approximately 245 children less than 12 years of age were prescribed TCAs.
    b. While many antidepressant therapies are not FDA-approved for children, most patients prescribed a SSRI or serotonin norepinephrine reuptake inhibitor (SNRI) had an FDA-approved or compendia-supported indication of depression, anxiety or adjustment reactions. Off-label use of TCAs was more common, and 48% of patients had no FDA-approved indication based on available claims data.
2. Prescriber types and specialties
    a. Pediatric physicians (25%) and providers with a mental health specialty (38%) were the most common prescribers of antidepressant therapy in children and adolescents. Non-specialists including family physicians, family nurse practitioners, and physician assistants accounted for 12%, 7% and 4% of prescribing, respectively.
3. Frequency of emergency department (ED) visits or hospitalizations
    a. There were no large differences in incidence of hospitalization or ED visits based on type of antidepressant. Overall, 17% of patients had an ED visit and 1% of patients had a hospitalization in the 90 days following prescription of an antidepressant.
4. Characteristics associated with TCA therapy
    a. Most patients (65%) with claims for a TCA were classified as treatment-naïve and had had no recent use of other antidepressant therapy in the 4 months prior to their first claim. Almost 33% of patients were prescribed ongoing TCA therapy and few had recent claims for other types of antidepressants.

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b. Common psychiatric diagnoses associated with TCA use included anxiety (25%), adjustment disorders (21%), attention deficit hyperactivity disorder (19%), and depression (12%). Common physical health diagnoses included various headache syndromes (36%), and gastrointestinal problems such as abdominal pain, pelvic pain or nausea, and sleep disorders.
c. Approximately 34% of patients were prescribed only short-term use of TCAs with less than 30 days of therapy. Over 45% of patients with claims for a TCA were prescribed therapy for more than 2 months.
d. The average dose for TCAs was less than 50% of the maximum FDA-approved dose in most patients (65-76%). Only a small proportion of patients with claims for TCAs had doses exceeding the FDA maximum dose.

Recommendations:

- Implement a safety edit for initiation of TCA therapy in children younger than the FDA-approved minimum age limit with the goal of preventing off-label use. Automatically approve requests for:
  - Children with prescriptions identified as being written by a mental health specialist, or
  - Children with ongoing TCA therapy, or
  - Children with a recent trial of a SSRI.
- Implement a retrospective drug use review safety net program to identify patients with denied claims and no subsequent follow-up in order to minimize interruptions and delays in therapy.

Background

Antidepressants are associated with significant safety concerns, particularly in children and adolescents. Many antidepressants are not approved for use in children and most antidepressants have an FDA box warning for increased risk of suicidal thoughts and behavior in pediatric and young adult patients. In particular, TCAs are rarely recommended in pediatric patients less than 12 years of age due to known safety concerns, frequency of adverse events, and limited data on efficacy. Current FDA-approved indications, ages, and maximum doses for TCAs are available in **Appendix 1**.

Recently updated guidance from the National Institute for Health and Care Excellence (NICE) provided recommendations for management of depression in children and young people.[1] Primary first-line therapies for moderate to severe depression include individual or family-based psychotherapy or cognitive behavioral therapy.[1] If pharmacotherapy is needed, fluoxetine is recommended in addition to non-pharmacotherapy for patients 5 to 18 years of age.[1] In patients with depression unresponsive to treatment, recurrent depression or psychotic depression, pharmacotherapy (including fluoxetine, sertraline, citalopram or augmentation with an antipsychotic) may be added to intensive psychological therapy.[1] Pharmacotherapy is not recommended except in combination with concurrent psychological therapy. Recommendations are made against use of paroxetine, venlafaxine, or TCAs for treatment of depression in children.[1]

A 2017 report by the Agency for Healthcare Research and Quality (AHRQ) evaluated evidence for treatment of anxiety in children.[2] Only 19 RCTs (n=2,498) were identified which evaluated pharmacotherapy compared to placebo.[2] SSRIs (fluoxetine, paroxetine, and sertraline) and SNRIs (atomoxetine, duloxetine and venlafaxine) improved primary anxiety symptoms compared to placebo based on moderate to high quality evidence.[2] SSRIs also demonstrated efficacy in improved remission rates, function, and clinical response compared to placebo (moderate to high strength of evidence).[2] TCAs and benzodiazepines lacked conclusive evidence of benefit.[2]

Similarly, guidelines from the American Academy of Neurology and American Headache Society recently updated recommendations for pharmacologic treatment of migraine prevention in pediatric patients and found insufficient evidence to support a reduction in headache frequency with use of amitriptyline monotherapy.[3] When used as monotherapy there was no difference in headache frequency based on one high quality study.[3] However, in patients aged 10-17 years, combined amitriptyline and cognitive behavioral therapy was associated with reduced headache frequency compared to amitriptyline and headache education alone (high strength evidence).[3] Evidence was significantly limited by high placebo response rates (30-61% of children with 50% reduction in headache frequency).[3] Due to the limited evidence available for pharmacologic treatment, recommendations are made to engage in shared decision-making with an adequate discussion of expected risks and benefits of therapy.[3] If benefits may outweigh risks, a short-term (at least 2 month) medication trial may be considered to evaluate utility of prophylactic amitriptyline therapy in combination with cognitive behavioral therapy.[3]

Methods:
Included patients were less than 18 years of age and had a paid FFS pharmacy claim for a drug in the antidepressant PDL class from January 1, 2018 to December 31, 2018. The index event (IE) was defined as the first paid antidepressant claim in the reporting period. Type of antidepressant was categorized according to pharmacologic class (**Appendix 1**) and a subgroup analysis was conducted in patients with an IE for a TCA. Patients were excluded if they had Medicare Part D coverage or less than 75% of covered days in the 120 days before the IE to 120 days after the IE. Baseline characteristics, including patient age, were assessed at the time of the IE.

The following definitions and categories were used for the analysis:

- Duration of therapy was defined using the average days of coverage in the assessment period.
- Prior history of antidepressant use was evaluated in the 120 days prior to the IE and categorized by antidepressant class.
- New start patients were defined as no antidepressant use in the 120 days prior to the IE.
- Prescriber type was identified using the primary provider taxonomy.
- Diagnoses were identified using ICD-10 codes on medical claims in the year prior to the IE (see **Appendix 1** for relevant ICD-10 codes)
- Average daily dose was defined as a percent of the maximum FDA-approved daily dose. If pediatric dosing was not available, maximum adult doses were used (see **Appendix 1**). Daily doses were stratified as greater than the max dose, 51 to 100% of the max dose, and 50% or less of the max dose.
- ED visits and hospitalizations were assessed in the 90 days following the IE. Psychiatric illnesses were defined as visits with a primary ICD-10 diagnosis code beginning with F.

Results:
Most patients with claims for an antidepressant were adolescents older than 13 years of age (68%), white (49%) and female (56%). Most patients prescribed antidepressants received prescriptions for an SSRI (74%), and approximately 53% had no recent history for other antidepressant therapy (**Table 1**). When classified by age, trazodone and mirtazapine were most commonly prescribed for children less than 5 years of age whereas fluoxetine and sertraline were most commonly prescribed in patients 5-17 years of age (**Table 2**). Use of TCAs and SNRIs was infrequent, prescribed for 5.6% (n=734) and 2.9% (n=378) of patients, respectively. The most commonly prescribed TCAs were amitriptyline and nortriptyline.

Over 90% of patients prescribed an SSRI or SNRI had an FDA-approved diagnosis in the year prior to the IE (**Table 3**). However, only 71% of patients prescribed other atypical antidepressants and 52% of patients prescribed TCAs had a documented FDA-approved diagnosis based on medical claims in the year prior to the IE. The most common identified diagnoses were depression, anxiety or panic disorder, and adjustment reactions. The most common prescribers of

antidepressants in children and adolescents were pediatric physicians (25%). The top 20 prescriber types are listed in **Table 4**. Practitioners who had a mental health specialty (either nurse practitioners or psychiatric physicians) also accounted for a large majority of prescribing.

Overall, there were no large differences in incidence of hospitalization or ED visits based on type of antidepressant. Approximately 17% of patients had an ED visit and 1% of patients had a hospitalization in the 90 days following prescription of an antidepressant (**Table 5**).

Figure 1. Per member per month (PMPM;unique patient count) from January 2016 to present for children <18 years of age prescribed an antidepressant.

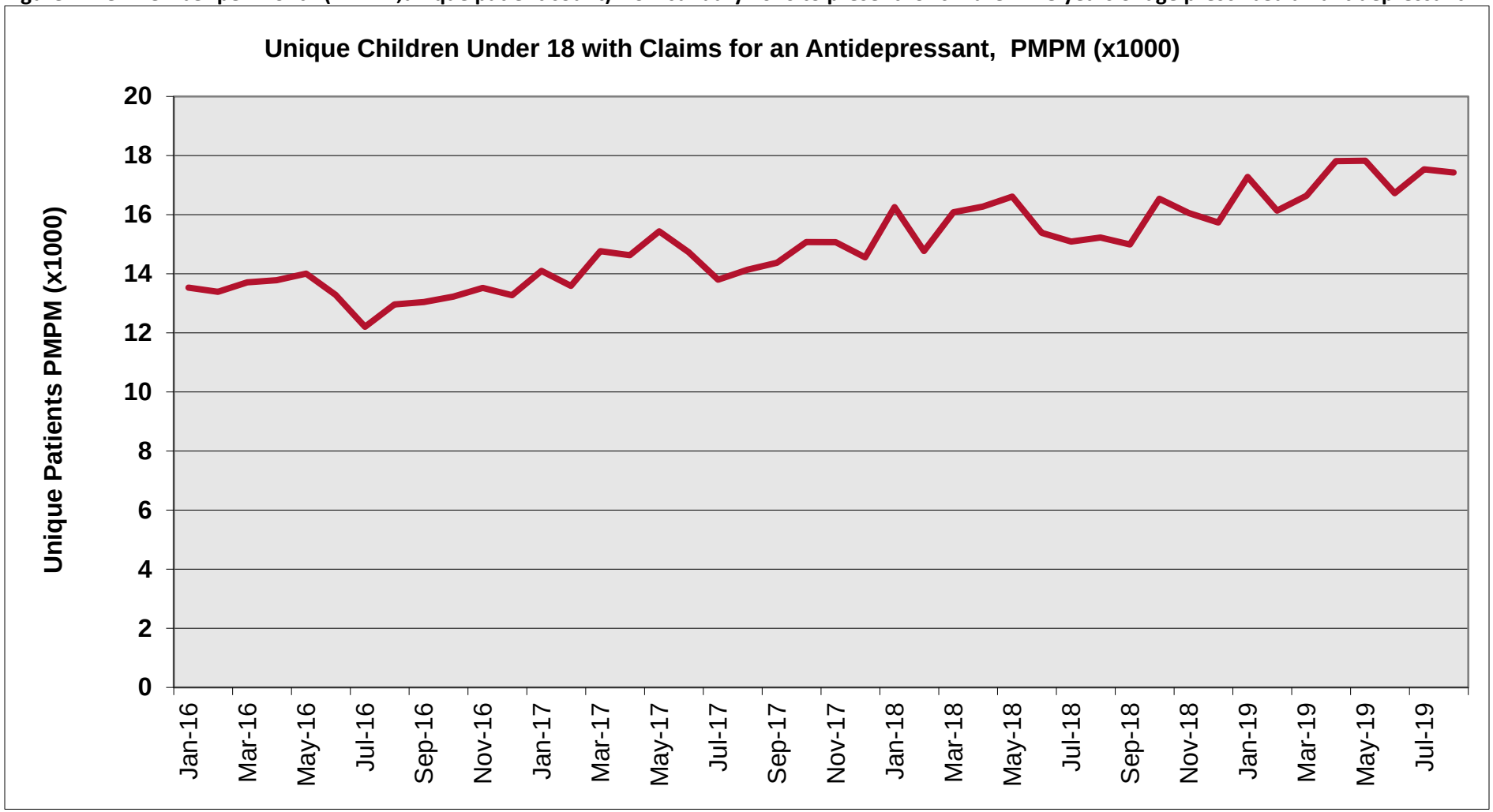

Table 1. Demographics.

	N=	13,058	%
Age			
Average (min - max)		13.3	(0-17)
0-4		58	0%
5-12		4,096	31%
13-17		8,904	68%
Female		7,312	56.0%
Race			
White		6,361	48.7%
Native American		649	5.0%
Other		876	6.7%
Unknown		5,172	39.6%
Antidepressant Class			
SSRI		9,632	73.8%
SNRI		378	2.9%
TCA		734	5.6%
Other		2,314	17.7%
Prior Antidepressant Use			
New start		6,896	52.8%
History of another antidepressant		6,162	47.2%

Table 2. Antidepressant Use by Age

	<5 years		5-12 years		13-18 years	
	58	%	4,096	%	8,904	%
Antidepressant Class						
SSRI	15	25.9%	2,946	71.9%	6,671	74.9%
SNRI	1	1.7%	44	1.1%	333	3.7%
TCA	6	10.3%	239	5.8%	489	5.5%
Other	36	62.1%	867	21.2%	1,411	15.8%

Top 20 Prescribed Antidepressants						
fluoxetine HCl	7	12.1%	1273	31.1%	2540	28.5%
sertraline HCl	6	10.3%	1158	28.3%	2386	26.8%
trazodone HCl	25	43.1%	562	13.7%	779	8.7%
escitalopram oxalate	1	1.7%	230	5.6%	974	10.9%
citalopram hydrobromide		0.0%	229	5.6%	600	6.7%
bupropion HCl		0.0%	106	2.6%	416	4.7%
amitriptyline HCl	**1**	**1.7%**	**134**	**3.3%**	**337**	**3.8%**
mirtazapine	11	19.0%	196	4.8%	200	2.2%
venlafaxine HCl		0.0%	24	0.6%	155	1.7%
duloxetine HCl	1	1.7%	15	0.4%	157	1.8%
paroxetine HCl	1	1.7%	19	0.5%	97	1.1%
fluvoxamine maleate		0.0%	37	0.9%	72	0.8%
nortriptyline HCl	**3**	**5.2%**	**16**	**0.4%**	**85**	**1.0%**
imipramine HCl		**0.0%**	**68**	**1.7%**	**28**	**0.3%**
doxepin HCl		**0.0%**	**11**	**0.3%**	**21**	**0.2%**
desvenlafaxine succinate		0.0%	5	0.1%	19	0.2%
clomipramine HCl		**0.0%**	**5**	**0.1%**	**11**	**0.1%**
vilazodone HCl		0.0%	2	0.0%	12	0.1%
desipramine HCl		**0.0%**	**5**	**0.1%**	**3**	**0.0%**
vortioxetine hydrobromide		0.0%	1	0.0%	4	0.0%

Table 3. Antidepressant Use by FDA-approved Diagnosis. Patients with multiple diagnoses may be counted more than once.

	SSRI		**SNRI**		**TCA**		**Other**	
	9,632	**%**	**378**	**%**	**734**	**%**	**2,314**	**%**
Any FDA-approved indication	8,689	90.2%	345	91.3%	381	51.9%	1,639	70.8%
Depression	4,925	51.1%	242	64.0%	115	15.7%	754	32.6%
Anxiety and Panic disorder	5,838	60.6%	258	68.3%	190	25.9%	898	38.8%
Bipolar Disorder	174	1.8%	16	4.2%	9	1.2%	150	6.5%
Adjustment Reactions	3,613	37.5%	158	41.8%	156	21.3%	859	37.1%
Other FDA-approved indication*	1,207	12.5%	71	18.8%	151	20.6%	285	12.3%
No FDA-approved indication	943	9.8%	33	8.7%	353	48.1%	675	29.2%

* Includes Bulimia nervosa and eating disorders, premenstrual dysphoric disorder/tension syndromes, OCD, smoking cessation (bupropion), diabetic neuropathy, fibromyalgia, chronic pain (SNRIs), and nocturnal enuresis (TCAs).

Table 4. Top 20 Prescriber Types for Antidepressants

Index Prescriber Taxonomy	Patients 13,058	%
PHYSICIAN-PEDIATRICS	3,254	24.9%
NURSE PRACTITIONER - PSYCHIATRIC/MENTAL HEALTH	1,684	12.9%
PHYSICIAN-FAMILY MEDICINE	1,551	11.9%
PHYSICIAN-PSYCHIATRY&NEUROLGY-CHILD&ADOLESCENT PSYCHIATRY	1,523	11.7%
PHYSICIAN-PSYCHIATRY&NEUROLOGY-PSYCHIATRY	1,231	9.4%
NURSE PRACTITIONER - FAMILY	965	7.4%
PHYSICIAN ASSISTANT	608	4.7%
NURSE PRACTITIONER - PEDIATRICS: PEDIATRICS	528	4.0%
PHYSICIAN ASSISTANT - MEDICAL	231	1.8%
PHYSICIAN-PEDIATRICS-DEVELOPMENTAL BEHAVORIAL PEDIATRICS	228	1.7%
STUDENT IN AN ORGANIZED HEALTH CARE EDUCATION/TRAINING PROGRAM	209	1.6%
NURSE PRACTITIONER	151	1.2%
REGISTERED NURSE - PSYCHIATRIC/MENTAL HEALTH	115	0.9%
CLINICAL NURSE SPECIALIST - PSYCHIATRIC/MENTAL HEALTH	99	0.8%
PHYSICIAN-INTERNAL MEDICINE	67	0.5%
PHYSICIAN-PSYCHIATRY&NEUROLOGY-NEUROLOGY	65	0.5%
PHYSICIAN-PEDIATRICS-PEDIATRIC GASTROENTEROLOGY	55	0.4%
PHYSICIAN-PSYCHIATRY&NEUROLOGY-NEUROLOGY WITH SPECIAL QUAL IN CHILD NEUROLO	52	0.4%
PHYSICIAN-PEDIATRICS-ADOLESCENT MEDICINE	38	0.3%
PHYSICIAN-EMERGENCY MEDICINE	36	0.3%

Table 5. Hospitalization and Emergency Department (ED) visits by Antidepressant Class in the 90 days following the IE.

	SSRI		SNRI		TCA		Other		Total	
	9,632	%	378	%	734	%	2,314	%	13,058	%
All ER visits	1,666	17.3%	81	21.4%	129	17.6%	371	16.0%	2,247	17.2%
All hospitalizations	139	1.4%	7	1.9%	17	2.3%	35	1.5%	198	1.5%
ER visit due to psychiatric illness	405	4.2%	23	6.1%	3	0.4%	80	3.5%	511	3.9%
Hospitalization due to psychiatric illness	108	1.1%	6	1.6%	7	1.0%	26	1.1%	147	1.1%

Subgroup analysis in patients with a TCA index event

Most common relevant psychiatric and physical diagnoses in patients with TCA use are listed in **Table 6**. Because medications are not associated with diagnoses codes, it is difficult to determine the exact diagnosis intended for the medication. TCAs have a wide variety of adverse effects and they are commonly used off-label despite insufficient or inconclusive evidence of benefit in pediatric populations. Documented off-label indications include various types of pain (e.g., headache, cancer pain, fibromyalgia, neuropathy), gastrointestinal syndromes (e.g., irritable bowel syndrome, nocturnal enuresis, urinary incontinence, neurogenic bladder), and psychiatric conditions (insomnia, ADHD, premenstrual dysphoric disorder, smoking cessation assistance, binge eating disorder).[4] In children prescribed TCAs, the most common psychiatric diagnoses included anxiety (25%), adjustment disorders (21%), ADHD (19%), and depression (12%). Common non-psychiatric diagnoses included various headache syndromes (36%), and gastrointestinal problems such as abdominal pain, pelvic pain or nausea, and sleep disorders.

Most patients with claims for a TCA were classified as treatment-naïve and had had no recent use of other antidepressant therapy in the 4 months prior to their first claim (65%; **Table 7**). Thirty-three percent of patients were prescribed ongoing TCA therapy, and only a small percent had claims indicating they may be switching from a different antidepressant class. Approximately 34% of patients were prescribed only short-term use of TCAs with less than 30 days of therapy. Over 45% of patients with claims for a TCA were prescribed therapy for more than 2 months. On average, the TCA dose was less than 50% of the maximum FDA approved dose in most patients (65-76%). Only a small proportion of patients had TCA doses prescribed above the recommended maximum dose (2-6%).

Table 6. Common Diagnoses in Patients Prescribed TCAs.

Diagnosis grouped by category using the first 3 characters of the ICD-10 code. ICD-10 codes beginning with Z (factors influencing health status) were excluded.

		TCA Patients	
Diagnosis in year prior to IE		**734**	**%**
Psychiatric Diagnoses			
F41	Other anxiety disorders	184	25.1%
F43	Reaction to severe stress, and adjustment disorders	156	21.3%
F90	Attention-deficit hyperactivity disorders	142	19.3%
F32	Major depressive disorder, single episode	91	12.4%
F91	Conduct disorders	54	7.4%
F07	Personality & behavioral disorders due to known physiological condition	47	6.4%
F33	Major depressive disorder, recurrent	46	6.3%
F34	Persistent mood [affective] disorders	36	4.9%
F51	Sleep disorders not due to a substance or known physiological condition	36	4.9%
Relevant Physical Diagnoses			
G43	Migraine	266	36.2%
R51	Headache	262	35.7%
R10	Abdominal and pelvic pain	206	28.1%
R11	Nausea and vomiting	170	23.2%
G44	Other headache syndromes	124	16.9%
G47	Sleep disorders	117	15.9%
M54	Dorsalgia	112	15.3%

K59	Other functional intestinal disorders	99	13.5%
N39	Other disorders of urinary system	99	13.5%
R53	Malaise and fatigue	83	11.3%
R42	Dizziness and giddiness	64	8.7%
E66	Overweight and obesity	63	8.6%
R19	Other symptoms and signs involving the digestive system and abdomen	63	8.6%
R07	Pain in throat and chest	62	8.4%
G89	Pain, not elsewhere classified	60	8.2%
R30	Pain associated with micturition	53	7.2%
K21	Gastro-esophageal reflux disease	51	6.9%
R41	Other symptoms and signs with cognitive functions and awareness	46	6.3%
R45	Symptoms and signs involving emotional state	44	6.0%
N92	Excessive, frequent and irregular menstruation	43	5.9%

Table 7. Prior Antidepressant Use in Patients with TCAs.

Utilization was assessed in the 120 days prior to the IE. Patients with claims for multiple types of antidepressants may be counted more than once.

	Patients with TCA IE	
	734	**%**
Treatment-naïve	477	65.0%
Prior Antidepressant Use		
SSRI	42	5.7%
SNRI	3	0.4%
TCA	239	32.6%
Other	20	2.7%

Table 8. Duration of TCA Use.

Assessed by the average days of coverage in 120 days following IE.

	Patients with TCA IE	
Days of Coverage	**734**	**%**
<=7 days	2	0.3%
8-30 days	250	34.1%
31-60 days	149	20.3%
61-120 days	333	45.4%

Table 9. TCA Dose at IE and for Patients Prescribed Continuous Therapy.

Maximum dose defined according to FDA-approved pediatric doses (when available) or adult maximum doses in **Appendix 1**. In patients with ongoing therapy for more than 60 days, average dose calculated based on most recent claim in the 120 days following IE.

	IE Dose		Patients with >60 days of coverage	
Average Daily Dose	**734**	**%**	**333**	**%**
<=50% of FDA max dose	558	76.0%	218	65.5%
51-100% of FDA max dose	157	21.4%	94	28.2%
> 100% of FDA max dose	19	2.6%	21	6.3%

Limitations:

Data presented in this report is based on Medicaid claims history and has several inherent limitations.

- Diagnostic accuracy: Diagnoses based on claims history may be inaccurate or incomplete. Because diagnoses are not associated with prescriptions, it is difficult to determine the intended indication for the drug, particularly when therapy is used off-label.
- Provider specialty: Information on provider specialty may be inaccurate, out-of-date, or incomplete for some providers. Prescribers with multiple specialties or designations may not be identified.
- Days of coverage: Estimates of covered days attempts to approximate the frequency which a patient takes a prescription, but accuracy of this method has not been validated, covered days may not accurately correlate to actual medication adherence, and patients may not always be categorized appropriately.
- Definitions for treatment-naïve patients: Prior use of antidepressants was only evaluated in the 120 days prior to the IE. Patients may have a remote history of antidepressant use beyond this date which could influence choice in current therapy.

References:

1. National Institute for Health and Care Excellence. Depression in children and young people: identification and management. Clinical Guideline. September 2017. Available at: www.NICE.org.uk. Accessed: July 30, 2019.
2. Wang Z WS, Sim L, et al. Anxiety in children. Comparative Effectiveness Review No. 192. AHRQ Publication No. 17-EHC023-EF. Rockville, MD. Agency for Healthcare Research and Quality. August 2017.
3. Oskoui M, Pringsheim T, Billinghurst L, et al. Practice guideline update summary: Pharmacologic treatment for pediatric migraine prevention. *Neurology*. 2019;93(11):500.
4. Micromedex Healthcare Series [internet database]. Greenwood Village, CO: Truven Health Analytics, Inc. Updated periodically. Accessed August 13, 2019.

Appendix 1: Coding Information

Table A1. Antidepressant Classes and FDA approved Ages[4]

Class	HSN	Generic Name	FDA Approval in Children
Other	001638	isocarboxazid	≥16 years
Other	001639	phenelzine sulfate	NA
Other	033510	selegiline	NA
Other	001640	tranylcypromine sulfate	NA
Other	036156	bupropion HBr	NA
Other	001653	bupropion HCl	NA
Other	011505	mirtazapine	NA
Other	009612	nefazodone HCl	NA
Other	001652	trazodone HCl	NA
Other	037597	vilazodone HCl	NA
Other	040637	vortioxetine hydrobromide	NA
SNRI	040202	desvenlafaxine	NA
SNRI	040692	desvenlafaxine fumarate	NA
SNRI	035420	desvenlafaxine succinate	NA
SNRI	026521	duloxetine HCl	≥7 years (anxiety)
SNRI	040632	levomilnacipran HCl	NA
SNRI	008847	venlafaxine HCl	NA
SSRI	010321	citalopram hydrobromide	NA
SSRI	024022	escitalopram oxalate	≥12 years (MDD)
SSRI	001655	fluoxetine HCl	≥7 years (MDD, OCD, bipolar)
SSRI	006338	fluvoxamine maleate	≥8 years (OCD)
SSRI	025800	olanzapine/fluoxetine HCl	≥10 years (bipolar)
SSRI	007344	paroxetine HCl	NA
SSRI	025796	paroxetine mesylate	NA
SSRI	006324	sertraline HCl	≥6 years (OCD)
TCA	001643	amitriptyline HCl	≥12 years (MDD)
TCA	001648	amoxapine	NA
TCA	004744	clomipramine HCl	≥10 years (OCD)
TCA	001645	desipramine HCl	NA
TCA	001650	doxepin HCl	≥12 years (anxiety, MDD)
TCA	001641	imipramine HCl	≥6 years (nocturnal enuresis)
TCA	001642	imipramine pamoate	NA
TCA	001651	maprotiline HCl	NA
TCA	001644	nortriptyline HCl	≥12 years (MDD)
TCA	001646	protriptyline HCl	≥12 years (MDD)
TCA	001649	trimipramine maleate	≥12 years (MDD)

Abbreviations: MDD = major depressive disorder; NA = not applicable; OCD = obsessive compulsive disorder; SNRI = serotonin norepinephrine reuptake inhibitor; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant

Table A2. TCA Max Dose Definitions[4]

Class	HSN	Generic	FDA Max Daily Dose	Source of max dose (pediatric if available or adult)
TCA	001643	amitriptyline HCl	50 mg	Pediatric
TCA	001648	amoxapine	400 mg	Adult
TCA	004744	clomipramine HCl	200 mg	Pediatric
TCA	001645	desipramine HCl	300 mg	Adult
TCA	001650	doxepin HCl	150 mg	Pediatric
TCA	001641	imipramine HCl	75 mg	Pediatric
TCA	001642	imipramine pamoate	200 mg	Adult
TCA	001651	maprotiline HCl	225 mg	Adult
TCA	001644	nortriptyline HCl	50 mg	Pediatric
TCA	001646	protriptyline HCl	60 mg	Adult
TCA	001649	trimipramine maleate	100 mg	Pediatric

Table A3. Antidepressant Dosing Calculations for Unique Formulations

GSN	Route	Form	Strength	Generic	Mg per Unit
046092	PO	ORAL CONC	10 mg/mL	doxepin HCl	10
046063	PO	SOLUTION	10 mg/5 mL	nortriptyline HCl	2
078426	PO	SOLUTION	20 mg/10 mL	nortriptyline HCl	2

Table A4. ICD-10 diagnosis codes

ICD10	ICD-10 Description	Category
F31xx	Bipolar disorder	Bipolar Disorder
F32xx (excluding F32.81)	Major depressive disorder, single episode	Depression
F33xx	Major depressive disorder, recurrent	Depression
F41xxx	Other anxiety disorders	Panic or anxiety disorder
F40xxx	Phobic anxiety disorders	Panic or anxiety disorder
F43xxx	Reaction to severe stress, and adjustment disorders	Adjustment disorders
F42XX	Obsessive-compulsive disorders	Other indications
N94.3	Premenstrual tension syndrome	Other indications
F32.81	Premenstrual dysphoric disorder	Other indications
F50xx	Eating disorders	Other indications
F17xx	Nicotine dependence	Other indications
E11.40	Diabetes with neuropathy	Other indications
M79.7	Fibromyalgia	Other indications
G89.2x	Chronic pain, not elsewhere classified	Other indications
N39.44	Nocturnal enuresis	Other indications

Tricyclic Antidepressants

Goal(s):

- Ensure safe and appropriate use of tricyclic antidepressants in children less than 12 years of age
- Discourage off-label use not supported by compendia

Length of Authorization:

Up to 12 months

Requires PA:

- Tricyclic antidepressants in children younger than the FDA-approved minimum age (new starts)
- Auto-PA approvals for:
  - Patients with a claim for an SSRI or TCA in the last 6 months
  - Prescriptions identified as being written by a mental health provider

Covered Alternatives:

- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Table 1. FDA-Approved Indications of Tricyclic Antidepressants

Drug	FDA-Approved Indications	Maximum Dose	Minimum FDA-Approved Age
amitriptyline HCl	Depression	50 mg	12
amoxapine	Depression	400 mg	18
clomipramine HCl	Obsessive-compulsive disorder	200 mg	10
desipramine HCl	Depression	300 mg	18
doxepin HCl	Depression Anxiety	150 mg	12
imipramine HCl	Depression Nocturnal enuresis	75 mg	6
imipramine pamoate	Depression	200 mg	18
maprotiline HCl	Depression Bipolar depression Dysthymia Mixed anxiety and depressive disorder	225 mg	18
nortriptyline HCl	Depression	50 mg	12

protriptyline HCl	Depression	60 mg	12
trimipramine maleate	Depression	100 mg	12

Approval Criteria		
1. What diagnosis is being treated?	Record ICD10 code.	
2. Is the diagnosis funded by OHP?	**Yes:** Go to #3	**No:** Pass to RPh. Deny; not funded by the OHP.
3. Does the dose exceed the maximum FDA-approved dose (**Table 1**)?	**Yes:** Pass to RPh. Deny; medical appropriateness.	**No:** Go to #4
4. Is the request for an FDA-approved indication and age (**Table 1**)?	**Yes:** Approve for up to 6 months	**No:** Go to #5
5. Is the request for prophylactic treatment of headache or migraine and is the therapy prescribed in combination with cognitive behavioral therapy?	**Yes**: Approve for up to 6 months	**No:** Go to #6
6. Is the drug prescribed by or in consultation with an appropriate specialist for the condition (e.g., mental health specialist, neurologist, etc.)?	**Yes**: Approve for up to 6 months	**No:** Pass to RPh. Deny; medical appropriateness.