Drug Use Research & Management Program
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New Drug Evaluation: lisdexamfetamine dimesylate capsule

New Indication: Binge Eating Disorder (BED)

Date of Review: May 2016
Generic Name: lisdexamfetamine
PDL Class: ADHD

End Date of Literature Search: Week 2, March 2016
Brand Name (Manufacturer): Vyvanse™ (Shire, Inc.)
AMCP Dossier Received: February 9, 2016

Research Questions:

- Is lisdexamfetamine more effective than currently available treatments at reducing binge-eating episodes (BEE) for patients with BED?
- Is lisdexamfetamine safer than currently available treatments for patients with BED?
- Is lisdexamfetamine more effective or safer than currently available treatments for any subgroup of patients with BED?

Conclusions:

- There is moderate quality evidence that lisdexamfetamine 50-70 mg daily is more efficacious than placebo at reducing BEE days per week and maintaining BEE cessation for 4 weeks (NNT:3-4) when used for 11 weeks in patients without mental health co-morbidities or substance abuse history. Comparisons to psychotherapy, behavioral weight loss therapy, topiramate or second-generation antidepressants have not been made.
- No new safety concerns were identified.
- Lisdexamfetamine has not been evaluated in patients with anorexia, bulimia, other mental health co-morbidities or substance abuse history.

Recommendations:

- After completion of the ADHD policy evaluation, recommend current PA criteria to include BED for lisdexamfetamine as appropriate **(Appendix 2).**

Background:

Lisdexamfetamine is currently "preferred" with a dose limit of 70 mg daily or 0.5 mg/kg/day and age limit of greater than 6 years old. Medical and psychotherapy of BED is a funded Oregon Health Plan condition (Line 386).

BED is characterized by recurrent episodes of eating more food in a discreet time period (e.g. 1-2 hours) than most people would under similar circumstances.[1] Patients often feel a lack of control during these events, experience shame or guilt but do not compensate with subsequent bulimia or anorexia and the episodes occur at least 1 day per week for 3 months.[2] The lifetime prevalence of BED in the United States (U.S.) is estimated to be 2.6% and up to 30% in weight-control program patients.[1,3] Lifetime prevalence is more common in women (3.5%) than men (2.0%) but it is not associated with race, marital status or employment.[1,3] The median age of onset is 23 years old and its persists an average of 14 years.[3] BED is commonly (78% of patients) comorbid with at least one other psychiatric diagnosis (e.g. social phobia, major depression, posttraumatic stress disorder or substance abuse).[3] BED patients are at increased risk of chronic pain, diabetes, hypertension and morbid obesity.[1,3]

Binge-eating episodes (BEE) vary greatly in size and duration; they are difficult for patients to objectively distinguish because they are distressed by the loss of control during even small episodes or ashamed to report large episodes.[1] Thus, self-reporting must be verified by clinicians using clear metrics and a structured clinical interview.[1] There are over 20 scales and tools used to diagnose and monitor BED.[1]

BED treatment currently focuses on reducing BEE and improving psychological feelings about eating, weight, body shape and distress[1,4] Comorbid concerns include treatment of coexisting metabolic health issues, depression, anxiety or substance abuse.[1,4] Current approaches include cognitive behavioral therapy, interpersonal psychotherapy, behavioral weight loss treatment or various off-label pharmacotherapies (e.g. second generation antidepressants and topiramate).[1,4] All drugs researched by the Agency for Health Quality Research and some forms of cognitive behavioral therapy are superior to placebo at achieving cessation of and reducing BEE but evidence is limited by few trials, small samples, short durations and heterogeneous outcome measures.[1] In January 2015, lisdexamfetamine became the first drug approved by the U.S. Food and Drug Administration (FDA) for BED treatment under a priority review.[5]

See **Appendix 1** for **Highlights of Prescribing Information** from the manufacturer, including Black Boxed Warning and Risk Evaluation Mitigation Strategies (if applicable), indications, dosage and administration, formulations, contraindications, warnings and precautions, adverse reactions, drug interactions and use in specific populations.

Methods: ClinicalTrials.gov identified 6 completed studies evaluating lisdexamfetamine for BED: NCT02009163 (Phase 3, no results available), NCT01657019 (open-label, safety extension), NCT01718509 (Phase 3),[6] NCT01718483 (Phase 3),[6] NCT01291173 (Phase 2)[7] and NCT01090713 (Phase 3, no results available). An Ovid Medline search including dates from 1946 until Week 2, March 2016 on the exploded terms "lisdexamfetamine dimesylate OR SPD489" AND "Binge-Eating Disorder" identified just 2 published papers but, only one[7] was a randomized controlled trial.

Clinical Efficacy: Clinical efficacy was established in 1 Phase 2 dose-ranging study (n=260)[7] and 2 Phase 3 trials (n=383, n=390).[6] All 3 trials had low risk of bias but were of short duration (12 weeks). The primary endpoint, change in number of BEE days per week at end of treatment, was based on a daily diary maintained by the patient and confirmed by clinician interview. All studies established statistical superiority over placebo for lisdexamfetamine 50-70mg daily on the primary outcome (see Comparative Evidence Table below) but, the clinical importance of the treatment effect is difficult to interpret because of the log-transformed scale used and short duration of the trial. The secondary outcome results in all 3 trials, total cessation of BEE for 4 weeks, was more impressive. Three to 4 patients would need to be treated with lisdexamfetamine 50-70mg daily rather than placebo for 11 weeks to achieve 4 weeks total cessation of BEE. Unfortunately, all trials excluded patients with any history of mental health comorbidity (including anorexia or bulimia) or substance abuse. So, it is difficult to extrapolate these results to a population where 78% of patients have mental health co-morbities. No comparison was made to current psychotherapy treatment or other drug options.

Clinical Safety: No new safety issues were raised in these trials. Cardiovascular effects (hypertension and increased heart rate) and substance abuse potential remain areas of concern.

Comparative Clinical Efficacy:

Clinically Relevant Endpoints:
1) Binge-Eating Episode Frequency
2) Binge-Eating Cessation Time

Primary Study Endpoint:
1) Change from baseline in binge-eating days per week @ week 12 or early termination using a mixed-effects model for repeated measured – least squares mean on a log-transformed scale

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Date: May 2016

Comparative Evidence Table

Ref./ Study Design	Intervention/ Duration	Patient Population	N	Efficacy Endpoints	RD/NNT	Safety Outcomes	RD/NNH	Risk of Bias / Applicability
1. Study 1 *(NCT01718483)* & Study 2 *(NCT01718509)*[6] Phase 3, R-PCT, PG, DB MC (93 with 85 U.S.) Nov 2012 – Sep 2013	1. LDX 50 - 70mg PO daily @ 0700 x 12 weeks. (wk 1 30mg; wk 2 50mg; wk 3 70mg; wk 4, if 70mg not tolerated, reduced to 50mg) -No other dose adjustments allowed 2. PCB PO daily @ 0700 x 12 weeks -All capsules identical appearance -Follow-up 1 week after week 12 or at early termination -Mean daily dose: Study 1/ 56.9mg Study 2/57.6 mg - mean follow-up Study 1/ ~76 days Study 2/ ~74 days -Patients screened 2-4 weeks.	Demographics: mean age: 37.1-38.7 years female: 82.7% -87.8% white: 71.8% - 78.1% obese: 67.2% -69.2% CGI-S moderately ill: 47.1% - 58.0% Key Inclusion Criteria: - 18-55 years old -BEE ≥ 3 days / wk x 2 consecutive wks AND CGI-S ≥ 4 AND confirmed BED using DSM-IV-TR - BMI ≥18 and ≤ 45 Key Exclusion Criteria: -current anorexia nervosa, bulimia nervosa, psychiatric disorders controlled with prohibited drugs or uncontrolled with any symptom that may confound clinical assessment -current psychotherapy or weight loss support -BED ≤ 3 months -use of stimulants for dieting for BED ≤ 6 months - MADR-S ≥ 18, suicide risk, ideation or previous attempt -lifetime history of psychosis, mania, hypomania, dementia, attention-deficit disorder - history of cardiovascular disease, hypertension, or arrhythmia -lifetime history of substance abuse (except nicotine)	ITT: *Study 1:* LDX: n=192 PCB: n=191 *Study 2:* LDX: n=195 PCB: n=195 mITT (excluded patients who do not take study drug or have <1 baseline assessment): *Study 1:* LDX: n=190 PCB: n=184 *Study 2:* LDX: n=174 PCB: n=176 Attrition (exclusions + loss to follow-up): *Study 1* LDX: 5/192=2.6% PCB: 15/191=7.6% *Study 2 (may include patients from 2 sites that were excluded after randomization)* LDX: 36/195=18.5% PCB : 37/195=19.0% Safety Analysis: *Study 1:* LDX: n=192 PCB: n=187 *Study 2:* LDX: n=181 PCB: n=185	Change from baseline in BEE days / wk @ week 12 or early termination (mixed-effects model for repeated measured – least squares mean) *Study 1:* LDX: -3.87 PCB: -2.51 Mean Difference: -1.35 95%CI (-1.70,-1.01) p < 0.001 *Study 2:* LDX:-3.92 PCB: -2.26 Mean Difference: -1.66 95%CI (-2.04,-1.28) p < 0.001 90% power assumptions met 4-wk binge-cessation @ wk 12 *Study 1:* LDX:76/190 (40.0%) PCB:26/184 (14.1%) *Study 2:* LDX:63/174 (36.2%) PCB:23/176 (13.1%)	NA NA RD: 25.9% 95%CI (17.3, 34.5) p<0.001 NNT=4 RD: 23.1% 95%CI (14.4,31.8) p<0.001 NNT=4	Withdrawal due to ADE: *Study 1:* LDX: 12/192= 6.3% PCB: 5/187= 2.7% *Study 2:* LDX: 7/181= 3.9% PCB: 5/185= 2.7% Serious ADE*: *Study 1:* LDX: 3/192= 1.6% PCB: 2/187= 1.1% *Study 2:* LDX: 1/181= 0.06% PCB: 2/185= 1.1% *anaphylaxis, syncope, cholecystitis, fibula fracture, agitation, anxiety, lumbar fracture	RD = 3.6% 95%CI (-8.2,0.08) NA RD = 1.2% 95%CI (-5.4, 2.8) NA RD= 0.05% 95%CI (-3.5,2.4) NA RD= 0.05% 95%CI (-2.1, 3.3) NA	**Risk of Bias**: **Probably Low despite some unclear reporting.** Selection Bias: Low; unclear sequence generation but interactive voice response system implies computer generated random sequence, good allocation concealment; groups even at baseline Performance Bias: Low; identical intervention Detection Bias: Unclear who outcome assessors were; but assume it was treating clinicians who were blinded. Attrition Bias: Unclear; low reported attrition despite mITT: slightly higher in study 1 placebo; Unclear if Study 2 withdrawal numbers included study site that was excluded; higher rate suggests they were. Reporting Bias: Low; all outcomes reported **Applicability**: Patient: Extensive exclusion of mental health comorbidities limits applicability Intervention: Oral capsule, easily reproducible; adherence monitoring not achievable in practice Comparator: placebo appropriate Outcomes: Subjective, but valid, clinically important outcome that includes patient reporting; authors made reasonable attempt to increase reliability with certified, trained clinician verification using standardized criteria. Outcomes may not be sustainable for longer durations. Setting: not described

2. *NCT01291173*[7] Phase 2, R-PCT, PG, DB MC (28 U.S.) May 2011 – Jan 2012	1. LDX 30mg x 11 wks 2. LDX 50mg (wk 1 30mg; wk 2 50mg x 10 wks) 3. LDX 70mg PO daily (wk 1 30mg; wk 2 50mg; wk 3 70mg x 9 wks) -No other dose adjustments allowed 2. PCB PO daily x 11 weeks -All capsules identical appearance and inert ingredients. -Follow-up 1 week after week 11 or at early termination	Demographics: Age: 38.7 years Female: 81.5% White: 78% Non-Latino: 88.8% Weight: 98.6 kg BMI 34.9 Obese: 58.7% Key Inclusion Criteria: - 18-55 years old - met DSM-IV-TR criteria for BED - BMI ≥ 25 and ≤ 45 Key Exclusion Criteria: - current bulimia/anorexia or another psychiatric disorder - lifetime history of bipolar disorder or psychosis -MADRS of ≥ 18 -weight loss intervention within 3 months -use of psychostimulant within 6 months -personal/family history of cardiovascular disease -history of suspected drug abuse -lifetime history of psychostimulant abuse -recent therapy with any psychoactive drug -nicotine allowed	ITT: PCB: n= 64 (1 did not receive study drug) LDX30: n= 66 LDX50: n= 65 LDX70: n= 65 mITT (excluded patients who do not take study drug or have <1 baseline assessment): PCB: n= 62 LDX30: n= 66 L-50: n= 64 L-70: n= 63 Attrition (exclusions + loss to follow-up): PCB: 6/64 = 9.4% LDX30: 6/66 = 9.1% LDX50: 4/65 = 6.2% LDX70: 4/65 = 6.2% Safety Analysis: PCB: n= 63 LDX30: n= 66 LDX50: n= 65 LDX70: n= 65	Change from baseline in BEE days / wk @ week 12 or early termination (mixed-effects model for repeated measured – least squares mean) on the log-transformed scale (BE days per week) + 1. Log-transformed, least-squared mean BE days (SE): PCB: -1.23 (0.069) LDX30: -1.24 (0.067) LDX50: -1.49 (0.066) LDX70: -1.57 (0.067) Mean difference in BEE days / wk vs. PCB: LDX30: -0.01 p=0.88 LDX 50: -0.26 p=0.008 LDX70: -0.35 p<0.001 4-wk binge-cessation @ wk 12 PCB: 21.3% LDX30: 34.8% LDX50: 42.2% LDX70: 50.0%	NA RD vs PCB: LDX30: 13.5% p=0.09 LDX50: 20.9% p=0.01 NNH=5 LDX70: 28.7% p<0.001 NNH= 3	Withdrawal due to ADE: PCB: 0/64 (0.0%) LDX30: 3/66 (4.5%) LDX50: 1/65 (1.5%) LDX70: 3/65 (4.6%) Serious ADE*: PCB: 0/64 (0.0%) LDX30: 2/66 (3.0%) LDX50: 0/65 (0.0%) LDX70: 1/65 (1.5%) *methamphetamine overdose, acute pancreatitis, appendicitis (all deemed unrelated to study drug)	NA NA	**Risk of Bias**: **Probably Low despite some unclear reporting.** Selection Bias: Low; unclear sequence generation but interactive voice response system implies computer generated random sequence, good allocation concealment; groups even at baseline Performance Bias: Low; identical intervention Detection Bias: Unclear who outcome assessors were; but assume it was treating clinicians who were blinded Attrition Bias: Unclear; low reported attrition despite mITT: Unclear if withdrawal numbers included study site that was excluded Reporting Bias: Low **Applicability**: Patient: Extensive exclusions applies to very narrow population of moderate to severe disease, obese & no mental health comorbidities Intervention: Oral capsule, easily reproducible; adherence monitoring not achievable in practice Comparator: placebo appropriate Outcomes: Subjective, but valid, clinically important outcome; authors attempt to increase reliability with certified, trained clinician verification using standardized criteria. Longer term studies are needed to determine if the treatment effect is sustained beyond 11 weeks. Setting: US, university clinics, psychiatric & research centers; implies a level of care not generalizable to community care and the same treatment effect may not be achieved

Abbreviations [alphabetical order]: ADE: adverse drug event; BED = binge-eating disorder; BEE = binge-eating episodes; BMI- body mass index; CI = confidence interval; CGI-S = Clinical Global Impressions-Severity score; ITT = intention to treat; DB = double-blind; DSM-IV-TR = Diagnostic and Statistical Manual of Mental Disorders, 4th ed. ;LDX = lisdexamfetamine; mITT = modified intention to treat; MADR-S = Montgomery-Asberg Depression Rating Scale; ; mITT = modified intention to treat; MC = multi-center; N = number of subjects; NA = not applicable; NNH = number needed to harm; NNT = number needed to treat; PCB = placebo; PG = parallel group; PP = per protocol; RD: risk difference; R-PCT = randomized, placebo-controlled trial; wk = week

References:

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Appendix 1: Highlights of Prescribing Information[8]

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use VYVANSE safely and effectively. See full prescribing information for VYVANSE.

VYVANSE® (lisdexamfetamine dimesylate) capsules, for oral use, CII

Initial U.S. Approval: 2007

WARNING: ABUSE AND DEPENDENCE

See full prescribing information for complete boxed warning.

- **CNS stimulants (amphetamines and methylphenidate-containing products), including VYVANSE, have a high potential for abuse and dependence (5.1, 9.2, 9.3)**
- **Assess the risk of abuse prior to prescribing and monitor for signs of abuse and dependence while on therapy (5.1, 9.2)**

----------RECENT MAJOR CHANGES----------

Indications and Usage (1)	01/2015
Dosage and Administration (2)	01/2015

----------INDICATIONS AND USAGE----------

VYVANSE is a central nervous system (CNS) stimulant indicated for the treatment of (1):

- Attention Deficit Hyperactivity Disorder (ADHD)
- Moderate to Severe Binge Eating Disorder (BED)

Limitation of Use: VYVANSE is not indicated for weight loss. Use of other sympathomimetic drugs for weight loss has been associated with serious cardiovascular adverse events. The safety and effectiveness of VYVANSE for the treatment of obesity have not been established.

----------DOSAGE AND ADMINISTRATION----------

Indication	Initial Dose	Titration Schedule	Recommended Dose	Maximum Dose
ADHD (2.2)	30 mg every morning	10 mg or 20 mg weekly	30 mg to 70 mg per day	70 mg per day
BED (2.3)	30 mg every morning	20 mg weekly	50 mg to 70 mg per day	70 mg per day

- Prior to treatment, assess for presence of cardiac disease (2.4)
- Severe renal impairment: Maximum dose is 50 mg/day (2.5)
- End stage renal disease (ESRD): Maximum dose is 30 mg/day (2.5)

----------DOSAGE FORMS AND STRENGTHS----------

Capsules: 10 mg, 20 mg, 30 mg, 40 mg, 50 mg, 60 mg, 70 mg (3)

----------CONTRAINDICATIONS----------

- Known hypersensitivity to amphetamine products or other ingredients in VYVANSE (4)
- Use with monoamine oxidase (MAO) inhibitor, or within 14 days of the last MAO inhibitor dose (4, 7.2)

----------WARNINGS AND PRECAUTIONS----------

- *Serious Cardiovascular Reactions:* Sudden death in children and adolescents with serious heart problems, as well as sudden death, stroke, and myocardial infarction in adults reported. Avoid use in patients with known structural cardiac abnormalities, cardiomyopathy, serious heart arrhythmia, or coronary artery disease (5.2)
- *Blood Pressure and Heart Rate Increases:* Monitor blood pressure and pulse. Consider benefits and risks before use in patients for whom blood pressure increases may be problematic (5.3)
- *Psychiatric Adverse Reactions:* May cause psychotic or manic symptoms in patients with no prior history, or exacerbation of symptoms in patients with pre-existing psychosis. Evaluate for bipolar disorder prior to stimulant use. (5.4)
- *Suppression of Growth:* Monitor height and weight in pediatric patients during treatment (5.5)
- *Peripheral Vasculopathy, including Raynaud's phenomenon:* Stimulants are associated with peripheral vasculopathy, including Raynaud's phenomenon. Careful observation for digital changes is necessary during treatment with stimulants (5.6)

----------ADVERSE REACTIONS----------

Most common adverse reactions (incidence ≥5% and at a rate at least twice placebo) in children, adolescents, and/or adults with ADHD were anorexia, anxiety, decreased appetite, decreased weight, diarrhea, dizziness, dry mouth, irritability, insomnia, nausea, upper abdominal pain, and vomiting (6.1)

Most common adverse reactions (incidence ≥5% and at a rate at least twice placebo) in adults with BED were dry mouth, insomnia, decreased appetite, increased heart rate, constipation, feeling jittery, and anxiety (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Shire US Inc. at 1-800-828-2088 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

----------DRUG INTERACTIONS----------

Acidifying and Alkalinizing Agents: Agents that alter urinary pH can alter blood levels of amphetamine. Acidifying agents decrease amphetamine blood levels, while alkalinizing agents increase amphetamine blood levels. Adjust VYVANSE dosage accordingly. (2.6, 7.1)

----------USE IN SPECIFIC POPULATIONS----------

- *Pregnancy:* Based on animal data, may cause fetal harm (8.1)
- *Nursing Mothers:* Discontinue drug or nursing taking into consideration importance of drug to the mother (8.3)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 12/2015

Appendix 2: Proposed Prior Authorization Criteria

Attention Deficit Hyperactivity Disorder (ADHD) Safety Edit

Goals:

- Cover ADHD medications only for diagnoses funded by the OHP and medications consistent with current best practices.
- Promote care by a psychiatrist for patients requiring therapy outside of best-practice guidelines.
- Promote preferred drugs in class.

Length of Authorization:

- Up to 12 months

Requires PA:

- Non-preferred drugs on the enforceable preferred drug list.
- Regimens prescribed outside of standard doses and age range (Tables 1 and 2)
- Non-standard polypharmacy (Table 3)

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 and OHP-funded Indications.

	STIMULANTS		NON-STIMULANTS		
Indication	**Methylphenidate and derivatives**	**Amphetamine and derivatives**	**Atomoxetine**	**Clonidine ER**	**Guanfacine ER**
ADHD	Age ≥6 years	Age ≥3 years	Age ≥6 years	Children age 6-17 years only	Children age 6-17 years only
Narcolepsy	Age ≥6 years	Age ≥6 years	Not approved	Not approved	Not approved
Binge-Eating Disorder	Not approved	lisdexamfetamine approved for ≥18 years	Not approved	Not approved	Not approved

Table 2. Standard Age and Maximum Daily Doses.

Drug Type	Generic Name	Minimum Age	Maximum Age	Maximum Daily Dose (adults or children <18 years of age unless otherwise noted)
CNS Stimulant	amphetamine/dextroamphetamine salts IR	3		60 mg
CNS Stimulant	amphetamine/dextroamphetamine salts ER	6		30 mg
CNS Stimulant	dexmethylphenidate IR	6		20 mg
CNS Stimulant	dexmethylphenidate LA	6		40 mg for adults or 30 mg if age <18 years
CNS Stimulant	dextroamphetamine IR	6		40 mg

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Date: May 2016

CNS Stimulant	dextroamphetamine LA	6		60 mg
CNS Stimulant	lisdexamfetamine	6		70 mg
CNS Stimulant	methamphetamine	6	17	not established
CNS Stimulant	methylphenidate IR	4		60 mg
CNS Stimulant	methylphenidate LA	6		72 mg
CNS Stimulant	methylphenidate transdermal	6	17	30 mg
Non-Stimulant	atomoxetine	6		100 mg
Non-Stimulant	clonidine LA	6	17	0.4 mg
Non-Stimulant	guanfacine LA	6	17	4 mg

Abbreviations: IR = immediate-release formulation; LA = long-acting formulation (extended-release, sustained-release, etc.)

Table 3. Standard Combination Therapy for ADHD

Age Group	Standard Combination Therapy
Age <6 years*	Combination therapy not recommended
Age 6-17 years*	1 CNS Stimulant Formulation (LA or IR) + Guanfacine LA 1 CNS Stimulant Formulation (LA or IR) + Clonidine LA
Age ≥18 years**	Combination therapy not recommended

Abbreviations: IR = immediate-release formulation; LA = long-acting formulation (extended-release, sustained-release, etc.)
* As recommended by the American Academy of Pediatrics 2011 Guidelines www.pediatrics.org/cgi/doi/10.1542/peds.2011-2654
**As identified by Drug Class Review: Pharmacologic Treatments for Attention Deficit Hyperactivity Disorder: Drug Effectiveness Review Project, 2011.

Approval Criteria		
1. What diagnosis is being treated?	Record ICD10 code.	
2. Is the treated diagnosis an OHP-funded condition?	**Yes:** Go to #3	**No:** Pass to RPh. Deny; not funded by OHP.
3. Is the requested drug on the PDL?	**Yes:** Go to #5	**No:** Go to #4
4. Will the prescriber consider a change to a preferred agent? Message: • Preferred drugs do not require co-pay and are evidence-based reviewed for comparative effectiveness and safety by the Oregon Pharmacy & Therapeutics (P&T) Committee.	**Yes:** Inform prescriber of preferred alternatives	**No:** Go to #5

Approval Criteria		
5. Is the request for an approved FDA indication defined in Table 1?	**Yes:** Go to #6	**No:** Go to #9
6. Are the patient's age and the prescribed dose within the limits defined in Table 2?	**Yes:** Go to #7	**No:** Go to #9
7. Is the prescribed drug the only stimulant or non-stimulant filled in the last 30 days?	**Yes:** Approve for up to 12 months	**No:** Go to #8
8. Is the multi-drug regimen considered a standard combination as defined in Table 3?	**Yes:** Approve for up to 12 months	**No:** Go to #9
9. Was the drug regimen developed by, or in consultation with, a psychiatrist, developmental pediatrician, psychiatric nurse practitioner, sleep specialist or neurologist?	**Yes:** Document name and contact information of consulting provider and approve for up to 12 months	**No:** Pass to RPh. Deny for medical appropriateness. Doses exceeding defined limits or non-recommended multi-drug regimens of stimulants and/or non-stimulants are only approved when prescribed by a psychiatrist or in consultation with a mental health specialist. May approve continuation of existing therapy once up to 90 days to allow time to consult with a mental health specialist.

P&T Review: *5/16 (KK); 3/16; 5/14; 9/09; 12/08; 2/06; 11/05; 9/05; 5/05; 2/01; 9/00; 5/00*
Implementation: *TBD; 10/9/14; 1/1/15; 9/27/14; 1/1/10; 7/1/06; 2/23/06; 11/15/05*