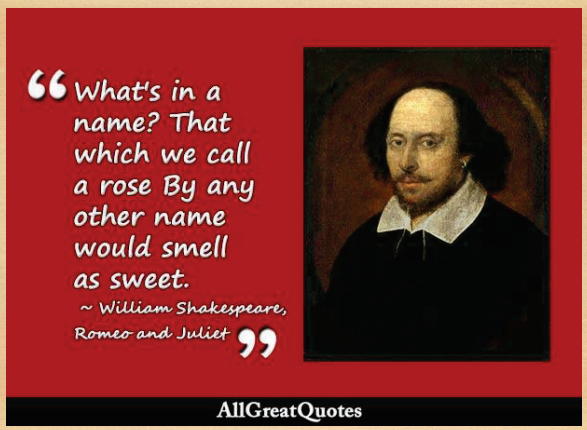
THE NAME GAME

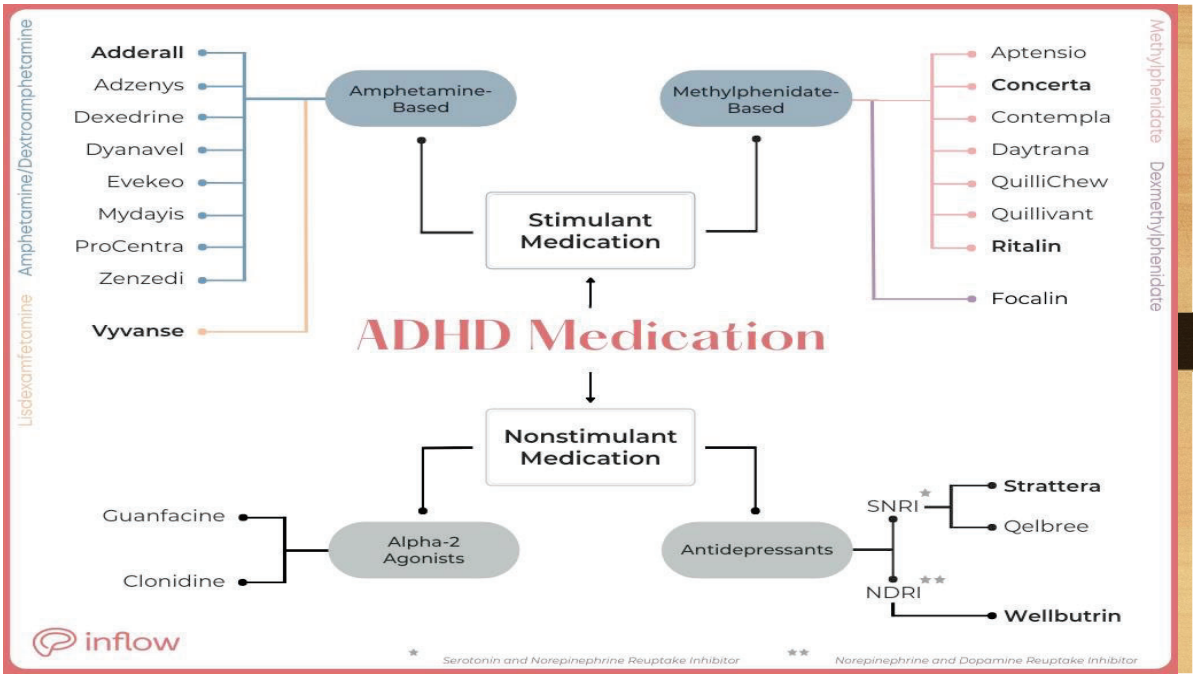
THE NAME GAME

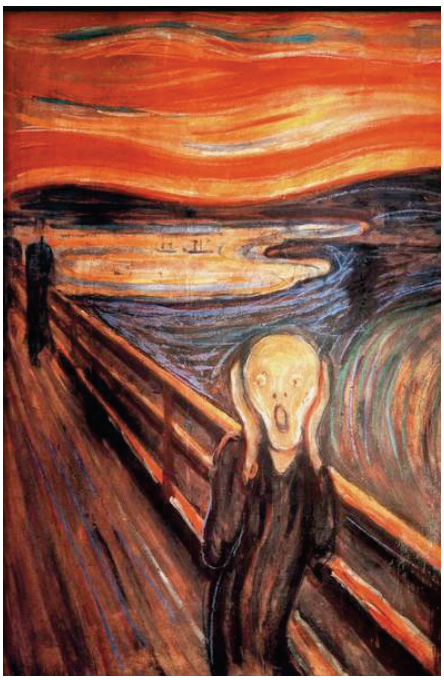
A MEDICATION BY THE SAME NAME MAY NOT BE AS SWEET



GENERIC MEDICATION NAMES

- Generic medication names do not tell what the equivalent brand name medication is





Mark S. Wright, M.D.

- Lily
- Shire/ Takeda
- Neos/Aytu
- Janssen
- Tris
- Supernus
- Alkermes
- Teva

DISCLAIMER

- I will be using brand names in the presentation to differentiate between products so that the participant can identify the current products on the marker to treat ADHD.

METHYLPHENIDATE IR

- Ritalin
- Methylin liquid

AMPHETAMINE IMMEDIATE RELEASE

- Adderall
- Dexedrine
- Dextrostat
- Zenzedi

AMPHETAMINE ER

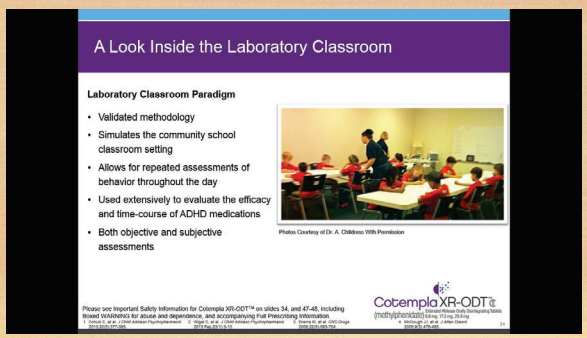
- Adderall XR
- Adzenys XR ODT
- Dexedrine Spansules *
- Dyanavel XR
- Evekeo/Benzedrine
- Mydayis
- Vyvanse*
- Xelstyrm*

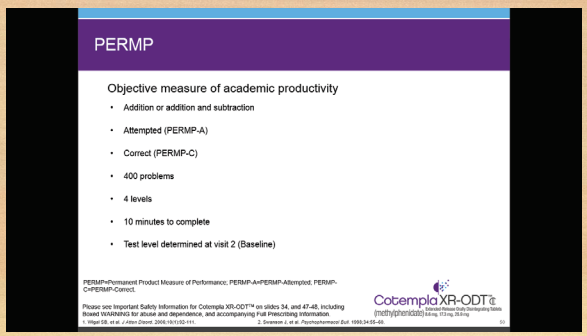
METHYLPHENIDATE EXTENDED RELEASE

- Adhansia XR
- Aptensio XR
- Azstarys
- Concerta
- Cotempla XR ODT
- Focalin XR
- Jornay PM
- Metadate CD
- Methylin ER
- Quillichew ER
- Quillivant XR
- Ritalin LA
- Ritalin SR

RELEASE MECHANISM

- WAX Matrix
- Diffucups
- OROS
- SODAS/MICROTROL
- PRODRUG
- PATCH
- MULTILAYER BEADS
- RESIN RELEASE
- LIQUI-XR
- DERIS

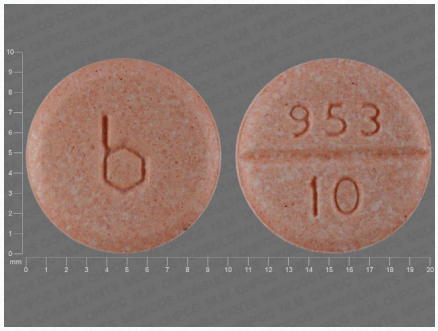




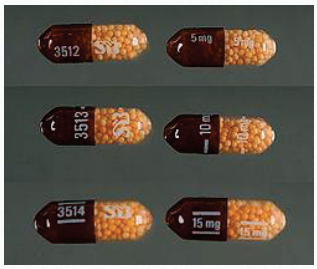
Dexedrine tablet and spansule

- Dexedrine comes in both long- and short-acting forms.
- The short-acting tablet comes in 5 mg and 10 mg dosages. This dose usually lasts about 2 hours.
- The longer-acting spansule is available in 5 mg, 10 mg, and 15 mg sizes and is typically effective for 8 to 10 hours after administration. This permits once-daily dosing with the spansule.

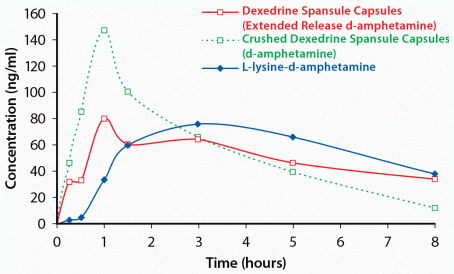
DEXEDRINE SHORT ACTING (Dextrostat)



DEXEDRINE SPANSULE



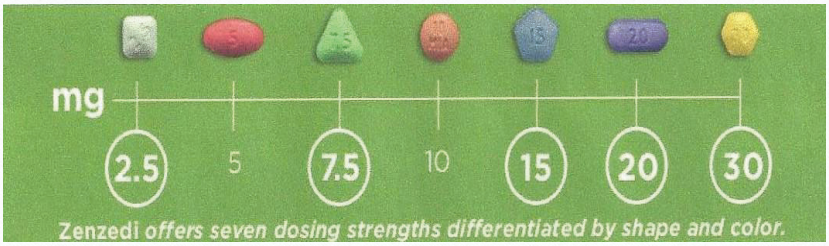
DEXEDRINE SPANSULE vs VYVANSE



Plasma concentrations of d-amphetamine levels following oral administration of Dexedrine Spansule® capsules, crushed Dexedrine Spansule® capsules, or L-lysine-d-amphetamine dimesylate (at dose 3 mg/kg d-amphetamine base) to rats (ELISA analysis).

Figure 20 from the Shire patent application for Vyvance®, recreated by aeon.

ZENZEDI
Immediate Release Dextroamphetamine



Zenzedi offers seven dosing strengths differentiated by shape and color.

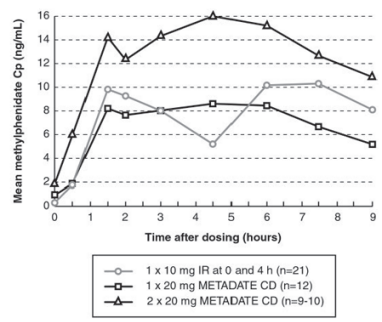
WAX MATRIX

- Ritalin SR
- Manufactured by Novartis (Ciba) March 30, 1982.
- Comes in 20 mg dose
- There is no legitimate generic of this medication

Diffucapps

- Metadate CR
  - Once a day capsule with biphasic release
  - Releases 30 % immediately
  - Releases 70 % gradually
  - Lasts about 8 hours
  - Discontinued in U.S.

METADATE CD vs RITALIN IR



OROS

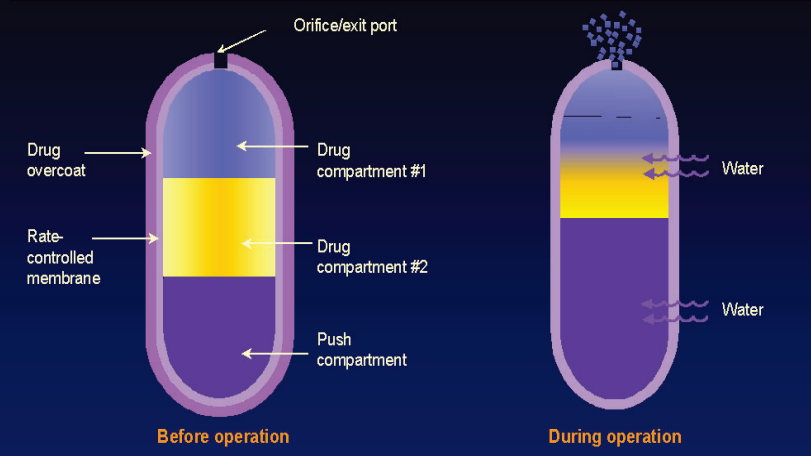
Osmotic Controlled Release Oral Delivery System

OROS

- ALZA Corporation
- Rigid tablet
- Semi-permeable outer membrane
- Laser drilled holes

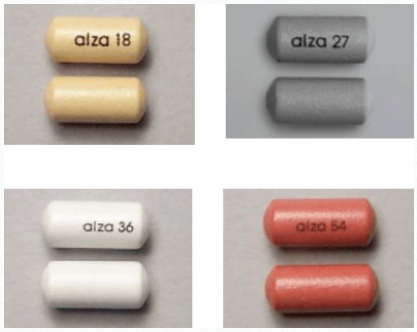
- As the tablet passes through GI tract, water is absorbed through the semipermeable membrane via osmosis
- Resulting osmotic pressure pushes active drug through the laser drilled openings in the tablet and into GI tract

OROS® Technology



Swanson JM et al. Comparison of efficacy and safety of Concerta™ (methylphenidate HCl) with Ritalin® and placebo in children with ADHD. Presented at Region IX and X Annual Meeting of the Ambulatory Pediatric Association; February 12-13, 2000; Carmel, CA.

Concerta



ADHD Roller Coaster 12/5/2022

- **1. Janssen has stopped the authorized generic.**
- The official cut-off date is 1/13/23. But the last supplies have been already distributed, according to a Janssen representative. You might still find pockets of availability. At least for a while.

SODAS

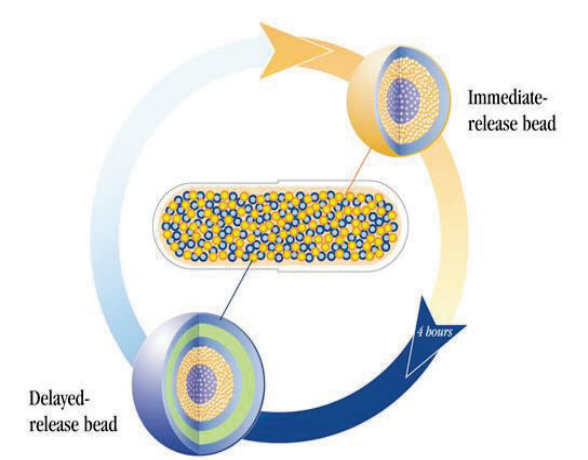
Spheroidal Oral Drug Absorption System

SODAS

- Elan Corporation
- Multiparticle drug delivery system
- Can be designed to release at specific pH in the GI tract
- Can be designed to release different quantities at different pHs

SPHEROIDAL ORAL DRUG ABSORPTION SYSTEM

SODAS Pulse Delivery System



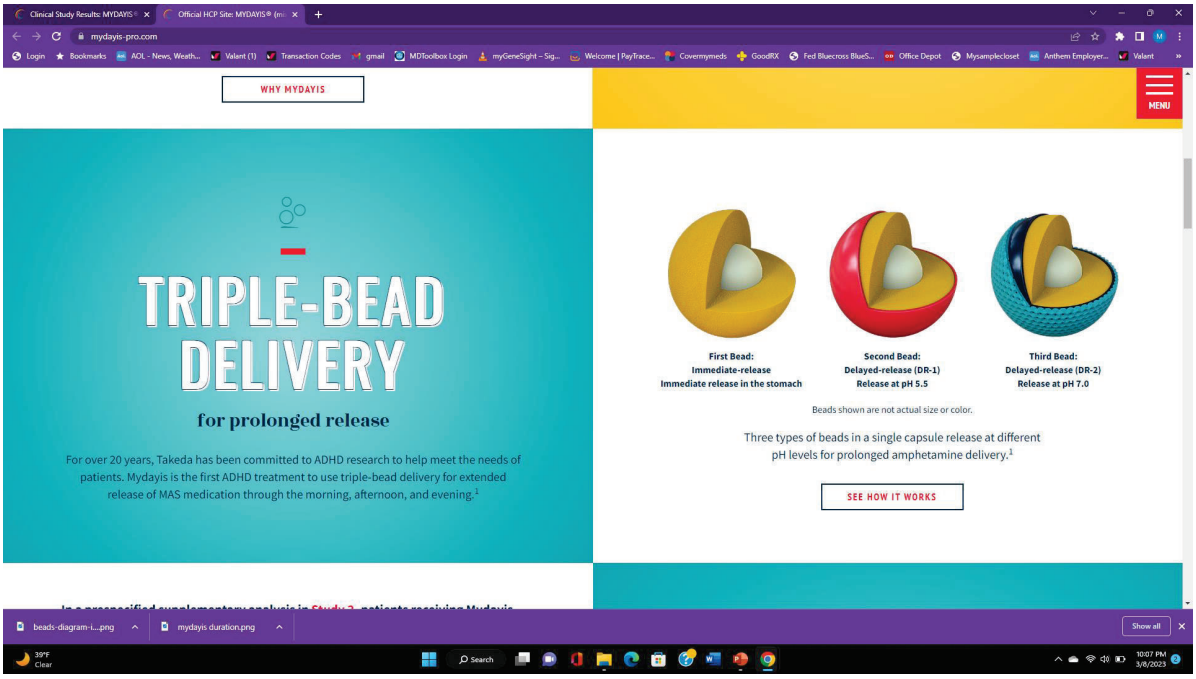
SODAS

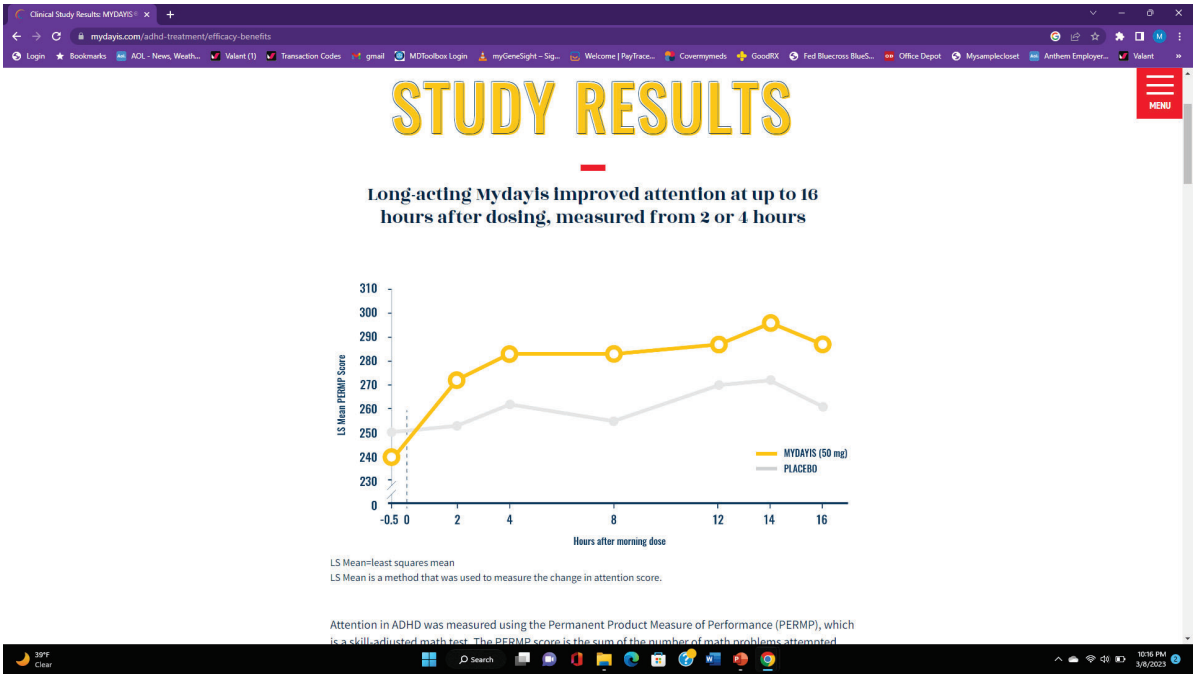
- Methylphenidate
  - Ritalin LA 50/50
  - Focalin XR 50/50
- Amphetamine salts
  - Adderall XR 50/50
  - Mydayis 33/33/33

Mydayis®
(mixed salts of a single-entity amphetamine product)
12.5 | 25 | 37.5 | 50 mg extended-release capsules

MYDAYIS – Triphasic Release

- Our **immediate-release** beads provide medication right after your daily dose and for the next few hours.
- Our first type of **delayed-release** beads continue to provide midday medication.
- Our second type of **delayed-release** beads provide medication release into the evening.





50% dextroamphetamine

50% levoamphetamine

EVEKEO® (II)

amphetamine sulfate

5 mg • 10 mg tablets, USP

INDICATION

Evekeo® (amphetamine sulfate tablets, USP) is a prescription medicine for the treatment of narcolepsy, attention deficit disorder with hyperactivity as an integral part of a total treatment program and exogenous obesity as a short term adjunct in a regimen of weight reduction.

Please see additional Important Safety Information on back of cover and attached full Prescribing Information.

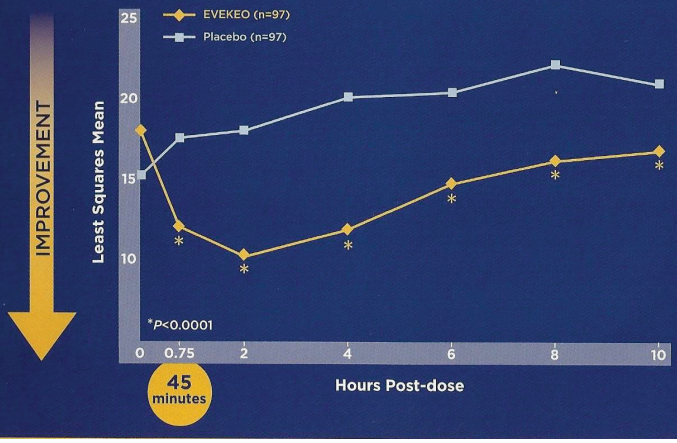
IMPORTANT SAFETY INFORMATION

Evekeo is a federally controlled substance (CII) with a high risk of abuse or dependence. Prolonged use may lead to drug dependence and must be avoided. Subjects may obtain Evekeo for illegal non-therapeutic use or distribution to others, and therefore it should be prescribed or dispensed sparingly.

Misuse of Evekeo may cause sudden death and serious cardiovascular adverse events.

EVEKEO: SKAMP-Combined[2]

A single dose of EVEKEO at 8 am demonstrated significant efficacy (*P*<0.0001) vs placebo at all measured time points[2]



- Improvement from 45 minutes through 10 hours post-dose[2]

Study details: Swanson, Kotkin, Agler, M-Flynn, and Pelham (SKAMP)-Combined measurement includes attention, deportment, quality of work, and compliance subscales and is a standardized, validated classroom assessment tool consisting of 13 items used for evaluating inattention and behavioral symptoms of ADHD.[2]

Study design: Results are from a phase 4 laboratory classroom study of children with ADHD aged 6 to 12 years. This was a multicenter, double-blind, placebo-controlled, crossover study. The study excluded children with significant psychiatric and medical comorbidities.[2]

Least squares mean: Mean calculated using a statistical model.

APTENSIO-XR

Small bead release

Actually not as illustrated

40 % immediate release

60 % gradual release

Not for potentiation

Can be sprinkled on apple sauce

Each capsule of Aptensio XR® (methylphenidate HCl extended-release) is filled with small beads that contain layers of medicine to be released at different times in a 12-hour day.

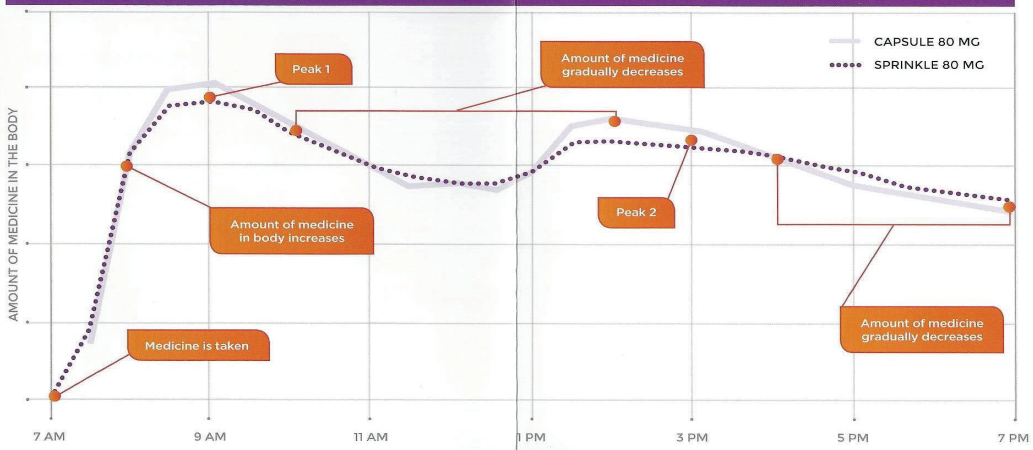
About 40% of the medicine in each bead is fast-acting and 60% is long-acting.

How Aptensio XR works

Medicine is released in the first hour after your child takes Aptensio XR® (methylphenidate HCl extended-release) and continues to work from hour 1 to hour 12.

The amount of medicine in your child's body peaks twice in a 12-hour day, at times he or she may need it most.

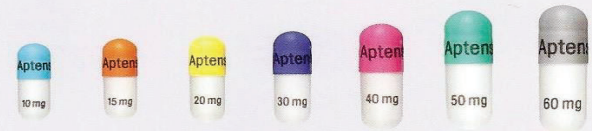
Aptensio XR peaks twice throughout your child's 12-hour day



How Aptensio XR is taken

Aptensio XR® (methylphenidate HCl extended-release) comes in 7 dosing strengths to help the doctor find the right dose for your child.

7 dosage strengths for personalized treatment



10 mg 15 mg 20 mg 30 mg 40 mg 50 mg 60 mg

Capsules are not shown at actual size.

Aptensio XR can be swallowed whole or the capsule can be opened and the contents sprinkled on applesauce.

- It is important that your child takes the entire contents of the capsule immediately, and does not chew the beads

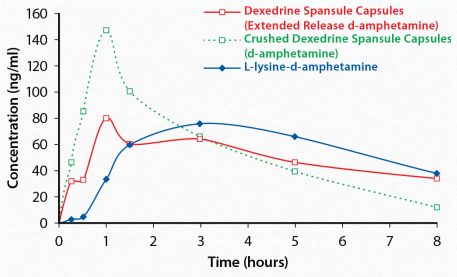
PRODRUG

- Inactive parent compound that is bound to an essential amino acid. Once the compound is absorbed, the amino acid is removed by enzymatic action that turns into the active drug.

PRODRUG

- Vyvanse (lysdextroamphetamine)
- Bound to lysine
- Continuous release up to 14 hours
- Azstarys (serdexmethylphenidate/ dexmethylphenidate)
- Bound to serine
- 30 % immediate release
- 70 % prodrug release

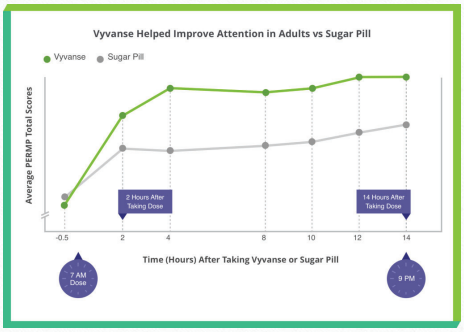
VYVNASE RELEASE



Plasma concentrations of d-amphetamine levels following oral administration of Dexedrine Spansule® capsules, crushed Dexedrine Spansule® capsules, or L-lysine-d-amphetamine dimesylate (at dose 3 mg/kg d-amphetamine base) to rats (ELISA analysis).

Figure 20 from the Shire patent application for Vyvance®, recreated by aeon.

VYVANSE SCHOOLROOM STUDY

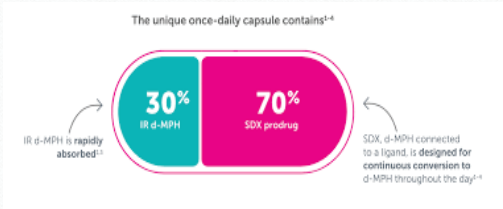


azstarys™ (C)

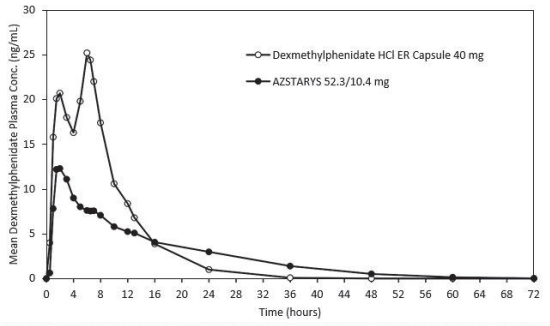
serdexmethylphenidate and dexmethylphenidate

26.1/5.2mg • 39.2/7.8mg • 52.3/10.4mg capsules

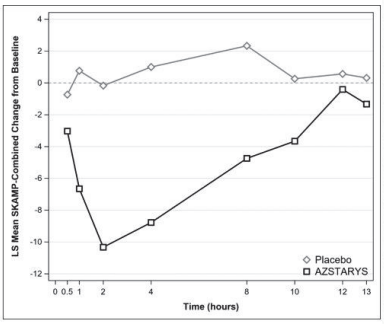
AZSTARYS



AZSTARYS vs FOCALIN XR



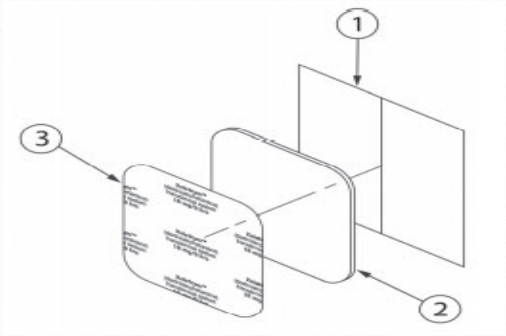
AZSTARYS DURATION



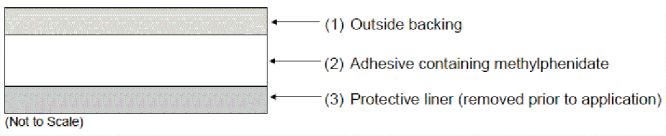
HOW MUCH?

PATCHES FROM NOVEN

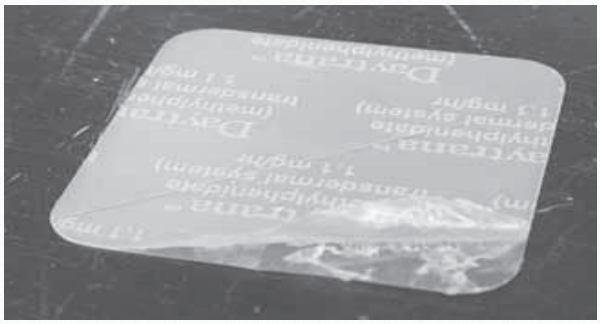
- Daytrana
- Methylphenidate
- Comes in 4 sizes
- Xelstyrm
- Dextroamphetamine
- Approved 2022
- Released Spring 2023



3 layer system

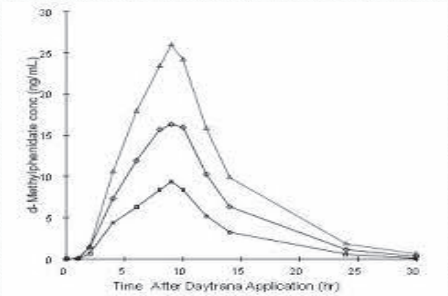


DAYTRANA PATCH



Daytrana comes in 4 sizes

DAYTRANA RELEASE

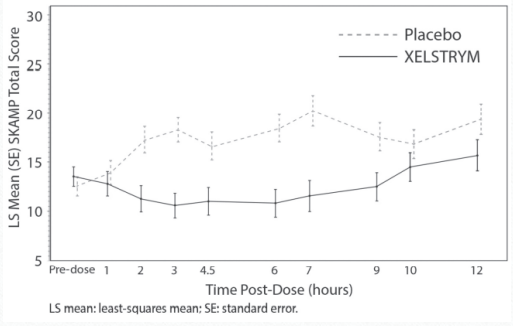


Xelstrym™

(dextroamphetamine) Ⓒ Ⅱ
transdermal system

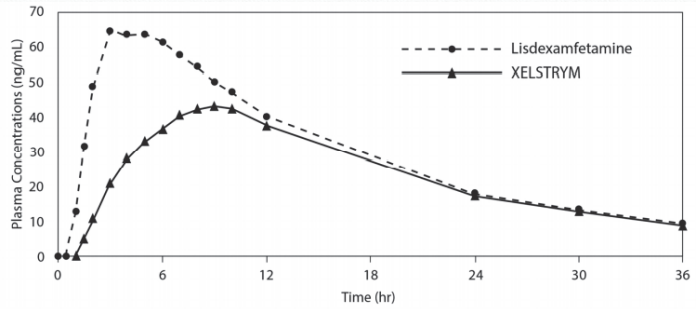
4.5mg/9 hours 9mg/9 hours 13.5mg/9 hours 18mg/9 hours

SKAMP CLASSROOM PERFORMANCE



LS mean: least-squares mean; SE: standard error.

XELSTRYM vs. VYVANSE



DERIS Release

- Delayed Extended Release IronShore
  - Delayed-release layer with hydrophobic pH-dependent properties
  - Extended-release layer composed of hydrophobic and soluble polymers providing a delayed period before drug is released
  - Immediate-release core that acts as a drug reservoir

Jornay

- Delayed release, extended release methylphenidate indicated for ADHD in children 6 and up
- Unlike other stimulants, Jornay is taken once a day close to bedtime
  - 6:30-9:30 PM
  - Same time every day
- Delayed release allows for drug control of symptoms upon awakening

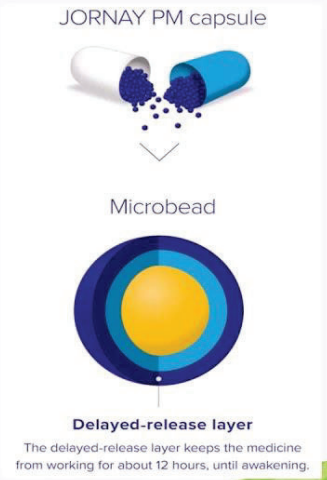


Image and content from https://www.jornaypm.com/

Gradually absorbed in the colon for long and consistent ADHD symptom control

jornay PM methylphenidate HCl extended-release capsules

Methylphenidate (MPH) is absorbed at a slower rate in the colon than in the upper bowel[6,7]

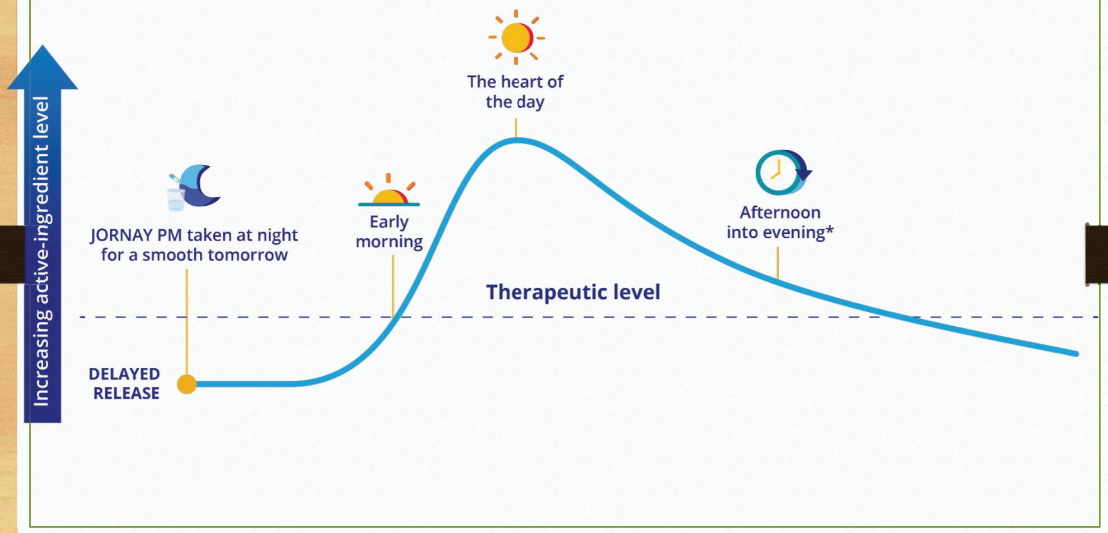
Dissolution and absorption of JORNAY PM is not dependent on any single factor (eg, pH, normal variations in GI transit time, site of release, etc)[6]

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS

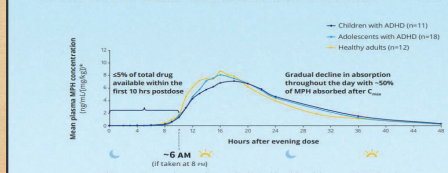
- *Serious Cardiovascular Reactions:* Sudden death, stroke, and myocardial infarction have been reported in adults treated with CNS stimulants at recommended doses. Sudden death has been reported in pediatric patients with structural cardiac abnormalities and other serious heart problems taking CNS stimulants at recommended doses for ADHD. Avoid use in patients with known structural cardiac abnormalities, cardiomyopathy, serious heart arrhythmias, coronary artery disease, and other serious cardiac problems.

Please see additional Important Safety Information throughout and on pages 6-7.
Please see accompanying Full Prescribing Information, including Boxed Warning.



Long, smooth pharmacokinetic profile with no immediate-release bolus[2,6]

jornay PM methylphenidate HCl extended-release capsules



*Concentrations are dose-weight-normalized in healthy adults, adolescents with ADHD, and children with ADHD. Results based on a 54-mg oral dose of JORNAY PM administered in the evening at 9 PM. Dose-weight-normalized exposure was similar among all age groups.[6]
C_{max} occurs between noon and 2 PM (16–18 hours postdose).[4]
C_{max}, peak plasma concentration; PK, pharmacokinetic.

Based on multiple-dose simulations, accumulation of JORNAY PM was predicted to be negligible[a]

IMPORTANT SAFETY INFORMATION (continued)

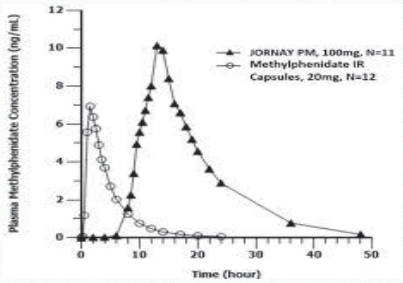
WARNINGS AND PRECAUTIONS (continued)

- *Blood Pressure and Heart Rate Increases:* CNS stimulants may cause an increase in blood pressure and heart rate. Monitor all patients for hypertension and tachycardia.

Please see additional Important Safety Information throughout and on pages 6-7.
Please see accompanying Full Prescribing Information, including Boxed Warning.

7 AM 8 AM 9 AM 10 AM 11 AM 12 PM 1 PM 2 PM 3 PM 4 PM 5 PM 6 PM 7 PM 8 PM

JORNAY PM vs RITALIN IR

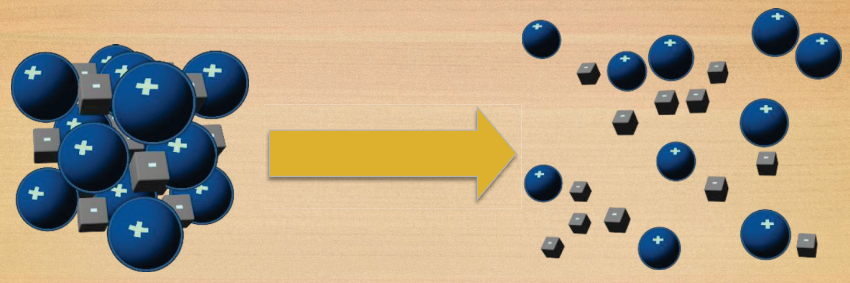


MICROPARTICLE RESIN RELEASE

Adzenys XR ODT

Cotempla XR ODT

STEP 1: Adzenys XR-ODT™ Technology Overview



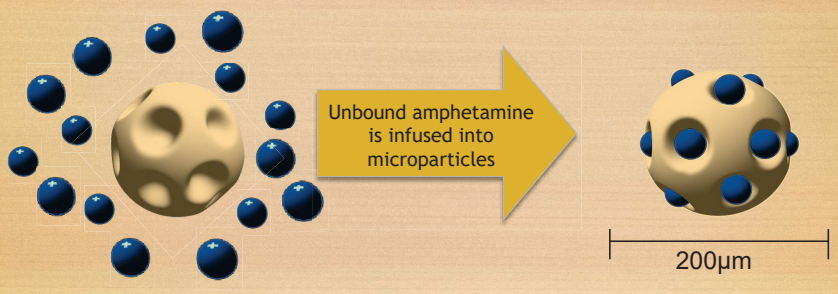
Amphetamine
Salt

Amphetamine-salt dissociates in solution

STEP 2: Adzenys XR-ODT™ Technology Overview

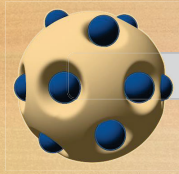
Amphetamine
Microparticle

Amphetamine-loaded microparticle



Data on File. Neos Therapeutics, Inc.

STEP 3: Adzenys XR-ODT™ Technology Overview



Amphetamine-loaded microparticles are split into two groups

1 **50% Immediate-Release (IR)**
- Microparticles remain uncoated for immediate-release (IR) amphetamine delivery

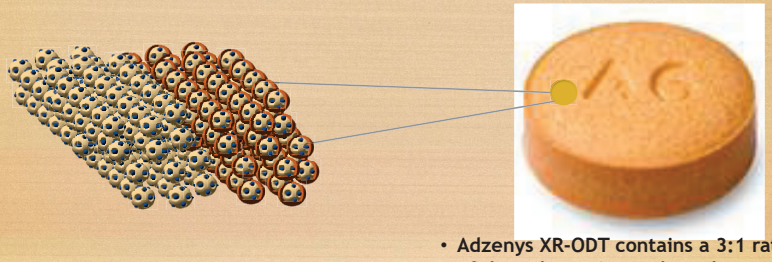
2 **50% Extended-Release (XR)**
- Microparticles are coated, which enables extended-release (XR) amphetamine delivery

Data on File. Neos Therapeutics, Inc.

STEP 4: Adzenys XR-ODT™ Technology Overview

Thousands of microparticles are compressed into a single ODT

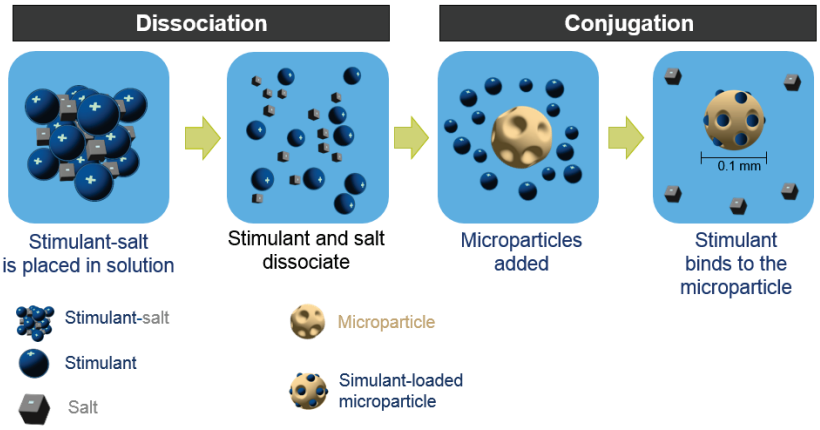
50% Immediate-Release (IR) **50% Extended Release (XR)**



- **Adzenys XR-ODT contains a 3:1 ratio of *d*-amphetamine to *l*-amphetamine**

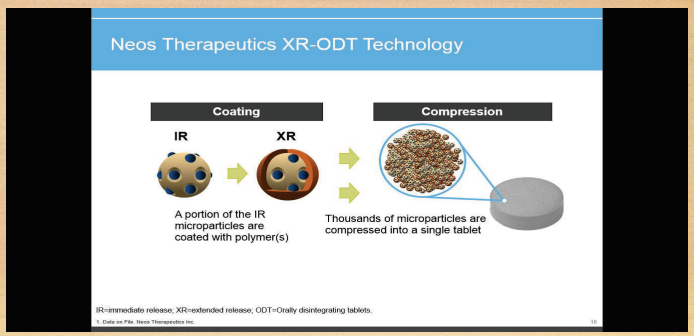
Data on File. Neos Therapeutics, Inc.

Neos Therapeutics XR-ODT Technology



1. Data on File. Neos Therapeutics Inc.

9

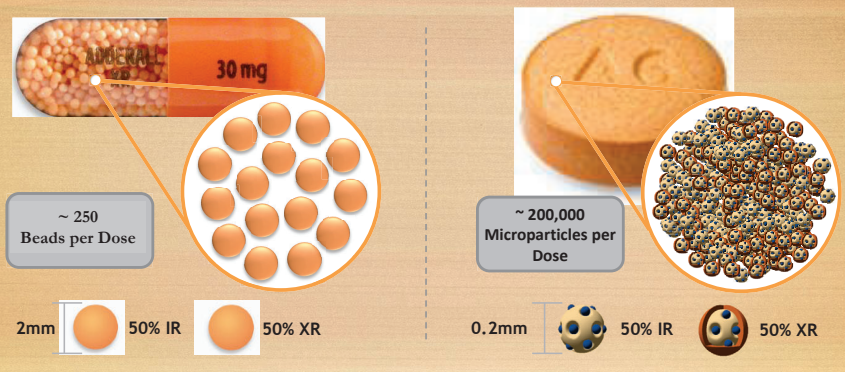


ADZENYS-XR ODT

Beaded Delivery System

Microparticle Delivery System

30 mg Adderall XR® and 18.8 mg Adzenys XR-ODT™ are Equivalent Doses



Above represents the physical characteristics of the products, not intended to compare safety or efficacy. Adzenys XR-ODT is therapeutically equivalent to Adderall XR.

79

Adzenys XR-ODT™ Dosing[1]

Available in 6 dosage strengths

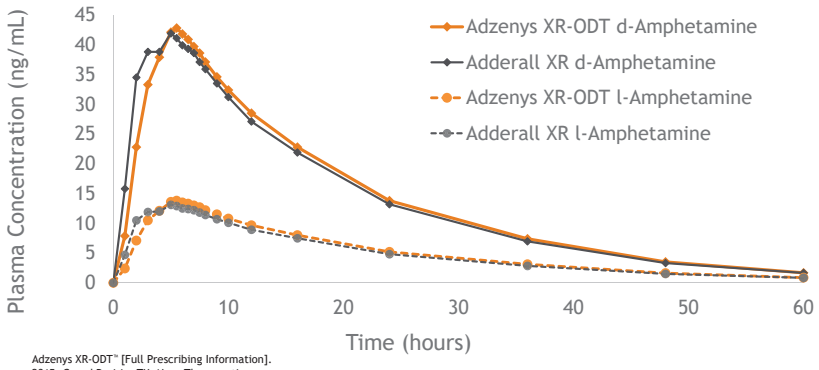
Treatment Considerations

- Prior to treating patients, assess for the presence of cardiac disease
- Tablet should not be crushed or chewed
- Assess the risk of abuse prior to prescribing, and monitor for signs of abuse and dependence while on therapy.
- Agents that alter urinary pH can alter blood levels of amphetamine. Acidifying agents can decrease amphetamine blood levels, while alkalinizing agents can increase amphetamine blood levels. Adjust Adzenys XR-ODT dosage accordingly

1. Adzenys XR-ODT™ [Full Prescribing Information]. 2015. Neos Therapeutics, Inc.

Therapeutically Equivalent to Adderall XR™

Fasted State – Adzenys XR-ODT (18.8 mg) and Adderall XR (30 mg)

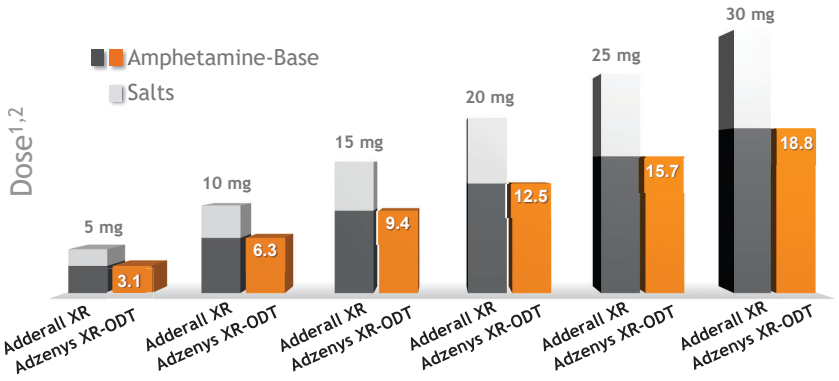


Adzenys XR-ODT™ [Full Prescribing Information]. 2015. Grand Prairie, TX: Neos Therapeutics.

CAUTION:
Not equivalent dosing with Adderall XR

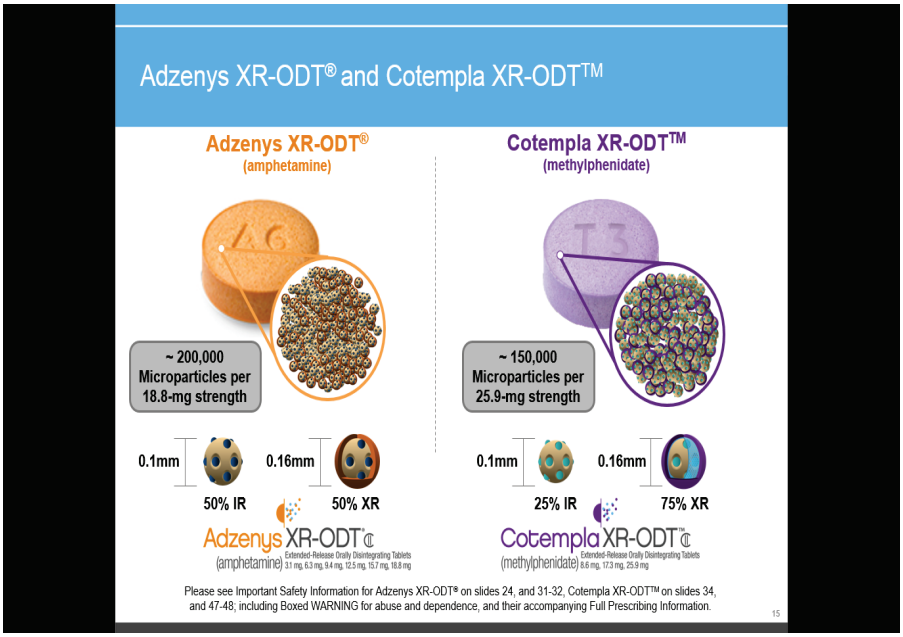
Adzenys XR-ODT™ (amphetamine) Extended-Release Orally Disintegrating Tablets 3.1 mg, 6.3 mg, 9.4 mg, 12.5 mg, 15.7 mg, 18.8 mg	3.1 mg	6.3 mg	9.4 mg	12.5 mg	15.7 mg	18.8 mg
Adderall XR	5 mg	10 mg	15 mg	20 mg	25 mg	30 mg

Adzenys XR-ODT™ and Adderall XR®: Same Amphetamine Base



3:1 ratio, *d*-to *l*-amphetamine

1. Adzenys XR-ODT™ [Full Prescribing Information]. 2015. Neos Therapeutics, Inc.
2. Adderall XR® [Full Prescribing Information]. 2015. Shire US, Inc.

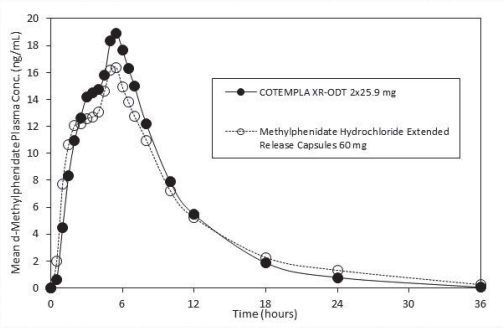


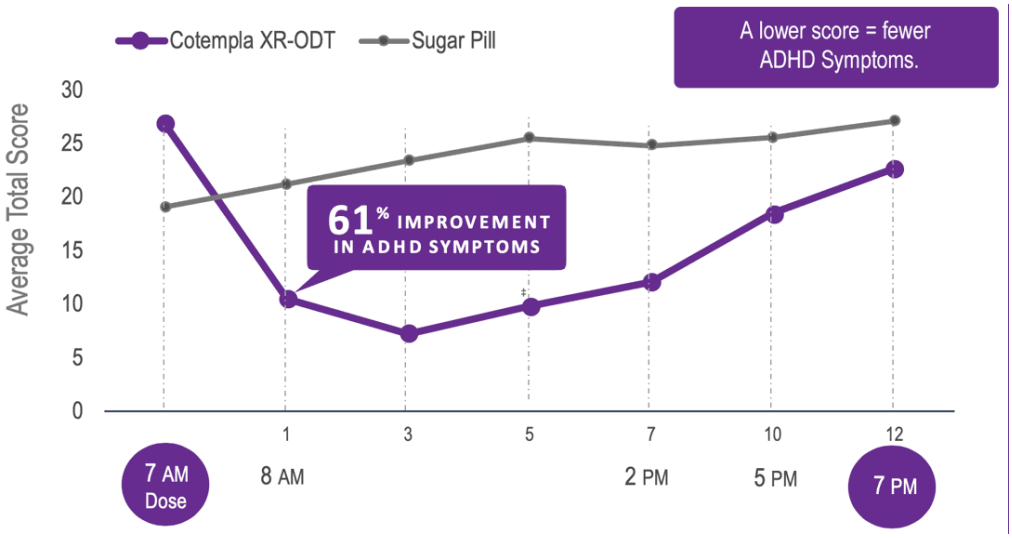
INDIVIDUALIZED DOSING OPTIONS TO FIT PATIENT NEEDS

8.6 mg	17.3 mg	25.9 mg	34.6 mg	51.8 mg
T1	T2	T3	T2 + T2	T3 + T3
	Starting Dose		17.3 mg + 17.3 mg	25.9 mg + 25.9 mg

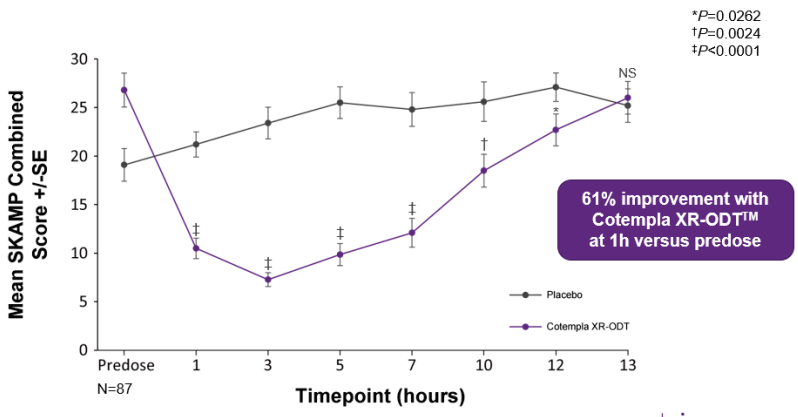
Tablets depicted are not actual size

COTEMPLA XR ODT RELEASE





SKAMP-Combined Score During the Classroom Testing Day (LS Mean)



Please see Important Safety Information for Cotempla XR-ODT™ on slides 34, and 47-48, including Boxed WARNING for abuse and dependence, and accompanying Full Prescribing Information.

1. Cotempla XR-ODT™ Prescribing Information. Neos Therapeutics Inc. Grand Prairie, TX. June 2017.

Cotempla XR-ODT™ (methylphenidate) Extended-Release Orally Disintegrating Tablets 8.6 mg, 17.3 mg, 25.9 mg

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CAUTION: NOT MG. PER MG.

	DOSING OPTIONS				
Cotempla XR-ODT	8.6 mg	17.3 mg	25.9 mg	17.3 mg + 17.3 mg	25.9 mg + 25.9 mg
		Recommended Starting Dose		34.6 mg	51.8 mg
	METHYLPHENIDATE BASE EQUIVALENTS				
ER MPH	10 mg	20 mg	30 mg	40 mg	60 mg

The Tris Product Portfolio Provides Multiple Treatment Options for Patients 6 Years and Older With ADHD

DYANAVEL XR (amphetamine) extended-release tablets 5 mg • 10 mg • 15 mg • 20 mg

Dyanavel XR (amphetamine) extended-release oral suspension 2.5 mg/mL

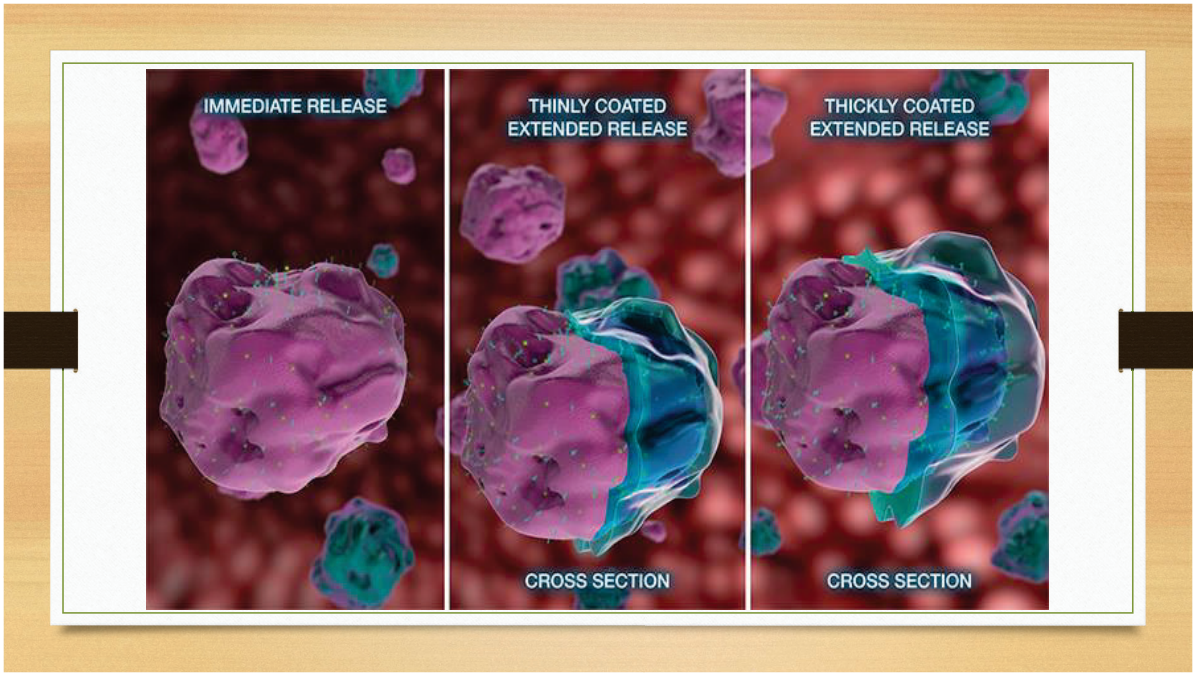
Tris PHARMA

QuilliChew ER methylphenidate HCl 20 mg, 30 mg, 40 mg extended-release chewable tablets

Quillivant XR methylphenidate HCl 25 mg/5 mL for extended-release oral suspension

Please see additional Important Safety Information throughout, and Full Prescribing Information for DYANAVEL XR, Quillivant XR, and QuilliChew ER, including Boxed Warning regarding Abuse and Dependence, provided at this presentation, and also available at TrisADHDHCP.com.

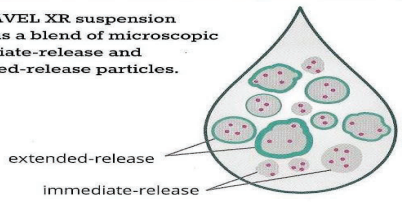
40



LiquiXR® Technology[1,2]

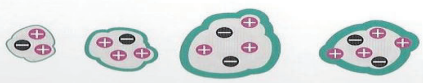
Ion exchange chemistry combined with the science of extended-release

DYANAVEL XR suspension contains a blend of microscopic immediate-release and extended-release particles.

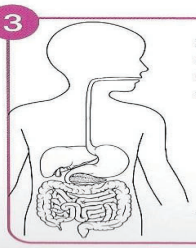


1 Initially, amphetamine ions bind with a negatively charged ion-exchange resin.

2 A coating of various thicknesses is applied. Coating thickness is a key factor in providing a continuous release of amphetamine.



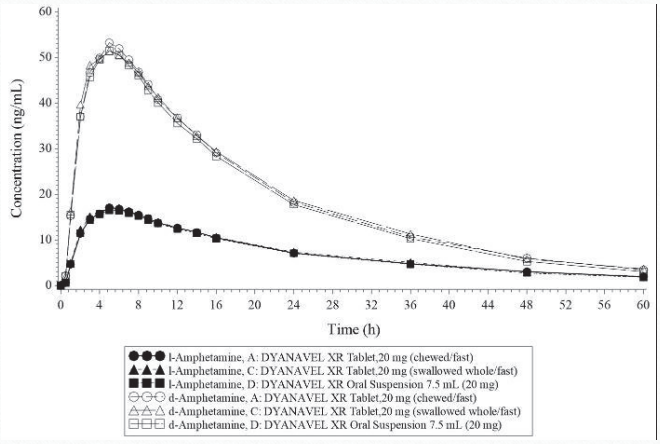
3 Positively charged ions from the GI tract displace the amphetamine from the resin; amphetamine is absorbed into the bloodstream.*



*After drug release the ion-exchange resin is excreted in the feces.

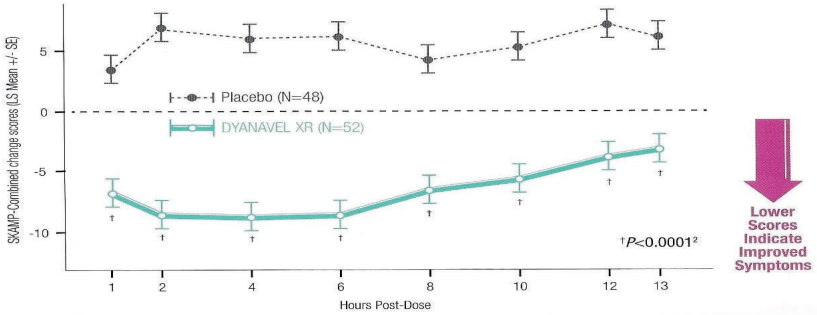
DYANAVEL XR LIQUID AND TABLET

Dosing/ Titration	Dispense	Take Once Daily in the Morning With or Without Food
20 mg/day (starting dose)	600-mg bottle (120 mL)	4 mL
10 mg/day	300-mg bottle (60 mL)	2 mL
30 mg/day	900-mg bottle (180 mL)	6 mL
40 mg/day	2×600-mg bottle (total 240 mL)	8 mL
50 mg/day	2×750-mg bottle (total 300 mL)	10 mL
60 mg/day (maximum dose)	2×900-mg bottle (total 360 mL)	12 mL



Continuous Symptom Control From 1 Hour to 13 Hours Post-Dose

Change from pre-dose in SKAMP*-Combined Score after treatment with DYANAVEL XR or Placebo

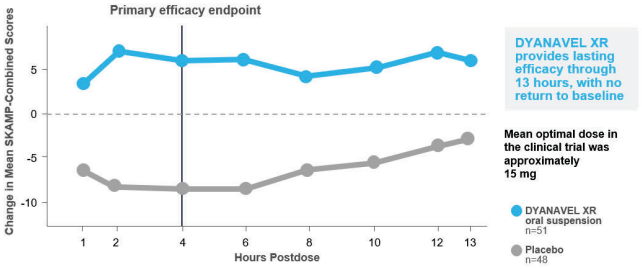


Results of the 1-week, randomized, double-blind, placebo-controlled laboratory classroom assessment of attention and behavior, scored by teachers and raters using the SKAMP Rating Scale in children aged 6 to 12 years (N=108) who met DSM-IV criteria for ADHD. Classroom assessment followed a 5-week, open-label dose-optimization period. The optimal dose was carried into the double-blind phase of the study. Primary efficacy endpoint was change from pre-dose in the SKAMP-Combined score at 4 hours post-dosing. The key secondary efficacy parameters were onset and duration of clinical effect. The change scores from pre-dose SKAMP-Combined scores at post-dose timepoints (1, 2, 4, 6, 8, 10, 12, and 13 hours) were used to evaluate key secondary efficacy parameters.

*** SKAMP** = Swanson, Kotkin, Agler, M-Flynn, and Pelham; a 13-item, teacher-rated, 7-point impairment scale that assesses manifestations of ADHD in a classroom setting.

DYANAVEL XR Oral Suspension Starts Fast and Lasts

Statistically Significant Improvement in Attention and Behavior With DYANAVEL XR vs Placebo



The primary endpoint—change from predose in SKAMP-Combined score at 4 hours postdose—was **significantly improved** in the DYANAVEL XR (amphetamine) group compared with that in the placebo group.

- LS mean: DYANAVEL XR oral suspension, -8.8; placebo, 6.0
- LS mean difference: -14.8 [95% CI: -17.9, -11.6; *P*<0.0001]

CI, confidence interval; LS, least squares; SKAMP, Swanson, Kotkin, Agler, M-Flynn, and Pelham Scale.

Reference: 1. Childress AC et al. *J Child Adolesc Psychopharmacol.* 2018;28(5):306-313.

Dyanavel XR (amphetamine) extended-release oral suspension 2.5 mg/mL

Amphetamine Base Equivalents for ADHD Formulations

DYANAVEL XR (amphetamine) Tablet and Oral Suspension Have Identical Dosing

DYANAVEL XR Tablet*	DYANAVEL XR Oral Suspension*	MAS ER Capsules
2.5 mg	2.5 mg (1 mL)	
5 mg	5 mg (2 mL)	5 mg (3.1-mg amphetamine base)
7.5 mg	7.5 mg (3 mL)	10 mg (6.3-mg amphetamine base)
10 mg	10 mg (4 mL)	15 mg (9.4-mg amphetamine base)
12.5 mg	12.5 mg (5 mL)	20 mg (12.5-mg amphetamine base)
15 mg	15 mg (6 mL)	25 mg (15.6-mg amphetamine base)
17.5 mg	17.5 mg (7 mL)	
20 mg	20 mg (8 mL)	30 mg (18.8-mg amphetamine base)

*DYANAVEL XR is a milligram-to-milligram amphetamine base.

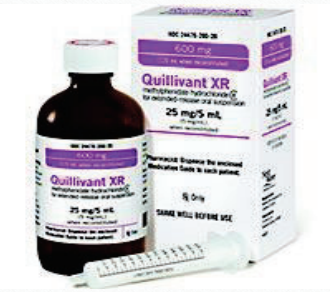
- DYANAVEL XR (amphetamine) extended-release oral suspension can be substituted with DYANAVEL XR extended-release tablet on a milligram-per-milligram basis
- When switching to DYANAVEL XR from other amphetamine products, discontinue that treatment and titrate with DYANAVEL XR as shown on previous slide
- Do not substitute for other amphetamine products on a milligram-per-milligram basis because of different amphetamine base compositions and differing pharmacokinetic profiles
- There are no data comparing the efficacy and safety of DYANAVEL XR and Adderall XR (mixed salts of a single-entity amphetamine product)

DYANAVEL XR has the most dosing options of any extended-release amphetamine product

Reference: Adderall XR [package insert]. Takeda Pharmaceuticals, U.S.A., Inc.

DYANAVEL XR (amphetamine) extended-release tablets 5 mg • 10 mg • 15 mg • 20 mg

QUILLIVANT AND QUILLICHEW



- Ability to titrate the dose in as little as 10-mg increments to meet the individual needs of patients
- 11 dosing options—the most dosing options in a tablet for ADHD

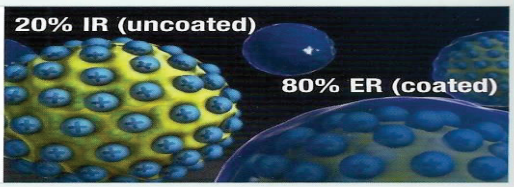
*The 20-mg and 30-mg tablets are scored. The 40-mg tablet is not scored.
Tablets are not actual size.

12

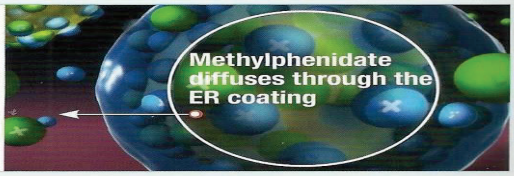
Quillivant XR™ (methylphenidate HCl): extended-release formulation

Quillivant XR uses proprietary LiquiXR™ technology, which provides a combination of approximately 20% immediate-release (IR) and 80% extended-release (ER) methylphenidate

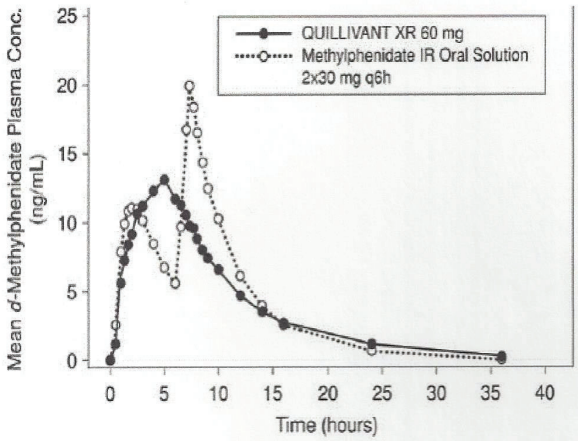
During the manufacturing process, drug/polymer complexes are created and some are coated with varying thicknesses of an ER coating. Some of the drug/polymer complexes remain uncoated.



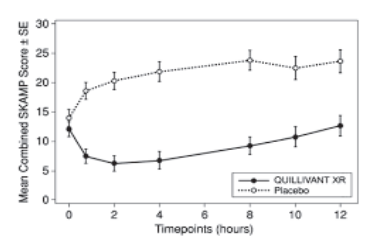
The uncoated complexes immediately release methylphenidate in the small intestine, while the coated complexes release methylphenidate at varying rates, depending on the thickness of the coating. The thicker the coating, the slower the release.

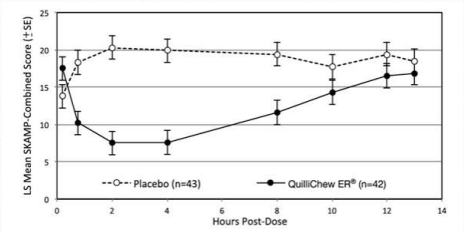


2/12/2017 RxList



QUILLIVANT vs. QUILLICHEW





The Tris Product Portfolio Provides Multiple Treatment Options for Patients 6 Years and Older With ADHD

DYANAVEL XR (amphetamine) extended-release tablets 5 mg • 10 mg • 15 mg • 20 mg

Dyanavel XR (amphetamine) extended-release oral suspension 2.5 mg/mL

Tris PHARMA

QuilliChew ER® methylphenidate HCl extended-release chewable tablets 20 mg 30 mg 40 mg

Quillivant XR® methylphenidate HCl for extended-release oral suspension 25 mg/5 mL

Please see additional Important Safety Information throughout, and Full Prescribing Information for DYANAVEL XR, Quillivant XR, and QuilliChew ER, including Boxed Warning regarding Abuse and Dependence, provided at this presentation, and also available at TrisADHDHCP.com.

40

NOW APPROVED
FOR ADULT ADHD

Focusing on ADHD Across the Ages: The Role of Qelbree in Treating Both Pediatric and Adult Patients

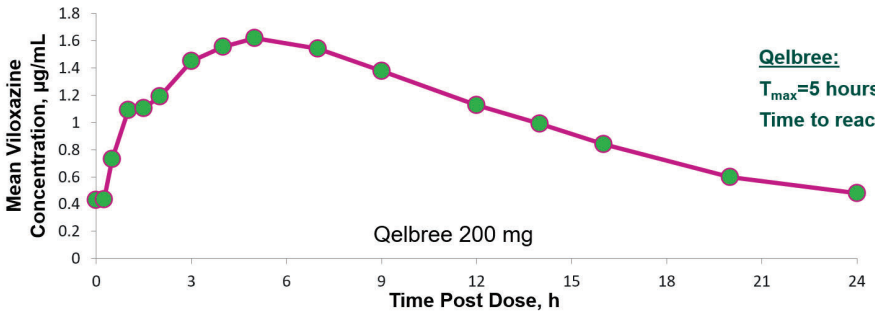
Now approved for the treatment of Attention-Deficit/Hyperactivity Disorder (ADHD) in patients 6 years and older

ONCE-DAILY Qelbree® viloxazine extended-release capsules

Please see full Important Safety Information, including Boxed Warning, on slides 25-26.

Qelbree: Once-Daily Dosing Provides Full-Day Exposure[1,2]

Mean Viloxazine Plasma Levels in Healthy Adults at Steady State (N=27)



Qelbree:

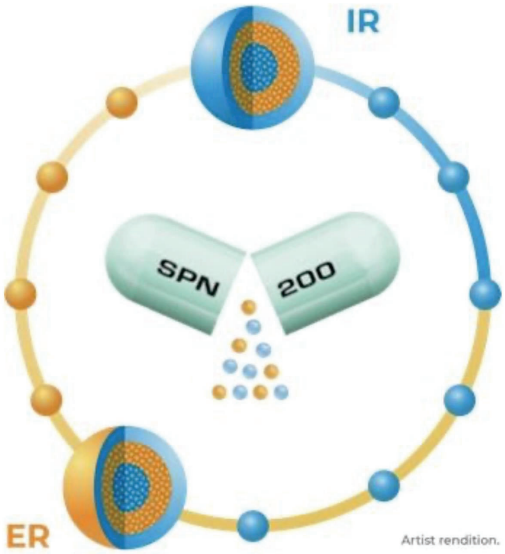
T_{max}=5 hours (median)

Time to reach steady state=2 days

Demonstrated gradual release of ER formulation for extended exposure throughout the day, with smooth tapering at the end of the dosing interval

ER, extended release; T_{max}, time to maximum plasma concentration.
1. Qelbree [package insert]. Rockville, MD: Supernus Pharmaceuticals, Inc. 2. Data on file. Supernus Pharmaceuticals, Inc.

Qelbree ONCE-DAILY viloxazine extended-release capsules



Children

Adolescents

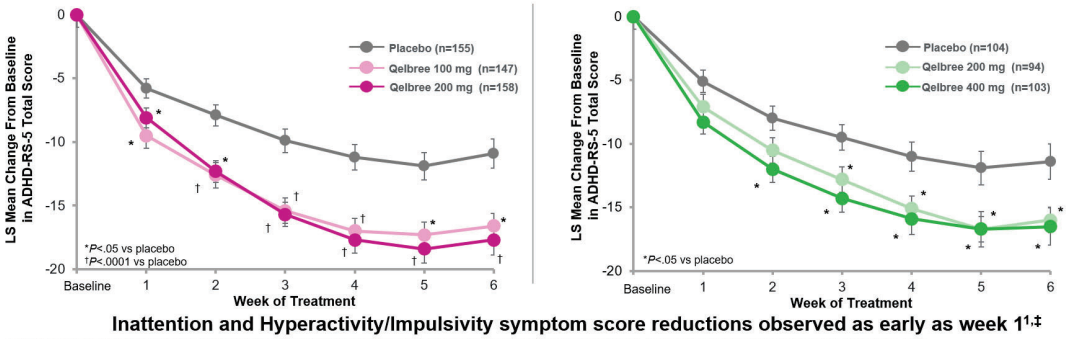
Inattention and Hyperactivity/Impulsivity Symptom Score Reductions Observed Early in Treatment

Proven efficacy in treating ADHD at EOS:

P301: Children Ages 6 to 11 Years[1,2]

P302: Adolescents Ages 12 to 17 Years[1,3]

Mean Change From Baseline in ADHD-RS-5 Total Score by Visit and Treatment Group



Inattention and Hyperactivity/Impulsivity symptom score reductions observed as early as week 1[1,‡]

‡Qelbree was studied in 4 clinical trials. In one study of children 6 to 11 years of age, ADHD symptom score reductions were statistically significant for 100 mg and 200 mg dose, beginning at week 1. In the study of adolescents 12 to 17 years of age, ADHD symptom score reductions were statistically significant for 400mg, beginning at week 2.

Vertical bars at each data point denote SE.

LS, least-squares.

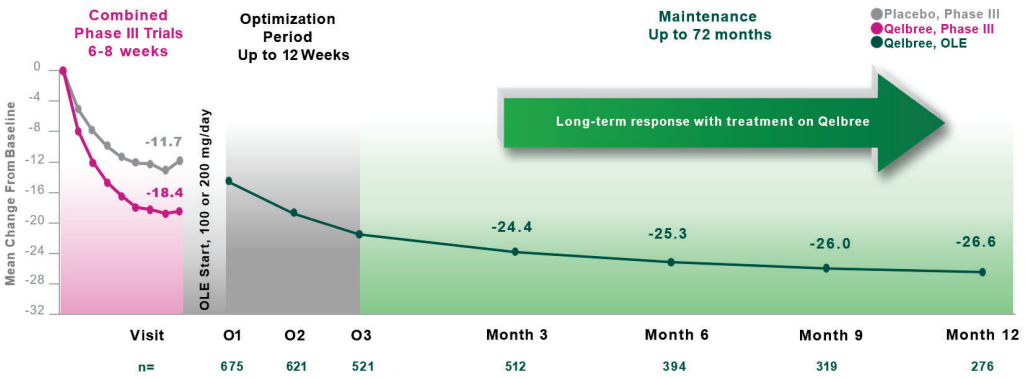
1. Qelbree [package insert]. Rockville, MD: Supernus Pharmaceuticals, Inc. 2. Nasser A et al. *Clin Ther.* 2020;42(8):1452-1466. 3. Nasser A et al. *J Clin Psychopharmacol.* 2021;41(4):370-380.

Qelbree ONCE-DAILY viloxazine extended-release capsules

Long-Term Response by the ADHD-RS-5 Scores in the OLE Interim Subpopulation Analysis at 12 Months

Children
Adolescents

Mean Change From Baseline in ADHD-RS-5 Total Score*



*Combined data include both children and adolescents.
Data on file. Supernus Pharmaceuticals, Inc.

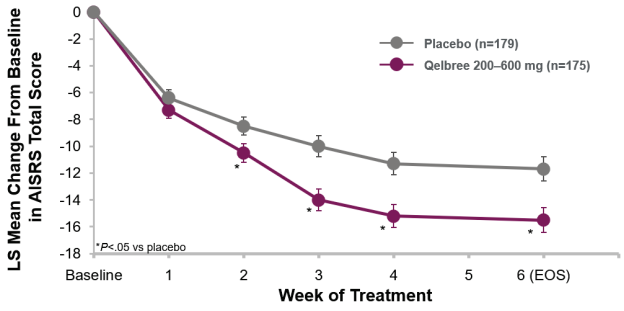
Qelbree ONCE-DAILY viloxazine extended-release capsules

Mean Change From Baseline vs Placebo in AISRS Total Score

Adults

Proven efficacy in treating ADHD at EOS:

P306: Adult Trial (N=354)[1,2]



Qelbree dosing at week 6 (EOS):[2]
- 8% were at 200 mg/day
- 32% were at 400 mg/day
- 60% were at 600 mg/day

Inattention and Hyperactivity/Impulsivity symptom score reductions observed as early as week 2[1,2]

No study visit was scheduled/performed at week 5.
1. Qelbree [package insert]. Rockville, MD: Supernus Pharmaceuticals, Inc. 2. Data on file. Supernus Pharmaceuticals, Inc.

Qelbree ONCE-DAILY viloxazine extended-release capsules

Once-Daily Flexible Dosing With Qelbree

Children
Adolescents
Adults

- Once-daily oral administration
- Capsules and their contents should not be cut, crushed, or chewed
- Can be taken with or without food
- Capsules can be taken whole, or entire contents can be sprinkled over a spoonful of soft food (pudding or applesauce). Consume the soft food mixture in its entirety, without chewing, within 15 minutes for pudding, or within 2 hours for applesauce; do not store for future use
- No dosage adjustment necessary in patients with hepatic impairment

Once-daily dosing with 3 dose strengths

SPN 100	100 mg
SPN 150	150 mg
SPN 200	200 mg

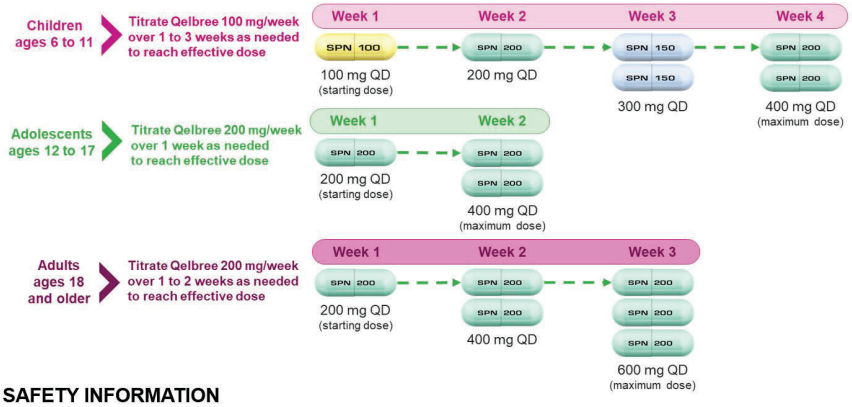
Capsules shown are not actual size.

*Dose will depend on response to medication. Maximum dose for 6-17 years is 400 mg and for adults is 600 mg.
Qelbree [package insert]. Rockville, MD: Supernus Pharmaceuticals, Inc.

Qelbree ONCE-DAILY viloxazine extended-release capsules

Qelbree: Titrate Weekly to Optimize ADHD Symptom Control

Children
Adolescents
Adults

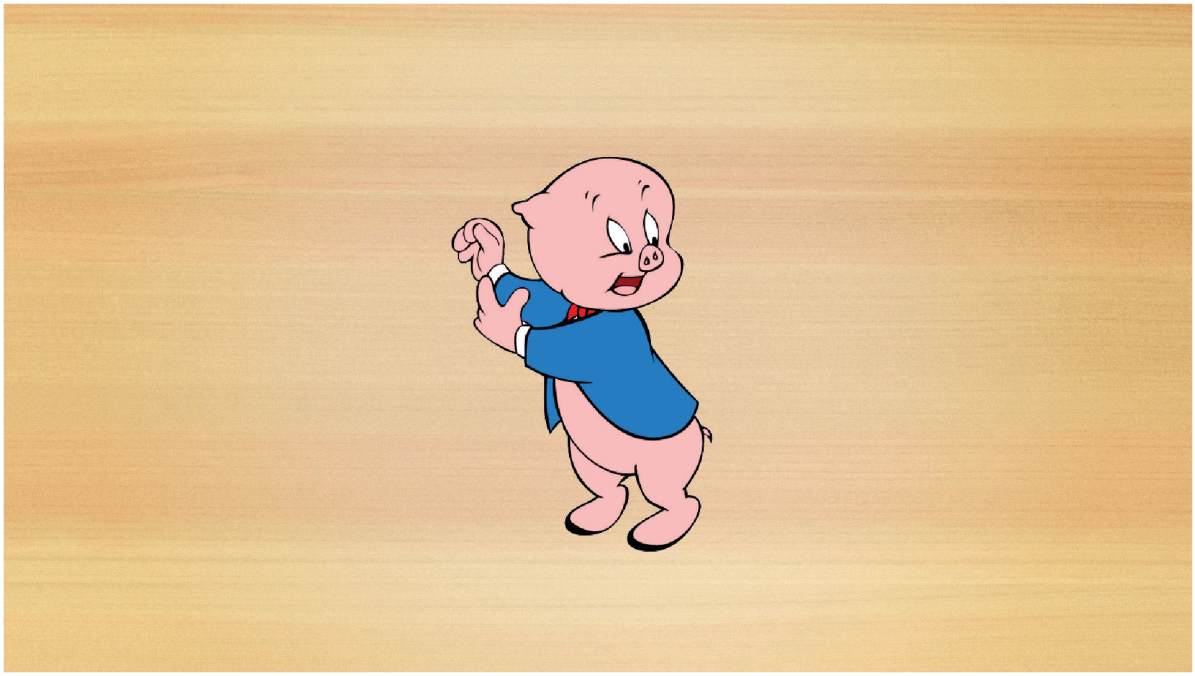


IMPORTANT SAFETY INFORMATION

- *Severe Renal Impairment:* Initiate Qelbree at 100 mg once daily and increase by 50 mg to 100 mg at weekly intervals to a maximum recommended dosage of 200 mg once daily

Capsules shown are not actual size.
QD, once daily.
Qelbree [package insert]. Rockville, MD: Supernus Pharmaceuticals, Inc.

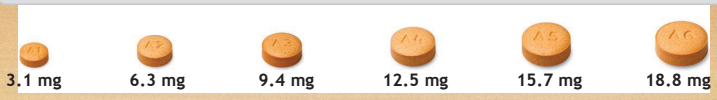
Qelbree ONCE-DAILY viloxazine extended-release capsules



THAT'S ALL, FOLKS!!

Adzenys XR-ODT™ Dosing[1]

Available in 6 dosage strengths



Treatment Considerations

- Prior to treating patients, assess for the presence of cardiac disease
- Tablet should not be crushed or chewed
- Assess the risk of abuse prior to prescribing, and monitor for signs of abuse and dependence while on therapy.
- Agents that alter urinary pH can alter blood levels of amphetamine. Acidifying agents can decrease amphetamine blood levels, while alkalinizing agents can increase amphetamine blood levels. Adjust Adzenys XR-ODT dosage accordingly

1. Adzenys XR-ODT™ [Full Prescribing Information]. 2015. Neos Therapeutics, Inc.

Adzenys XR-ODT™ Dosing Conversion Chart

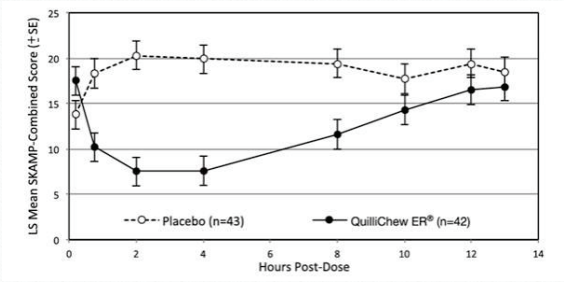
Patients taking Adderall XR® may be switched to Adzenys XR-ODT at the equivalent dose taken once daily

	Equivalent Doses[1,2]					
Adzenys XR-ODT	3.1 mg	6.3 mg	9.4 mg	12.5 mg	15.7 mg	18.8 mg
Adderall XR*	5 mg	10 mg	15 mg	20 mg	25 mg	30 mg

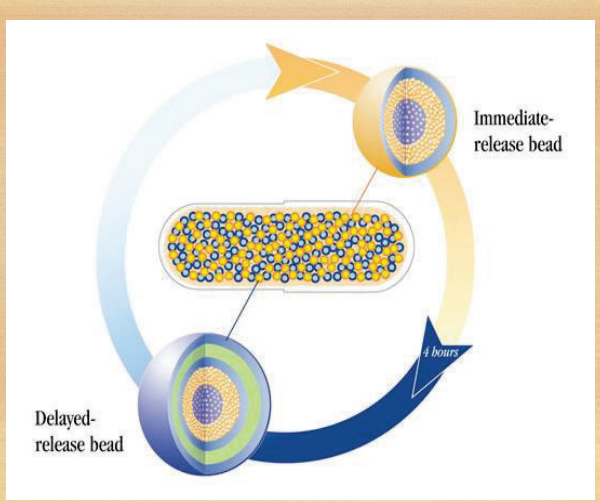
*Adderall XR® is a registered trademark of Shire US, Inc. Wayne, PA

1. Adzenys XR-ODT™ [Full Prescribing Information]. 2015. Neos Therapeutics, Inc.
2. Adderall XR® [Full Prescribing Information]. 2015. Shire US, Inc.

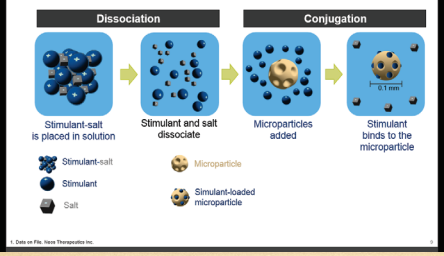
- Therapeutically equivalent to Adderall XR
- See accompanying Prescribing Information for full dosage and administration instructions



SODAS Pulse Delivery System

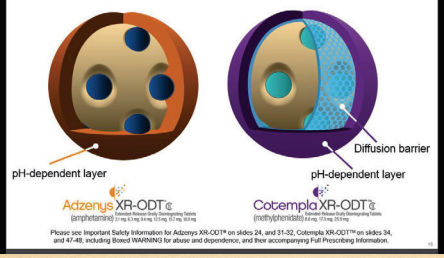


Neos Therapeutics XR-ODT Technology



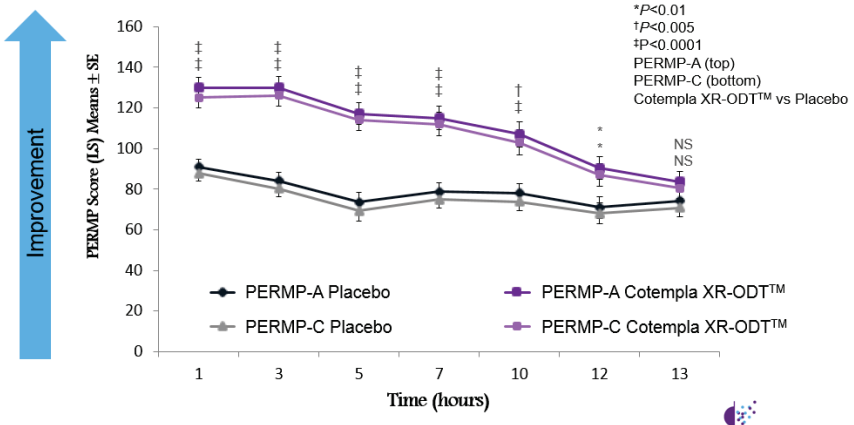
1. Data on File, Neos Therapeutics Inc.

Expanded View of Adzenys XR-ODT® and Cotempla XR-ODT™ XR Microparticles



Please see Important Safety Information for Adzenys XR-ODT® on slides 24, and 31-32, Cotempla XR-ODT™ on slides 34, and 47-48, including Boxed WARNING for abuse and dependence, and their accompanying Full Prescribing Information.

PERMP-A and PERMP-C During the Classroom Testing Day

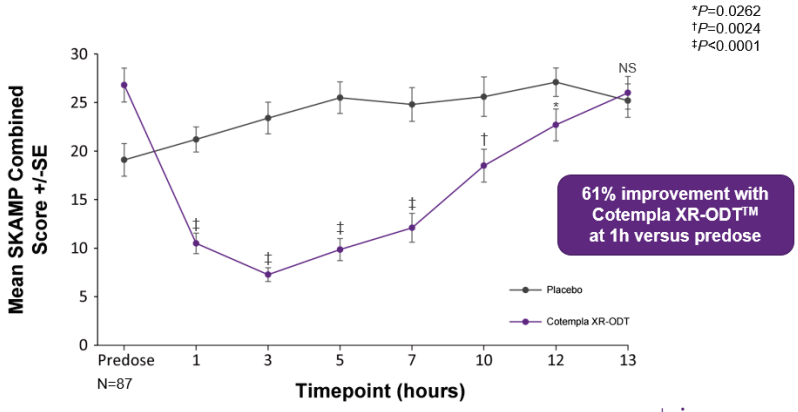


Please see Important Safety Information for Cotempla XR-ODT™ on slides 34, and 47-48, including Boxed WARNING for abuse and dependence, and accompanying Full Prescribing Information.

1. Childress AC, et al. *J Child Adolesc Psychopharmacol*. 2017;27(1):66-74.

Cotempla XR-ODT™ (methylphenidate) Extended-Release Orally Disintegrating Tablets 8.6 mg, 17.3 mg, 25.9 mg

SKAMP-Combined Score During the Classroom Testing Day (LS Mean)



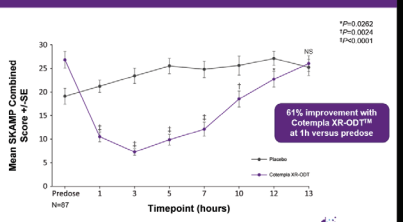
Please see Important Safety Information for Cotempla XR-ODT™ on slides 34, and 47-48, including Boxed WARNING for abuse and dependence, and accompanying Full Prescribing Information.

1. Cotempla XR-ODT™ Prescribing Information. Neos Therapeutics Inc. Grand Prairie, TX. June 2017.

Cotempla XR-ODT™ (methylphenidate) Extended-Release Orally Disintegrating Tablets 8.6 mg, 17.3 mg, 25.9 mg

39

SKAMP-Combined Score During the Classroom Testing Day (LS Mean)



Please see Important Safety Information for Cotempla XR-ODT™ on slides 34, and 47-48, including Boxed WARNING for abuse and dependence, and accompanying Full Prescribing Information.

1. Cotempla XR-ODT™ Prescribing Information. Neos Therapeutics Inc. Grand Prairie, TX. June 2017.

Cotempla XR-ODT™ Laboratory Classroom Study

- **Study design:**
  - Randomized, multicenter, double-blind, placebo-controlled, parallel group study of Cotempla XR-ODT™ (equivalent to 20, 30, 40, or 60 mg of methylphenidate ER hydrochloride) in children (ages 6-12 years) with ADHD
- **Objective:**
  - To determine the efficacy, safety, and tolerability of Cotempla XR-ODT™ versus placebo in a laboratory classroom setting
- **Primary efficacy endpoint:**
  - SKAMP-Combined Score – averaged over the classroom study day (13 hours)
- **Secondary efficacy endpoints:**
  - Key endpoints: onset and duration of effect
  - Additional efficacy endpoints:
    - SKAMP-Attention and SKAMP-Deportment
    - PERMP-Attempted and PERMP-Correct scores

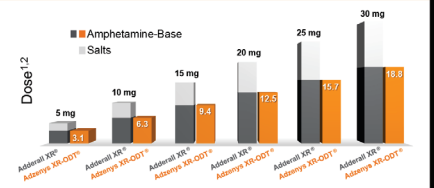
SKAMP=Swanson, Kotkin, Agler, M-Flynn, and Pelham rating score; PERMP=Permanent Product Measure of Performance

Please see Important Safety Information for Cotempla XR-ODT™ on slides 34, and 47-48, including Boxed WARNING for abuse and dependence, and accompanying Full Prescribing Information.

1. Childress AC, et al. *J Child Adolesc Psychopharmacol*. 2017;27(1):66-74.

Cotempla XR-ODT™ (methylphenidate) Extended-Release Orally Disintegrating Tablets 8.6 mg, 17.3 mg, 25.9 mg

Adzenys XR-ODT® and Adderall XR®: Same Amphetamine Base

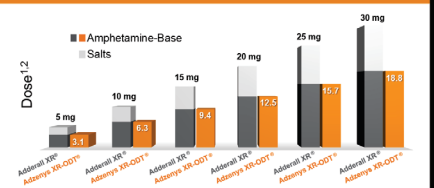


3:1 ratio, *d*-to *l*-amphetamine

Please see Important Safety Information for Adzenys XR-ODT® on slides 24, and 31-32, including Boxed WARNING for abuse and dependence, and accompanying Full Prescribing Information.

1. Adzenys XR-ODT® Prescribing Information. Neos Therapeutics, Inc. January 2017. 2. Adderall XR® Prescribing Information. Shire US, Inc. January 2017.

Adzenys XR-ODT® and Adderall XR®: Same Amphetamine Base



3:1 ratio, *d*-to *l*-amphetamine

Please see Important Safety Information for Adzenys XR-ODT® on slides 24, and 31-32, including Boxed WARNING for abuse and dependence, and accompanying Full Prescribing Information.

1. Adzenys XR-ODT® Prescribing Information. Neos Therapeutics, Inc. January 2017. 2. Adderall XR® Prescribing Information. Shire US, Inc. January 2017.

Adzenys XR-ODT® Dosing Conversion Chart

Patients taking Adderall XR® may be switched to Adzenys XR-ODT® at the equivalent dose taken once daily

	Equivalent Doses[1,2]					
Adzenys XR-ODT®	**3.1 mg**	**6.3 mg**	**9.4 mg**	**12.5 mg**	**15.7 mg**	**18.8 mg**
Adderall XR®	**5 mg**	**10 mg**	**15 mg**	**20 mg**	**25 mg**	**30 mg**

- Therapeutically equivalent to Adderall XR®
- See accompanying Prescribing Information for full dosage and administration instructions

Please see Important Safety Information for Adzenys XR-ODT® on slides 24, and 31-32, including Boxed WARNING for abuse and dependence, and accompanying Full Prescribing Information.

1. Adzenys XR-ODT® Prescribing Information. Neos Therapeutics, Inc. January 2017. 2. Adderall XR® Prescribing Information. Shire US, Inc. January 2017.

A Look Inside the Laboratory Classroom

Laboratory Classroom Paradigm

- Validated methodology
- Simulates the community school classroom setting
- Allows for repeated assessments of behavior throughout the day
- Used extensively to evaluate the efficacy and time-course of ADHD medications
- Both objective and subjective assessments

Photos Courtesy of Dr. A. Childress With Permission

APTENSIO-XR

Small bead release

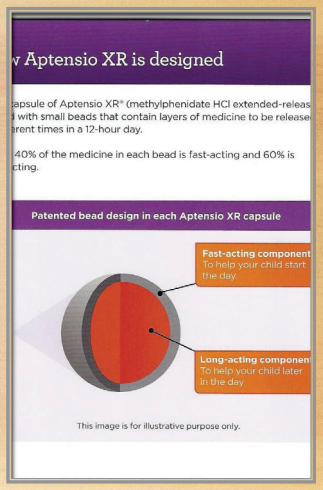
Actually not as illustrated

40 % immediate release

60 % gradual release

Not for potentiation

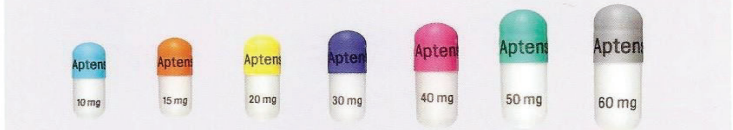
Can be sprinkled on apple sauce



How Aptensio XR is taken

Aptensio XR® (methylphenidate HCl extended-release) comes in 7 dosing strengths to help the doctor find the right dose for your child.

7 dosage strengths for personalized treatment



Capsules are not shown at actual size.

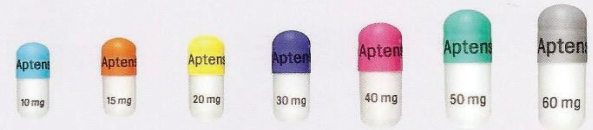
Aptensio XR can be swallowed whole or the capsule can be opened and the contents sprinkled on applesauce.

- It is important that your child takes the entire contents of the capsule immediately, and does not chew the beads

How Aptensio XR is taken

Aptensio XR® (methylphenidate HCl extended-release) comes in 7 dosing strengths to help the doctor find the right dose for your child.

7 dosage strengths for personalized treatment



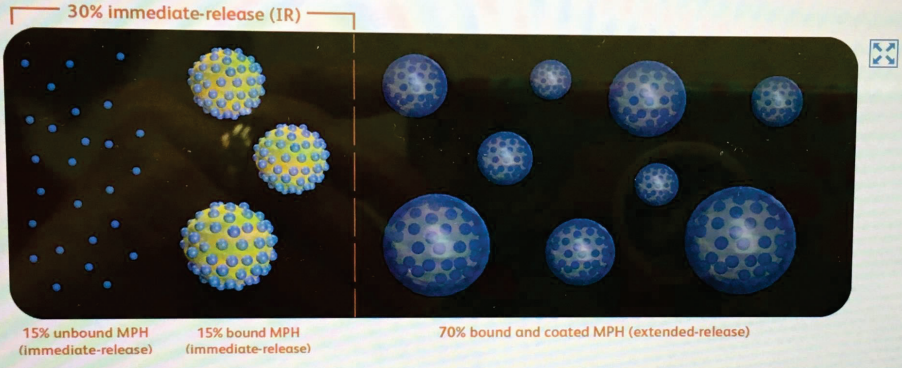
Capsules are not shown at actual size.

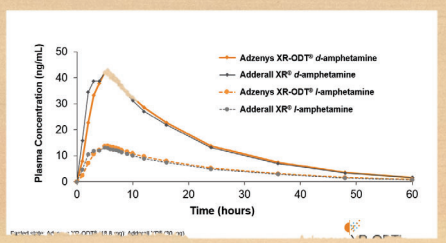
Aptensio XR can be swallowed whole or the capsule can be opened and the contents sprinkled on applesauce.

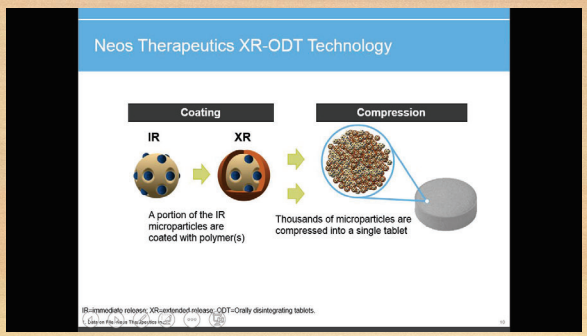
- It is important that your child takes the entire contents of the capsule immediately, and does not chew the beads

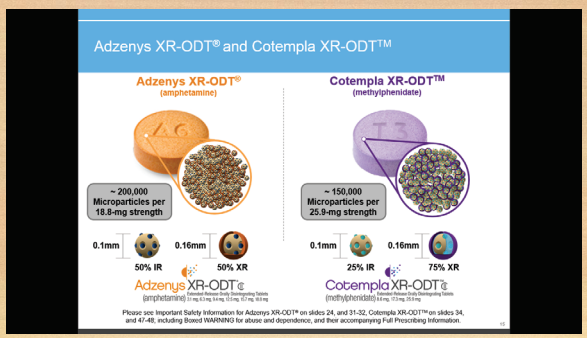
QuilliChew ER™ methylphenidate HCl extended-release chewable tablets 20 mg 30 mg 40 mg

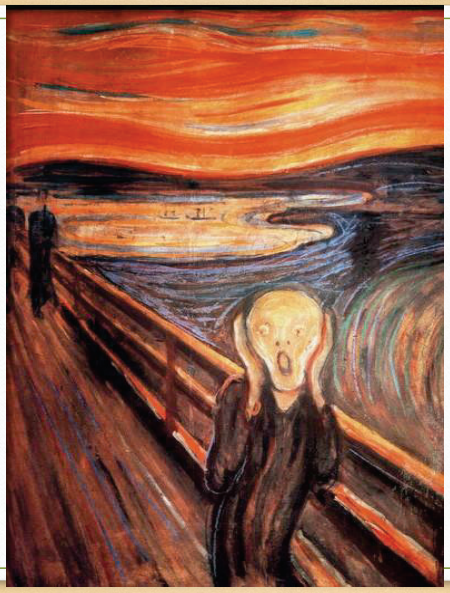
QuilliChew ER uses proprietary extended-release technology, which provides a combination of approximately 30% immediate-release (IR) and 70% extended-release (ER) methylphenidate.

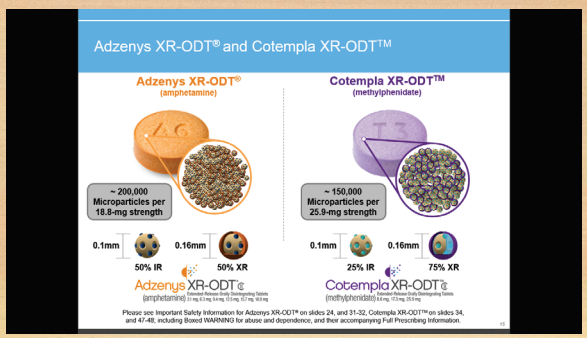



Plasma Concentration (ng/mL)
50
40
30
20
10
0
0
10
20
30
40
50
60
Time (hours)
Adzenys XR-ODT® d-amphetamine
Adderall XR® d-amphetamine
Adzenys XR-ODT® l-amphetamine
Adderall XR® l-amphetamine


Neos Therapeutics XR-ODT Technology
Coating
IR
XR
A portion of the IR microparticles are coated with polymer(s)
Compression
Thousands of microparticles are compressed into a single tablet
IR=immediate release; XR=extended release; ODT=Orally disintegrating tablets.


Adzenys XR-ODT® and Cotempla XR-ODT™
Adzenys XR-ODT®
(amphetamine)
Cotempla XR-ODT™
(methylphenidate)
~ 200,000 Microparticles per 18.8-mg strength
~ 150,000 Microparticles per 25.9-mg strength
0.1mm
0.16mm
50% IR
50% XR
0.1mm
0.16mm
25% IR
75% XR
Please see Important Safety Information for Adzenys XR-ODT™ on slides 24, and 31-32, Cotempla XR-ODT™ on slides 34, and 47-48, including Boxed WARNING for abuse and dependence, and their accompanying Full Prescribing Information.





Adzenys XR-ODT® Bioequivalence Study

Study	Objectives	Participants	PK Parameters of Interest
Bioequivalence Phase 1	To compare rate of absorption and oral bioavailability to a reference product (Adderall XR®)	42 healthy adults ≥18 years of age	Primary endpoint: *d*- and *l*-amphetamine C_{max}, AUC_{last}, and AUC_{inf} Secondary endpoint: *d*- and *l*-amphetamine AUC_{0-5}, AUC_{5-last}

AUC_{inf} = area under the concentration-time curve from time 0 extrapolated to infinity; AUC_{0-5} = area under the concentration-time curve from time 0 to 5 hours; AUC_{last} = area under the concentration-time curve from time 0 to the time of the last quantifiable concentration; AUC_{5-last} = area under the concentration-time curve from 5 hours to the time of the last quantifiable concentration ; C_{max}= peak plasma concentration.

Adderall XR® is a registered trademark of Shire LLC.

Please see Important Safety Information for Adzenys XR-ODT® on slides 24, and 31-32, including Boxed WARNING for abuse and dependence, and accompanying Full Prescribing Information.

1. Data on File. Neos Therapeutics Inc.

Adzenys XR-ODT (amphetamine) Extended-Release Orally Disintegrating Tablets 3.1 mg, 6.3 mg, 9.4 mg, 12.5 mg, 15.7 mg, 18.8 mg

Adzenys XR-ODT® Bioequivalence Study

Study	Objectives	Participants	PK Parameters of Interest
Bioequivalence Phase 1	To compare rate of absorption and oral bioavailability to a reference product (Adderall XR®)	42 healthy adults ≥18 years of age	Primary endpoint: *d*- and *l*-amphetamine C_{max}, AUC_{last}, and AUC_{inf} Secondary endpoint: *d*- and *l*-amphetamine AUC_{0-5}, AUC_{5-last}

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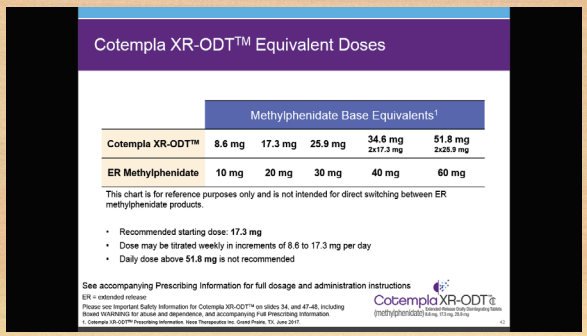
Adzenys XR-ODT (amphetamine) Extended-Release Orally Disintegrating Tablets 3.1 mg, 6.3 mg, 9.4 mg, 12.5 mg, 15.7 mg, 18.8 mg

22


Cotempla XR-ODT™ Equivalent Doses
Methylphenidate Base Equivalents†
Cotempla XR-ODT™
8.6 mg
17.3 mg
25.9 mg
34.6 mg
2x17.3 mg
51.8 mg
2x25.9 mg
ER Methylphenidate
10 mg
20 mg
30 mg
40 mg
60 mg
This chart is for reference purposes only and is not intended for direct switching between ER methylphenidate products.
Recommended starting dose: 17.3 mg
Dose may be titrated weekly in increments of 8.6 to 17.3 mg per day
Daily dose above 51.8 mg is not recommended
See accompanying Prescribing Information for full dosage and administration instructions
ER = extended release
Please see Important Safety Information for Cotempla XR-ODT™ on slides 34, and 47-48, including Boxed WARNING for abuse and dependence, and accompanying Full Prescribing Information.
1. Cotempla XR-ODT™ Prescribing Information. Neos Therapeutics Inc. Grand Prairie, TX. June 2017.
Cotempla XR-ODT
(methylphenidate) Extended-Release Orally Disintegrating Tablets
8.6 mg, 17.3 mg, 25.9 mg