Select Drugs for Attention Deficit Hyperactivity Disorder (ADHD)

Policy # 00601
Original Effective Date: 01/17/2018
Current Effective Date: 03/10/2025

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider select drugs for attention deficit hyperactivity disorder (ADHD), including but not limited to Cotempla XR-ODT™‡ (methylphenidate), branded Amphetamine ER oral suspension, Relexxii™‡ (methylphenidate), branded Methylphenidate ER, Jornay PM™‡ (methylphenidate), Adhansia XR™‡ (methylphenidate), Evekeo ODT™‡ (amphetamine), Qelbree™‡ (viloxazine), Dyanavel XR®‡ tablets (amphetamine), Xelstrym™‡ (dextroamphetamine), Metadate CD®‡ (methylphenidate), and Onyda™‡ XR (clonidine) extended release oral suspension to be **eligible for coverage**** when the patient selection criteria are met.

Patient Selection Criteria

Coverage eligibility for select drugs for ADHD, including but not limited to Cotempla XR-ODT (methylphenidate), branded Amphetamine ER oral suspension, Relexxii (methylphenidate), branded Methylphenidate ER, Jornay PM (methylphenidate), Adhansia XR (methylphenidate), Evekeo ODT (amphetamine), Qelbree (viloxazine), Dyanavel XR tablets (amphetamine), Xelstrym (dextroamphetamine), Metadate CD (methylphenidate), and Onyda XR (clonidine) extended release oral suspension will be considered when the following criteria are met for the requested drug:

- Cotempla XR-ODT:
  - Patient has a diagnosis of ADHD; AND
  - Patient is 6 to 17 years of age; AND
  - Patient has tried and failed (e.g., intolerance or inadequate response) TWO of the following generic products for ADHD: methylphenidate ER or CD capsules, dexmethylphenidate ER capsules, or dextroamphetamine-amphetamine mixed salt ER capsules unless there is clinical evidence or patient history that suggests the alternatives will be ineffective or cause an adverse reaction to the patient.
    *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*

- branded Amphetamine ER oral suspension:
  - Patient has a diagnosis of ADHD; AND
  - Patient is 6 to 17 years of age; AND
    *(Note: The use of this product in patients 6-17 years of age is an additional Company requirement for coverage eligibility. Requests for patients 18 years of age and above will be denied as not medically necessary**. Requests for patients under 6 years of age will be denied as investigational*)*
  - Patient has tried and failed (e.g., intolerance or inadequate response) TWO of the following generic products for ADHD: dextroamphetamine oral solution, dextroamphetamine/amphetamine mixed salts immediate release tablet, dextroamphetamine/amphetamine mixed salts extended release capsule, methylphenidate oral solution, methylphenidate chewable tablet, or methylphenidate ER or CD capsules unless there is clinical evidence or patient history that suggests the alternatives will be ineffective or cause an adverse reaction to the patient.
    *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
- Relexxii, branded Methylphenidate ER:
  - Patient has a diagnosis of ADHD; AND
  - Patient is 6 to 65 years of age; AND
  - Patient has tried and failed (e.g., intolerance or inadequate response) TWO of the following generic products for ADHD: methylphenidate ER or CD capsules, dexmethylphenidate ER capsules, or dextroamphetamine-amphetamine mixed salt ER capsules unless there is clinical evidence or patient history that suggests the alternatives will be ineffective or cause an adverse reaction to the patient.
    *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
- Jornay PM, Adhansia XR:
  - Patient has a diagnosis of ADHD; AND Patient is 6 years of age or older; AND
  - Patient has tried and failed (e.g., intolerance or inadequate response) TWO of the following generic products for ADHD: methylphenidate ER or CD capsules, dexmethylphenidate ER capsules, or dextroamphetamine-amphetamine mixed salt ER capsules unless there is clinical evidence or patient history that suggests the alternatives will be ineffective or cause an adverse reaction to the patient.
    *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
- Evekeo ODT:
  - Patient has a diagnosis of ADHD;
  - Patient meets one of the following:
    - Patient is 6 to 17 years of age AND patient has tried and failed (e.g., intolerance or inadequate response) TWO of the following generic products for ADHD: dextroamphetamine oral solution, dextroamphetamine/amphetamine mixed salts immediate release tablet, dextroamphetamine/amphetamine mixed salts extended release capsule,

methylphenidate oral solution, methylphenidate chewable tablet, or methylphenidate ER or CD capsules unless there is clinical evidence or patient history that suggests the alternatives will be ineffective or cause an adverse reaction to the patient; OR
*(Note: The portion of this patient selection criterion requiring alternative products prior to the requested product is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*

- Patient is 3-5 years of age.

- Qelbree:
  - Patient has a diagnosis of ADHD; AND
  - Patient is 6 years of age or older; AND
  - Patient has tried and failed (e.g., intolerance or inadequate response) ONE of the following generic products for ADHD: methylphenidate ER or CD capsules, dexmethylphenidate ER capsules, dextroamphetamine-amphetamine mixed salt ER capsules, atomoxetine capsules, clonidine ER tablets, or guanfacine ER tablets unless there is clinical evidence or patient history that suggests the alternatives will be ineffective or cause an adverse reaction to the patient.
    *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
- Dyanavel XR tablets
  - Patient has a diagnosis of ADHD; AND
  - Patient is 6 years of age or older; AND
  - Patient has tried and failed (e.g., intolerance or inadequate response) TWO of the following generic products for ADHD: methylphenidate ER or CD capsules, dexmethylphenidate ER capsules, or dextroamphetamine-amphetamine mixed salt ER capsules unless there is clinical evidence or patient history that suggests the alternatives will be ineffective or cause and adverse reaction to the patient.
    *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
- Xelstrym:
  - Patient has a diagnosis of ADHD; AND
  - Patients is 6 years of age or older; AND
  - Patient has tried and failed (e.g., intolerance or inadequate response) TWO of the following generic products for ADHD: dextroamphetamine oral solution, dextroamphetamine/amphetamine mixed salts immediate release tablet, dextroamphetamine/amphetamine mixed salts extended release capsule, methylphenidate oral solution, methylphenidate chewable tablet, or methylphenidate ER or CD capsules unless there is clinical evidence or patient history that suggests the alternatives will be ineffective or cause an adverse reaction to the patient.
    *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*

- Metadate CD:
  - Patient has a diagnosis of ADHD; AND
  - Patient is 6 years of age or older; AND
  - Patient has tried and failed (e.g., intolerance or inadequate response) TWO of the following generic products for ADHD: methylphenidate ER or CD capsules, dexmethylphenidate ER capsules, or dextroamphetamine-amphetamine mixed salt ER capsules unless there is clinical evidence or patient history that suggests the alternatives will be ineffective or cause an adverse reaction to the patient.
    (*Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met*)
- Onyda XR (clonidine) extended release oral suspension:
  - Patient has a diagnosis of ADHD; AND
  - Patient is 6 to 17 years of age; AND
    *(Note: The use of this product in patients over 17 years of age is an additional Company requirement for coverage eligibility. Requests for patients 18 years of age and above will be denied as not medically necessary**)*
  - Patient has tried and failed (e.g., intolerance or inadequate response) generic clonidine ER tablets unless there is clinical evidence or patient history that suggests the alternative will be ineffective or cause an adverse reaction to the patient.
    (*Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met*)

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of select drugs for ADHD, including but not limited to Cotempla XR-ODT (methylphenidate), branded Amphetamine ER oral suspension, Relexxii (methylphenidate), branded Methylphenidate ER, Jornay PM (methylphenidate), Adhansia XR (methylphenidate, Evekeo ODT (amphetamine) [for ages 6 to 17 years only], Dyanavel XR tablets (amphetamine), Xelstrym (dextroamphetamine), and Metadate CD (methylphenidate) when at least TWO of the listed generic alternatives for the requested ADHD drug have NOT been tried and failed to be **not medically necessary.****

Based on review of available data, the Company considers the use of Qelbree (viloxazine) when the patient has not tried and failed ONE of the listed generic alternatives to be **not medically necessary.****

Based on review of available data, the Company considers the use of branded Amphetamine ER oral suspension or Onyda XR (clonidine) extended release oral suspension when a member is 18 years of age or older to be **not medically necessary.****

Based on review of available data, the Company considers the use of Onyda XR (clonidine) extended release oral suspension when the patient has not tried and failed generic clonidine ER tablets to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of select drugs for ADHD, including but not limited to Cotempla XR-ODT (methylphenidate), branded Amphetamine ER oral suspension, Relexxii (methylphenidate), branded Methylphenidate ER, Jornay PM (methylphenidate), Adhansia XR (methylphenidate), Evekeo ODT (amphetamine), Qelbree (viloxazine), Dyanavel XR tablets (amphetamine), Xelstrym (dextroamphetamine), Metadate CD (methylphenidate), and Onyda XR (clonidine) extended release oral suspension for any non-FDA approved request (e.g. indication) to be **investigational.***

Based on review of available data, the Company considers the use of Cotempla XR-ODT (methylphenidate), branded Amphetamine ER oral suspension, Qelbree (viloxazine), Relexxii (methylphenidate), branded Methylphenidate ER, Jornay PM (methylphenidate), Adhansia XR (methylphenidate), Dyanavel XR tablets (amphetamine), Xelstrym (dextroamphetamine), Metadate CD (methylphenidate), or Onyda XR (clonidine) extended release oral suspension when a member is less than 6 years of age to be **investigational.***

Based on review of available data, the Company considers the use of Evekeo ODT (amphetamine) when a member is less than 3 years of age to be **investigational.***

Based on review of available data, the Company considers the use of Relexxii (methylphenidate) and branded Methylphenidate ER when a member is greater than 65 years of age to be **investigational.***

Based on review of available data, the Company considers the use of Evekeo ODT (amphetamine) when a member is greater than 17 years of age to be **investigational.***

Background/Overview

The treatment of ADHD includes using stimulant medications such as methylphenidate, dexmethylphenidate, serdexmethylphenidate, dextroamphetamine/amphetamine salts, or some variant of those ingredients. Non-stimulant medications, such as atomoxetine, are also used to treat ADHD. Medications may vary based on product release, formulations, etc. Multiple generic products exist in this class of medications, including methylphenidate ER or CD capsules, dexmethylphenidate ER capsules, or dextroamphetamine-amphetamine mixed salt ER capsules. Typically, new medications in this class that are FDA approved (such as those targeted in this policy) as branded products do not show superior efficacy to the existing generic products on the market. Qelbree is a medication new to the ADHD non-stimulant class and is the fourth non-stimulant drug approved by the FDA for ADHD. It shares a similar mechanism of action as atomoxetine. Dyanavel XR is available in tablet and oral suspension form, but only the tablets are targeted in this policy. Xelstrym is the first FDA approved amphetamine containing transdermal patch. If a member is over

17 years of age, they should be able to use an alternative generic drug in tablet, capsule, or solution form in lieu of requesting the branded Amphetamine ER oral suspension or Onyda XR oral suspension. Generic methylphenidate extended-release capsules and extended release dextroamphetamine-amphetamine capsules may be opened and sprinkled on one tablespoon of applesauce for those that may have issues swallowing. The generic products in this class offer a more economical, yet equally efficacious, option over the brand name products in this class.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Cotempla XR-ODT is approved for the treatment of ADHD in patients 6 to 17 years of age.

Branded Amphetamine ER oral suspension is approved for the treatment of ADHD in patients 6 years of age or older.

Both Relexxii and branded Methylphenidate ER are indicated for the treatment of ADHD in children 6 years of age and older, adolescents, and adults up to the age of 65.

Both Jornay PM and Adhansia XR are indicated for the treatment of ADHD in patients 6 years of age and older.

Evekeo ODT is indicated for the treatment of ADHD in patients 3 to 17 years of age.

Qelbree is indicated for the treatment of ADHD in adults and pediatric patients 6 years of age and older.

Dyanavel XR is indicated for the treatment of ADHD in patients 6 years of age and older.

Xelstrym is indicated for the treatment of ADHD in adults and pediatric patients 6 years of age and older.

Metadate CD is indicated for the treatment of ADHD in pediatric patients 6 to 15 years of age.

Onyda XR is indicated for the treatment of ADHD as monotherapy and as adjunctive therapy to central nervous system (CNS) stimulant medications in pediatric patients 6 years of age and older.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

This policy is in place to ensure that the targeted drugs in this policy are used according to their FDA label, and this policy is also intended to ensure that efficacious and economically sensible options are utilized prior to branded products.

References

1. Cotempla XR-ODT [package insert]. Neos Therapeutics Brands, LLC. Grand Prairie, TX. Updated June 2017.
2. Relexxii [package insert]. Vertical Pharmaceuticals, LLC. Bridgewater, New Jersey. Updated June 2018.
3. Methylphenidate ER [package insert]. Trigen Laboratories, LLC. Bridgewater, New Jersey. Updated February 2018.
4. Jornay PM [package insert]. Ironshore Pharmaceuticals, Inc. Cherry Hill, New Jersey. April 2019.
5. Adhansia XR [package insert]. Purdue Pharmaceuticals. Wilson, North Carolina. July 2019.
6. Evekeo ODT [package insert]. Arbor Pharmaceuticals. Atlanta, Georgia. April 2021.
7. Amphetamine ER oral suspension [package insert]. Prasco Laboratories. Mason, Ohio. Updated August 2019.
8. Qelbree [package insert]. Catalent Pharma Solutions. Winchester, Kentucky. Updated April 2022.
9. Qelbree Drug Evaluation. Express Scripts. Updated April 2021.
10. Dyanavel XR [package insert]. Tris Pharma, Inc. Monmouth Junction, New Jersey. Updated May 2022.
11. Xelstrym [package insert]. Noven Pharmaceuticals, Inc. Miami, Florida. Updated March 2022.
12. Metadate CD [package insert]. Aytu Biopharma. Denver, CO. Updated October 2023.
13. Onyda XR [package insert}. Tris Pharma, Inc. Monmouth Junction, NJ. July 2024.

Policy History

Original Effective Date: 01/17/2018
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01/04/2018	Medical Policy Committee review
01/17/2018	Medical Policy Implementation Committee approval. New policy.
07/05/2018	Medical Policy Committee review
07/11/2018	Medical Policy Implementation Committee approval. Added new product, Adzenys ER suspension, to the policy.
02/07/2019	Medical Policy Committee review
02/20/2019	Medical Policy Implementation Committee approval. Added Relexxii and branded Methylphenidate ER to the policy. Updated relevant sections.
12/05/2019	Medical Policy Committee review
12/11/2019	Medical Policy Implementation Committee approval. Added three new products, Jornay PM, Adhansia XR, and Evekeo ODT, to the policy.

12/03/2020	Medical Policy Committee review
12/09/2020	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
03/04/2021	Medical Policy Committee review
03/10/2021	Medical Policy Implementation Committee approval. Added a new product, branded Amphetamine ER suspension, to the policy.
07/01/2021	Medical Policy Committee review
07/14/2021	Medical Policy Implementation Committee approval. Updated Evekeo ODT to reflect an expansion of the age range by the FDA from 6 to 17 years of age to 3 to 17 years of age. Added a new drug, Qelbree, and its criteria to the policy.
11/04/2021	Medical Policy Committee review
11/10/2021	Medical Policy Implementation Committee approval. Added a new product, Azstarys, to the policy with criteria. Split out the Adzenys ER oral suspension and branded Amphetamine ER oral suspension age requirement into investigational and not medically necessary.
07/07/2022	Medical Policy Committee review
07/13/2022	Medical Policy Implementation Committee approval. Updated eligibility and regulatory approval section to reflect expanded age range approved by the FDA for Qelbree.
10/06/2022	Medical Policy Committee review
10/11/2022	Medical Policy Implementation Committee approval. Updated age requirement of Azstarys to reflect the age approved by the FDA, which is 6 years of age and older. Added a new product, Dyanavel XR tablets, to the policy with criteria. Removed Adzenys ER from policy since it has been discontinued. Updated Investigational section of policy to include denials of patients who do not meet the covered age requirements. Updated and revised Background section of policy.
02/02/2023	Medical Policy Committee review
02/08/2023	Medical Policy Implementation Committee approval. Added new drug, Xelstrym, to the policy with criteria and updated relevant sections.
08/03/2023	Medical Policy Committee review
08/09/2023	Medical Policy Implementation Committee approval. Updated Qelbree criteria to require a patient to try and fail one generic stimulant alternative or non-stimulant alternative instead of both. Added generic clonidine extended release tablets and generic guanfacine extended release tablets to the listed alternatives that must be tried and failed prior to therapy with Qelbree.
07/02/2024	Medical Policy Committee review
07/10/2024	Medical Policy Implementation Committee approval. Added the product Metadate CD along with its criteria to the policy. Removed Azstarys and its criteria from the policy.

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02/06/2025 Medical Policy Committee review
02/12/2025 Medical Policy Implementation Committee approval. Added the product Onyda XR along with its criteria to the policy. Removed Qelbree criterion requiring that the patient be unable to swallow tablets and/or capsules AND not taking other medications in tablet and/or capsule form.
Next Scheduled Review Date: 02/2026

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.