Selective Serotonin Reuptake Inhibitors (SSRIs)/Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)

Policy # 00360
Original Effective Date: 08/21/2013
Current Effective Date: 02/13/2023

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.

For Patients With “Step Therapy” (generic before brand) ONLY:
Based on review of available data, the Company may consider brand name selective serotonin reuptake inhibitor (SSRI) or serotonin-norepinephrine reuptake inhibitor (SNRI) products (including, but not limited to Paxil® [paroxetine], Paxil® CR [paroxetine], Zoloft® [sertraline], Sertraline 150 mg and 200 mg capsules, Prozac® [fluoxetine], Prozac® Weekly [fluoxetine], Luvox CR® [fluvoxamine], Celexa® [citalopram], Citalopram 30 mg capsules, Effexor® [venlafaxine], Effexor® XR [venlafaxine], Venlafaxine ER 112.5 mg tablets, Lexapro® [escitalopram], Pexeva® [paroxetine], Pristiq® [desvenlafaxine succinate], Fetzima® [levomilnacipran], Khedezla® [desvenlafaxine], Trintellix® [vortioxetine], Drizalma Sprinkle™ [duloxetine] or Viibryd® [vilazodone])‡ to be eligible for coverage** when one of the below patient selection criteria is met:

Patient Selection Criteria
Coverage eligibility for brand name selective serotonin reuptake inhibitor (SSRI) or serotonin-norepinephrine reuptake inhibitor (SNRI) products will be considered when one of the following criteria is met:

- Requested drug is ANY brand name selective serotonin reuptake inhibitor (SSRI) or serotonin-norepinephrine reuptake inhibitor (SNRI) product: There is clinical evidence or patient history that suggests the generically available products will be ineffective or cause an adverse reaction to the patient; OR
- Requested drug is ANY brand name selective serotonin reuptake inhibitor (SSRI) or serotonin-norepinephrine reuptake inhibitor (SNRI) product: Patient has tried and failed one
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- Requested drug is a selective serotonin reuptake inhibitor (SSRI) or serotonin-norepinephrine reuptake inhibitor (SNRI) that is not available as a generic product (e.g. Pexeva, Trintellix, Khedezla, Fetzima, Drizalma Sprinkle): Patient meets one of the following:
  - Patient is currently taking the requested medication in the form of samples OR the patient has been paying 100% out of pocket for at least 4 weeks and is stabilized on the requested drug; OR
  - Patient was on the requested drug on a previous occasion; OR
  - Prescribing physician is a psychiatrist; OR
  - Patient is a child or adolescent less than or equal to 18 years of age; OR
  - Patient has suicidal ideations.

When Services Are Considered Not Medically Necessary
Based on review of available data, the Company considers the use of brand name selective serotonin reuptake inhibitor (SSRI) or serotonin-norepinephrine reuptake inhibitor (SNRI) products when the patient selection criteria are not met to be not medically necessary.**

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.

For Patients With “Prior Authorization” ONLY:
Based on review of available data, the Company may consider Drizalma Spinkle (duloxetine), Sertraline 150 mg and 200 mg capsules, Citalopram 30 mg capsules, or Venlafaxine ER 112.5 mg tablets to be eligible for coverage** when the below patient selection criteria are met for the requested drug.
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Patient Selection Criteria
Coverage eligibility will be considered for Drizalma Spinkle (duloxetine), Sertraline 150 mg and 200 mg capsules, Citalopram 30 mg capsules, or Venlafaxine ER 112.5 mg tablets when the following criteria are met for the requested drug:

- For Drizalma Sprinkle requests:
  - Patient has a gastrostomy tube (G-tube) or is otherwise unable to swallow tablets and/or capsules; AND
  - Patient is not currently taking any medication in tablet or capsule form; AND
  - Patient has tried and failed (e.g., intolerance or inadequate response) at least TWO generic alternative antidepressants unless there is clinical evidence or patient history that suggests the generic alternative antidepressants will be ineffective or cause an adverse reaction to the patient. Note: generic alternative antidepressants that can be administered in a liquid or suspension form (e.g., opened and mixed with applesauce or liquid formulations) include citalopram solution, escitalopram solution, sertraline solution/concentrate, or venlafaxine capsules; OR
  (Note: These patient selection criteria are additional Company requirements for coverage eligibility and will be denied as not medically necessary** if not met.)
- For Sertraline 150 mg or 200 mg capsule requests:
  - Patient has been receiving sertraline at a dose of 100 mg or 125 mg for at least 1 week; AND
  - Patient is unable to achieve the desired dose of sertraline using the generically available sertraline tablets; OR
  (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.)
- For Citalopram 30 mg capsule requests:
  - Patient has been receiving citalopram at a dose of 20 mg or 40 mg for at least one week; AND
  - Patient is unable to achieve the desired dose of citalopram using the generically available citalopram tablets.
  (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.)
- For Venlafaxine ER 112.5 mg tablet requests:
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- Patient has received at least 75 mg of another venlafaxine extended-release product for at least 4 days; AND
- Patient is unable to achieve the desired dose of venlafaxine using the generically available venlafaxine extended-release capsules.

(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 Drizalma Spinkle (duloxetine) when the patient selection criteria are not met to be not medically necessary.**

Based on review of available data, the Company considers the use of Sertraline 150 mg or 200 mg capsules, Citalopram 30 mg capsules, or Venlafaxine ER 112.5 mg tablets when the patient is able to achieve the desired dose of the requested medication using a generically available formulation 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 Sertraline 150 mg or 200 mg capsules, Citalopram 30 mg capsules, or Venlafaxine ER 112.5 mg tablets when the patient has not been receiving another dosage form of the requested drug for at least one week to be investigational.*

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.

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For Patients With BOTH “Prior Authorization” AND “Step Therapy”:
Based on review of available data, the Company may consider brand name selective serotonin reuptake inhibitor (SSRI) or serotonin-norepinephrine reuptake inhibitor (SNRI) products (including, but not limited to Paxil [paroxetine], Paxil CR [paroxetine], Zoloft [sertraline], Sertraline 150 mg or 200 mg capsules, Prozac [fluoxetine], Prozac Weekly [fluoxetine], Luvox CR [fluvoxamine], Celexa [citalopram], Citalopram 30 mg capsules, Effexor [venlafaxine], Effexor XR [venlafaxine], Venlafaxine ER 112.5 mg tablets, Lexapro [escitalopram], Pexeva [paroxetine], Pristiq [desvenlaxafine succinate], Fetzima [levomilnacipran], Khedezla [desvenlafaxine], Trintellix [vortioxetine], Drizalma Sprinkle [duloxetine], or Viibryd [vilazodone]) to be eligible for coverage when the patient selection criteria for the requested drug is met:

- For Drizalma Sprinkle requests:
  - Patient has a gastrostomy tube (G-tube) or is otherwise unable to swallow tablets and/or capsules; AND
  - Patient is not currently taking any medication in tablet or capsule form; AND
  - Patient has tried and failed (e.g. intolerance or inadequate response) at least TWO generic alternative antidepressants unless there is clinical evidence or patient history that suggests the generic alternative antidepressants will be ineffective or cause an adverse reaction to the patient. Note: generic alternative antidepressants that can be administered in a liquid or suspension form (e.g. open and mixed with applesauce or liquid formulations) include citalopram solution, escitalopram solution, sertraline solution/concentrate, or venlafaxine capsules.

  (Note: These patient selection criteria are additional Company requirements for coverage eligibility and will be denied as not medically necessary if not met.)

- For Sertraline 150 mg or 200 mg capsule requests:
  - Patient has been receiving sertraline at a dose of 100 mg or 125 mg for at least 1 week; AND
  - Patient is unable to achieve the desired dose of sertraline using the generically available sertraline tablets; OR

  (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.)

- For Citalopram 30 mg capsule requests:
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- Patient has been receiving citalopram at a dose of 20 mg or 40 mg for at least one week; AND
- Patient is unable to achieve the desired dose of citalopram using the generically available citalopram tablets.
  
  *(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.)*

- For Venlafaxine ER 112.5 mg tablet requests:
  - Patient has received at least 75 mg of another venlafaxine extended-release product for at least 4 days; AND
  - Patient is unable to achieve the desired dose of venlafaxine using the generically available venlafaxine extended-release capsules.
  
  *(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.)*

- For ALL other branded SSRI/SNRI requests:
  - There is clinical evidence or patient history that suggests the generically available products will be ineffective or cause an adverse reaction to the patient; OR
  - Patient has tried and failed one generic selective serotonin reuptake inhibitor (SSRI) or one generic serotonin-norepinephrine reuptake inhibitor (SNRI) (e.g. citalopram, escitalopram, sertraline, fluoxetine, venlafaxine); OR
  - Requested drug is a selective serotonin reuptake inhibitor (SSRI) or serotonin-norepinephrine reuptake inhibitor (SNRI) that is not available as a generic product (e.g. Pexeva, Trintellix, Khedezla, Fetzima, but NOT Drizalma Sprinkle): Patient meets one of the following:
    - Patient is currently taking the requested medication in the form of samples OR the patient has been paying 100% out of pocket for at least 4 weeks and is stabilized on the requested drug; OR
    - Patient was on the requested drug on a previous occasion; OR
    - Prescribing physician is a psychiatrist; OR
    - Patient is a child or adolescent less than or equal to 18 years of age; OR
    - Patient has suicidal ideations.
  
  *(Note: These patient selection criteria are additional Company requirements for coverage eligibility and will be denied as not medically necessary** if not met.)*
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When Services Are Considered Not Medically Necessary
Based on review of available data, the Company considers the use of brand name selective serotonin reuptake inhibitor (SSRI) or serotonin-norepinephrine reuptake inhibitor (SNRI) products when the patient selection criteria are not met to be not medically necessary.**

Based on review of available data, the Company considers the use of Sertraline 150 mg or 200 mg capsules, Citalopram 30 mg capsules, or Venlafaxine ER 112.5 mg tablets when the patient is able to achieve the desired dose of the requested medication using a generically available formulation 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 Sertraline 150 mg or 200 mg capsules, Citalopram 30 mg capsules, or Venlafaxine ER 112.5 mg tablets when the patient has not been receiving another dosage form of the requested drug to be investigational.*

Background/Overview
SSRIs and SNRIs are common drugs used for the treatment of depression. Some of the drugs in these classes have other uses including anxiety management and the treatment of neuropathic pain.

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 federal regulations, other plan medical policies, and accredited national guidelines.

Regarding step therapy, the patient selection criteria presented in this policy take into consideration clinical evidence or patient history that suggests the available generic SSRI or SNRI products will
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be ineffective or cause an adverse reaction to the patient. This policy also takes into consideration certain reasons for the prescribing of a brand name medication within these two classes. Based on a review of the data, in the absence of the above mentioned caveats, there is no advantage of using a brand name SSRI or SNRI product over the available generic SSRI or SNRI products. Generic drugs are considered to have equal bioavailability and efficacy in comparison to brand name drugs.

Regarding prior authorization, there is no meaningful clinical advantage with the use of Drizalma Sprinkle. There are other anti-depressant products that can be opened and mixed with applesauce or liquid formulations. These include citalopram solution, escitalopram solution, sertraline solution/concentrate, or venlafaxine capsules. These products are available in generic form. The branded Sertraline and Citalopram capsules and Venlafaxine tablets also present no meaningful clinical advantage as these are available in generic formulations of different strengths. Additionally, the package insert for these products requires the patient to have initiated therapy using one of the other formulations.

References
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Policy History
Original Effective Date: 08/21/2013
Current Effective Date: 02/13/2023
08/01/2013 Medical Policy Committee review
08/21/2013 Medical Policy Implementation Committee approval. New policy.
08/07/2014 Medical Policy Committee review
08/20/2014 Medical Policy Implementation Committee approval. Added new drugs that recently came out (Fetzima, Khedezla, Brintellix). They fall into existing criteria.

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08/06/2015  Medical Policy Committee review
08/19/2015  Medical Policy Implementation Committee approval. No change to coverage.
08/04/2016  Medical Policy Committee review
08/17/2016  Medical Policy Implementation Committee approval. Changed Brintellix to Trintellix secondary to the changing of the product’s name.
08/03/2017  Medical Policy Committee review
08/23/2017  Medical Policy Implementation Committee approval. Corrected drug name misspelling. Removed Pristiq from portion regarding drugs not having a generic. Pristiq now has a generic.
08/09/2018  Medical Policy Committee review
08/15/2018  Medical Policy Implementation Committee approval. No change to coverage.
08/01/2019  Medical Policy Committee review
08/14/2019  Medical Policy Implementation Committee approval. No change to coverage.
06/04/2020  Medical Policy Committee review
06/10/2020  Medical Policy Implementation Committee approval. Added a new drug, Drizalma Sprinkle, to the policy. Split the policy into step only, PA only, and PA/step sections.
06/03/2021  Medical Policy Committee review
06/09/2021  Medical Policy Implementation Committee approval. No change to coverage.
06/02/2022  Medical Policy Committee review
06/08/2022  Medical Policy Implementation Committee approval. Added new single source brand Sertraline 150 and 200 mg capsules and Citalopram 30 mg capsules to policy with relevant criteria.
01/05/2023  Medical Policy Committee review
01/11/2023  Medical Policy Implementation Committee approval. Added in new single source brand venlafaxine besylate ER to policy with relevant criteria and removed Viibryd from section for brands without available generics since generic is now available.

Next Scheduled Review Date:  01/2024

*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:
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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.

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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.