Clinical Policy: Quetiapine Extended-Release (Seroquel XR)

Reference Number: CP.PMN.64
Effective Date: 09.01.15
Last Review Date: 02.24
Line of Business: Commercial, HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Quetiapine extended-release (Seroquel XR®) is an atypical antipsychotic.

FDA Approved Indication(s)

Seroquel XR is indicated for the treatment of:

- Schizophrenia in adults and adolescents (13-17 years)
- Bipolar I disorder, manic or mixed episodes, in adults and children/adolescents (10-17 years)
- Bipolar disorder, depressive episodes, in adults
- Major depressive disorder (MDD), as adjunctive therapy with antidepressants, in adults

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Seroquel XR is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Schizophrenia (must meet all)**:**

1. Diagnosis of schizophrenia;
2. Age ≥ 13 years;
3. Member meets one of the following (a or b):
   a. Request is for the treatment of a member in a State with limitations on step therapy in certain mental health settings (*see Appendix D*);
   b. Failure of a ≥ 4-week trial of quetiapine immediate-release (IR) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
4. Member meets one of the following (a or b):
   a. Request is for the treatment of a member in a State with limitations on step therapy in certain mental health settings (*see Appendix D*);
   b. For Seroquel XR requests, member must use generic quetiapine extended-release (ER), unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed both of the following (a and b):
   a. 800 mg per day;
   b. 2 tablets per day.

Approval duration:

Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Bipolar Disorder (must meet all)**:**
1. Diagnosis of bipolar disorder;
2. Age ≥ 10 years;
3. Member meets one of the following (a or b):
   a. Request is for the treatment of a member in a State with limitations on step therapy in certain mental health settings (*see Appendix D*);
   b. Failure of a ≥ 4-week trial of quetiapine IR at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
4. Member meets one of the following (a or b):
   a. Request is for the treatment of a member in a State with limitations on step therapy in certain mental health settings (*see Appendix D*);
   b. For Seroquel XR requests, member must use generic quetiapine ER, unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed one of the following (a or b):
   a. Adults (i and ii)
      i. 800 mg per day;
      ii. 2 tablets per day;
   b. Children and adolescents (i and ii):
      i. 600 mg per day;
      ii. 2 tablets per day.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

C. Major Depressive Disorder (must meet all)**:**
1. Diagnosis of MDD;
2. Age ≥ 18 years;
3. Member meets one of the following (a or b):
   a. Request is for the treatment of a member in a State with limitations on step therapy in certain mental health settings (*see Appendix D*);
   b. For all other requests, both of the following (i and ii):
      i. Failure of THREE antidepressants from at least TWO different classes (e.g., selective serotonin reuptake inhibitor [SSRI], serotonin-norepinephrine reuptake inhibitor [SNRI], tricyclic antidepressant [TCA], bupropion, mirtazapine) at up to maximally indicated doses, each used for ≥ 4 weeks, unless member is unable to satisfy this requirement due to clinically significant adverse effects experienced, member's age ≥ 65 years, or contraindication(s) to multiple antidepressants;
      ii. Failure of a ≥ 4-week trial of aripiprazole at up to maximally indicated doses, used concurrently with an antidepressant, unless contraindicated or clinically significant adverse effects are experienced;
4. Seroquel XR is prescribed concurrently with an antidepressant;

5. Member meets one of the following (a or b):
   a. Request is for the treatment of a member in a State with limitations on step therapy in certain mental health settings (*see Appendix D*);
   b. For Seroquel XR requests, member must use generic quetiapine ER, unless contraindicated or clinically significant adverse effects are experienced;
6. Dose does not exceed both of the following (a and b):
   a. 300 mg per day;
   b. 2 tablets per day.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

D. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Member meets one of the following (a, b, or c):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Documentation supports that member is currently receiving Seroquel XR for schizophrenia or bipolar disorder and has received this medication for at least 30 days;
   c. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy;
3. For Seroquel XR requests, member must use generic quetiapine ER, unless contraindicated or clinically significant adverse effects are experienced;

4. If request is for a dose increase, new dose does not exceed any of the following (a, b, or c):
   a. Schizophrenia (i and ii):
      i. 800 mg per day;
      ii. 2 tablets per day;
   b. Bipolar disorder, one of the following (i or ii):
      i. Adults (1 and 2):
         1) 800 mg per day;
         2) 2 tablets per day;
      ii. Children and adolescents (1 and 2):
         1) 600 mg per day;
         2) 2 tablets per day;
   c. MDD (i and ii):
      i. 300 mg per day;
      ii. 2 tablets per day.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:
A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.
B. Dementia-related psychosis.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
ER: extended-release
IR: immediate-release
MDD: major depressive disorder
SNRI: serotonin/norepinephrine reuptake inhibitor
SSRI: selective serotonin reuptake inhibitor
TCA: tricyclic antidepressant
XR: extended-release

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Antipsychotics		
quetiapine immediate-release (Seroquel®)	**Schizophrenia** Initial: 25 mg PO BID; target: 400 to 800 mg/day **Bipolar Disorder** Initial: 50 mg PO BID; target: 400 to 800 mg/day	800 mg/day
Selective Serotonin Reuptake Inhibitors (SSRIs)		
citalopram (Celexa®)	**Major Depressive Disorder** Refer to prescribing information	40 mg/day
escitalopram (Lexapro®)		20 mg/day
fluoxetine (Prozac®)		Immediate-release: 80 mg/day (20 mg/day if pediatric) Delayed-release: 90 mg/week
fluvoxamine* (immediate-release) (Luvox®)		150 mg/day
paroxetine (Paxil®, Paxil CR®)		Immediate-release: 50 mg/day (40 mg/day if geriatric) Extended-release: 62.5 mg/day (50 mg/day if geriatric)
sertraline (Zoloft®)		200 mg/day (20 mg/day if age 6-11 years)
Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)		
desvenlafaxine (Pristiq®)	**Major Depressive Disorder** Refer to prescribing information	400 mg/day
duloxetine (Cymbalta®)		120 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Fetzima® (levomilnacipran)		120 mg/day
venlafaxine (Effexor®, Effexor XR®)		Extended-release: 225 mg/day
Tricyclic Antidepressant (TCAs)		
amitriptyline (Elavil®)	**Major Depressive Disorder** Refer to prescribing information	150 mg/day
amoxapine		400 mg/day (300 mg/day if geriatric)
clomipramine* (Anafranil®)		250 mg/day (200 mg/day if pediatric)
desipramine (Norpramin®)		300 mg/day (100 mg/day if pediatric)
doxepin		300 mg/day
imipramine HCl		200 mg/day (150 mg/day if geriatric or pediatric)
imipramine pamoate		200 mg/day (100 mg/day if geriatric or pediatric)
nortriptyline (Pamelor®)		150 mg/day
protriptyline		60 mg/day (30 mg/day if geriatric or pediatric)
trimipramine		200 mg/day (100 mg/day if geriatric or pediatric)
Monoamine Oxidase Inhibitors		
Marplan® (isocarboxazid)	**Major Depressive Disorder** Refer to prescribing information	60 mg/day
phenelzine (Nardil®)		90 mg/day
selegiline (EMSAM® transdermal; Eldepryl®, Zelapar®)		Transdermal: 12 mg/24 hr Oral: 30 mg/day
tranylcypromine (Parnate®)		60 mg/day
Other Antidepressants		
bupropion (Aplenzin®, Forfivo XL®, Wellbutrin®, Wellbutrin SR®, Wellbutrin XL®)	**Major Depressive Disorder** Refer to prescribing information	Immediate-release: 450 mg/day (300 mg/day if pediatric) Sustained-release: 400 mg/day Extended-release (HCl): 450 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
		Extended-release (HBr): 522 mg/day
mirtazapine (Remeron®)		45 mg/day
perphenazine/ amitriptyline		16 mg/day perphenazine and 200 mg/day amitriptyline
nefazodone		600 mg/day
trazodone (Oleptro®)		Immediate-release: 400 mg/day Extended-release: 375 mg/day
Trintellix® (vortioxetine)		20 mg/day
vilazodone (Viibryd®)		40 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): known hypersensitivity to Seroquel XR or any components in the formulation
- Boxed warning(s): increased mortality in elderly patients with dementia-related psychosis; and suicidal thoughts and behaviors in children, adolescents, and young adults taking antidepressants.

Appendix D: States with Limitations against Redirections in Certain Mental Health Settings

State	Step Therapy Prohibited?	Notes
AR	Yes	**Applies to HIM requests only** For the treatment of psychosis and serious mental illness through antipsychotic prescription drugs, no step therapies allowed. Note: For Seroquel XR requests, member must use generic quetiapine extended-release (ER), unless contraindicated or clinically significant adverse effects are experienced
NV	No	**Applies to Medicaid requests only** • Schizophrenia/bipolar disorder: Failure of generic quetiapine extended-release (ER) or quetiapine immediate-release (IR), unless clinically significant adverse effects are experienced or both are contraindicated. • MDD: Failure of one of the following at up to maximally indicated doses, used for ≥ 4 weeks, unless member is unable to satisfy this requirement due to clinically significant adverse effects experienced, member's age ≥ 65 years, or contraindication(s) to multiple antidepressants: generic

State	Step Therapy Prohibited?	Notes
		quetiapine ER, aripiprazole, or an antidepressant (e.g., selective serotonin reuptake inhibitor [SSRI], serotonin-norepinephrine reuptake inhibitor [SNRI], tricyclic antidepressant [TCA], bupropion, mirtazapine).
TX	No	**Applies to HIM requests only** For MDD ONLY: Failure of aripiprazole or an antidepressant (e.g., selective serotonin reuptake inhibitor [SSRI], serotonin-norepinephrine reuptake inhibitor [SNRI], tricyclic antidepressant [TCA], bupropion, mirtazapine) at up to maximally indicated doses, each used for ≥ 4 weeks, unless member is unable to satisfy this requirement due to clinically significant adverse effects experienced, member's age ≥ 65 years, or contraindication(s) to multiple antidepressants. Note: For Seroquel XR requests, member must use generic quetiapine extended-release (ER), unless contraindicated or clinically significant adverse effects are experienced

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Schizophrenia	Adults: Initial: 300 mg PO QD Target: 400 to 800 mg/day Adolescents: Initial: 50 mg PO QD Target: 400 to 800 mg/day	800 mg/day
Bipolar I disorder	**Manic or mixed episodes** Adults: Initial: 300 mg PO QD Target: 400 to 800 mg/day Children and adolescents Initial: 50 mg PO QD Target: 400 to 600 mg/day **Depressive episodes** Adults: Initial: 50 mg PO QD Target: 300 mg/day	Manic or mixed episodes Adults: 800 mg/day Children and adolescents: 600 mg/day Depressive episodes 300 mg/day
MDD	Adults: Initial: 50 mg PO QD Target: 150 to 300 mg/day	300 mg/day

VI. Product Availability

Extended-release tablets: 50 mg, 150 mg, 200 mg, 300 mg, 400 mg

VII. References

1. Seroquel XR Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals LP; January 2022. Available at: www.seroquelxr.com. Accessed November 10, 2023.
2. Hirschfeld RMA, Bowden CL, Gitlin MJ, et al. Practice guideline for the treatment of patients with bipolar disorder, second edition. Arlington, VA: American Psychiatric Association; April 2002. Available online at: http://www.psychiatryonline.org/guidelines. Accessed November 10, 2023.
3. Washburn JJ, West AE, and Heil JA. Treatment of pediatric bipolar disorder: a review. Minerva Psichiatr. 2011 March;52(1):21-35.
4. Patino LR, Bruns KM, Witt NM, et al. Management of bipolar disorder in children and adolescents. Focus 2015;13(1): 25-36.
5. Gelenberg AJ, Freeman MP, Markowitz JC, et al. Practice guideline for the treatment of patients with major depressive disorder, third edition. Arlington, VA: American Psychiatric Association; May 2010. Available online at: http://www.psychiatryonline.org/guidelines. Accessed November 10, 2023.
6. Keepers G, Fochtmann L, Anzia J, et al. APA Practice guideline for the treatment of patients with schizophrenia, third edition. Am J Psychiatry. 2020 Sept;177(9):868-872.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2020 annual review: no significant changes; references reviewed and updated.	11.30.19	02.20
Allowed members 65 years old or older to bypass redirections to TCA for major depressive disorder.	03.27.20	08.20
1Q 2021 annual review: no significant changes; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	11.29.20	02.21
1Q 2022 annual review: no significant changes; changed Commercial line of business auth duration from Length of Benefit to 12 months or duration of request, whichever is less; references reviewed and updated.	11.13.21	02.22
Template changes applied to other diagnoses/indications and continued therapy section.	10.10.22	
1Q 2023 annual review: added must use generic quetiapine XR language; for bipolar disorder, added max 600 mg per day for children and adolescents; addition of dementia related psychosis to section III; added references reviewed and updated.	10.27.22	02.23
Added redirection bypass for members in a State with limitations on step therapy in certain mental health settings along with Appendix D, which includes Arkansas.	07.05.23	
For MDD, added Texas to Appendix D with requirements for single drug redirection for HIM requests.	07.20.23	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Added Nevada to Appendix D with requirements for single drug redirection for Medicaid requests.	08.31.23	
1Q 2024 annual review: no significant changes; removed commercially unavailable branded products from appendix B; references reviewed and updated.	11.10.23	02.24

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.