Clinical Policy: Quetiapine Extended-Release (Seroquel XR)

Reference Number: ERX.NPA.50
Effective Date: 02.01.17
Last Review Date: 02.22
Line of Business: Commercial, 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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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. 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. Dose does not exceed 800 mg (2 tablets) per day.

Approval duration:
Commercial – Length of Benefit
Medicaid – 12 months

B. Bipolar Disorder (must meet all)**:**
1. Diagnosis of bipolar disorder;
2. Age ≥ 10 years;
3. 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. Dose does not exceed 800 mg (2 tablets) per day.

Approval duration:
Commercial – Length of Benefit
Medicaid – 12 months

C. Major Depressive Disorder (must meet all)**:**
1. Diagnosis of MDD;
2. Age ≥ 18 years;

3. Failure of THREE antidepressants (e.g., selective serotonin reuptake inhibitor, serotonin/norepinephrine reuptake inhibitor, tricyclic antidepressant, bupropion, mirtazapine) from at least TWO different classes 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, member's age is ≥ 65, or contraindication(s) to multiple antidepressants;
4. Failure of a ≥ 4 week trial of aripiprazole used concurrently with an antidepressant at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
5. Seroquel XR is prescribed concurrently with an antidepressant;
6. Dose does not exceed 300 mg (2 tablets) per day.

Approval duration:
Commercial – Length of Benefit
Medicaid – 12 months

D. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
   b. Documentation supports that member is currently receiving Seroquel XR for bipolar disorder or schizophrenia and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed (a or b):
   a. Schizophrenia or bipolar disorder: 800 mg (2 tablets) per day;
   b. MDD: 300 mg (2 tablets) per day.

Approval duration:
Commercial – Length of Benefit
Medicaid – 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration	MDD: major depressive disorder
IR: immediate-release	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®, Pexeva®)		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
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 (Sinequan®)		300 mg/day
imipramine HCl (Tofranil®)		200 mg/day (150 mg/day if geriatric or pediatric)
imipramine pamoate (Tofranil PM®)		200 mg/day (100 mg/day if geriatric or pediatric)
nortriptyline (Pamelor®)		150 mg/day
protriptyline (Vivactil®)		60 mg/day (30 mg/day if geriatric or pediatric)
trimipramine (Surmontil®)		200 mg/day (100 mg/day if geriatric or pediatric)
Monoamine Oxidase Inhibitors		
isocarboxazid (Marplan®)	**Major Depressive Disorder** Refer to prescribing information	60 mg/day
phenelzine (Nardil®)		90 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
selegiline (EMSAM®, transdermal; Eldepryl®, Zelapar®, Carbex®)		Transdermal: 12 mg/24 hr Oral: 30 mg/day
tranylcypromine (Parnate®)		60 mg/day
Other Antidepressants		
bupropion (Aplenzin®, Budeprion SR® , Budeprion XL®, 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 Extended-release (HBr): 522 mg/day
mirtazapine (Remeron®)		45 mg/day
perphenazine/ amitriptyline (Triavil®)		16 mg/day perphenazine and 200 mg/day amitriptyline
maprotiline (Ludiomil®)		150 mg/day
nefazodone (Serzone®)		600 mg/day
trazodone (Desyrel®, Oleptro®)		Immediate-release: 400 mg/day Extended-release: 375 mg/day
vortioxetine (Trintellix®)		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

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

Indication	Dosing Regimen	Maximum Dose
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; September 30, 2020. Available at: www.seroquelxr.com. Accessed November 13, 2021.
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3. Dixon L, Perkins D, Calmes C. Guideline watch: practice guideline for the treatment of patients with schizophrenia. Arlington, VA: American Psychiatric Association; September 2009. Available online at http://www.psychiatryonline.org/guidelines. Accessed November 30, 2019.
4. 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 30, 2019.
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6. 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 30, 2019.
7. 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
1Q18 annual review: Approval durations increased from 12/12 months to length of benefit; References reviewed and updated.	11.02.17	02.18
1Q 2019 annual review: no significant changes; references reviewed and updated.	10.30.18	02.19
1Q 2020 annual review: no significant changes; added Medicaid line of business with 12 month approval durations; references reviewed and updated.	12.02.19	02.20
Allowed members 65 years old or older to bypass redirections to any TCA throughout the policy.	03.27.20	08.20
1Q 2021 annual review: no significant changes; references reviewed and updated.	12.02.20	02.21
1Q 2022 annual review: no significant changes; references reviewed and updated.	11.13.21	02.22

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.

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