Clinical Policy Title:	quetiapine extended-release
Policy Number:	RxA.279
Drug(s) Applied:	Seroquel XR®
Original Policy Date:	02/07/2020
Last Review Date:	09/14/2021
Line of Business Policy Applies to:	All lines of business

Background

Quetiapine extended-release (Seroquel XR®) is an atypical antipsychotic.
It 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, as adjunctive therapy with antidepressants, in adults

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
quetiapine extended-release (Seroquel XR®)	Schizophrenia	Adults: Initial: 300 mg orally once daily dose increases may occur at intervals of at least 1 day in increments of up to 300 mg/day* Target: 400 to 800 mg/day Adolescents: Initial: 50 mg orally once daily increase to 100 mg once daily on day 2, then increase in 100 mg/day increments each day until a target dose of 400 mg once daily is reached on day 5 Target: 400 to 800 mg/day*	800 mg/day
	Bipolar I disorder	**Manic or mixed episodes** Adults: Initial: 300 mg orally once daily. Increase to 600 mg once daily on day 2 Target: 400 to 800 mg/day* Children and adolescents Initial: 50 mg orally once daily. Increase to 100 mg once daily on day 2, then increase in 100 mg/day increments	Manic or mixed episodes Adults: 800 mg/day Children and adolescents: 600 mg/day Depressive episodes 300 mg/day

		each day until a target dose of 400 mg once daily is reached on day 5* Target: 400 to 600 mg/day Depressive episodes Adults: Initial: 50 mg orally once daily Increase to 100 mg once daily on day 2, then increase in 100 mg/day increments each day until a target dose of 300 mg once daily is reached on day 4 Target: 300mg/day*	
	Major depressive disorder	<u>Adults:</u> Initial: 50 mg orally once daily in evening Increase to 150 mg once daily in the evening on day 3 Target: 150 to 300 mg/day*	300 mg/day

* Hepatic Impairment: Lower starting dose (50 mg/day) and slowly increase dose by 50 mg once daily to effective dose.

Dosage Forms

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

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

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: 12 months
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: 12 months
Medicaid: 12 months

C. Major Depressive Disorder (must meet all):
1. Diagnosis of major depressive disorder;
2. Age ≥ 18 years;
3. Failure of three antidepressants (e.g., selective serotonin reuptake inhibitor [SSRI], serotonin-norepinephrine reuptake inhibitor [SNRI], tricyclic antidepressant [TCA], 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 or contraindication(s) to multiple antidepressants;
4. 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;
5. Seroquel XR® is prescribed concurrently with an antidepressant;
6. Dose does not exceed 300 mg (2 tablets) per day.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

II. Continued Therapy Approval

A. All Indications in Section I (must meet all):
1. Member meets one of the following (a or b):
   a. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
   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;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed:
   a. Schizophrenia, bipolar disorder: 800 mg (2 tablets) per day;
   b. Major depressive disorder: 300 mg (2 tablets) per day.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
IR: immediate-release
SNRI: serotonin/norepinephrine reuptake inhibitor
SSRI: selective serotonin reuptake inhibitor
TCA: tricyclic antidepressant

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Antipsychotics		

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
quetiapine immediate-release (Seroquel®)	**Schizophrenia** Initial: 25 mg orally twice daily; target: 400 to 800 mg/day **Bipolar Disorder** Initial: 50 mg orally twice daily; 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)		300 mg/day
paroxetine (Paxil®, Paxil CR®, Pexeva®)		Immediate-release: 60 mg/day (40mg/day if geriatric) Extended-release: 75 mg/day (50 mg/day if geriatric)
sertraline (Zoloft®)		200 mg/day
Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)		
desvenlafaxine (Pristiq®)	**Major Depressive Disorder** Refer to prescribing information	400 mg/day
duloxetine (Cymbalta®)		120 mg/day
levomilnacipran (Fetzima®)		120 mg/day
venlafaxine (Effexor®, Effexor XR®)		Extended-release: 225 mg/day
Tricyclic Antidepressant (TCAs)		
amitriptyline		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)

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Doxepin (Silenor)	**Major Depressive Disorder** Refer to prescribing information	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		
isocarboxazid (Marplan®)	**Major Depressive Disorder** Refer to prescribing information	60 mg/day
selegiline (EMSAM® transdermal; Eldepryl® , Zelapar® , Carbex®)		Transdermal: 12 mg/24 hr Oral*: 30 mg/day
tranylcypromine (Parnate®)		60 mg/day
Other Antidepressants		
bupropion (Aplenzin®, Forfivo XL®, 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		16 mg/day perphenazine and 200 mg/day amitriptyline
maprotiline		225 mg/day
nefazodone		600 mg/day
trazodone		Immediate-release: 400 mg/day Extended-release: 375 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Trintellix®		20 mg/day
Viibryd®		40 mg/day

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

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: General Information

- Concomitant use of strong CYP3A4 inhibitors: Reduce quetiapine dose to one-sixth when co-administered with strong CYP3A4 inhibitors (e.g., Ketoconazole, ritonavir).
- Concomitant use of strong CYP3A4 inducers: Increase quetiapine dose to up to five fold when used in combination with a chronic treatment (more than 7-14 days) of potent CYP3A4 inducers (e.g. phenytoin, rifampin, St. John's wort).
- Discontinuation of strong CYP3A4 inducers: Reduce quetiapine dose by five fold within 7-14 days of discontinuation of CYP3A4 inducers.

References

1. Seroquel XR Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals LP; September 2020. Available at: www.seroquelxr.com. Accessed July 12, 2021.
2. Lehman AF, Lieberman JA, Dixon LB, et al. Practice guideline for the treatment of patients with schizophrenia, second edition. Arlington, VA: American Psychiatric Association; February 2004. Available online at http://www.psych.org/psych_pract/treatg/pg/prac_guide.cfm. Accessed July 06, 2020. Accessed July 12, 2021.
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.psych.org/psych_pract/treatg/pg/prac_guide.cfm. Accessed July 12, 2021.
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.psych.org/psych_pract/treatg/pg/prac_guide.cfm. Accessed July 12, 2021.
5. Hirschfeld RMA. Guideline watch: practice guideline for the treatment of patients with bipolar disorder. Arlington, VA: American Psychiatric Association; November 2005. Available online at http://www.psych.org/psych_pract/treatg/pg/prac_guide.cfm. Accessed July 12, 2021.
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.psych.org/psych_pract/treatg/pg/prac_guide.cfm. Accessed July 12, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy was reviewed: 1. Dosing Information- Dosages regimen updated on daily basis 2. Initial Therapy & Continued Therapy- Approval duration updated from Length of benefit updated to 12 months. 3. Continued Therapy II.A.1. was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." 4. Reference reviewed and updated.	07/06/2020	09/14/2020
Policy was reviewed: 1. Dosing Information was updated to include footnote regarding hepatic impairment dosing, "*Hepatic Impairment: Lower starting dose (50 mg/day) and slowly increase dose by 50 mg once daily to effective dose.". 2. Statement about provider sample ''The provision of provider samples does not guarantee coverage…" was added to Clinical Policy. 3. Initial Approval Criteria and Continued Therapy approval Criteria were updated to remove HIM approval duration. 4. Continued Therapy Approval Criteria II.A.1.a was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". 5. Therapeutic Alternatives verbiage was rephrased to "Below are suggested therapeutic alternatives based on clinical guidance..". 6. Appendix B: Therapeutic Alternatives maximum dose for fluvoxamine was updated from "150mg/day" to "300mg/day". 7. Appendix B: Therapeutic Alternatives was updated to remove inactive/unavailable drug names Luvox, Elavil, Sinequan, Tofranil, Tofranil PM, Vivactil, Surmontil, Budeprion SR, Budeprion XL, Wellbutrin, Triavil, Ludiomil, Serzone, Desyrel, Oleptro, vortioxetine, and vilazodone. 8. Appendix B: Therapeutic Alternatives maximum dose for paroxetine was updated	07/12/2021	9/14/2021

Review/Revision History	Review/Revised Date	P&T Approval Date
from “50mg/day” to “60mg/day” for immediate-release formulation and updated from “62.5mg/day” to “75mg/day” for extended-release formulation. 9. Appendix B: Therapeutic Alternatives maximum dose for sertraline was updated to remove age criteria, “if age 6-12 years”. 10. Appendix B: Therapeutic Alternatives maximum dose for maprotiline was updated from “150mg/day” to “225mg/day”. 11. Statement about drug listing format in Appendix B is rephrased to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only". 12. Appendix D was updated to include Warnings and Precautions, “Concomitant use of strong CYP3A4 inhibitors: Reduce quetiapine…”, “Concomitant use of strong CYP3A4 inducers: Increase quetiapine dose…”, and “Discontinuation of strong CYP3A4 inducers: Reduce quetiapine…”. 13. References were reviewed and updated.		