Clinical Policy: Non-Preferred Second-Generation Antipsychotics (Abilify MyCite, Saphris, Secuado, Rexulti, Vraylar, Caplyta, Fanapt, Zyprexa Relprevv, Symbyax, Lybalvi, Invega)

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Line of Business: Arizona Medicaid (AzCH-CCP and Care1st)

Revision Log

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

For children under 18, *refer to Clinical Policy: Antipsychotic Medications in Children Under 18: AZ.CP.PMN.08.*

Description

The following are second generation (atypical) antipsychotics requiring prior authorization: Aripiprazole (Abilify Mycite®), Asenapine (Saphris®, Secuado®), Brexpiprazole (Rexulti®), Cariprazine (Vraylar®), Lumateperone (Caplyta®), Iloperidone (Fanapt®), Olanzapine (Zyprexa Relprevv™), Olanzapine/fluoxetine (Symbyax®), Olanzapine/samidorphan (Lybalvi™), Paliperidone (Invega®)

FDA Approved Indication(s)

Abilify Mycite is indicated for the treatment of schizophrenia and as an adjunctive treatment of adults with major depressive disorder (MDD) in adults.
Abilify Mycite is also indicated for bipolar I disorder:

- Acute treatment of adults with manic and mixed episodes as monotherapy and as adjunct to lithium or valproate
- Maintenance treatment of adults as monotherapy and as adjunct to lithium or valproate

Saphris and Secuado are indicated for the treatment of schizophrenia in adults.
Saphris is also indicated for bipolar I disorder:

- Acute monotherapy treatment of manic or mixed episodes
- Adults and pediatric patients 10 to 17 years of age
- Adjunctive treatment to lithium or valproate in adults
- Maintenance monotherapy treatment in adults

Rexulti is indicated for the:

- Adjunctive treatment of major depressive disorder (MDD)
- Treatment of schizophrenia

Vraylar is indicated for:

- Treatment of schizophrenia in adults
- Acute treatment of manic or mixed episodes associated with bipolar I disorder in adults
- Treatment of depressive episodes associated with bipolar I disorder (bipolar depression) in adults

Zyprexa Relprevv, Caplyta and Fanapt are indicated for the treatment of schizophrenia in adults.

Symbyax is indicated for the treatment of:
- Acute depressive episodes in Bipolar I Disorder in adults and adolescents age 10-17
- Treatment resistant depression (Major Depressive Disorder in patient who do not respond to 2 separate trials of different antidepressants of adequate dose and duration in the current episode)

Lybalvi is indicated for the treatment of:
- Schizophrenia in adults
- Bipolar I disorder in adults
  - Acute treatment of manic or mixed episodes as monotherapy and as adjunct to lithium or valproate
  - Maintenance monotherapy treatment

Invega is indicated for the treatment of:
- Schizophrenia in adults and adolescents age 12-17
- Schizoaffective disorder as monotherapy, as an adjunct to mood stabilizers, and/or antidepressants in adults.

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of Arizona Complete Health-Complete Care Plan and Care1st that Abilify Mycite, Caplyta, Fanapt, Invega, Lybalvi, Rexulti, Saphris, Secuado, Symbyax, Vraylar, and Zyprexa Relprevv are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Aripiprazole (Abilify MyCite) (must meet all):

1. Diagnosis of one of the following (a, b, or c):
   a. Bipolar I Disorder, and failure of one preferred second-generation antipsychotic (e.g. aripiprazole, Latuda, olanzapine, quetiapine, risperidone, ziprasidone), Abilify Maintena, and Risperdal Consta at maximum indicated doses, each trialed for ≥ 4 weeks, unless all are contraindicated or clinically significant adverse effects are experienced;
   b. Major Depressive Disorder, and failure of aripiprazole, olanzapine, and quetiapine as adjunct to an antidepressant;
   c. Schizophrenia spectrum disorder (schizophrenia, schizoaffective disorder, schizophreniform disorders), and failure of 3 preferred second-generation long-acting injectables (e.g., Abilify Maintena, Aristada, Invega Sustenna, Invega

Trinza, Risperdal Consta, Perseris) at maximum indicated doses, each trialed for ≥ 4 weeks, unless all are contraindicated or clinically significant adverse effects are experienced;

2. Prescriber is a behavioral health specialist and is registered with AHCCCS;
3. Age ≥ 18 years;
4. Member is currently prescribed aripiprazole and established tolerability;
5. Member has history of ≥ 1 hospitalization within the last 6 months due to lack of medication adherence;
6. Failure of ALL of the following strategies to improve adherence:
   a. Reminder tools: alarm or phone alert, text reminder, reminder app, medication calendar, etc;
   b. Pill box;
7. Prescriber acknowledges that Abilify MyCite has not been shown to improve patient compliance or modify aripiprazole dosage;
8. Prescriber agrees to monitor and document adherence of Abilify MyCite through online portal provided by the manufacturer;
9. Dose does not exceed the following (a or b):
   a. Bipolar I Disorder or Schizophrenia spectrum disorder: 30 mg per day;
   b. Major Depressive Disorder: 15 mg per day.

Approval duration: 12 months

B. Asenapine (Saphris, Secuado) (must meet all):

1. Diagnosis of one of the following (a or b):
   a. Schizophrenia spectrum disorder (schizophrenia, schizoaffective disorder, schizophreniform disorders), and failure of 3 preferred second-generation antipsychotics (e.g., aripiprazole, clozapine, Latuda, olanzapine, quetiapine, risperidone, ziprasidone) at maximum indicated doses, each trialed for ≥ 4 weeks, unless all are contraindicated or clinically significant adverse effects are experienced;
   b. Bipolar I Disorder, most recent episode manic or mixed, and BOTH of the following (i and ii):
      i. Failure of 2 preferred second-generation antipsychotics (e.g. aripiprazole, Latuda, olanzapine, quetiapine, risperidone, ziprasidone) at up to maximum indicated doses, each trialed for ≥ 4 weeks, unless all are contraindicated or clinically significant adverse effects are experienced;
      ii. Failure of both Lithium and Valproic Acid, and one combination of Lithium or Valproic Acid, plus one preferred second-generation antipsychotic at maximum indicated doses, each trialed for ≥ 4 weeks, unless all are contraindicated or clinically significant adverse effects are experienced;
2. Prescriber is a behavioral health specialist and is registered with AHCCCS;
3. Age ≥ 18 years;
4. Member must be capable of following strict administration instructions sublingual administration and no food or drink for ten minutes after administration;

5. Member does not have severe hepatic impairment (Child-Pugh C);
6. Member is on no other antipsychotics (cross tapers up to 60 days are allowed);
7. Dose does not exceed the following (a or b):
   a. Schizophrenia spectrum disorder – Saphris: 20 mg (2 tablets) per day; Secuado: 7.6 mg (1 patch) per day;
   b. Bipolar I Disorder – Saphris: 10 mg sublingually twice per day (2 tablets per day).

Approval duration: 12 months

C. Brexpiprazole (Rexulti) (must meet all):

1. Diagnosis of one of the following (a or b):
   a. Major depressive disorder (MDD), and both of the following (i and ii):
      i. 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 all are contraindicated or clinically significant adverse effects are experienced;
      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;
   b. Schizophrenia spectrum disorder (schizophrenia, schizoaffective disorder, schizophreniform disorders), and one of the following (i or ii):
      i. Failure of 3 preferred second-generation antipsychotics (e.g., clozapine, Latuda, olanzapine, quetiapine, risperidone, ziprasidone), one of which must be aripiprazole at up to maximally indicated doses, each trialed for ≥ 4 weeks, unless all are contraindicated or clinically significant adverse effects are experienced;
      ii. If concern for weight gain due to comorbidities such as diabetes mellitus or body mass index (BMI) > 30, failure of aripiprazole, Latuda (lurasidone), and ziprasidone at up to maximally indicated doses, each used for ≥ 4 weeks, unless all are contraindicated or clinically significant adverse effects are experienced;
2. Prescriber is a behavioral health specialist and is registered with AHCCCS;
3. Age ≥ 18 years;
4. If for MDD, Rexulti is prescribed concurrently with an antidepressant;
5. Dose does not exceed the following:
   a. MDD: 3 mg (1 tablet) per day;
   b. Schizophrenia spectrum disorder: 4 mg (1 tablet) per day.

Approval duration: 12 months

D. Cariprazine (Vraylar) (must meet all):

1. Diagnosis of bipolar disorder or schizophrenia spectrum disorder (schizophrenia, schizoaffective disorder, schizophreniform disorders);
2. Prescriber is a behavioral health specialist and is registered with AHCCCS;
3. Age ≥ 18 years;

4. Member meets one of the following (a or b):
   a. For treatment of depressive episodes of Bipolar I disorder: Failure of quetiapine, Latuda (lurasidone), and olanzapine, at up to maximally indicated doses, each trialed for ≥ 4 weeks, unless all are contraindicated or clinically significant adverse effects are experienced;
   b. For treatment of Schizophrenia spectrum disorder or manic or mixed episodes of Bipolar I disorder: Failure of 3 preferred second-generation antipsychotics, one of which must be aripiprazole, at up to maximally indicated doses, each trialed for ≥ 4 weeks, unless all are contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed the following:
   a. Schizophrenia or manic or mixed episodes of bipolar I disorder: 6 mg (1 capsule) per day;
   b. Depressive episodes of bipolar I disorder: 3 mg (1 capsule) per day.

Approval duration: 12 months

E. Lumateperone (Caplyta) (must meet all)**:**
1. Diagnosis of Schizophrenia spectrum disorder (schizophrenia, schizoaffective disorder, schizophreniform disorders);
2. Prescriber is a behavioral health specialist and is registered with AHCCCS;
3. Age ≥ 18 years;
4. Member meets one of the following (a or b):
   a. Failure of 3 preferred second-generation antipsychotics (e.g., aripiprazole, clozapine, Latuda, olanzapine, quetiapine, risperidone, ziprasidone) at up to maximally indicated doses, each used for ≥ 4 weeks, unless all are contraindicated or clinically significant adverse effects are experienced;
   b. If concern for weight gain due to comorbidities such as diabetes mellitus or body mass index (BMI) > 30, failure of aripiprazole, Latuda (lurasidone), and ziprasidone at up to maximally indicated doses, each used for ≥ 4 weeks, unless all are contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed 42 mg (1 capsule) per day.

Approval duration: 12 months

F. Iloperidone (Fanapt) (must meet all):
1. Diagnosis of schizophrenia spectrum disorder (schizophrenia, schizoaffective disorder, schizophreniform disorders);
2. Prescriber is a behavioral health specialist and is registered with AHCCCS;
3. Age ≥ 18 years;
4. Failure of 3 preferred second-generation antipsychotics (e.g., aripiprazole, clozapine, Latuda, olanzapine, quetiapine, risperidone, ziprasidone) at maximum indicated doses, each trialed for ≥ 4 weeks, unless all are contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed 24 mg per day (2 tablets per day).

Approval duration: 12 months

G. Olanzapine (Zyprexa Relprevv) (must meet all):
1. Diagnosis of schizophrenia spectrum disorder (schizophrenia, schizoaffective disorder, schizophreniform disorders);
2. Prescriber is a behavioral health specialist and is registered with AHCCCS;
3. Age ≥ 18 years;
4. Failure of 3 preferred second-generation long-acting injectables (e.g., Abilify Maintena, Aristada, Invega Sustenna, Invega Trinza, Risperdal Consta, Perseris) at maximum indicated doses, each trialed for ≥ 4 weeks, unless all are contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed 405 mg per 4 weeks or 300 mg per 2 weeks.

Approval duration: 12 months

H. Olanzapine/fluoxetine (Symbyax) (must meet all):
1. Diagnosis of Bipolar I disorder or Treatment resistant depression;
2. Prescriber is a behavioral health specialist and is registered with AHCCCS;
3. Age is one of the following (a or b):
   a. Treatment resistant depression: ≥ 18 years;
   b. Bipolar I disorder: ≥ 10 years;
4. Member meets one of the following (a or b):
   a. <u>For treatment of depressive episodes of Bipolar I disorder</u>: Failure of quetiapine, Latuda (lurasidone), and divalproex, at up to maximally indicated doses, each trialed for ≥ 4 weeks, unless all are contraindicated or clinically significant adverse effects are experienced;
   b. <u>For treatment resistant depression</u>: 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 all are contraindicated or clinically significant adverse effects are experienced;
5. Medical justification* supports inability to use the individual drug products concurrently (e.g., contraindications to the excipients of all alternative products);
   **Use of samples or of a copay card or discount card does not constitute medical necessity and is not allowed by plan*
6. Dose does not exceed 12 mg olanzapine/50 mg fluoxetine per day.

Approval duration: 12 months

I. Olanzapine/samidorphan (Lybalvi) (must meet all):
1. Diagnosis of Bipolar I disorder or Schizophrenia spectrum disorder (schizophrenia, schizoaffective disorder, schizophreniform disorders);
2. Prescriber is a behavioral health specialist and is registered with AHCCCS;
3. Age ≥ 18 years;

4. Member meets one of the following (a or b):
   a. Failure of 3 preferred second-generation antipsychotics, one of which must be olanzapine (e.g., aripiprazole, Latuda, olanzapine, quetiapine, risperidone, ziprasidone) at up to maximally indicated doses, each used for ≥ 4 weeks, unless all are contraindicated or clinically significant adverse effects are experienced;
   b. If concern for weight gain due to comorbidities such as diabetes mellitus or body mass index (BMI) > 30, failure of aripiprazole, Latuda (lurasidone), and ziprasidone at up to maximally indicated doses, each used for ≥ 4 weeks, unless all are contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed 20 mg olanzapine/10 mg samidorphan per day.

Approval duration: 12 months

J. Paliperidone (Invega) (must meet all)**:**
1. Diagnosis of schizophrenia or schizoaffective disorder;
2. Prescriber is a behavioral health specialist and is registered with AHCCCS;
3. Age ≥ 12 years;
4. Failure of 3 preferred second-generation antipsychotics, one of which must be risperidone (e.g., aripiprazole, clozapine, Latuda, olanzapine, quetiapine, risperidone, ziprasidone) at up to maximally indicated doses, each trialed for ≥ 4 weeks unless all are contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed the following:
   a. Adults: 12 mg/day (1 tablet/day or lowest pill burden available);
   b. Adolescents < 51 kg: 6 mg/day (1 tablet/day);
   c. Adolescents ≥ 51kg: 12 mg/day (1 tablet/day or lowest pill burden available).

Approval duration: 12 months

K. Other diagnoses/indications/non-preferred second-generation antipsychotics
1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): AZ.CP.PMN.53 for Arizona Medicaid;
2. Refer to the Non-Preferred Drugs and Brand Name Override policy if the non-preferred second-generation antipsychotic is NOT specifically listed under section I (Initial Approval Criteria): AZ.CP.PMN.16 for Arizona Medicaid.

II. Continued Therapy

A. All Drugs in Section I (must meet all)**:**
1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving the non-preferred second-generation antipsychotic for bipolar disorder, treatment resistant depression, or schizophrenia spectrum 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 maximum dose indicated in Section V.

Approval duration: 12 months

B. Other diagnoses/indications/non-preferred second-generation antipsychotics (must meet 1, 2, or 3)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): AZ.CP.PMN.53 for Arizona Medicaid; or
3. Refer to the Non-Preferred Drugs and Brand Name Override policy if the non-preferred second-generation antipsychotic is NOT specifically listed under section I (Initial Approval Criteria): AZ.CP.PMN.16 for Arizona 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 policy AZ.CP.PMN.53 for Arizona Medicaid.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration

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
Oral Second-generation Antipsychotics		
aripiprazole (Abilify®)	**Bipolar Disorder and Schizophrenia** Adults: 10 to 15 mg PO QD	30 mg/day
clozapine	**Schizophrenia** 12.5 mg-450 mg in divided doses	900mg/day
ziprasidone (Geodon®)	**Schizophrenia** 20 mg PO BID **Bipolar Disorder** Initial: 40 mg PO BID; target: 40 to 80 mg PO BID	160 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Latuda® (lurasidone)	**Schizophrenia** Initial: 40 mg PO QD with food **Bipolar Disorder** Initial: 20 mg PO QD with food	160 mg/day
risperidone (Risperdal®)	**Schizophrenia** Initial: 1 mg PO BID or 2 mg PO QD; target: 4 to 8 mg PO QD **Bipolar Disorder** 2 to 3 mg PO QD	16 mg/day
quetiapine (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
olanzapine (Zyprexa®)	**Schizophrenia** Initial: 5 to 10 mg PO QD; target: 10 mg PO QD **Bipolar Disorder** Monotherapy: 10 to 15 mg PO QD; adjunct to lithium or valproate: 10 mg PO QD	20 mg/day
Long-Acting Injectable Second Generation Antipsychotics		
Abilify Maintena® (aripiprazole monohydrate)	**Bipolar Disorder and Schizophrenia** 400 mg IM monthly	400 mg/month
Aristada® (aripiprazole lauroxil)	**Schizophrenia** 441 mg, 662 mg, or 882 mg IM monthly; 882 mg IM every 6 weeks; or 1064 mg IM every 2 months	1064 mg/2 months
Aristada Initio® (aripiprazole lauroxil)	**Schizophrenia** *(therapy initiation only)* Single dose of Aristada Initio 675 mg IM	675 mg once
Invega Sustenna® (paliperidone)	**Schizophrenia**	234 mg/month

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Initial: 234 mg IM on day 1 and 156 mg one week later (day 8) Maintenance: 39-234 mg IM monthly **Schizoaffective disorder** Initial: 234 mg IM on day 1 and 156 mg one week later (day 8) Maintenance: 78-234 mg IM monthly	
Invega Trinza® (paliperidone)	**Schizophrenia** To be used only after Invega Sustenna® (1-month paliperidone palmitate extended-release injectable suspension) has been established as adequate treatment for at least four months. 273 mg, 410 mg, 546 mg, or 819 mg IM every 3 months	819 mg/3 months
Risperdal Consta® (risperidone)	**Bipolar disorder and Schizophrenia** 25 mg to 50 mg IM every 2 weeks	50 mg/2 weeks
Perseris® (risperidone)	**Schizophrenia** 90 mg or 120 mg SC once monthly	120 mg/4 weeks
SSRI		
citalopram (Celexa®)	20 mg PO QD; may increase to 40 mg PO QD after one week	40 mg/day (≤ 60 years) 20 mg/day (> 60 years)
escitalopram (Lexapro®)	10 mg PO QD; may increase to 20 mg PO QD after 1 week	20 mg/day
fluoxetine (Prozac®, Prozac Weekly®)	Prozac: 20 mg PO QD; may increase by 10-20 mg after several weeks Prozac Weekly: 90 mg PO q week beginning 7 days after the last daily dose	Prozac: 80 mg/day Prozac Weekly: 90 mg/week
paroxetine (Paxil®, Paxil CR®, Pexeva®)	Paxil, Pexeva: 20 mg PO QD; may increase by 10 mg every week as needed Paxil CR: 25 mg PO QD; may increase by 12.5 mg every week as needed	Paxil, Pexeva: 50 mg/day Paxil CR: 62.5 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
sertraline (Zoloft®)	50 mg PO QD; may increase every week as needed	200 mg/day
SNRIs		
duloxetine (Cymbalta®)	20 mg PO BID or 30 mg PO BID or 60 mg PO QD	120 mg/day
venlafaxine (Effexor®, Effexor XR®)	Effexor: 75 mg/day PO in 2-3 divided doses; may increase by 75 mg every 4 days as needed Effexor XR: 75 mg PO QD; may increase by 75 mg every 4 days as needed	Effexor: 225 mg/day (outpatient) or 375 mg/day (inpatient) Effexor XR: 225 mg/day
TCAs		
amitriptyline (Elavil®)	25 to 50 mg/day PO QD or divided doses	150 mg/day
amoxapine	25 to 300 mg/day PO in divided doses	400 mg/day (300 mg/day if geriatric)
clomipramine* (Anafranil®)	12.5 to 150 mg/day PO QD	250 mg/day (200 mg/day if pediatric)
desipramine (Norpramin®)	25 to 300 mg/day PO QD	300 mg/day (100 mg/day if pediatric)
doxepin (Sinequan®)	25 to 300 mg/day PO QD	300 mg/day
imipramine HCl (Tofranil®)	25 to 200 mg/day PO QD or divided doses	200 mg/day (150 mg/day if geriatric or pediatric)
imipramine pamoate (Tofranil PM®)	25 to 200 mg/day PO QD or divided doses	200 mg/day (100 mg/day if geriatric or pediatric)
nortriptyline (Pamelor®)	25 to 150 mg/day PO QD	150 mg/day
protriptyline (Vivactil®)	10 to 60 mg/day PO in divided doses	60 mg/day (30 mg/day if geriatric or pediatric)
trimipramine (Surmontil®)	25 to 200 mg/day PO QD	200 mg/day (100 mg/day if geriatric or pediatric)
Other Antidepressants		

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
bupropion (Aplenzin®, Budeprion SR® , Budeprion XL®, Forfivo XL®, Wellbutrin®, Wellbutrin SR®, Wellbutrin XL®)	Varies	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
buspirone*	15 to 20 mg/day PO in 2 divided doses	60 mg/day
mirtazapine (Remeron®)	15 to 15 mg PO QD	45 mg/day
lithium*	300 mg PO QD or BID; up to 600 to 1,200 mg PO daily in divided doses	1,200 mg/day
thyroid hormone*	25 to 50 mcg/day PO	50 mcg/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.
**Off-label*

Appendix C: Contraindications/Boxed Warnings
Refer to drug specific Prescribing Information.

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Aripiprazole (Abilify Mycite)	Bipolar Disorder and Schizophrenia	Adults: 10-15 mg PO QD	30 mg/day
Asenapine sublingual tablets (Saphris)	Schizophrenia	5 to 10 mg SL BID	20 mg/day
	Bipolar in adults		
	Bipolar in pediatric members	2.5 to 10 mg SL BID	
Asenapine transdermal system (Secuado)	Schizophrenia	3.8 to 7.6 mg TD QD	7.6 mg/day

Drug Name	Indication	Dosing Regimen	Maximum Dose
Brexpiprazole (Rexulti)	Adjunctive treatment of MDD	0.5 mg or 1 mg PO QD, up to the target dosage of 2 mg once daily	3 mg/day
	Schizophrenia	1 mg PO QD, up to target dosage of 2 mg to 4 mg once daily	4 mg/day
Cariprazine (Vraylar)	Schizophrenia	1.5 mg to 6 mg PO QD	6 mg/day
	Bipolar I disorder	Manic or mixed episodes: 3 mg to 6 mg PO QD Depressive episodes: 1.5 mg or 3 mg PO QD	Manic or mixed episodes: 6 mg/day Depressive episodes: 3 mg/day
Lumateperone (Caplyta)	Schizophrenia	42 mg PO QD	42 mg/day
Iloperidone (Fanapt)	Schizophrenia	Initial: 1 mg, 2 mg, 4 mg, 6 mg, 8 mg, 10 mg, and 12 mg PO BID on consecutive days from Day 1 to Day 7 Maintenance: 12 to 24 mg/day PO BID	24 mg/day
Olanzapine (Zyprexa Relprevv)	Schizophrenia	IM: 150 mg/2 weeks, 300 mg/4 weeks, 210 mg/2 weeks, 405 mg/4 weeks, or 300 mg/2 weeks Zyprexa Relprevv should be administered by a healthcare professional.	405 mg every 4 weeks or 300 mg every 2 weeks
Olanzapine/fluoxetine (Symbyax)	Bipolar I disorder	Initial: olanzapine 6 mg/fluoxetine 25 mg PO QD Maintenance: olanzapine 6 to 12 mg/fluoxetine 25 to 50 mg PO QD	12 mg/50 mg/day
	Treatment-resistant depression	Initial: olanzapine 6 mg/fluoxetine 25 mg PO QD Maintenance: olanzapine 6 to 18 mg/fluoxetine 25 to 50 mg PO QD	12 mg/50 mg/day

Drug Name	Indication	Dosing Regimen	Maximum Dose
Olanzapine/samidorphan (Lybalvi)	Schizophrenia	Initiate at 5 mg/10 mg or 10 mg/10 mg PO QD. The recommended dosage is 10 mg/10 mg, 15 mg/10 mg, or 20 mg/10 mg. Dosage may be adjusted at weekly intervals of 5 mg (based on the olanzapine component) depending upon clinical response and tolerability.	20 mg/10 mg/day
	Bipolar I disorder	Monotherapy: Initiate at 10 mg/10 mg or 15 mg/10 mg PO QD. The recommended dosage is 10 mg/10 mg, 15 mg/10 mg, or 20 mg/10 mg PO QD. Dosage adjustments should occur at intervals of not less than 24 hours. When dosage adjustments are necessary, dose increments/decrements of 5 mg (based on the olanzapine component) are recommended. Maintenance monotherapy: Administer at 5 mg/10 mg, 10 mg/10 mg, 15 mg/10 mg, or 20 mg/10 mg PO QD.	20 mg/10 mg/day
Paliperidone (Invega)	Schizophrenia	Adults Initial dose: 6 mg PO QD Target dose: 3 to 12 mg PO QD Adolescents Initial dose: 3 mg PO QD Target dose: • Weight < 51 kg: 3 to 6 mg PO QD • Weight ≥ 51 kg 3 to 12 mg PO QD	Adults and adolescents weighing ≥ 51 kg: 12 mg/day Adolescents weighing < 51 kg: 6 mg/day
	Schizoaffective disorder	Initial dose: 6 mg PO QD Target dose: 3 to 12 mg PO QD	12 mg/day

VI. Product Availability

Drug	Availability
Aripiprazole (Abilify Mycite®)	**Tablets**: 2 mg, 5 mg, 10 mg, 15 mg, 20 mg, 30 mg
Asenapine	**Generic, sublingual tablets**: 2.5 mg, 5 mg, 10 mg **Saphris®, sublingual tablets**: 2.5 mg, 5 mg, 10 mg
	Secuado®, transdermal patch – 24 hour: 3.8 mg/24hr, 5.7 mg/24hr, 7.6 mg/24hr
Brexpiprazole (Rexulti®)	**Tablets**: 0.25 mg, 0.5 mg, 1 mg, 2 mg, 3 mg, 4 mg
Cariprazine (Vraylar®)	**Capsules**: 1.5 mg, 3 mg, 4.5 mg, 6 mg
Lumateperone (Caplyta®)	**Capsules**: 42 mg
Iloperidone (Fanapt®)	**Tablets**: 1 mg, 2 mg, 4 mg, 6 mg, 8 mg, 10 mg, 12 mg, Fanapt Titration Pack
Olanzapine (Zyprexa Relprevv™)	**Powder for Suspension**: 210 mg, 300 mg, 405 mg
Olanzapine/fluoxetine (Symbyax®)	**Generic, Capsules**: 3 mg/25 mg, 6 mg/25 mg, 6 mg/50 mg, 12 mg/25 mg, 12 mg/50 mg **Symbyax®, Capsules**: 3 mg/25 mg, 6 mg/25 mg, 6 mg/50 mg, 12 mg/50 mg
Olanzapine/samidorphan (Lybalvi™)	**Tablets**: 5 mg/10 mg, 10 mg/10 mg, 15 mg/10 mg, 20 mg/10 mg
Paliperidone (Invega®)	**Generic, Tablets, Extended-release**: 1.5 mg, 3 mg, 6 mg, 9 mg **Invega®, Tablets, Extended-release**: 1.5 mg, 3 mg, 6 mg, 9 mg

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	09.13.21	11.21
1Q 2022 annual review: no significant changes; references reviewed and updated.	01.25.22	01.22

Important Reminder

CLINICAL POLICY
Non-Preferred Second-Generation Antipsychotics

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.

For Health Insurance Marketplace members, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the formulary exception policy.