STEP THERAPY CRITERIA

DRUG CLASS	**ATYPICAL ANTIPSYCHOTICS (BRAND PRODUCTS ONLY)**
BRAND NAME* (generic)	**ABILIFY (ORAL TABLET & ORAL SOLUTION ONLY) (BRAND ONLY) (aripiprazole)** **ABILIFY MYCITE (BRAND ONLY) (aripiprazole)** **FANAPT (BRAND ONLY) (iloperidone)** **GEODON (BRAND ONLY) (ziprasidone)** **INVEGA (ORAL TABLET) (BRAND ONLY) (paliperidone)** **LATUDA (BRAND ONLY) (lurasidone hydrochloride)** **REXULTI (BRAND ONLY) (brexpiprazole)** **SAPHRIS (BRAND ONLY) (asenapine)** **SEROQUEL, SEROQUEL XR (BRAND ONLY) (quetiapine)** **VRAYLAR (BRAND ONLY) (cariprazine)**
Status: CVS Caremark Criteria	
Type: Initial Step Therapy; Post Step Therapy Prior Authorization	***Ref # 657-D***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Abilify

Abilify Oral Tablets and Oral Solution are indicated for the treatment of:

- Schizophrenia

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- Acute Treatment of Manic and Mixed Episodes associated with Bipolar I Disorder
- Adjunctive Treatment of Major Depressive Disorder
- Irritability Associated with Autistic Disorder
- Treatment of Tourette's Disorder

Abilify Mycite
Abilify Mycite, a drug-device combination product comprised of aripiprazole tablets embedded with an Ingestible Event Marker (IEM) sensor intended to track drug ingestion, is indicated for the treatment of:

- Adults with schizophrenia
- Treatment of 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
- Adjunctive treatment of adults with Major Depressive Disorder

Limitations of Use
The ability of the Abilify Mycite to improve patient compliance or modify aripiprazole dosage has not been established. The use of Abilify Mycite to track drug ingestion in "real-time" or during an emergency is not recommended because detection may be delayed or not occur.

Fanapt
Fanapt tablets are indicated for the treatment of adults with schizophrenia. Efficacy was established in two short-term (4- and 6-week) placebo- and active-controlled studies of adult patients with schizophrenia. When deciding among the alternative treatments available for this condition, the prescriber should consider the finding that Fanapt is associated with prolongation of the QTc interval. Prolongation of the QTc interval is associated in some other drugs with the ability to cause torsade de pointes-type arrhythmia, a potentially fatal polymorphic ventricular tachycardia which can result in sudden death. In many cases this would lead to the conclusion that other drugs should be tried first. Whether Fanapt will cause torsade de pointes or increase the rate of sudden death is not yet known. Patients must be titrated to an effective dose of Fanapt. Thus, control of symptoms may be delayed during the first 1 to 2 weeks of treatment compared to some other antipsychotic drugs that do not require a similar titration. Prescribers should be mindful of this delay when selecting an antipsychotic drug for the treatment of schizophrenia. The effectiveness of Fanapt in long-term use, that is, for more than 6 weeks, has not been systematically evaluated in controlled trials. Therefore, the physician who elects to use Fanapt for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient.

Geodon
Geodon is indicated for the treatment of schizophrenia, as monotherapy for the acute treatment of Bipolar manic or mixed episodes, and as an adjunct to lithium or valproate for the maintenance treatment of Bipolar disorder. Geodon intramuscular is indicated for acute agitation in schizophrenic patients. When deciding among the alternative treatments available for the condition needing treatment, the prescriber should consider the finding of ziprasidone's greater capacity to prolong the QT/QTc interval compared to several other antipsychotic drugs. Prolongation of the QTc interval is associated in some other drugs with the ability to cause torsade de pointes-type arrhythmia, a potentially fatal polymorphic ventricular tachycardia, and sudden death. In many cases this would lead to the conclusion that other drugs should be tried first. Whether ziprasidone will cause torsade de pointes or increase the rate of sudden death is not yet known.
Schizophrenia
Geodon is indicated for the treatment of schizophrenia. The efficacy of oral ziprasidone was established in four short-term (4-week and 6-week) controlled trials of adult schizophrenic inpatients and in one maintenance trial of stable adult schizophrenic inpatients.
Bipolar I Disorder
Geodon is indicated as monotherapy for the acute treatment of manic or mixed episodes associated with Bipolar I disorder. Efficacy was established in two 3-week monotherapy studies in adult patients.
Geodon is indicated as an adjunct to lithium or valproate for the maintenance treatment of Bipolar I disorder. Efficacy was established in a maintenance trial in adult patients. The efficacy of Geodon as monotherapy for the maintenance treatment of Bipolar I disorder has not been systematically evaluated in controlled clinical trials.
Acute Treatment of Agitation in Schizophrenia

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Geodon intramuscular is indicated for the treatment of acute agitation in schizophrenic patients for whom treatment with ziprasidone is appropriate and who need intramuscular antipsychotic medication for rapid control of agitation. The efficacy of intramuscular ziprasidone for acute agitation in schizophrenia was established in single day controlled trials of agitated schizophrenic inpatients. "Psychomotor agitation" is defined in DSM-IV as "excessive motor activity associated with a feeling of inner tension." Schizophrenic patients experiencing agitation often manifest behaviors that interfere with their diagnosis and care, e.g., threatening behaviors, escalating or urgently distressing behavior, or self-exhausting behavior, leading clinicians to the use of intramuscular antipsychotic medications to achieve immediate control of the agitation. Since there is no experience regarding the safety of administering ziprasidone intramuscular to schizophrenic patients already taking oral ziprasidone, the practice of co-administration is not recommended.
Ziprasidone intramuscular is intended for intramuscular use only and should not be administered intravenously.

Invega
Schizophrenia
Invega (paliperidone) Extended-Release Tablets are indicated for the treatment of schizophrenia. The efficacy of Invega in schizophrenia was established in three 6-week trials in adults and one 6-week trial in adolescents, as well as one maintenance trial in adults.
Schizoaffective Disorder
Invega (paliperidone) Extended-Release Tablets are indicated for the treatment of schizoaffective disorder as monotherapy and an adjunct to mood stabilizers and/or antidepressant therapy. The efficacy of Invega in schizoaffective disorder was established in two 6-week trials in adults.

Latuda
Latuda is indicated for:
- Treatment of adult and adolescent patients age 13 to 17 years with schizophrenia
- Monotherapy treatment of adult and pediatric patients (10 to 17 years) with major depressive episodes associated with Bipolar I disorder (bipolar depression)
- Adjunctive treatment with lithium or valproate in adult patients with major depressive episodes associated with Bipolar I disorder (bipolar depression)

Rexulti
Rexulti is indicated for:
- Adjunctive treatment of major depressive disorder (MDD)
- Treatment of schizophrenia

Saphris
Saphris is indicated for:
- Schizophrenia in adults
- Acute monotherapy of manic or mixed episodes in Bipolar I disorder, in adults and pediatric patients 10 to 17 years of age
- Adjunctive treatment to lithium or valproate in Bipolar I disorder in adults
- Maintenance monotherapy treatment in Bipolar I disorder in adults

Seroquel
Schizophrenia
Seroquel is indicated for the treatment of schizophrenia. The efficacy of Seroquel in schizophrenia was established in three 6-week trials in adults and one 6–week trial in adolescents (13–17 years). The effectiveness of Seroquel for the maintenance treatment of schizophrenia has not been systematically evaluated in controlled clinical trials.
Bipolar Disorder
Seroquel is indicated for the acute treatment of manic episodes associated with Bipolar I disorder, both as monotherapy and as an adjunct to lithium or divalproex. Efficacy was established in two 12-week monotherapy trials in adults, in one 3-week adjunctive trial in adults, and in one 3-week monotherapy trial in pediatric patients (10-17 years).
Seroquel is indicated as monotherapy for the acute treatment of depressive episodes associated with Bipolar disorder. Efficacy was established in two 8-week monotherapy trials in adult patients with Bipolar I and Bipolar II disorder.

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Seroquel is indicated for the maintenance treatment of Bipolar I disorder, as an adjunct to lithium or divalproex. Efficacy was established in two maintenance trials in adults. The effectiveness of Seroquel as monotherapy for the maintenance treatment of Bipolar disorder has not been systematically evaluated in controlled clinical trials.
Special Considerations in Treating Pediatric Schizophrenia and Bipolar I Disorder
Pediatric schizophrenia and Bipolar I disorder are serious mental disorders, however, diagnosis can be challenging. For pediatric schizophrenia, symptom profiles can be variable, and for Bipolar I disorder, patients may have variable patterns of periodicity of manic or mixed symptoms. It is recommended that medication therapy for pediatric schizophrenia and Bipolar I disorder be initiated only after a thorough diagnostic evaluation has been performed and careful consideration given to the risks associated with medication treatment. Medication treatment for both pediatric schizophrenia and Bipolar I disorder is indicated as part of a total treatment program that often includes psychological, educational and social interventions.

Seroquel XR
Schizophrenia
Seroquel XR is indicated for the treatment of schizophrenia. The efficacy of Seroquel XR in schizophrenia was established in one 6- week and one maintenance trial in adults with schizophrenia. Efficacy was supported by three 6-week trials in adults with schizophrenia and one 6-week trial in adolescents with schizophrenia (13-17 years) treated with Seroquel.
Bipolar Disorder
Seroquel XR is indicated for the acute treatment of manic or mixed episodes associated with Bipolar I disorder, both as monotherapy and as an adjunct to lithium or divalproex. The efficacy of Seroquel XR in manic or mixed episodes of Bipolar I disorder was established in one 3-week trial in adults with manic or mixed episodes associated with Bipolar I disorder. Efficacy was supported by two 12-week monotherapy trials and one 3-week adjunctive trial in adults with manic epsidoes associated with Bipolar I disorder as well as one 3-week monotherapy trial in children and adolescents (10-17 years) with manic episodes associated with Bipolar I disorder treated with Seroquel.
Seroquel XR is indicated for the acute treatment of depressive episodes associated with Bipolar disorder. The efficacy of Seroquel XR was established in one 8-week trial in adults with Bipolar I or II disorder and supported by two 8-week trials in adults with Bipolar I or II disorder treated with Seroquel.
Seroquel XR is indicated for the maintenance treatment of Bipolar I disorder, as an adjunct to lithium or divalproex. Efficacy was extrapolated from two maintenance trials in adults with Bipolar I disorder treated with Seroquel. The effectiveness of monotherapy for the maintenance treatment of Bipolar I disorder has not been systematically evaluated in controlled clinical trials.
Adjunctive Treatment of Major Depressive Disorder (MDD)
Seroquel XR is indicated for use as adjunctive therapy to antidepressants for the treatment of MDD. The efficacy of Seroquel XR as adjunctive therapy to antidepressants in MDD was established in two 6-week trials in adults with MDD who had an inadequate response to antidepressant treatment.
Special Considerations in Treating Pediatric Schizophrenia and Bipolar I Disorder
Pediatric schizophrenia and Bipolar I disorder are serious mental disorders, however, diagnosis can be challenging. For pediatric schizophrenia, symptom profiles can be variable, and for Bipolar I disorder, patients may have variable patterns of periodicity of manic or mixed symptoms. It is recommended that medication therapy for pediatric schizophrenia and Bipolar I disorder be initiated only after a thorough diagnostic evaluation has been performed and careful consideration given to the risks associated with medication treatment. Medication treatment for both pediatric schizophrenia and Bipolar I disorder is indicated as part of a total treatment program that often includes psychological, educational and social interventions.

Vraylar
Vraylar is indicated for:
- Treatment of schizophrenia in adults
- Acute treatment of manic or mixed episodes associated with Bipolar I disorder in adults

INITIAL STEP THERAPY
If the patient has filled a prescription for a 30 day supply of generic aripiprazole, olanzapine, paliperidone, risperidone, quetiapine (regular or extended release), or ziprasidone within the past 180 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. If the patient does not meet the

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initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- Patient is currently taking the requested drug with evidence of improvement.
  OR
- Patient has experienced an inadequate treatment response to generic aripiprazole, olanzapine, risperidone (any dosage form), quetiapine (regular or extended release), paliperidone, or ziprasidone after a trial of at least 30 days.
  OR
- Patient has an intolerance, drug interaction, or contraindication to generic aripiprazole, olanzapine, risperidone (any dosage form), quetiapine (regular or extended release), paliperidone or ziprasidone that would prohibit a 30 day trial.
  OR
- Patient has a clinical condition for which there is no generic alternative or the generic alternatives are not recommended based on published guidelines or clinical literature.

RATIONALE

If the patient has filled a prescription for a 30 day supply of aripiprazole, olanzapine, risperidone, quetiapine (regular or extended release), paliperidone or ziprasidone within the past 180 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.

If the patient does not meet the initial step therapy criteria, then prior authorization is required.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines.

The American Psychiatric Association (APA) considers certain atypical (second-generation) antipsychotic agents (e.g., aripiprazole, olanzapine, quetiapine, risperidone, ziprasidone) first-line drugs for the management of the acute phase of schizophrenia (including first psychotic episodes), principally because of the decreased risk of adverse extrapyramidal effects and tardive dyskinesia, with the understanding that the relative advantages, disadvantages, and cost-effectiveness of conventional and atypical antipsychotic agents remain controversial. The APA states, with the possible exception of clozapine for the management of treatment-resistant symptoms, there currently is no definitive evidence that one atypical antipsychotic agent will have superior efficacy compared with another agent in the class, although meaningful differences in response may be observed in individual patients. The American Psychiatric Association (APA) considers atypical (second-generation) antipsychotics preferred over typical antipsychotics because of their more benign side effect profile with most of the evidence supporting the use of olanzapine or risperidone with alternatives ziprasidone and quetiapine in lieu of another antipsychotic for bipolar disorder, severe manic or mixed episodes. The American Psychiatric Association (APA) considers that second-generation antipsychotic medications (e.g., aripiprazole, olanzapine, quetiapine, risperidone) may increase the rates of response or remission of depressive symptoms in patients who typically have not responded to more than two antidepressant medication trials, even when psychotic symptoms are not present. Patient response and tolerance to antipsychotic agents are variable, and patients who do not respond to or tolerate one drug may be successfully treated with an agent from a different class or with a different adverse effect profile.[11-14]

Approval is allowed if the patient is currently taking the requested drug with evidence of improvement. Approval is also allowed if the patient had an inadequate response to a 30 day trial or intolerance, drug interaction, or contraindication to aripiprazole, olanzapine, risperidone (any dosage form), quetiapine (regular or extended release), paliperidone, or ziprasidone. If the patient has a clinical condition for which there is no generic alternative or the listed generic alternatives are not recommended based on published guidelines or clinical literature, then the requested drug will also be approved.

REFERENCES

1. Abilify [package insert]. Rockville, MD: Otsuka America Pharmaceutical, Inc.; February 2017.

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Written by:	UM Development (RP)
Date Written:	06/2011
Revised:	11/2011 (removed Zyprexa), 12/2011 (added olanzapine to initial step), 04/2012 (added quetiapine regular release and ziprasidone to initial step), 05/2012; (NB) 10/2012 (extended duration); (PL) 05/2013; (MS) 05/2014; (CF) 02/2015 (added Tourette's indication for Abilify); (MS) 05/2015 (Clarified target drug dosage forms, Added generic aripiprazole to automated step, to question 3 and 4. Changed Abilify to BRAND ONLY), 07/2015 (added Rexulti), 09/2015 (added Vraylar), (NB) 05/2016 (no clinical changes), (JK) 05/2017 (Changed all targets to BRAND ONLY, added paliperidone as pre-req), (ME) 05/2018 (no clinical changes), 02/2019 (added Abilify Mycite)
Reviewed:	Medical Affairs (KP) 06/2011, 11/2011, 12/2011, 04/2012; (LB) 05/2012; (KP) 10/2012; (LCB) 05/2013; (SS) 05/2014; (SES) 02/2015; (DC) 05/2015; (MM) 07/2015; (LS) 09/2015, (TP) 05/2017, (AN) 02/2019 External Review: 10/2011, 12/2011, 10/2012, 08/2013, 08/2014, 08/2015, 08/2015, 08/2017, 08/2018, 04/2019 (FYI P&T)

CRITERIA FOR APPROVAL

1	Is the patient currently taking the requested drug with evidence of improvement? [If yes, then no further questions.]	Yes	No
2	Has the patient experienced an inadequate treatment response to aripiprazole, olanzapine, risperidone (any dosage form), quetiapine (regular or extended release), paliperidone, or ziprasidone after a trial of at least 30 days? [If yes, then no further questions.]	Yes	No
3	Did the patient have an intolerance, drug interaction, or contraindication to aripiprazole, olanzapine, risperidone (any dosage form), quetiapine (regular or extended release), paliperidone or ziprasidone that would prohibit a 30 day trial? [If yes, then no further questions.]	Yes	No
4	Does the patient have a clinical condition for which there is no generic alternative or the generic alternatives are not recommended based on published guidelines or clinical literature?	Yes	No

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Mapping Instructions			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Approve, 36 months	Go to 2	
2.	Approve, 36 months	Go to 3	
3.	Approve, 36 months	Go to 4	
4.	Approve, 36 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet one of these conditions: - You are currently taking this medicine and have shown improvement - You tried another medicine first and it did not work for you - You cannot use another medicine Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance or contraindication to generic formulary alternatives]

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