

## MTF Formulary Management for Atypical Antipsychotic (AAP) Drugs

Defense Health Agency Pharmacy Operations Division

### Bottom Line

- Aripiprazole was added to the Basic Core Formulary. Military Treatment Facilities are encouraged to switch patients to generic aripiprazole.
- Generics for Seroquel XR are expected in November 2016.
- Lurasidone (Latuda) was added to the Uniform Formulary.
- Fanapt and Saphris remain nonformulary. The new drugs, Rexulti and Vraylar, offer no compelling advantages over existing agents and were designated nonformulary.
- The safety profiles of individual atypical antipsychotic drugs are well known, in terms of metabolic, neurologic, and cardiovascular effects.
- Choice of treatment should be influenced by the relationship between the efficacy, tolerability, and individual patient characteristics.

**Uniform Formulary (UF) Decision:** The Director, DHA, approved the recommendations from the May 2016 DoD P&T Committee meeting on July 28, 2016, with an implementation date of November 2, 2016.

Uniform Formulary (UF)		Nonformulary (NF) Agents
MTFs must have on formulary	MTFs <u>may</u> have on formulary	MTFs <u>must not</u> have on formulary
<ul style="list-style-type: none"> <li>• risperidone tablets and ODT</li> <li>• quetiapine IR</li> <li>• quetiapine XR (Seroquel XR)</li> <li>• aripiprazole tablets</li> </ul>	<ul style="list-style-type: none"> <li>• aripiprazole ODT and oral solution</li> <li>• clozapine tablets and ODT</li> <li>• lurasidone (Latuda)</li> <li>• olanzapine tablets and ODT</li> <li>• olanzapine/Fluoxetine</li> <li>• paliperidone</li> <li>• ziprasidone</li> </ul>	<ul style="list-style-type: none"> <li>• asenapine (Saphris)</li> <li>• brexpiprazole (Rexulti)</li> <li>• cariprazine (Vraylar)</li> <li>• iloperidone (Fanapt)</li> </ul>

ODT – orally dissolving tablets

### Formulary Management Issues

- The AAP Drug Class was previously reviewed for formulary placement in May 2011. There are currently 13 oral AAP drugs available in the United States. Six branded agents remain in the class including Seroquel XR, Fanapt, Saphris, Latuda, Vraylar, and Rexulti.
- This review focused only on the oral AAP drugs, not the injectable agents, and particularly on the remaining brand name agents.
- Cariprazine (Vraylar) and brexpiprazole (Rexulti) are new agents in the class that have not been previously reviewed.
- Since the last class review, many agents have become available in generic form, including aripiprazole. Seroquel XR generics are expected in November 2016.

### Brexpiprazole (Rexulti)

- Brexpiprazole is a new AAP that is FDA approved to treat schizophrenia and as an adjunct to antidepressant therapy for major depressive disorder (MDD).
  - In schizophrenia, brexpiprazole showed individual changes from baseline in Positive and Negative Symptom Scale (PANSS) score that were clinically significant from baseline, but not when compared to placebo.
  - Limitations of the schizophrenia studies included lack of active comparators and short duration (six weeks).
  - In depression, higher doses of brexpiprazole were statistically significant and clinically significant, but not at the lowest dose (1 mg).

## Cariprazine (Vraylar)

- Cariprazine is a new AAP that is FDA approved to treat schizophrenia and bipolar disorder.
  - In schizophrenia, cariprazine showed individual changes from baseline in PANSS score that were clinically significant, but not when compared to placebo.
  - Limitations include the short duration of the studies and no head-to-head comparisons with other AAP drugs.
  - In bipolar disorder, cariprazine was superior to placebo but there are no head-to-head studies with other AAP drugs.

## Safety and Tolerability

- The safety profiles of individual AAP drugs are well known in terms of metabolic, neurologic, and cardiovascular effects.
- Brexpiprazole and cariprazine have similar safety and tolerability concerns as the other drugs in the class.
- Cariprazine has an active metabolite with a long half-life (one to three weeks) that may extend adverse effects in those affected.

## Summary

- There are no significant efficacy or safety updates since the May 2011 drug class review.
- Brexpiprazole and cariprazine offer no clinically compelling advantages over existing UF agents.
- According to the Institute for Quality and Efficiency in Health Care (IQWiG), manufacturer claims of fewer adverse events with lurasidone compared to risperidone, olanzapine, and quetiapine XR could not be proven. However, lurasidone is dosed once daily and is the only Pregnancy Category B drug, besides clozapine.
- AAP drugs with new pediatric indications include asenapine for bipolar disorder (ages 10-17 years) and paliperidone for schizophrenia (ages 12-17 years), although several other drugs have similar pediatric indications.
- Generic AAP drugs currently on the UF are adequate to meet the needs of the majority of DoD patients with schizophrenia, bipolar disorder, and adjunct to MDD.
- Choice of treatment should be based on efficacy, tolerability, and individual patient characteristics.

## Prior Authorization for Brexpiprazole

- All new users of brexpiprazole are required to undergo the manual prior authorization (PA) process.
- For MDD, patients must be at least 18 years old and have tried and failed at least two other antidepressant augmentation therapies (one of which must be aripiprazole). Brexpiprazole must be used in conjunction with an antidepressant.
- For schizophrenia, patients must be at least 18 years old and have tried and failed at least two other AAP therapies (one of which must be aripiprazole).
- The PA for brexpiprazole limits use to FDA-approved indications.

**References**

- DoD P&T Committee minutes:  
<http://www.health.mil/PandT>
- Current/future drug classes under review by the DoD P&T Committee  
<http://www.health.mil/About-MHS/Other-MHS-Organizations/DoD-PT-Committee>
- TRICARE Formulary Search Tool:  
<http://www.health.mil/formulary>
- Prior Authorization/Medical Necessity forms:  
 See Formulary Search Tool above.
- Formulary Management Documents (including this one) available at:  
<http://www.health.mil/DoDPTResources>
- Point of contact for additional information:  
[dha.jbsa.pharmacy.list.poduf@mail.mil](mailto:dha.jbsa.pharmacy.list.poduf@mail.mil)

AAP Drugs – MTF Dose/Price Comparison	
<b>Basic Core Formulary</b>	
risperidone, risperidone ODT	<b>\$ = Most Cost-Effective</b>
quetiapine (Seroquel IR/XR)	
aripiprazole tabs	
<b>Uniform Formulary</b>	
clozapine	<b>\$\$ = Less Cost-Effective</b>
olanzapine, olanzapine ODT	
olanzapine/fluoxetine	
ziprasidone	
aripiprazole ODT/oral solution	
paliperidone	<b>\$\$\$ = Less Cost Effective</b>
lurasidone (Latuda)	
<b>Nonformulary</b>	
iloperidone (Fanapt)	<b>\$\$\$\$ = Least Cost-Effective</b>
asenapine (Saphris)	
brexpiprazole (Rexulti)	
cariprazine (Vraylar)	
Legend: <b>\$</b> = "Most Cost-Effective" represents Rx's with the <u>lowest cost</u> and best clinical efficacy <b>\$\$</b> = "Less Cost-Effective" represents <u>higher cost</u> Rx's with similar clinical efficacy <b>\$\$\$</b> = "Less Cost-Effective" represents <u>next higher cost</u> Rx's with similar clinical efficacy <b>\$\$\$\$</b> = "Least Cost-Effective" represents Rx's with the <u>highest cost</u> with similar clinical efficacy	