Treating Bipolar Disorders: The State of the Science and the Art

Terence A. Ketter, M.D.
## Disclosure Information

### Research Support / Consultant / Speaker

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<table>
<thead>
<tr>
<th>Medication</th>
<th>Company</th>
<th>Relationships</th>
</tr>
</thead>
<tbody>
<tr>
<td>asenapine (Saphris™)</td>
<td>Allergan Pharmaceuticals</td>
<td>Advisory, consultant</td>
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<td>cariprazine (Vraylar™)</td>
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<td>esketamine</td>
<td>Janssen Pharmaceutica</td>
<td>Spouse employee &amp; stockholder</td>
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<tr>
<td>paliperidone (Invega™)</td>
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<td>risperidone (Risperdal™)</td>
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<td>lamotrigine (Lamictal™)</td>
<td>GlaxoSmithKline</td>
<td>Speaker fee</td>
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<tr>
<td>lurasidone (Latuda™)</td>
<td>Sunovion Pharmaceuticals</td>
<td>Research contract, advisory, speaker fee</td>
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<td>suvorexant (Belsomra™)</td>
<td>Merck Pharmaceuticals</td>
<td>Research contract, advisory</td>
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Overview

- Recent FDA indications
- Comparative Effectiveness Studies
Recent FDA indications

- **Olanzapine plus fluoxetine**
  - Pediatric acute bipolar I depression (2013)

- **Lurasidone (monotherapy or adjunctive)**
  - Adult acute bipolar I depression (2013)

- **Asenapine monotherapy**
  - Pediatric acute mania (2015)

- **Cariprazine monotherapy**
  - Adult acute mania (2015)
Comparative Effectiveness Studies

- 52-wk bipolar depression (CEQUEL, 2016)
  - Comp Eval of QUEtiapine + Lamotrigine vs. Quetiapine in Bipolar Depression
  - Lamotrigine + Quetiapine > Placebo + Quetiapine

- 24-wk bipolar disorder (Bipolar CHOICE, 2016)
  - Clinical Health Outcomes Initiative in Comparative Effectiveness
  - Lithium + other meds = Quetiapine + other meds
FDA-Approved Agents for Adult Bipolar Disorder

**Acute Mania**
- 1970 Lithium
- 1973 Chlorpromazine
- 2000 Olanzapine*
- 2003 Risperidone*
- 2004 Quetiapine, XR (2008)*
- 2004 Ziprasidone
- 2004 Aripiprazole*
- 2004 Carbamazepine ERC
- 2009 Asenapine*
- 2015 Cariprazine

**Acute Depression**
- 2003 Olanzapine+fluoxetine combination
- 2006 Quetiapine, XR (2008)
- 2013 Lurasidone*

**Longer-Term**
- 1974 Lithium
- 2003 Lamotrigine
- 2004 Olanzapine
- 2005 Aripiprazole*
- 2008 Quetiapine, XR (adjunct)
- 2009 Risperidone LAI*
- 2009 Ziprasidone (adjunct)

*Adjunctive and monotherapy; LAI = Long-Acting Injectable

Unmet Need

Unmet Need
FDA-Approved Agents for Pediatric Bipolar Disorder

**Acute Mania**
- 1970 Lithium \(^a\)
- 2007 Risperidone \(^b\)
- 2008 Aripiprazole \(^b,(*->e)\)
- 2009 Quetiapine \(^b\)
- 2009 Olanzapine \(^c\)
- 2015 Asenapine \(^b\)

**Acute Depression**
- 2013 Olanzapine + fluoxetine combination \(^b\)

**Longer-Term**
- 1974 Lithium \(^a\)
- 2008 Aripiprazole \(b->e)\)

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* Adjunctive (as well as monotherapy); \(^a\)Age ≥ 12-17; \(^b\)Age 10-17; \(^c\)13-17; \((->e)\)Extrapolated indication
Take-Away Points

- New treatments available
- Combination treatments common
- Balance benefits & harms
Bipolar Disorder Clinic Studies, 2016

- **Adjunctive Belsomra™ in Bipolar Disorder with Insomnia**
  - Bipolar disorder with insomnia
  - 1-week double-blind placebo-controlled Belsomra™
  - 3-month open Belsomra™
  - Actigraphy

- **From Affective Illness to Recovery - STudent Access to Rapid Treatment (FAIŘ START)**
  - Community college students with any insurance
  - Access to Stanford bipolar diagnosis & mood stabilization Rx

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