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

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Disclosure Information

Research Support / Consultant / Speaker

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Medication	Company	Relationships
asenapine (Saphris™) cariprazine (Vraylar™)	Allergan Pharmaceuticals	Advisory, consultant
esketamine paliperidone (Invega™) risperidone (Risperdal™)	Janssen Pharmaceutica	Spouse employee & stockholder
lamotrigine (Lamictal™)	GlaxoSmithKline	Speaker fee
lurasidone (Latuda™)	Sunovion Pharmaceuticals	Research contract, advisory, speaker fee
suvorexant (Belsomra™)	Merck Pharmaceuticals	Research contract, advisory

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

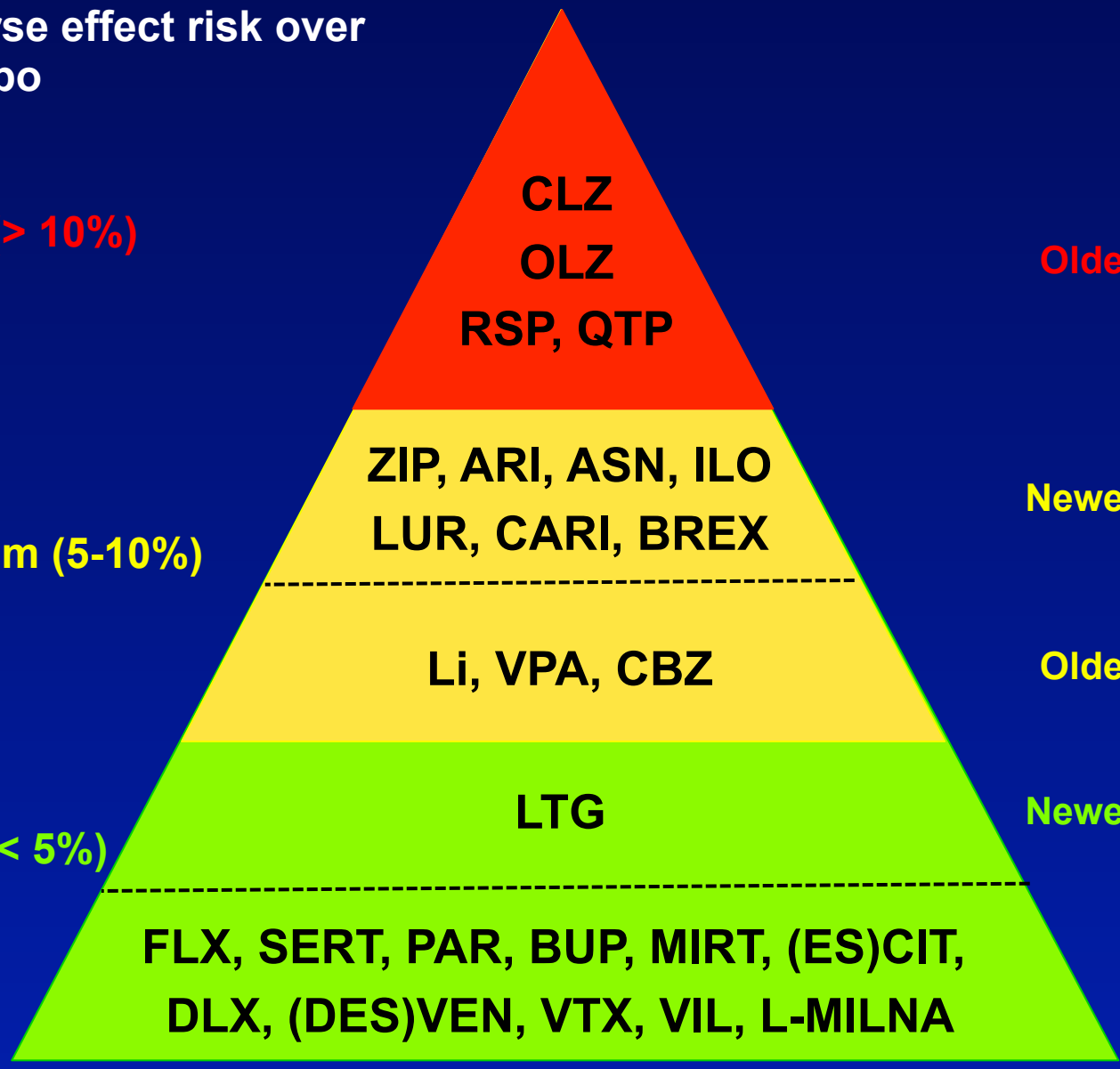
Psychotropic Medication Adverse Effect Schematic

Adverse effect risk over placebo

High (> 10%)

Medium (5-10%)

Low (< 5%)



Medication Class

Older
Second-Generation
Anti-psychotics

Newer

Older
Mood
Stabilizers

Newer

Anti-depressants

Ketter TA, et al. J Affect Disord 2014;169(Suppl 1):S24-33.

FDA-Approved Agents for Adult Bipolar Disorder

Acute Mania

1970 Lithium
1973 Chlorpromazine
1994 Divalproex, ER (2005)
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*

**Unmet
Need**

Longer-Term

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

**Unmet
Need**

*Adjunctive and monotherapy; LAI = Long-Acting Injectable

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

Unmet
Need

Longer-Term

- 1974 Lithium ^a
- 2008 Aripiprazole ^(b->e)

Unmet
Need

*Adjunctive (as well as monotherapy); ^aAge ≥ 12-17; ^bAge 10-17; ^c13-17; (->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 (**FAIR START**)**
 - Community college students with any insurance
 - Access to Stanford bipolar diagnosis & mood stabilization Rx
- **For additional information contact Dennis Do at**
 - (650) 498-8459; denniso@stanford.edu