BRINGING BIPOLAR I TO LIGHT

CONNECTING ON DIAGNOSIS AND TREATMENT CHALLENGES

THERAPY DECISION TOOL

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Tips for Utilizing the Therapy Decision Tool With Patients During a Shared Decision Making Conversation

Note: this tool is intended to facilitate discussion with your patients but **is not intended** to be a full comprehensive review of each treatment option and does not list all potential side effects.

For in-office visits

- **Print** out the therapy decision tool before a patient visit
- **Share** this tool with your patient after the clinical interview as a summary of key points regarding best medication options and opportunity for further dialogue for shared decision making
  - The clinical interview will help you to narrow down the treatments you will discuss with the patient using the tool
- **Introduce the tool** as something that you will plan to revisit with the patient throughout his/her treatment journey whenever a change in the treatment plan is being considered
- **Date the tool and cross out** any treatments that you do not consider good/appropriate options for this patient at that current date
  - Emphasize to the patient that the current medication regimen may not be as effective as other options might be and review the pros and cons of alternative available medications; treatment decisions often change from one time point to another
- Using the therapy decision tool, **begin by introducing the list of treatment options** that you'd like to consider with the patient during that visit and share the basic attributes of these treatments
  - **Listen to patient comments** about which attributes are most important to him/her
  - **Ask the patient clarifying questions** to probe what is most valued by the patient
- **Discuss the potential benefits and harms** of each treatment option with the patient
- **Ask the patient about the questions** he/she may have about each option
- If the patient needs additional time to make a decision, allow the patient to review the therapy decision tool at home and return to the next appointment with additional questions that can help guide deliberation and discussion
  - Note: this tool is not intended for patients to initially review on their own
- Plan to print out a new version of the tool for this patient when a new treatment discussion is needed
- Note: the first time you utilize this tool with a patient, it should take longer than subsequent times

Modifications for Telehealth Appointments

- Instead of printing out the tool, plan to have the tool open on your computer and share your screen with your patient so that he/she can see the tool
- Electronically cross out any treatments you don't consider to be good options for this patient at that current date using Adobe®'s tools for drawing markups
- If the patient needs additional time to make a decision, send the patient an electronic copy of the tool

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Therapy Decision Tool for Patients With Bipolar I Disorder: Mood Stabilizers

	Lithium	Divalproex	Carbamazepine	Lamotrigine
Year of FDA Approval in Bipolar Disorder				
Mania	1970	1995	2004	---
Depression	---	---	---	---
Maintenance	1978	---	---	2003
Dosing	Acute: 600 mg PO TID titrated to serum level; maintenance: 300 mg PO TID or QID titrated to serum level	Initial: (delayed release): 750 mg/day titrated rapidly to therapeutic blood level; (extended release): oral loading at 25 mg/kg in divided doses as tolerated	Initial: (extended release): 400 mg/day (divided), increase by 200 mg/day (max 1600 mg/day)	Initial (monotherapy): 25 mg/day for 2 weeks then 50 mg/day for 2 weeks then 100 mg/day for 1 week then target of 200 mg/day; dose at half this rate with divalproex cotherapy and twice this rate with carbamazepine cotherapy
Half-Life	18-36 hours	9-16 hours	35 hours	29 hours
Therapeutic Drug Monitoring	In mania, serum levels of 1.0-1.5 mEq/L per manufacturer In maintenance, serum levels of 0.6-1.2 mEq/L per manufacturer	In mania, 50-125 µg/ml	Not established in bipolar disorder	Not established in bipolar disorder
Efficacy in Mania	✓	✓	✓	Unproven
Efficacy in Depression	Less robust than in mania	Less robust than in mania	Poorly studied	Moderate, off-label
Efficacy in Mixed Features	Less robust than in pure mania	✓	✓	Unknown
Maintenance Efficacy	✓	Unproven (but often used off-label)	Modest data suggesting inferiority to lithium	✓ (more robust prevention of depression than mania)
Impact of Multi-Episode	Better when begun in first few episodes	✓	Unknown	Unknown
Impact of Rapid Cycling	Modest efficacy	Possibly more robust than lithium, likely better in combination with lithium	Modest efficacy	Modest relapse prevention data, mainly in bipolar II disorder
Impact of Psychosis	Poorer response when psychosis is present	✓ (ER indication includes "with or without psychotic features")	Modest data suggesting possible advantage over lithium	Unknown
Most Common Adverse Effects	Tremor, urinary frequency, thirst, GI upset	Somnolence, GI upset, tremor, weight gain, alopecia	Dizziness, drowsiness, blurry vision, nausea	Dizziness, drowsiness, headache, GI upset, rash

ER=extended release; FDA=US Food and Drug Administration; GI=gastrointestinal; PO=by mouth; TID=three times a day; QID=one a day.

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Therapy Decision Tool for Patients With Bipolar I Disorder: Antipsychotics

	Chlorpromazine	Aripiprazole	Olanzapine	OFC	Risperidone	Quetiapine	Asenapine	Ziprasidone	Lurasidone	Cariprazine
Year of FDA Approval in Bipolar Disorder										
Mania	1973	2004	2000	---	2003	2003; (2008[XR])	2009	2004	---	2015
Depression	---	---	---	2003	---	2008 (XR)	---	---	2013; 2018 (pediatric)	2017
Maintenance	---	2005; 2017 (LAI)	2004	---	2009 (LAI)	2007 (with Li^+ or DVPX)	---	2009 (with Li^+ or DVPX)	---	---
Dosing	30-75 mg initially; 200-800 mg/day	Initial (mania): 15 mg/day; range 15-30 mg/day Short-acting IM: 9.75 or 15 mg Pediatric mania: 2 mg/day	Initial (mania): 10-15 mg/day (max 20 mg/day) Short-acting IM: 5-10 mg q2-4 hours, max dose= 30 mg/day Pediatric mania: 2.5-5 mg/day, target= 10 mg/day	Initial: 6 mg/25 mg, may increase to 12 mg/50 mg	Initially 2-3 mg PO daily; target=1.6 mg PO daily LAI: 25 mg IM q2 weeks (max 50 mg IM q2 weeks) Pediatric mania: 0.5 mg/day titrated to 2.5 mg/day (maximum 6 mg/day)	Mania: IR: day 1=100 mg, titrate to 400 mg by day 4, max= 800 mg by day 6 XR: 300 mg day 1, 600 mg day 2; day 3+ target= 400-800 mg/day Depression: day 1=50 mg; day 2=100 mg; day 3=200 mg; day 4=400 mg Pediatric: 25 mg PO BID, target 400-600 mg/day	5-10 mg SL BID Pediatric mania: 2.5 mg SL BID, target 2.5-10 mg SL BID	Day 1: 40 mg PO BID with food; Day 2: 60-80 mg PO BID; mean target= 120 mg/day Short-acting IM (schizophrenia): 10-20 mg q2-4 hours, max dose= 40 mg/day	20-120 mg/day (adult or pediatric)	Initial (mania): 1.5 mg/day; usual= 3-6 mg/day Depression: 1.5-3 mg/day

BID=twice daily; DVPX=divalproex; IM=intramuscular; IR=immediate release; LAI=long-acting injectable; Li=lithium; OFC=olanzapine and fluoxetine hydrochloride; q2-4=every 2-4; SL=sublingually; XR=extended release.

Therapy Decision Tool for Patients With Bipolar I Disorder: Antipsychotics (cont.)

	Chlorpromazine	Aripiprazole	Olanzapine	OFC	Risperidone	Quetiapine	Asenapine	Ziprasidone	Lurasidone	Cariprazine
Half-Life	30 hours	75 hours	21-54 hours	8-9 days	3 hours	6 hours	24 hours	7 hours	18 hours	2-4 days
Acute Agitation	✓	✓ (oral or IM)	✓ (oral or short-acting IM)	No data (unlikely useful)	✓ (oral)	✓ (oral)	No data on immediate effect	✓ (oral; short-acting IM approved only in schizophrenia)	No data on immediate effect	No data
Efficacy in Mania	✓	✓	✓	Contraindicated	✓	✓	✓	✓	No data	✓
Efficacy in Depression	Unknown	No	✓	✓	No	✓	Unknown	No	✓	✓
Efficacy in Mixed Features	No data	✓	✓	No data	✓	✓	✓	✓	✓	✓
Maintenance Efficacy	No data	✓	✓	Unknown	✓ (LAI)	✓ (with Li^+ or DVPX)	✓	✓	Unproven	No data
Pediatric Data	No data	✓ (mania)	✓ (mania)	✓ (depression)	✓ (mania)	✓ (mania)	✓ (mania)	No data	✓ (depression)	No data
Impact of Multi-Episode	No data	No data	No data	No data	No data	No data	No data	No data	No data	No data
Impact of Rapid Cycling	No data	✓ (mania)	✓ (mania)	No data	Minimal data	✓ (acute mania)	No data	No data	No data	No data
Impact of Psychosis	✓	✓	✓	✓	✓	✓	✓	✓	Unstudied but presumed	✓
Long-Acting Preparation	None	✓	✓ (approved only in schizophrenia)	None	✓	None	None	None	None	None
Common Adverse Effects	Somnolence, orthostatic hypotension, extrapyramidal reactions, dry mouth, amenorrhea, galactorrhea, weight gain	Extrapyramidal reactions, dizziness, drowsiness, tremor, weight gain	Asthenia, dry mouth, constipation, increased appetite, somnolence, dizziness, tremor	Dry mouth, fatigue, edema, weight gain, increased appetite, somnolence	Parkinsonism, dystonia, somnolence	Somnolence, dry mouth, dizziness, constipation, increased appetite	Oral hypoesthesia, fatigue, somnolence, extrapyramidal reactions, akathisia	Headache, nausea, somnolence, dizziness, extrapyramidal reactions, akathisia	Nausea, somnolence, extrapyramidal reactions, akathisia	Nausea, vomiting, extrapyramidal reactions, akathisia, headache

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DRUG PRESCRIBING INFORMATION

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Asenapine: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/022117s020s021lbl.pdf

Carbamazepine: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/016608s115_018281_s058_018927s055_020234_s047.pdf

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Risperidone (LAI): https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/021346s063lbl.pdf

Risperidone (oral): https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/020272s085,020588s072,021444s058lbl.pdf

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