

Canmat and ISBD 2018 Guidelines

Hierarchical rankings of first and second-line treatments recommended for management of acute mania

	Level of evidence by phase of treatment					Considerations for treatment selection				
						Acute		Maintenance		Risk of depressive switch
	Acute mania	Prevention of any mood episode	Prevention of mania	Prevention of depression	Acute depression	Safety concerns	Tolerability concerns	Safety concerns	Tolerability concerns	
First-line treatments: Monotherapies										
Lithium	●	●	●	●	●	+	+	++	++	–
Quetiapine	●	●	●	●	●	+	++	++	++	–
Divalproex	●	●	●	●	●	–	+	++*	+	–
Asenapine	●	●	●	n.d. ^a	n.d.	–	+	–	+	–
Aripiprazole	●	●	●	n.d. ^a	■	–	+	–	+	–
Paliperidone (>6 mg)	●	●	●	n.d. ^a	n.d.	–	+	+	++	–
Risperidone	●	●	●	n.d.	n.d.	–	+	+	++	–
Cariprazine	●	n.d.	n.d.	n.d.	●	–	+	–	–	–
First-line treatments: Combination therapies										
Quetiapine + Li/DVP	●	●	●	●	● ^b	+	++	+++*	++	–
Aripiprazole + Li/DVP	●	●	●	n.d. ^b	●	+	+	++*	++	–
Risperidone + Li/DVP	●	●	●	n.d.	●	+	++	+++*	++	–
Asenapine + Li/DVP	●	●	●	n.d.	●	+	+	++*	+	–
Second-line treatments: Combination therapies										
Olanzapine	●	●	●	●	● ^c	+	++	+++	++	–
Carbamazepine	●	●	●	●	●	++	+	++*	++	–
Olanzapine + Li/DVP	●	●	●	●	n.d.	+	++	+++*	++	–
Lithium + DVP	●	●	●	n.d.	n.d.	+	++	++	++	–
Ziprasidone	●	●	●	n.d.	■	++	++	++	+	–
Haloperidol	●	n.d.	●	■	n.d.	+	++	+++	++	++
ECT	●	●	●	●	●	+	++	+	++	–

DVP, divalproex; ECT, electroconvulsive therapy; Li, lithium.

●, level 1 evidence; ●, level 2 evidence; ●, level 3 evidence; ●, level 4 evidence; ■, level 1 negative evidence; ■, level 2 negative evidence; ■, level 3 negative evidence; ■, level 4 negative evidence; n.d., no data; – Limited impact on treatment selection; +, minor impact on treatment selection; ++, moderate impact on treatment selection; +++, significant impact on treatment selection.

^aAlthough monotherapies are listed above combination therapies in the hierarchy, combination therapies may be indicated as the preferred choice in patients with previous history of partial response to monotherapy and in those with psychotic mania or in situations where rapid response is desirable.

^bDid not separate from placebo in those with index mania; no studies available in index depression.

^cNo controlled trials; however, clinical experience suggests that it is a useful strategy.

^dDid not separate from placebo on core symptoms of depression.

^eDivalproex and carbamazepine should be used with caution in women of childbearing age.