

49 - References

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312 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 2 References

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4. Mahajan V, et al. Efficacy and safety of asenapine versus olanzapine in combination with divalproex for acute mania: a randomized controlled trial. *J Clin Psychopharmacol* 2019; 39:305–311.
5. Huang W, et al. Comparative efficacy, safety, and tolerability of pharmacotherapies for acute mania in adults: a systematic review and network meta-analysis of randomized controlled trials. *Mol Psychiatry* 2024; doi: 10.1038/s41380-024-02705-3. Table 2.7 Mania: other possible treatments.* Treatment Comments Allopurinol (300–600mg/day) A meta-analysis of five studies of adjunct allopurinol found an effect size of just less than 0.3.⁵⁰ Celecoxib (400mg/day)⁵¹ Small RCT (n = 46) suggests benefit when used as adjunct to valproate. Clonidine (450–900mcg/day)⁵² Limited data Clozapine^{53–55} Established treatment option for refractory mania/bipolar disorder. Rapid titration has been reported.⁵⁶ Endoxifen⁵⁷ (4–8mg/day) RCT evidence of efficacy. Major metabolite of tamoxifen. Gabapentin⁵⁸ (up to 2.4g/day) Probably only effective by virtue of an anxiolytic effect. Rarely used. Possibly useful as prophylaxis.⁵⁹ Levetiracetam (up to 1500mg/day) Effective as adjunctive treatment in two RCTs.^{60,61} One case of levetiracetam causing mania.⁶² Melatonin (6mg/day)⁶⁷ Preliminary evidence of benefit as an adjunct to standard treatment. One small negative study.⁶⁸ Memantine⁶³ (10–30mg/day) Conflicting evidence^{64–66} Oxcarbazepine^{69–76} (around 300–3000mg/day) Probably effective acutely and as prophylaxis although one controlled study (conducted in youths) was negative.⁷⁷ Phenytoin⁷⁸ (300–400mg/day) Rarely used. Limited data. Complex kinetics with narrow therapeutic range. Ritanserin⁷⁹ (10mg/day) Supported by a single RCT. Well tolerated. May protect against EPSEs. Tamoxifen⁸⁰ (20–140mg/day) Good evidence for efficacy as adjunct and as monotherapy, with large effect size. May provoke switch to depression. Topiramate⁸¹ (up to 300mg/day) Probably not effective. Less effective than lithium.² Tryptophan depletion⁸² Supported by a small RCT. Ziprasidone^{83–85} Supported by three RCTs. Widely used outside UK. *Entries are given in alphabetical order; no preference is implied by order in the table. Consult specialist and

primary literature before using any treatment listed. EPSEs, extrapyramidal side effects; RCT, randomised controlled trial.

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