39 - Summary and recommendations

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36 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 1 RCTs have demonstrated some benefit for selegiline,65,66 pramiprexole,67 topical testosterone,68 ondansetron,69 granisetron,70 palmitoylethanolamide (an endogenous analogue of anandamide, an endocannabinoid) added to risperidone71 and pimavanserin, a potent 5-HT2A inverse agonist and antagonist.72,73 The 5HT2 antagonist roluperidone may also be effective.74,75 ■ ■Other experimental treatments for which promising data exist include pregnenolone,76 raloxifene (in women),77 levetiracetam,78 clonidine,79 nanocurcumin,80 xanomeline (as Cobenfy)81 and the anti-inflammatory drugs berberine82 and fingolimod.61 ■ ■The findings from studies of repetitive transcranial magnetic stimulation (rTMS) are mixed but promising.83 Transcranial direct current stimulation (tDCS) may also have some potential as a treatment for negative symptoms, but the evidence thus far is limited and rather inconsistent.18,84–87 Patients who misuse psychoactive substances may experience less severe negative symptoms than patients who do not.88 But rather than any pharmacological effect, it may be that this association at least partly reflects that those people who develop psychosis in the context of substance use, specifically cannabis, have fewer neurodevelopmental risk factors and thus better cognitive and social function.89,90 Summary and recommendations These recommendations are derived from the British Association for Psychopharmacology (BAP) schizophrenia guideline (2020),91 Galderisi et al. (2021),87 Veerman et al. (2017),10 Aleman et al. (2017)18 and Howes et al. (2023).38 ■ ■There are no well--replicated, large trials or meta-analyses of trials with negative symptoms as the primary outcome measure that have yielded convincing evidence for enduring and clinically significant benefit. ■ ■Where some improvement has been demonstrated in clinical trials, this may be limited to secondary negative symptoms. ■ ■Psychotic illness should be identified and treated as early as possible, as this may offer some protection against the development of negative symptoms. ■ ■For any given patient, the antipsychotic medication that provides the best balance between overall efficacy and adverse effects should be used, at the lowest dose that maintains control of positive symptoms. ■ ■Where negative symptoms persist beyond an acute episode of psychosis: ■ ■Ensure that EPS (specifically bradykinesia) and depression are detected and treated if present, and consider the contribution of the environment to negative symptoms (e.g. institutionalisation, lack of stimulation). ■ ■There is insufficient evidence at present to support a recommendation for

any specific pharmacological treatment for negative symptoms. Nevertheless, a trial of add-on medication for which there is some RCT evidence for efficacy, such as an antidepressant or an antipsychotic, may be worth considering in some cases, ensuring that the choice of the augmenting agent is based on minimising the potential for compounding adverse effects through pharmacokinetic or pharmacodynamic drug interactions.

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