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362 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 3 Psychotic depression Psychotic depression represents a severe manifestation of depression. It is diagnosed in people experiencing a major depressive illness accompanied by psychotic symptoms such as hallucinations and/or delusions. It can occur in the context of both MDD and bipolar disorder. Psychotic depression has a lifetime prevalence of 1%.¹ However, it is often under-diagnosed and is commonly not adequately identified despite requiring a different treatment approach.^{2,3} When compared with non-psychotic depression, psychotic depression is associated with greater illness severity, impairment and episode duration.⁴ Once an individual has experienced psychotic symptoms during a depressive episode there is a risk of their recurrence in future episodes.^{4,5} Furthermore, long-term outcomes are generally poorer for psychotic than non-psychotic depression.⁶⁻⁸ Patients with psychotic depression may also have a poorer response to combined pharmacological and psychological treatment than those with non-psychotic depression.⁹ People with psychotic depression are much more likely than those with non-psychotic depression to attempt and complete suicide.^{8,10} Acute treatment While it is important to acknowledge that no treatments have been granted regulatory approval specifically for psychotic depression,¹¹ there is sufficient evidence to guide treatment decisions. Oliva and colleagues¹² conducted a systematic review and network meta-analysis of pharmacological treatments for psychotic depression in 2024. This network meta-analysis included 14 randomised controlled trials including patients in the acute phase of their illness. It found that, compared with placebo, the combination of an SSRI and an SGA, particularly fluoxetine and olanzapine, resulted in the highest proportion of participants with a treatment response.¹² Overall, this specific combination also showed a good balance between efficacy and tolerability and specifically improved depressive symptom scores compared with placebo.¹² The network meta-analysis concluded that this treatment option is the most appropriate choice in people with psychotic depression.¹² When different treatment options were compared directly, a combination of antipsychotics and antidepressants was also found to have greater efficacy than monotherapy with either antipsychotic or antidepressant alone.¹² Prior meta-analyses support this outcome, although they were not able to provide specific recommendations on individual drugs because of methodological restrictions.^{13,14} UK NICE guidance from 2022, although written some time before the latest network meta-analysis, also advocates this approach.^{11,15} The 2024 network meta-analysis also compared monotherapies and found that TCAs (amoxapine and imipramine) were more efficacious than serotonin-noradrenaline reuptake inhibitors (SNRIs; venlafaxine) and noradrenergic and specific serotonergic reuptake inhibitors (mirtazapine) when overall treatment response was assessed.¹² It is important to consider that this network meta-analysis only included patients in the acute phase of their illness. Continuation and maintenance studies were excluded. In addition, it only included studies published up to 2013, so drugs used in clinical practice more

recently could not be examined.

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