Medication management during electroconvulsant therapy

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Abstract: Electroconvulsive therapy (ECT) has demonstrated to be highly effective and safe, even life saving for many psychiatric disorders such as major depression, bipolar disorder and schizophrenia. Most patients who require ECT are also on concurrent pharmacotherapy. As such, the objective of this article is to provide a review of the most recent literature focusing on the medications used during an ECT procedure and on the effects of concurrent psychiatric and non-psychiatric medications on the effectiveness and safety of ECT. The review also attempts to summarize the recommendations derived from existing documents to guide pharmacotherapy decisions for patients undergoing ECT. For this purpose, using electronic databases, an extensive search of the current literature was made using ECT and medications or drug classes as keywords.

Keywords: ECT, medications, drug interactions

Introduction
Several evidence-based documents on the use of electroconvulsive therapy (ECT) indicate that it is a safe and effective treatment for a variety of psychiatric disorders.1–3 Although major depression refractory to antidepressant medications is the primary indication for ECT, there is also significant evidence to support its use in other psychiatric disorders such as catatonia, psychotic depression, mania, bipolar disorder and schizophrenia.1–3

The goal of ECT is to produce a controlled and monitored seizure lasting from 30 to 90 seconds in duration to be considered therapeutic.1,4–6 Although the exact mechanism of ECT is unknown, the induced seizure affects nearly every neurotransmitter system, including \( \beta \)-adrenergic, serotonin, muscarinic, cholinergic, and dopaminergic systems.6,7 Brain-derived neurotrophic factor may also play a role in the efficacy of ECT.8 There are no absolute contraindications to ECT; nevertheless, ECT can induce side effects and may be physically risky for certain individuals. As such, all patients must be assessed prior to ECT for the presence of conditions such as cardiovascular disease, space-occupying intracranial lesion with the evidence of elevated intracranial pressure, recent cerebral hemorrhage or stroke, bleeding or otherwise unstable vascular aneurysm, and severe pulmonary disease, as all of these can be associated with increased risk of complications from the general anesthesia and induction of seizure activity.1 ECT is considered safe with a mortality of \(~1/10,000\) patients or \(~1/80,000\) treatments.6 Most patients report some adverse cognitive effects during and after a course of ECT, such as postictal confusion state (the result of both anesthesia and the seizure), anterograde amnesia (decreased ability to retain newly acquired...
Medications during the ECT procedure

Table 1 lists common medications that patients may receive during an ECT procedure. These include anesthetic induction agents, anticholinergic agents, muscle relaxants, antihypertensives, and narcotics.

Anesthetic agents and muscle relaxants are used to induce a state of insensibility and to decrease the likelihood of bone and soft tissue injury. Due to the brief nature of ECT, an ideal anesthetic agent should rapidly induce hypnosis and allow for rapid emergence from anesthesia without significantly shortening seizure activity or causing hemodynamic instability. Among the barbiturates, methohexital and thiopental, which have minimal anticonvulsant properties compared with other barbiturates, were considered as gold standard as ECT anesthetic induction agents, but due to recent worldwide shortages of these agents, other drugs such as propofol, etomidate and ketamine have become more widely used.

The advantages of propofol over methohexital include a quicker and smoother emergence from anesthesia and a somewhat more favorable hemodynamic profile. Disadvantages are its much greater anticonvulsant effect and higher cost. Etomidate is an alternative particularly in patients who have seizures of short duration or hard to elicit. Ketamine has shown to be slightly proconvulsant and has intrinsic antidepressant properties. Disadvantages include hypertension and occasional transient dissociative symptoms on wake up. A recent systematic review concluded that robust evidence to recommend a particular induction agent for ECT is lacking and indicated that anesthetic agents should

![Image of Table 1](https://example.com/table1.png)

**Table 1 Medications during the ECT procedure**

<table>
<thead>
<tr>
<th>Anesthetic induction agents</th>
<th>Methohexital</th>
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<tbody>
<tr>
<td>Thiopental</td>
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<td>Propofol</td>
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<td>Etomidate</td>
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<td>Ketamine</td>
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<tr>
<th>Neuromuscular blocking agents</th>
<th>Succinylcholine (suxamethonium)</th>
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<tr>
<td>Rocuronium</td>
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<tr>
<td>Atracurium</td>
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<td>Mivacurium</td>
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<thead>
<tr>
<th>Antihypertensives</th>
<th>β-blockers (atenolol, esmolol, and labetalol)</th>
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<tr>
<td>Calcium channel blockers</td>
<td>(nifedipine and nicardipine)</td>
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<table>
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<tr>
<th>Anticholinergic agents</th>
<th>Glycopyrrolate</th>
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<tr>
<td>Atrazine</td>
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<tr>
<td>Fentanyl</td>
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<tr>
<td>Remifentanyl</td>
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<td>Alfentanly</td>
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**Abbreviation:** ECT, electroconvulsive therapy.
be chosen on the basis of adverse effect profile, emergence, and how these medications affect seizure duration.^{18} Opioids, such as remifentanil and alfentanil, combined with anesthetic agents have been used to increase the seizure duration by an induction agent dose-sparing effect.^{17,22–24} Caffeine, in the form of caffeine sodium benzoate intravenous injection 250–1,000 mg, and other methylxanthines have also been administered prior to ECT to increase the seizure duration but do not appear to reduce seizure threshold.^{24} However, because the potential cardiac and other complications of caffeine use are known, this augmenting strategy is not generally recommended, especially in the elderly.^{24,25} Muscle relaxation during the application of the stimulus, as well as for the duration of the motor portion of the seizure, prevents musculoskeletal injury; this is especially important if the patient has osteoporosis or a history of spinal injury.^{1,6,7} Because of the short duration of ECT, succinylcholine (also known as suxamethonium) is the drug of choice for neuromuscular blockade.^{1,17,26} Succinylcholine is a depolarizing neuromuscular blocker with an ultrashort duration of action, slightly less than that of the anesthetic agent. The duration of muscle paralysis is, thus, very brief, and spontaneous respirations return shortly after the seizure ends. In patients in whom its use is contraindicated, rocuronium or other nondepolarizing agents are alternatives.^{1,26}

During ECT, significant changes in autonomic function can occur. Initially a parasympathetic surge can result in significant bradycardia, hypotension, and, in some cases, brief asystole.^{1,6} Patients already on β-blockers may be at risk of bradycardia if stimulation is given but a seizure is not induced.^{4,7} To counteract the parasympathetic effect, anticholinergic medications (eg, glycopyrrolate and atropine) may be given, although this is not routinely required. Glycopyrrolate is preferred over atropine since it does not cross the blood–brain barrier, which reduces unwanted cognitive effects after ECT.^{6}

Following stimulus termination, the resulting seizure is accompanied by a profound sympathetic surge, typically associated with tachycardia and hypertension.^{1,27} Deteriorous sympathetic effects may be controlled with β-blockers either pre- (atenolol) or intraprocedurally (labetalol and esmolol).^{13,17} There is controversy, however, regarding whether labetalol and esmolol reduce seizure duration.^{20} Sublingual nifedipine and intravenous nicardipine have been used (although tachycardia can occur), as has diltiazem, although it also may reduce seizure duration.^{27} Preoperative α-2 agonists, such as dexmedetomidine, also blunt the hyperdynamic response as does glyceryl trinitrate, which should be considered in patients at high risk of myocardial ischemia.^{17,27,28}

### Interactions between regularly prescribed medications and ECT

The majority of patients requiring ECT are likely to be receiving concurrent regularly prescribed medications for treating psychiatric, medical, and comorbid conditions. Therefore, not surprisingly, drug interactions can occur between psychotropic agents, drugs prescribed for chronic medical conditions, anesthesia-inducing agents, and other medications used for the ECT procedure itself. These drug interactions can be classified into the following categories: 1) interactions with medications used during the ECT procedure, 2) interactions that affect the efficacy of ECT (ie, suppressing seizure activity), and 3) interactions that can increase the risks associated with ECT (eg, increase risk of complications, such as prolonged seizures and cardiotoxicity).

In general, medications that raise seizure threshold or impede seizure propagation (interfere with induction or spread of a robust seizure) should be avoided if possible, or the dose decreased (eg, anticonvulsants and benzodiazepines). Cardiac medications, antihypertensives, and antiasthmatic medications can typically be continued. Table 2 provides a summary of the most often reported drug interactions based on the major classes of commonly used medications by patients undergoing ECT. For each specific drug interaction, the possible undesired effect and how it can be managed are also included for easy reference. There are no studies exploring the effects of herbal medicines on ECT; however, several direct and indirect mechanisms whereby such use may impact the ECT procedure are also summarized in Table 2.

### Conclusion

Despite the vast potential for drug interactions in patients receiving ECT, available evidence on those interactions that are clinically significant is scarce, and it is almost exclusively retrospective in nature, or derived from case reports or case series. A summary of the existing evidence as presented in this article can inform clinicians on the potential and documented consequences of these interactions, and assist them weighing the risks and benefits before making decisions on the concurrent use of medications in patients receiving ECT.
Table 2 Drug interactions reported in patients undergoing ECT

<table>
<thead>
<tr>
<th>Class</th>
<th>Evidence</th>
<th>Possible undesired effect</th>
<th>Management strategies</th>
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<tbody>
<tr>
<td><strong>Anticonvulsants/mood stabilizers</strong></td>
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| Lithium6,29–31                 |          | • Combination has a significant risk of delirium, prolonged seizures, toxic lithium levels, and prolonged neuromuscular blockade | • Avoid combination if possible  
• If lithium cannot be discontinued, give at a dose to maintain a blood level in the lowest therapeutic range and/or hold day before ECT  
• If patient is already taking lithium without clear benefit, stop lithium before ECT. A washout period is unnecessary unless high blood level is present  
• Alternatively, substitute lithium for another mood stabilizer (eg, atypical antipsychotic) to provide protection against mania while ECT is being given for depression  
• Nondepolarizing neuromuscular blockers should be administered in incremental and reduced doses and titrated to the degree of block required |
|                               |          | • Combination not an absolute contraindication. In certain emergencies where the benefits clearly outweigh the risks, combined therapy could be considered |                                              |
|                               |          | • Case reports in elderly patients indicate that only 24 hours of holding lithium therapy might result in a lithium level sufficient to contribute to delirium after ECT |                                              |
| **VPA**14,32–34                |          | • Case reports of difficulty in eliciting seizures with patients on VPA  
• Possible drug–drug interaction competing for protein binding, which can elevate VPA levels  
• Decrease in the propofol dose required to induce anesthesia during ECT in the presence of VPA | • Dose reduction or withholding doses (eg, the morning of, or the evening or morning prior to the ECT procedure)  
• Changing the anesthetic regimen (addition of remifentanil to a lower dose of methohexital, or etomidate instead of methohexital), to produce adequate seizures |
|                               |          | • Case reports show mixed results. Some indicate no negative effect of CBZ on ECT, and others report difficulty in eliciting seizures  
• CBZ–ECT group compared to control group had a shorter duration of seizures and a higher stimulus dose when unilateral treatments were used  
• Development of moderately severe postictal confusion has also been reported  
• CBZ may prolong the action of succinylcholine (few clinical implications)  
• Long-term CBZ demonstrated resistance to nondepolarizing neuromuscular blockers (except mivacurium) | • Seizure inhibition or difficulty in eliciting adequate seizures during ECT  
• Theoretically, the anticonvulsant activity of VPA may interact with the efficacy of ECT  
• Seizure inhibition  
• Accelerated recovery and need for increased doses to achieve complete neuromuscular block (induce a mild upregulation of neuromuscular acetylcholine) |
| **CBZ**14,32,33                |          | • Seizure inhibition or difficulty in eliciting adequate seizures during ECT  
• Theoretically, the anticonvulsant activity of VPA may interact with the efficacy of ECT  
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• Accelerated recovery and need for increased doses to achieve complete neuromuscular block (induce a mild upregulation of neuromuscular acetylcholine) | • Dose reduction or withholding doses (eg, the morning of, or the evening or morning prior to the ECT procedure)  
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• CBZ may prolong the action of succinylcholine (few clinical implications)  
• Long-term CBZ demonstrated resistance to nondepolarizing neuromuscular blockers (except mivacurium) | • Neuromuscular blockade: if suxamethonium is contraindicated, mivacurium seems to be the preferred neuromuscular blocker in patients receiving CBZ therapy |

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Table 2 (Continued)

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<thead>
<tr>
<th>Class</th>
<th>Evidence</th>
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<th>Management strategies</th>
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<tbody>
<tr>
<td>LTG</td>
<td>14,32,34,35</td>
<td>Case reports/series show minimal or no influence on seizures and/or seizure duration</td>
<td>Theoretically, seizure inhibition</td>
</tr>
<tr>
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<td>Interaction with halothane; reducing effect of LTG on glutamate release, either at the receptor or via effects at the inactivated sodium channel</td>
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<tr>
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<td>ECT attenuates the inhibitory dose-dependent effects of LTG on synaptic transmission at a low frequency. Clinical significance remains unknown</td>
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<tr>
<td>Others: gabapentin and topiramate</td>
<td>16,32,34</td>
<td>No complications were found in two case reports using gabapentin</td>
<td>Theoretically, seizure inhibition</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No interactions have as yet been reported between gabapentin or topiramate and the anesthetics used for ECT</td>
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<td></td>
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<td>The use of topiramate for post-ECT headaches did not result in adverse ECT outcomes</td>
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<tr>
<td>Antidepressants</td>
<td>MAOI</td>
<td>No evidence of an interaction between ECT and MAOI use</td>
<td>Theoretically, risk of hypertensive crisis if combined with indirect acting sympathomimetics</td>
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<tr>
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<td>A prospective study looked at the risks associated with the combination of MAOIs and ECT, no differences between the study and control groups were reported</td>
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<tr>
<td></td>
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<td>Ketamine should be avoided as it causes sympathetic stimulation. Propofol and etomidate can be used safely with MAOIs</td>
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<tr>
<td>TCA</td>
<td>14,35,40</td>
<td>Retrospective review of the literature found that the use of TCAs in combination with ECT was associated with better outcomes and shorter total seizure time than with ECT alone</td>
<td>Theoretically, reduced seizure threshold and an increased risk of cardiotoxicity</td>
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<td>No differences were found in the measures of confusion and cardiac adverse effects, and there was even a trend toward fewer adverse effects in the groups receiving the ECT and TCA combination</td>
<td>Chronic therapy with TCAs depletes cardiac catecholamines, potentiating the cardiac depressant effects of anesthetic agents</td>
</tr>
<tr>
<td>Others</td>
<td>14,35,45</td>
<td>Minimal effect on ECT-related seizure duration has been reported with SSRIs, SNRIs, or trazodone</td>
<td>Theoretically, reduced seizure threshold with SSRIs and SNRIs</td>
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<td>Seizure length may increase when ECT is administered during bupropion treatment</td>
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Table 2 (Continued)

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</table>
| Anxiolytics BZD            | • The impact of BZDs on seizure adequacy may be low if the BZD has been routinely used | • Increased seizure threshold, decreased seizure duration, and decreased potential efficacy of ECT | • If possible, stop BZD before ECT. Many BZDs are long acting and may need to be discontinued some days before ECT  
• If the BZD cannot be discontinued, the use of higher stimulus or using flumazenil just before ECT to temporarily reverse effects of the BZD has been suggested  
• The dose of thiopental or propofol used for induction of anesthesia should be titrated to the desired effect |
| Antipsychotics FGA         | • The combination of FGAs, particularly phenothiazines (eg, chlorpromazine) and ECT has been reported to cause prolonged seizures | • Theoretically, FGAs reduce seizure threshold                                           | • None have been recommended  
• Their anticholinergic and anticholinergic effects are unpredictable, and caution in the use of drugs with similar effects during anesthesia should be exercised  
• For patients on clozapine, a dose reduction prior to ECT may be considered |
| SGA                       | • Some data suggest beneficial and additive efficacy when in combination, particularly with clozapine | • Clozapine is known to decrease the seizure threshold in a dose-dependent manner (usually at doses >600 mg/d) | • None have been recommended  
• For patients on clozapine, a dose reduction prior to ECT may be considered |
| CNS stimulants methylphenidate | • Methylphenidate was shown to reduce sedation and improve respiratory function in patients recovering from halothane anesthesia | • Theoretically, there is an increased risk for potentiating seizure activity, thereby leading to prolonged seizures or a risk for status epilepticus  
• Methylphenidate can also produce dysrhythmias and elevate blood pressure during anesthesia | • None have been recommended |
| Miscellaneous cholinesterase inhibitors | • No evidence of adverse incidents involving concurrent use with ECT  
• Successful use of donepezil in treating cognitive deficits associated with maintenance ECT has been reported  
• Ineffective in ameliorating the robust sympathetic response associated with ECT | • Theoretically, synergistic effects with neuromuscular blocking agents. This combination also has the potential to induce significant bradycardia, cardiac arrhythmias, and asystole | • Caution has been recommended particularly with neuromuscular blocking agents  
• Recommended to be used only in life threatening situations to control heart rate, when β-blockers are not available or are contraindicated |
| Lidocaine                  | • Ineffective in ameliorating the robust sympathetic response associated with ECT | • Seizure inhibition  
• Potentially useful for reducing tachycardia in high-risk patients and reducing the severity of propofol injection pain | • Recommended to be used only in life threatening situations to control heart rate, when β-blockers are not available or are contraindicated |
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</table>
| Theophylline | • Reports of status epilepticus after ECT  
• High levels of theophylline during ECT associated with status epilepticus | • Can increase seizure duration and increase risk of status epilepticus | • If possible, discontinue theophylline by tapering the dose. Continue with a regimen of bronchodilators and inhaled glucocorticoids  
• Alternatively, decrease dose to the lowest therapeutic drug level and monitor levels closely  
• Provide standard treatment during an asthma exacerbation (inhaled β-agonists and, if necessary, glucocorticoids, before proceeding with ECT) |
| Antigastric agents (eg, antacids and proton pump inhibitors) | • No evidence of adverse incidents involving concurrent use with ECT | | • Continue as patients with GERD may have worsened symptoms undergoing ECT due to vagal stimulation  
• Measure blood glucose levels before and after ECT treatment. Give half the usual amount of long-acting insulin in the morning of the procedure  
• Withhold oral agents until patient can eat. Provide short-acting insulin to treat elevations in blood glucose level |
| Diabetic agents (eg, oral hypoglycemics and insulin) | • Individual ECT treatments raise blood glucose levels in patients with diabetes to the same degree as in patients without diabetes | • Can cause hypoglycemia | | |
| Warfarin | • A retrospective case review found that over one-third of the patients INRs during ECT were subtherapeutic  
• However, ECT appears to be safe in patients who require long-term anticoagulation | • The potential for methohexital to increase the metabolism of warfarin, decrease the INR, and possibly affect warfarin’s efficacy exists | • Continue anticoagulation to maintain an INR of up to 3.5, unless there is an increased risk of intracranial hemorrhage (eg, intracranial mass or aneurysm) |
| Herbals | Mechanism of action and potential effect on ECT | | Management strategies |
| Ginkgo biloba | • GABA agonist: potentiates CNS depressant effects of barbiturates and BZDs and may increase ECT seizure threshold  
• Inhibit platelet activating factor: increase risk of cerebral hemorrhage  
• May contain convulsive agent: lower ECT seizure threshold  
• Cerebral arterial vasodilation: increased intracranial pressure  
• Induce CYP3A4: increase metabolism of barbiturates and BZDs | | • For all herbal medicines: assess its potential impact on the procedure, weigh benefits, and risk  
• Similar considerations when assessing conventional pharmacotherapy |
| Ginseng | • CNS depressant: potentiates CNS depressant effects of barbiturates and BZDs and may increase ECT seizure threshold  
• CNS stimulant: may increase anesthetic requirement and decrease ECT seizure threshold  
• Facilitates acetylcholine release: parasympathetically mediated bradycardia | | |
| St Johns Wort | • GABA agonist: potentiates CNS depressant effects of barbiturates and BZDs and may increase ECT seizure threshold  
• Reduces cholinesterase levels: potentiates neuromuscular blockade effect (eg, succinylcholine)  
• Inhibits MAO and COMT: hypertension or cardiovascular collapse | | |
Table 2 (Continued)

<table>
<thead>
<tr>
<th>Herbs</th>
<th>Mechanism of action and potential effect on ECT</th>
<th>Management</th>
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<tbody>
<tr>
<td>Valerian</td>
<td>CNS depressant, GABA agonist, inhibits GABA uptake and metabolism; potentiates CNS effects of barbiturates and BZDs and may increase ECT seizure threshold</td>
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</tr>
<tr>
<td>Kava kava</td>
<td>CNS depressant, GABA agonist: potentiates CNS effects of barbiturates and BZDs and may increase ECT seizure threshold</td>
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</table>

Abbreviations: BZD, benzodiazepine; CBZ, carbamazepine; ECT, electroconvulsive therapy; FGA, first-generation antipsychotics; LTG, lamotrigine; MAOI, monoamine oxidase inhibitor; SGA, second-generation antipsychotics; SNRIs, serotonin norepinephrine reuptake inhibitors; SSRIs, serotonin reuptake inhibitors; TCA, tricyclic antidepressant; VPA, valproic acid; CNS, Central Nervous System; GERD, Gastroesophageal Reflux Disease; INR, International Normalization Ratio; COMT, Catecholl-O-Amine Transferase; GABA, Gamma Amino-Butiric Acid.

Disclosure

The author reports no conflicts of interest in this work.

References