

Buspirone: A forgotten friend



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This older medication offers several advantages when treating anxiety or depression

In general, when a medication goes off patent, marketing for it significantly slows down or comes to a halt. Studies have shown that physicians' prescribing habits are influenced by pharmaceutical representatives and companies.¹ This phenomenon may have an unforeseen adverse effect: once an effective and inexpensive medication "goes generic," its use may fall out of favor. Additionally, physicians may have concerns about prescribing generic medications, such as perceiving them as less effective and conferring more adverse effects compared with brand-name formulations.² One such generic medication is buspirone, which originally was branded as BuSpar.

Anxiety disorders are the most common psychiatric diagnoses, and at times are the most challenging to treat.³ Anecdotally, we often see benzodiazepines prescribed as first-line monotherapy for acute and chronic anxiety, but because these agents can cause physical dependence and a withdrawal reaction, alternative anxiolytic medications should be strongly considered. Despite its age, buspirone still plays a role in the treatment of anxiety, and its off-label use can also be useful in certain populations and scenarios. In this article, we delve into buspirone's mechanism of action, discuss its advantages and challenges, and what you need to know when prescribing it.

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How buspirone works

Buspirone was originally described as an anxiolytic agent that was pharmacologically unrelated to traditional anxiety-reducing medications (ie, benzodiazepines and barbiturates).⁴ It has a high affinity for the 5-hydroxytryptamine 1A (5HT1A) receptor and may also act as a central dopamine antagonist at D2 receptors.^{4,5} It is FDA-approved only for the treatment of generalized anxiety disorder (GAD).⁴ Buspirone also is commonly used as an augmenting agent to selective serotonin reuptake inhibitors (SSRIs) in the treatment of medication-resistant or partially treated depression.⁶ When a patient who is depressed appears to have marginal to no response to an adequate trial of a first-line agent, buspirone is thought to replenish depleted stores and/or increase synthesis of serotonin. Additionally, it acts directly on 5HT1A autoreceptors to achieve the desired desensitization of those receptors. All of these proposed mechanisms are thought to improve symptoms of depression.⁶

The antidepressants vortioxetine and vilazodone exhibit dual-action at both serotonin reuptake transporters and 5HT1A receptors; thus, they work like an SSRI and buspirone combined.⁶ Although some patients may find it more convenient to take a dual-action pill over 2 separate ones, some insurance companies do not cover these newer agents. Additionally, prescribing buspirone separately allows for more precise dosing, which may lower the risk of adverse effects.

Buspirone is a major substrate for cytochrome P450 (CYP) 3A4 and a minor for CYP2D6, so caution must be advised if considering buspirone for a patient receiving any CYP3A4 inducers and/or inhibitors,⁷ including grapefruit juice.⁸

Dose adjustments are not necessary for age and sex, which allows for highly consistent dosing.⁴ However, as with prescribing medications in any geriatric population, lower starting doses and slower titration of buspirone may be necessary to avoid potential adverse effects due to the alterations of pharmacodynamic and pharmacokinetic processes that occur as patients age.⁹

Advantages of buspirone

Works well as an add-on to other medications. While buspirone in adequate doses may be helpful as monotherapy in GAD, it can also be helpful in other, more complex psychiatric scenarios. Sumiyoshi et al¹⁰ observed improvement in scores on the Digit Symbol Substitution Test when buspirone was added to a second-generation antipsychotic (SGA), which suggests buspirone may help improve attention in patients with schizophrenia. It has been postulated that buspirone may also be helpful for cognitive dysfunction in patients with Alzheimer's disease.¹¹ Buspirone has been used to treat comorbid anxiety and alcohol use disorder, resulting in reduced anxiety, longer latency to relapse, and fewer drinking days during a 12-week treatment program.¹² Buspirone has been more effective than placebo for treating post-stroke anxiety.¹³

Patients who receive an SSRI, such as citalopram, but are not able to achieve a substantial improvement in their depressive and/or anxious symptoms may benefit from the addition of buspirone to their treatment regimen.^{14,15}

A favorable adverse-effect profile. There are no absolute contraindications to buspirone except a history of hypersensitivity.⁴ Buspirone generally is well tolerated and carries a low risk of adverse effects. The most common adverse effects are dizziness and nausea.⁶ Buspirone is not sedating.

Potentially safe for patients who are pregnant. Unlike many other first-line agents for anxiety, such as SSRIs, buspirone has an FDA Category B classification, meaning animal studies have shown no adverse events during pregnancy.⁴ The FDA Pregnancy and Lactation Labeling Rule applies only to medications that entered the market on or after June 30, 2001; unfortunately, buspirone is excluded from this updated categorization.¹⁶ As with any medication being considered for pregnant or lactating women, the prescriber and patient must weigh the benefits vs the risks to determine if buspirone is appropriate for any individual patient.

Clinical Point

Buspirone is commonly used as an augmenting agent to SSRIs in patients with treatment-resistant depression



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Buspirone for anxiety and depression

Clinical Point

Unlike benzodiazepines, buspirone does not have an immediate onset of action

Table

Prescribing buspirone: Clinical pearls

The maximum daily dose of buspirone is 60 mg/d. Doses >60 mg/d do not appear to have been examined in the published literature

Be wary of drug–drug interactions with cytochrome P450 3A4 inducers and inhibitors, because buspirone levels will be greatly affected by these medications

Buspirone is not recommended for patients with hepatic and/or renal failure, but if it must be prescribed, do so with caution; lower doses will be necessary

The adverse-effects profile of buspirone is generally favorable, and no dose adjustments are needed based on a patient's age or sex

Food may decrease the bioavailability of buspirone, but it also decreases first-pass metabolism, so buspirone could be taken with or without food as long as administration is consistent

Source: Reference 4

No adverse events have been reported from abrupt discontinuation of buspirone.¹⁷

Inexpensive. Buspirone is generic and extremely inexpensive. According to GoodRx.com, a 30-day supply of 5-mg tablets for twice-daily dosing can cost \$4.¹⁸ A maximum daily dose (prescribed as 2 pills, 15 mg twice daily) may cost approximately \$18/month.¹⁸ Thus, buspirone is a good option for uninsured or underinsured patients, for whom this would be more affordable than other anxiolytic medications.

May offset certain adverse effects. Sexual dysfunction is a common adverse effect of SSRIs. One strategy to offset this phenomenon is to add bupropion. However, in a randomized controlled trial, Landén et al¹⁹ found that sexual adverse effects induced by SSRIs were greatly mitigated by adding buspirone, even within the first week of treatment. This improvement was more marked in women than in men, which is helpful because sexual dysfunction in women is generally resistant to other interventions.²⁰ Unlike bupropion, buspirone is not contraindicated in patients with seizure

and/or eating disorders.⁴ Additionally, the American Psychiatric Association practice guidelines for the treatment of major depressive disorder identify buspirone as a useful strategy in treating erectile dysfunction and orgasmic dysfunction due to SSRI treatment.¹⁵

Unlikely to cause extrapyramidal symptoms (EPS). Because of its central D2 antagonism, buspirone has a low potential (<1%) to produce EPS. Buspirone has even been shown to reverse haloperidol-induced EPS.²¹

The *Table*⁴ highlights key points to bear in mind when prescribing buspirone.

Challenges with buspirone

Response is not immediate. Unlike benzodiazepines, buspirone does not have an immediate onset of action.²² With buspirone monotherapy, response may be seen in approximately 2 to 4 weeks.²³ Therefore, patients transitioning from a quick-onset benzodiazepine to buspirone may not report a good response. However, as noted above, when using buspirone to treat SSRI-induced sexual dysfunction, response may emerge within 1 week.¹⁹ Buspirone also lacks the euphoric and sedative qualities of benzodiazepines that patients may prefer.

Not for patients with hepatic and renal impairment. Because plasma levels of buspirone are elevated in patients with hepatic and renal impairment, this medication is not ideal for use in these populations.⁴

Contraindicated in patients receiving MAOIs. Buspirone should not be prescribed to patients with depression who are receiving treatment with a monoamine oxidase inhibitor (MAOI) because the combination may precipitate a hypertensive reaction.⁴ A minimum washout period of 14 days from the MAOI is necessary before initiating buspirone.⁹

Idiosyncratic adverse effects. As with all pharmaceuticals, buspirone may produce idiosyncratic adverse effects. Faber and

Sansone²⁴ reported a case of a woman who experienced hair loss 3 months into treatment with buspirone. After cessation, her alopecia resolved.

Questionable efficacy for some anxiety subtypes. Buspirone has been studied as a treatment of other common psychiatric conditions, such as social phobia and anxiety in the setting of smoking cessation. However, it has not proven to be effective over placebo in treating these anxiety subtypes.^{25,26}

Short half-life. Because of its relatively short half-life (2 to 3 hours), buspirone requires dosing 2 to 3 times a day, which could increase the risk of noncompliance.⁴ However, some patients might prefer multiple dosing throughout the day due to perceived better coverage of their anxiety symptoms.

Limited incentive for future research.

Because buspirone is available only as a generic formulation, there is little financial incentive for pharmaceutical companies and other interested parties to study what may be valuable uses for buspirone. For example, there is no data available on comparative augmentation of buspirone and SGAs with antidepressants for depression and/or anxiety. There is also little data available about buspirone prescribing trends or why buspirone may be underutilized in clinical practice today.

Unfortunately, historical and longitudinal data on the prescribing practices of buspirone is limited because the original branded medication, BuSpar, is no longer on the market. However, this medication offers multiple advantages over other agents used to treat anxiety, and it should not be forgotten when formulating a

Clinical Point

Buspirone is a good option for patients who are uninsured or underinsured because it is extremely inexpensive



Buspirone for anxiety and depression

Clinical Point

Buspirone is not recommended for patients with hepatic or renal impairment

Related Resources

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Drug Brand Names

Bupropion • Wellbutrin, Haloperidol • Haldol
Zyban, Vilazodone • Viibryd
Buspirone • BuSpar, Vortioxetine • Trintellix
Citalopram • Celexa

treatment regimen for patients with anxiety and/or depression.

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Bottom Line

Buspirone is a safe, low-cost, effective treatment option for patients with anxiety and may be helpful as an augmenting agent for depression. Because of its efficacy and high degree of tolerability, it should be prioritized higher in our treatment algorithms and be a part of our routine pharmacologic armamentarium.