The seasonality of depression: a clinical perspective of recognizing and preventing SAD

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Dr. Brayden Kameg and Dr. Seemin Qureshi have been diagnosing and treating patients for seasonal affective disorder (SAD) for 8 years and 10 years, respectively. As medical experts in patient care, mental health, depression, and associated diagnoses, they share key signs and considerations.

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Dr. Brayden Kameg and Dr. Seemin Qureshi are paid consultants for Bausch Health Companies Inc. or its affiliates.

RECOGNIZING THE SYMPTOMS

We live in a world where patients come in telling us their diagnosis. Or at least what they think they might have. They have done their Internet research and are looking for us to confirm and agree. But patients can often be misinformed, and diagnosing SAD requires clinical experience and medical knowledge about the mental health field.

And while we are seeing a broader acceptance of discussing mental health, many individuals won't immediately seek that help from a psychiatric specialist and those who do are often running into barriers due to provider shortages.[1,2] Instead, patients may go to a primary care office and talk about their symptoms, but not necessarily the seasonality of them.

To add to the complexity, patients can often come in with a suggested diagnosis by a prescriber who may not specialize in mental health. When we first meet a patient, SAD may be an additional diagnosis that we need to make, or even correct from a previous misdiagnosis. Of course, labs such as a complete blood count and thyroid function panel are always done in advance to rule out any other underlying medical cause of symptoms.

Whether patients are being referred by a previous prescriber or they've spent time online searching their symptoms, it is important to listen to what they say and evaluate overall symptoms. Opening the dialogue about treating the patient's mental health and educating about the specific condition is a crucial step in this process. For proper diagnosis and treatment of SAD, recognizing the seasonality of symptoms and treatment is especially critical.

"I always ask, 'Are you sleeping more than usual? Are you eating more than usual? Is it a struggle to get out of bed?' And because, just generally, SAD affects more women and more young women than it does other populations, that's especially the target audience that I make sure that they ask those kinds of questions."

—Dr. Seemin Qureshi, DMSc, PA-C

DIAGNOSING A SEASONAL CONDITION

It is key to distinguish SAD from other diagnoses, like major depressive disorder (MDD).* With SAD, in particular, it is important to pay attention to the seasonality of when the symptoms are appearing and/or waning. Patients often try to self-manage their symptoms to get themselves through at first; however, they may decide to visit a healthcare professional for an initial diagnosis if they feel SAD symptoms continuing after the holidays.

One of our most reliable tools to aid in determining a SAD diagnosis is the SIGH-SAD HAM-D questionnaire. The SIGH-SAD builds on the 21-item HAM-D to include 8 additional items that are common in patients experiencing SAD. These include social withdrawal, weight gain, appetite increase, increased eating, carbohydrate craving, hypersomnia, fatigability, and reverse diurnal (afternoon slump).[3,4]

In fact, one of our telltale signs that a patient has SAD often accompanies or can be associated with the SIGH-SAD symptoms of fatigue and reverse diurnal: low motivation with a seasonal onset. Patients who seasonally feel they lack that "get-up-and-go" attitude and describe their lives as if they are "dragging themselves to everything throughout the day" are key candidates for a SAD diagnosis.

Still, patients may not realize the seasonality or even severity of their symptoms, or that it is a medically recognized condition for which there is preventative treatment. Asking patients to describe their past experiences can help to determine if a seasonal pattern exists. Focusing on those previously noted additional items from the SIGH-SAD, and then getting that longitudinal history as far as the timeline of symptom onset and symptom remission, helps in making the diagnosis. Asking about family history may also be helpful.

"Oftentimes, by the time patients are seeing me, they will say this [symptom] has been going on and off for years. They have not put together that their symptoms are occurring in the winter and then they feel better in the summer."

—Dr. Brayden Kameg, DNP, PMHNP-BC, CARN, CNE

INITIATING TREATMENT

In our experience, medication is a critical part of the puzzle when it comes to treating SAD. Finding the appropriate medication can help patients manage, or even help prevent, their symptoms.

***When prescribing treatment for SAD in an EHR (electronic health record), it is important to note that it may also be referred to as *Major Depressive Disorder with Seasonal Pattern* or similar.**

IMPORTANT SAFETY INFORMATION (cont)

APLENZIN is **contraindicated** in:

- patients with a seizure disorder
- patients with a current or prior diagnosis of bulimia or anorexia nervosa, due to a higher incidence of seizures
- patients undergoing abrupt discontinuation of alcohol, benzodiazepines, barbiturates, or antiepileptic drugs
- patients taking other bupropion products, including Zyban
- The concomitant use of MAOIs (intended to treat psychiatric disorders) and APLENZIN, or within 14 days of each other, is contraindicated due to an increased risk of hypertensive reactions. Starting APLENZIN in a patient treated with reversible MAOIs such as linezolid or intravenous methylene blue is contraindicated.
- APLENZIN is contraindicated in patients with known hypersensitivity to bupropion or other ingredients of APLENZIN. Anaphylactoid/anaphylactic reactions and Stevens-Johnson syndrome have been reported.

Please see additional Important Safety Information throughout. Click here for full Prescribing Information, including Boxed Warning regarding suicidal thoughts and behaviors.

Once diagnosed, it is important that patients start treatment along with recommended lifestyle changes. In fact, we've found that patients have difficulty starting these recommended lifestyle changes because of their SAD symptoms.

As medical professionals, we appreciate having a treatment for SAD that allows us to write a prescription as indicated. This ensures our patients' condition is being treated and managed for the prevention of SAD.[5] Bupropion hydrobromide, or APLENZIN, is our treatment of choice in this case as it is FDA-approved for the prevention of seasonal major depressive episodes.[6]

"I'll tell patients that we have to mimic the summer for you. I want to make sure you make it a point to eat more fresh fruits and vegetables, get that exercise, take a vitamin D supplement."

—Dr. Seemin Qureshi, DMSc, PA-C

CONSIDERING APLENZIN

We've found that many of the characteristics of APLENZIN are important to our patients with SAD and make APLENZIN worth considering as a possible treatment option. Let's start with dosing. For SAD, the recommended dosing for APLENZIN aligns with the timing of the patient's symptoms. Also, patients may be more willing to try APLENZIN knowing they may not require long-term treatment and can taper off with professional oversight as SAD symptoms dissipate.[7] It is also helpful that APLENZIN is one tablet, taken once a day, and is available in 3 different dosage strengths that can be adjusted based on patients' needs.[5]

Other common areas of concern for patients are weight gain and sexual side effects, which can often occur with antidepressants and can be a reason for patients to be hesitant about starting and staying on treatment.[8-12] In our experience, and in clinical trials, APLENZIN has demonstrated a low incidence of weight gain or orgasm dysfunction.[5,13†] We make sure to explain the possibility to patients to help avoid a potential non-start or lack of adherence.

Of course, the proven efficacy of APLENZIN is a reason to consider the medication for treatment of SAD. We have found it to be effective in many of our patients, which aligns with results from clinical trials. In clinical trials, patients experienced about half the number of seasonal depressive episodes over the course of treatment.[14‡]

Once we've diagnosed and started patients on APLENZIN, we can approach their treatment more longitudinally. We'll continue regular visits while they are on treatment. Then, come early spring, we can taper their APLENZIN and reinitiate treatment in early fall. We can also individualize treatment when needed and allow patients to stay on treatment year-round.[5] When patients taper their APLENZIN, we'll monitor them carefully while tapering and usually have at least one appointment midsummer.

†APLENZIN is not indicated for weight loss. In clinical trials in MDD (up to 6 weeks), weight gain was 3% with 300 mg/day bupropion HCl sustained-release vs 4% with placebo. In clinical trials in SAD (up to 6 months), weight gain was 11% with 150-300 mg/day bupropion HCl extended-release vs 21% with placebo. In clinical trials using bupropion HCl extended-release, orgasm dysfunction was 15% in MDD vs 9% with placebo (pooled data).[5,13]

‡Three 4- to 6-month placebo-controlled trials in patients with seasonal MDD used 300 mg/day bupropion HCl extended-release. Combined patient population: bupropion HCl extended-release, n=534; placebo, n=508. Bupropion HCl extended-release protected against the recurrence of seasonal major depressive episodes, reducing their frequency by an average of 44% across the 3 studies relative to that observed in the placebo group.[5,14]

IMPORTANT SAFETY INFORMATION (cont)

Warnings and Precautions

- APLENZIN is not approved for smoking cessation treatment; however, bupropion HCl sustained-release is approved for this use. Postmarketing reports of serious or clinically significant neuropsychiatric adverse events with smoking cessation treatment have included changes in mood (including depression and mania), psychosis, hallucinations, paranoia, delusions, homicidal ideation, aggression, hostility, agitation, anxiety, and panic, as well as suicidal ideation, suicide attempt, and completed suicide. Observe patients attempting to quit smoking with APLENZIN for the occurrence of such symptoms and instruct them to discontinue APLENZIN and contact a healthcare provider if they experience such adverse events.
- Bupropion is associated with a dose-related risk of seizures. The dose should not exceed 522 mg once daily. Increase the dose gradually. Discontinue APLENZIN and do not restart treatment if the patient experiences a seizure. Use with extreme caution in patients with a history of seizure or cranial trauma, or in patients treated with other medications that lower the seizure threshold.

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It is important to remember to initiate APLENZIN in the autumn, prior to the onset of depressive episodes. Treatment should then be continued through the winter season and tapered and discontinued in early spring.[5§]

CONTINUING TREATMENT

Staying on treatment is key in managing any diagnosis, and our experience shows that patients typically are able to continue taking their medication as instructed. In 3 clinical trials measuring discontinuation rates due to adverse reactions (up to 6 months), about 90% of patients with SAD stayed on treatment.[5,14‖] Also, we find that once our patients have taken APLENZIN for a season, they return to reinitiate treatment ahead of the fall/winter season. We typically schedule another visit for late summer or early fall, where we can reinitiate treatment to help prevent their SAD episodes from returning.

"It's nice when that diagnosis has been established to start offering some anticipatory guidance come August or September. We can initiate treatment early rather than waiting until holiday time, later in the winter where symptoms can continue to go untreated."

—Dr. Brayden Kameg, DNP, PMHNP-BC, CARN, CNE

Often, patients are regularly seeing therapists who can help to remind patients of setting up an appointment to get restarted on APLENZIN. For offices that do not specialize in mental health services, it can be helpful to include signage around the office and even bring up the subject during a visit to raise awareness among patients.

It is important to note that APLENZIN is indicated for the prevention of SAD episodes, so treatment should ideally be reinitiated before patients experience a SAD episode.[5] This can help put them in a better position going into the winter season. We believe that taking the appropriate treatment can often help patients avoid feeling apprehensive about the upcoming fall and winter season.

LOOKING FORWARD

Integrating treatment initiation into patients' late summer/fall routines may help them approach the season with less apprehension or concern. This not only helps patients manage and prevent their episodes of SAD, but also often helps cultivate a richer relationship with their healthcare professional. By fostering a relationship built on trust with patients seeking to improve their mental health, we can hope and expect to see better overall patient outcomes.

[§]For patients treated with 348 mg per day, decrease the dose to 174 mg once daily before discontinuing APLENZIN. Individualize the timing of initiation, and duration of treatment should be individualized based on the patient's historical pattern of seasonal MDD episodes.[5]

[‖]300 mg/day bupropion HCl sustained-release in MDD (n=376) and bupropion HCl extended-release in SAD (n=537); compared with 96% for patients on placebo in MDD trials (n=385) and 95% for patients on placebo in SAD trials (n=511).[5,14]

APLENZIN has been demonstrated to be bioequivalent to bupropion HCl extended-release. Bupropion HCl extended-release has been demonstrated to have similar bioavailability both to the immediate-release and sustained-release formulations of bupropion.[5]

IMPORTANT SAFETY INFORMATION (cont)
Warnings and Precautions (cont)

- Treatment with APLENZIN can result in elevated blood pressure and hypertension. Assess blood pressure before initiating treatment with APLENZIN, and monitor periodically during treatment.
- Antidepressant treatment can precipitate a manic, mixed, or hypomanic manic episode. Prior to initiating APLENZIN, screen patients for a history of bipolar disorder and the presence of risk factors for bipolar disorder (e.g., family history of bipolar disorder, suicide, or depression). APLENZIN is not approved for the treatment of bipolar depression.
- Depressed patients treated with bupropion have had a variety of neuropsychiatric signs and symptoms, including delusions, hallucinations, psychosis, concentration disturbance, paranoia, and confusion. Some of these patients had a diagnosis of bipolar disorder. In some cases, these symptoms abated upon dose reduction and/or withdrawal of treatment. Discontinue APLENZIN if these reactions occur.
- The pupillary dilation that occurs following use of many antidepressant drugs including APLENZIN may trigger an angle closure attack (Angle-Closure Glaucoma) in a patient with anatomically narrow angles who does not have a patent iridectomy.

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IMPORTANT SAFETY INFORMATION (cont)

Adverse Reactions

- The most common adverse reactions that occurred in at least 5% of patients treated with bupropion HCl sustained-release (300 mg and 400 mg per day) and at a rate at least twice the placebo rate were: anorexia, dry mouth, nausea, insomnia, dizziness, pharyngitis, abdominal pain, agitation, anxiety, tremor, palpitation, sweating, tinnitus, myalgia, urinary frequency, and rash.

Drug Interactions

- An increased dose of bupropion may be necessary if co-administered with CYP2B6 inducers based on clinical exposure but should not exceed the maximum recommended dose. Bupropion inhibits CYP2D6 and can increase concentrations of: antidepressants, antipsychotics, beta-blockers, and Type 1C antiarrhythmics. Consider dose reduction when using with bupropion. Dose bupropion with caution when used with drugs that lower seizure threshold. CNS toxicity can occur when bupropion is used concomitantly with dopaminergic drugs.
- APLENZIN can cause false-positive urine test results for amphetamines.

Use in Special Populations

- Pregnancy: Use only if benefit outweighs potential risk to the fetus. Healthcare providers are encouraged to register patients in the Pregnancy Exposure Registry by calling 1-844-405-6185 or visiting https://womensmentalhealth.org/research/pregnancyregistry/.
- In patients with moderate to severe hepatic impairment (Child-Pugh score: 7 to 15), the maximum dose is **174 mg every other day**. In patients with mild hepatic impairment (Child-Pugh score: 5 to 6) or renal impairment (glomerular filtration rate <90 mL/min), consider reducing the dose and/or frequency of dosing.
- Advise patients to read the FDA-approved patient labeling (Medication Guide). Inform patients, their families, and their caregivers about the benefits and risks associated with treatment with APLENZIN and counsel them in its appropriate use.

To report SUSPECTED ADVERSE REACTIONS, contact Bausch Health at 1-800-321-4576 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Click here for full Prescribing Information, including Boxed Warning regarding suicidal thoughts and behaviors.

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