Treating Panic Disorder

A Quick Reference Guide

Based on *Practice Guideline for the Treatment of Patients With Panic Disorder,* Second Edition, originally published in January 2009. A guideline watch, summarizing significant developments in the scientific literature since publication of this guideline, may be available at http://www.psychiatryonline.com/pracGuide/pracGuideTopic_9.aspx.

INTRODUCTION

Treating Panic Disorder: A Quick Reference Guide is a synopsis of the American Psychiatric Association's *Practice Guideline for the Treatment of Patients With Panic Disorder,* Second Edition, which was originally published in the *American Journal of Psychiatry* in January 2009 and is available through American Psychiatric Publishing, Inc. The psychiatrist using this Quick Reference Guide (QRG) should be familiar with the full-text practice guideline on which it is based. The QRG is not designed to stand on its own and should be used in conjunction with the full-text practice guideline. For clarification of a recommendation or for a review of the evidence supporting a particular strategy, the psychiatrist will find it helpful to return to the full-text practice guideline.

STATEMENT OF INTENT

The Practice Guidelines and the Quick Reference Guides are not intended to be construed or to serve as a standard of medical care. Standards of medical care are determined on the basis of all clinical data available for an individual patient and are subject to change as scientific knowledge and technology advance and practice patterns evolve. These parameters of practice should be considered guidelines only. Adherence to them will not ensure a successful outcome for every individual, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgment regarding a particular clinical procedure or treatment plan must be made by the psychiatrist in light of the clinical data presented by the patient and the diagnostic and treatment options available. The development of the APA Practice Guidelines and Quick Reference Guides has not been financially supported by any commercial organization.

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A. PSYCHIATRIC MANAGEMENT

Establish a therapeutic alliance.

- Give careful attention to the patient's preferences and concerns with regard to treatment.
- Provide education about panic disorder and its treatment in language that is readily understandable to the patient.
- Support the patient through phases of treatment that may be anxiety provoking (e.g., anticipating medication side effects, confronting agoraphobic situations).

Perform the psychiatric assessment.

- Evaluation generally includes the components described in Table 1.
- Assess clinical features that may influence treatment planning, including the presence of agoraphobia and the extent of situational fear and avoidance; the presence of co-occurring psychiatric conditions, including substance use; and the presence of general medical conditions.
- Consider if the patient's panic attacks are best diagnosed as a symptom of DSM-IV-TR panic disorder or whether they are related to substance use or a general medical condition (e.g., thyroid disease) or a side effect of medications prescribed to treat such conditions (e.g., oral corticosteroids).
- Note that panic disorder may also co-occur with many general medical conditions (Table 2) and with many psychiatric disorders, especially personality disorders, substance use disorders, and mood disorders.

Tailor the treatment plan for the individual patient.

- Take into account the nature of the individual patient's symptoms as well as symptom frequency, symptom triggers, and co-occurring conditions.

TABLE 1. COMPONENTS OF A PSYCHIATRIC EVALUATION FOR PATIENTS WITH PANIC DISORDER

History of the present illness and current symptoms
Past psychiatric history
General medical history
History of substance use, including illicit drugs, prescribed and over-the-counter medications, and other substances (e.g., caffeine) that may produce physiological effects that can trigger or exacerbate panic symptoms
Personal history (e.g., major life events)
Social, occupational (including military), and family history
Review of the patient's medications
Previous treatments
Review of systems
Mental status examination
Physical examination
Appropriate diagnostic tests (to rule out possible causes of panic symptoms)

TABLE 2. GENERAL MEDICAL CONDITIONS MORE PREVALENT IN PATIENTS WITH PANIC DISORDER THAN IN THE GENERAL POPULATION

Thyroid disease	Migraine
Cancer	Mitral valve prolapse
Chronic pain	Vestibular disorders
Cardiac disease	Allergic conditions
Irritable bowel syndrome	Respiratory disease

- To better assess symptoms, consider having the patient monitor them, for example, by keeping a diary. A diary may also help with ongoing assessment of the patient's psychiatric status and response to treatment.
- Consider the role of ethnicity and cultural factors in the patient's presentation—for example, by using the DSM-IV-TR Outline on Cultural Formulation—and tailor treatment accordingly.

Evaluate the safety of the patient.

- Carefully assess suicide risk (Table 3). Panic disorder has been shown to be associated with an elevated risk of suicidal ideation and behavior, even in the absence of co-occurring conditions such as major depression.
- Decide whether the patient can safely be treated as an outpatient, or whether hospitalization is indicated.

Evaluate types and severity of functional impairment.

- Consider the impact of panic disorder on the patient's functioning in domains such as work, school, family, social relationships, and leisure activities.
- Aim to minimize impairment in these domains through treatment.

TABLE 3. COMPONENTS OF A SUICIDE RISK ASSESSMENT FOR PATIENTS WITH PANIC DISORDER

Identification of specific psychiatric symptoms known to be associated with suicide attempts or suicide
Assessment of past suicidal behavior, family history of suicide and mental illness, and current stressors
Assessment of potential protective factors such as positive reasons for living
Specific inquiry about suicidal thoughts, intent, plans, means, and behaviors

Establish treatment goals.

- Reduce the frequency and intensity of panic attacks, anticipatory anxiety, and agoraphobic avoidance, optimally with full remission of symptoms and return to a premorbid level of functioning.
- Treat co-occurring psychiatric disorders when they are present.

Monitor the patient's psychiatric status.

- Monitor all symptoms originally presented by the patient.
- Understand that symptoms may resolve in stages (e.g., panic attacks may remit before agoraphobic avoidance does) and that new symptoms may emerge that were not initially noted.
- Consider using rating scales to help monitor the patient's status at each session.

Provide education to the patient and, when appropriate, to the family.

- Provide education about the disorder and its treatment.
- Inform the patient that panic attacks are not life-threatening, are almost never acutely dangerous, are not uncommon, and will abate. This information and reassurance alone may relieve some symptoms.
- Consider encouraging the patient to read educational books, pamphlets, and trusted web sites. Useful resources are listed in the appendix of the full-text practice guideline.
- When appropriate, also provide education to the family. This may include discussion of how changes in the patient's status can impact the family system, and how responses of family members can help or hinder treatment.

- Promote healthy behaviors such as exercise; sleep hygiene; and decreased use of caffeine, tobacco, alcohol, and other potentially deleterious substances.

Coordinate the patient's care with other clinicians.

- Communicate with other health care professionals who are evaluating or treating the patient.
- Ensure that a general medical evaluation is done (either by the psychiatrist or by another health care professional) to rule out medical causes of panic symptoms. Extensive or specialized testing for medical causes of panic symptoms is usually not indicated but may be conducted on the basis of individual characteristics of the patient.

Enhance treatment adherence.

- Whenever possible, assess and acknowledge potential barriers to treatment adherence (Table 4) and work collaboratively with the patient to minimize their influence.
- Encourage the patient to articulate his or her fears about treatment.
- Educate the patient about when to expect improvement so that treatment is not prematurely abandoned.
- Encourage the patient to raise concerns or questions, including by telephone if between visits.

Work with the patient to address early signs of relapse.

- Reassure the patient that symptoms can fluctuate during treatment before remission is attained.
- After remission, provide the patient a plan for responding to symptoms that linger or recur.

TABLE 4. FACTORS THAT MAY CONTRIBUTE TO TREATMENT NONADHERENCE

Avoidance that is a manifestation of panic disorder
Logistical barriers (e.g., economic factors, transportation, child care)
Cultural or language barriers
Problems in the therapeutic relationship
Short-term intensification of anxiety associated with treatment (e.g., due to medication side effects or exposure to fear cues)

B. INITIATING TREATMENT

Choose a treatment setting.

- Treatment is generally conducted on an outpatient basis.
- Hospitalization may be necessary under certain circumstances, for example, to address acute suicide risk or substance intoxication, or rarely, to treat very severe panic disorder with agoraphobia when outpatient treatment has been ineffective or is impractical.
- Home visits are another treatment option for severely agoraphobic patients who are limited in their ability to travel or leave the house.
- When accessibility to mental health care is limited (e.g., in remote or underserved areas), telephone- or web-based treatments may be considered.

Choose an initial treatment modality.

- Table 5 describes factors to consider.
- The use of a selective serotonin reuptake inhibitor (SSRI), serotonin-norepinephrine reuptake inhibitor (SNRI), tricyclic antidepressant (TCA), or cognitive-behavioral therapy (CBT) as the initial treatment for panic disorder is strongly supported by demonstrated efficacy in numerous randomized controlled trials. In the absence of a co-occurring mood disorder, monotherapy with a benzodiazepine is also an appropriate initial treatment.

TABLE 5. FACTORS TO CONSIDER WHEN CHOOSING AN INITIAL TREATMENT MODALITY

General Factors
Patient preference
Risks and benefits of the treatment, including risk of medication side effects
The patient's treatment history
Presence of co-occurring general medical and psychiatric conditions
Cost for the patient
Availability of the treatment
Factors Favoring Psychosocial Treatment
Patient prefers nonmedication treatment.
Patient can invest the time and effort needed for this modality.
Patient is pregnant, nursing, or planning to become pregnant.
Patient has co-occurring personality disorder.
Factors Favoring Pharmacotherapy
Patient prefers this modality.
Patient does not have time or other resources needed for psychosocial treatment.
Factors Favoring Combined Treatment
Patient has failed to respond to standard monotherapies.
Patient prefers immediate control of distressing symptoms (with pharmacotherapy).
Patient prefers to reduce future need for medications.

- A particular form of psychodynamic psychotherapy, panic-focused psychodynamic psychotherapy (PFPP), was effective in one randomized controlled trial and could be offered as an initial treatment.
- There is insufficient evidence to recommend any of these pharmacological or psychosocial interventions as superior to another, or to routinely recommend a combination of treatments over monotherapy, although a combination may be chosen based on individual circumstances.

- For women with panic disorder who are pregnant, nursing, or planning to become pregnant, psychosocial interventions should be considered in lieu of pharmacotherapy. Pharmacotherapy may also be indicated but requires weighing and discussing potential benefits and risks with the patient, her obstetrician, and, whenever possible, her partner. Such discussions should also consider the potential risks to the patient and the child of untreated panic disorder and any co-occurring psychiatric conditions.

When selecting a pharmacotherapy, consider the factors described in Table 6 and the following:

- The relatively favorable safety and side-effect profile of SSRIs and SNRIs makes them the best initial pharmacotherapy choice for many patients with panic disorder.
- Although TCAs are effective, their side effects and greater toxicity in overdose often limit their clinical utility and acceptability to patients.
- SSRIs, SNRIs, and TCAs are all preferable to benzodiazepines as monotherapies for patients with co-occurring depression or substance use disorders. Benzodiazepines may be especially useful adjunctively with antidepressants to treat residual anxiety symptoms. Benzodiazepines may be preferred (as monotherapies or in combination with antidepressants) for patients with very distressing or impairing symptoms in whom rapid symptom control is critical. The benefit of more rapid response to benzodiazepines must be balanced against the possibilities of troublesome side effects (e.g., sedation) and physiological dependence that may lead to difficulty discontinuing the medication.
- MAOIs appear effective for panic disorder, but because of their safety profile, they are generally reserved for patients who have failed to respond to several first-line treatments.
- Other medications with less empirical support (e.g., mirtazapine, anticonvulsants such as gabapentin) may be considered as

TABLE 6. FACTORS TO CONSIDER WHEN CHOOSING A PHARMACOTHERAPY FOR PANIC DISORDER

Side effects (including any applicable warnings of the U.S. Food and Drug Administration)
Cost
Pharmacological properties
Potential drug interactions
The patient's treatment history
Co-occurring general medical and psychiatric conditions
Strength of the evidence base for the particular medication

monotherapies or adjunctive treatments for panic disorder on the basis of individual circumstances or a lack of response to several standard treatments.

When selecting a psychotherapy, consider the factors described in Table 7 and the following:

- CBT for panic disorder is supported by multiple positive randomized controlled trials and is recommended with substantial clinical confidence. Group CBT is supported by multiple controlled studies. Self-directed CBT is supported by several controlled studies.
- Exposure therapy is also well studied and recommended with substantial clinical confidence.
- PFPP is supported by one randomized controlled trial. Evidence for the use of other psychodynamic psychotherapy approaches for panic disorder is limited to case reports and experience of psychodynamic psychotherapy experts.
- Other psychosocial treatments have not been formally tested for panic disorder or have proven ineffective (e.g., eye movement desensitization and reprocessing [EMDR]) or inferior (e.g., supportive psychotherapy) to standard treatments such as CBT.

TABLE 7. FACTORS TO CONSIDER WHEN CHOOSING A PSYCHOTHERAPY FOR PANIC DISORDER

Patient preference
Cost and availability
The patient's treatment history
Strength of the evidence base for the particular psychotherapy
Presence of co-occurring personality disorder

- Other group therapies (including patient support groups) are not recommended as monotherapies for panic disorder, but they may be useful adjunctive treatments for some patients.
- Couples or family therapy alone is not recommended as a treatment for panic disorder, although it may be helpful in addressing co-occurring relationship dysfunction.

C. IMPLEMENTING TREATMENT

Stabilize the medication dose.

- Table 8 describes usual dosing for antidepressant and benzodiazepine pharmacotherapy for panic disorder. Important safety considerations are described in Table 9.
- Because patients with panic disorder can be sensitive to medication side effects, low starting doses of SSRIs, SNRIs, and TCAs are recommended (approximately half of the starting doses given to depressed patients). The low dose is maintained for several days then gradually increased to a full therapeutic dose over subsequent days and as tolerated by the patient.
- Underdosing of antidepressants (i.e., starting low and never reaching full therapeutic doses) is common in the treatment of panic disorder and is a frequent source of partial response or nonresponse.

TABLE 8. DOSING OF ANTIDEPRESSANTS AND BENZODIAZEPINES FOR PANIC DISORDER

	Starting Dose and Incremental Dose (mg/day)	Usual Therapeutic Dose (mg/day)[a]
SSRIs		
Citalopram	10	20–40
Escitalopram	5–10	10–20
Fluoxetine	5–10	20–40
Fluvoxamine	25–50	100–200
Paroxetine	10	20–40
Paroxetine CR	12.5	25–50
Sertraline	25	100–200
SNRIs		
Duloxetine	20–30	60–120
Venlafaxine ER	37.5	150–225
TCAs		
Imipramine	10	100–300
Clomipramine	10–25	50–150
Desipramine	25–50	100–200
Nortriptyline	25	50–150
Benzodiazepines		
Alprazolam	0.75–1.0[b]	2–4[b]
Clonazepam	0.5–1.0[c]	1–2[c]
Lorazepam	1.5–2.0[b]	4–8[b]

[a]Higher doses are sometimes used for patients who do not respond to the usual therapeutic dose.
[b]Usually split into three or four doses given throughout the day.
[c]Often split into two doses given morning and evening.

TABLE 9. SAFETY CONSIDERATIONS FOR MEDICATIONS USED FOR PANIC DISORDER

Medication	Safety Risk	Implementation Recommendations
SSRIs	Suicidal ideation and behavior	Carefully monitor for self-harming or suicidal thoughts or behaviors and for side effects (e.g., anxiety, agitation, insomnia, irritability) that may influence such behaviors.
	Upper gastrointestinal bleeding	Consider possible increase in risk, particularly when an SSRI is prescribed in combination with a nonsteroidal anti-inflammatory drug or with aspirin.
	Falls and fractures	Prescribe carefully to elderly patients.
SNRIs	Suicidal ideation and behavior	See above for SSRIs.
Venlafaxine, extended release	Sustained hypertension in a small proportion of patients	Assess blood pressure during treatment, particularly when venlafaxine is titrated to higher doses.
TCAs	Suicidal ideation and behavior	See above for SSRIs.
	Anticholinergic effects	Do not prescribe TCAs for patients who have acute narrow-angle glaucoma or clinically significant prostatic hypertrophy.
	Falls and fractures	See above for SSRIs.
	Significant or fatal arrhythmia	Consider obtaining a baseline ECG for patients with preexisting cardiac conduction abnormalities.
	Significant cardiac toxicity and fatality on overdose	Prescribe TCAs judiciously in suicidal patients.

TABLE 9. SAFETY CONSIDERATIONS FOR MEDICATIONS USED FOR PANIC DISORDER *(continued)*

Benzodiazepines	Sedation, fatigue, ataxia, slurred speech, memory impairment, and weakness	
	Falls and fractures	See above for SSRIs.
	Increased risk of motor vehicle accidents	Warn patients about driving or operating heavy machinery.
	Additive effects of benzodiazepines and alcohol	Advise patients about these effects, particularly about combined sedative and respiratory effects.
	Potential misuse of the benzodiazepine or relapse of a substance use disorder	Prescribe cautiously to patients with a history of substance use disorders and monitor carefully, e.g., dispense in limited quantities, supervise medication administration, assess nonadherence, increase office visit frequency.
	Cognitive effects	Monitor the patient for development of cognitive impairment, which may be more problematic at higher doses and in patients performing complex information-processing tasks at work. Prescribe with caution to elderly patients or those with preexisting cognitive impairment.

- When benzodiazepines are prescribed, a regular dosing schedule rather than a PRN ("as needed") schedule is preferred for patients with panic disorder. The goal is to prevent panic attacks rather than reduce symptoms once the attack has already occurred.
- Patients are typically seen every 1–2 weeks when first starting a medication, then every 2–4 weeks until the dose is stabilized. After the dose is stabilized and symptoms have decreased, patients will most likely require less frequent visits.

Ensure that psychosocial treatments are conducted by professionals with an appropriate level of training and expertise.

- CBT for panic disorder generally includes psychoeducation, self-monitoring, countering anxious beliefs, exposure to fear cues, modification of anxiety-maintaining behaviors, and relapse prevention. The clinician may opt to emphasize certain components depending on the patient's symptom profile and response to different CBT techniques. For most patients, exposure proves to be the most challenging but often the most potent component of CBT.
- Exposure therapy focuses almost exclusively on systematic exposure to fear cues.
- Possible benefits of group CBT include decreasing shame and stigma; providing opportunities for modeling, inspiration, and reinforcement; and providing an exposure environment for patients who fear having panic symptoms in social situations.
- PFPP utilizes the general principles of psychodynamic psychotherapy, with special focus on the transference as the therapeutic agent promoting change, and encourages patients to confront the emotional significance of their panic symptoms with the aim of promoting greater autonomy, symptom relief, and improved functioning.
- Other psychodynamic psychotherapies may focus more broadly on emotional and interpersonal issues.

Deliver psychosocial treatments for an appropriate period of time and in an appropriate format.

- CBT is generally delivered in 10–15 weekly sessions. It can be successfully administered individually or in a group format.
- Self-directed forms of CBT may be useful for patients who do not have ready access to a trained CBT therapist.
- In research settings, PFPP has been administered on an individual basis twice weekly for 12 weeks.

Evaluate if the initial treatment is working.

- Effective treatment should produce a decrease in the patient's key symptom domains, such as frequency and intensity of panic attacks, level of anticipatory anxiety, degree of agoraphobic avoidance, and severity of interference and distress related to panic disorder.
- Some domains may change more quickly than others (e.g., the frequency of panic attacks may decrease before agoraphobic avoidance decreases). Furthermore, the pattern of symptom resolution varies depending on the individual patient; for example, some experience "sudden gains" in which they manifest a significant decrement in symptoms in a brief period of time, whereas others experience steady and gradual improvement over a period of many weeks.
- As described in Section A ("Psychiatric Management"), rating scales can be a useful adjunct to ongoing clinical assessment in evaluating treatment outcome.
- The severity of co-occurring conditions also should be assessed at regular intervals, as treatment of panic disorder can influence co-occurring conditions.

D. CHANGING TREATMENT

If the patient's response to a first-line treatment is unsatisfactory, first consider possible contributing factors.

- Common factors are described in Table 10. These potential impediments to successful treatment should be addressed as early as possible.
- If panic-related concerns are leading the patient to downplay the impact of avoidance or accept functional limitations, the patient should be encouraged to think through the costs and benefits of accepting versus treating functional limitations.
- Clinicians should aim for remission whenever feasible rather than view partial improvement as a satisfactory outcome.

If the patient's response to a first-line treatment remains unsatisfactory, despite an adequate trial, consider adding or switching to another first-line treatment.

- Decisions about how to address treatment resistance are usually highly individualized and based on clinical judgment, because few studies have tested the effects of specific switching or augmentation strategies.
- Augmentation is generally a reasonable approach if some significant benefits were observed with the original treatment. For example, a second pharmacological agent may be added (e.g., add a benzodiazepine to an antidepressant), or pharmacotherapy may be combined with psychotherapy or vice versa.
- If the original treatment did not provide a significant alleviation of the patient's symptoms, a switch in treatment may be more useful.

TABLE 10. CLINICAL FACTORS THAT MAY CONTRIBUTE TO UNSATISFACTORY TREATMENT RESPONSE

Underlying untreated medical illness
Interference by co-occurring general medical or psychiatric conditions (including depression and substance use)
Inadequate treatment adherence
Problems in the therapeutic alliance
Presence of psychosocial stressors
Motivational factors
Inability to tolerate treatment

- If the treatment options with the most robust evidence have been unsuccessful (because of either lack of efficacy or patient intolerance to the treatment), other options with some empirical support can be considered (e.g., MAOI, PFPP).
- After first- and second-line treatments and augmentation strategies have been exhausted, less well-supported treatment strategies may be considered. These include monotherapy or augmentation with gabapentin or a second-generation antipsychotic or with a psychotherapy other than CBT or PFPP.

If significant symptoms persist despite a lengthy course of a particular treatment, reassess the treatment plan and consider consultation with another qualified professional.

E. MAINTAINING OR DISCONTINUING TREATMENT

After acute response, maintain treatment for an appropriate time to promote further symptom reduction and decrease risk of recurrence.

- Pharmacotherapy should generally be continued for 1 year or more. Clinical trials suggest that therapeutic effects of antidepressants are maintained for as long as the medication is continued. Clinical experience suggests that many patients can be maintained on stable doses of benzodiazepines for many years with no recurrence of symptoms.
- For patients who receive psychotherapy, maintenance psychotherapy (e.g., monthly "booster" sessions focused on relapse prevention) may help maintain positive response; however, more systematic study on this issue is needed.

Before discontinuing pharmacotherapy, consider factors described in Table 11 as well as the following:

- The decision to discontinue pharmacotherapy should be made collaboratively with the patient.
- Discussion should address possible outcomes of discontinuation, including recurrence of panic symptoms and discontinuation symptoms.

TABLE 11. FACTORS TO CONSIDER BEFORE DISCONTINUING AN EFFECTIVE PHARMACOTHERAPY FOR PANIC DISORDER

The patient's level of motivation
Duration of the patient's symptom stability or remission
Stability of co-occurring conditions
Current or impending psychosocial stressors in the patient's life
Psychosocial supports
Availability of alternative treatments

When discontinuing an effective pharmacotherapy, taper the medication gradually (i.e., over several weeks or months); watch for recurrence; and if necessary, reinitiate the medication at a previously effective dose.

- SSRIs, SNRIs, and TCAs may be tapered by one dosage step every month or two. Under urgent conditions (e.g., the patient is pregnant and the decision is made to discontinue medications immediately), these medications can also be discontinued much more quickly.
- Withdrawal symptoms and symptomatic rebound are common with benzodiazepine discontinuation, can occur throughout the taper, and may be especially severe toward the end of the taper. This argues for tapering benzodiazepines very slowly for patients with panic disorder, probably over 2–4 months and at rates no higher than 10% of the dose per week. CBT may be added to facilitate withdrawal from benzodiazepines.