

Generalized Anxiety Disorder, Panic Disorder, and Social Anxiety Disorder (GAD)



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LEARNING OBJECTIVES

● Upon completion of the chapter, the reader will be able to:

1. Describe pathophysiology of generalized anxiety, panic, and social anxiety disorders (SAD).
2. List common presenting symptoms of generalized anxiety, panic, and SAD.
3. Identify the desired therapeutic outcomes for patients with generalized anxiety, panic, and SAD.
4. Discuss appropriate lifestyle modifications and over-the-counter medication use in these patients.
5. Recommend psychotherapy and pharmacotherapy interventions for patients with generalized anxiety, panic, and SAD.
6. Develop a monitoring plan for anxiety patients placed on specific medications.
7. Educate patients about their disease state and appropriate lifestyle modifications, as well as psychotherapy and pharmacotherapy for effective treatment.

Anxiety disorders

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graph TD; A[Anxiety disorders] --> B[General Anxiety Disorder (GAD)]; A --> C[Panic Disorder (PD)]; A --> D[Social Anxiety Disorder (SAD)]; A --> E[Posttraumatic stress disorder (PTSD)];
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General Anxiety
Disorder
(GAD)

Panic Disorder
(PD)

Social Anxiety
Disorder
(SAD)

Posttraumatic
stress disorder
(PTSD)

Epidemiology and Etiology

Epidemiology:

- Anxiety disorders are among the most frequent mental disorders encountered by clinicians.
- Anxiety disorders are more prevalent among women than men(2:1).
- Prevalence rates across the anxiety spectrum increase from the younger age group (18–29 years) to older age groups (30–44 and 45–59 years); however, rates are substantially lower for those older than age 59 years.

Course of Illness:

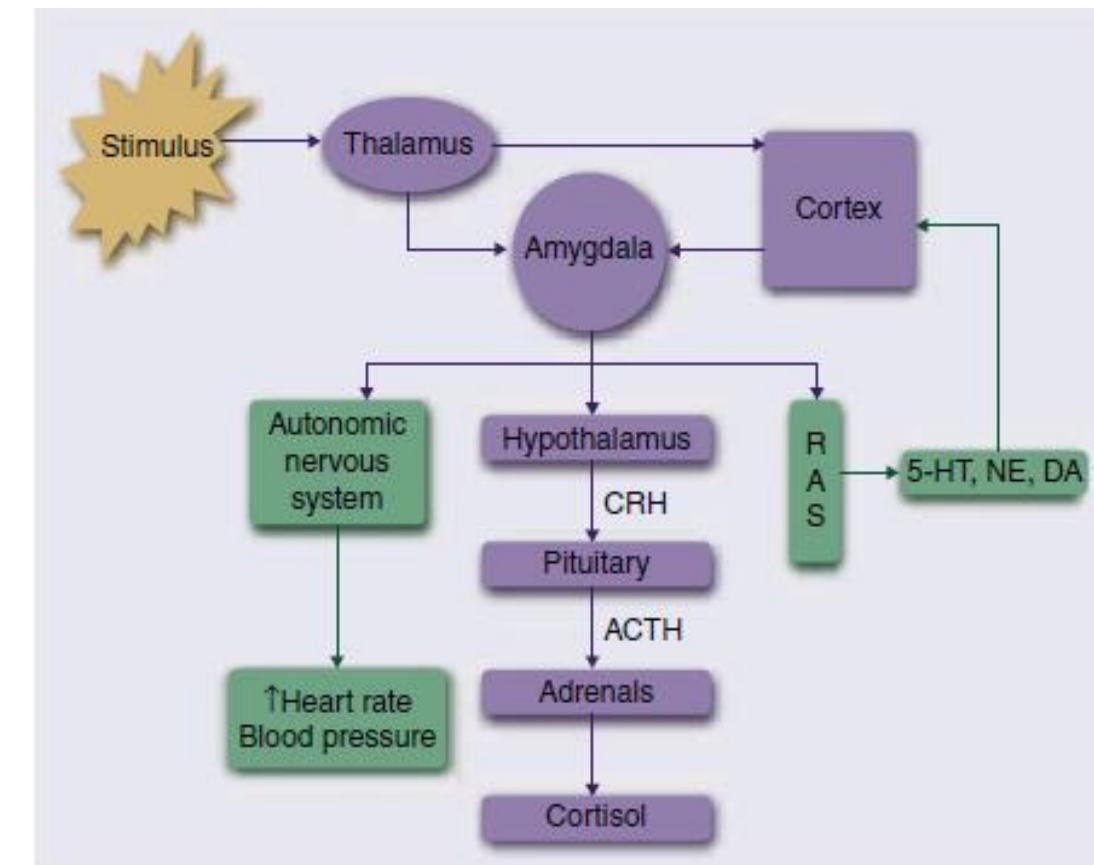
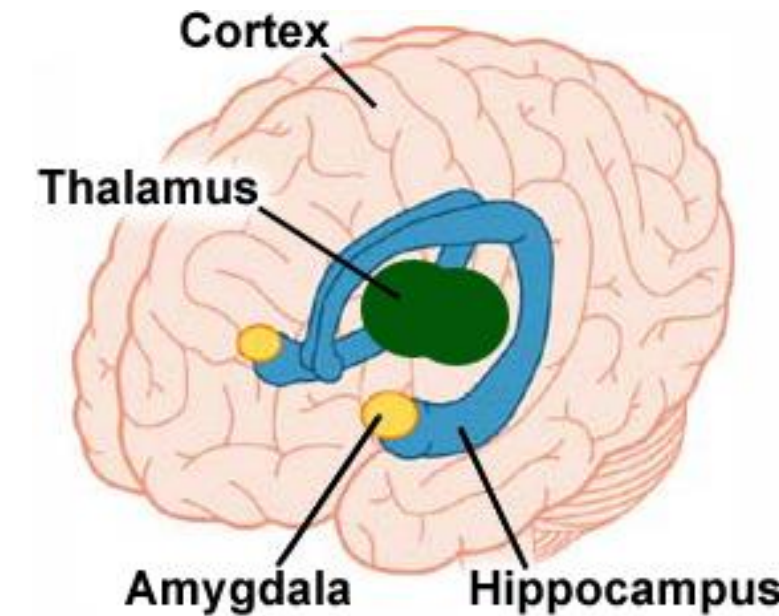
- PTSD, PD, and GAD have median ages of onset of 23, 24, and 31 years, respectively, whereas SAD develops earlier, 13 years.
- Anxiety disorders are chronic, and symptoms tend to wax and wane, with fewer than one-third of patients experiencing spontaneous symptom remission.
- The risk for relapse and recurrence of symptoms is also high for anxiety disorders.(recurrence rates ranged from 39% for SAD , 45% for GAD and 56% of PD,.

Comorbidity

- **More than 90% of individuals** with an anxiety disorder have a lifetime history of one or more other psychiatric disorders.
- **Depression** is the most common comorbidity, followed by alcohol and substance use disorders, as well as other co-occurring anxiety disorders, especially GAD and PD.
- Etiology:
- Both **genetic** and **psychosocial** factors appear to play a role in the initiation and expression of anxiety disorders.
- **Genetics** may create a susceptible phenotype for an anxiety disorder, and an individual's life stressors may play a role in precipitation and continued expression of the anxiety disorder.

PATHOPHYSIOLOGY

- The **thalamus** and **amygdala** are important in the generation of a **normal fear response** and **play a central role in most anxiety disorders**.
- The thalamus provides the first real processing region to organize sensory data obtained from the environment.
- It passes information to higher cortical centers for finer processing and to the amygdala for rapid assessment of highly charged emotional information.
- **Anxiety becomes an anxiety disorder when the fear-response system leads to maladaptive behavior or distress.**



PATHOPHYSIOLOGY

- connections to the reticular activating system (RAS) help to *regulate* arousal, vigilance, and fear.
 - These connections are modulated by *serotonin (5-HT)* and *norepinephrine (NE)*, which have their primary origins in the RAS.
- The amygdala sends projections to the hypothalamus, thus influencing the autonomic nervous system to affect *heart rate*, *blood pressure*, and *stress-associated changes*. It also influences the hypothalamic–pituitary–adrenal (HPA) axis, leading to a *cascade of stress hormones*, Such as cortisol which, if elevated for prolonged periods, can damage the brain and other organs.

General Anxiety Disorder (GAD)

Clinical Presentation and Diagnosis of GAD

Onset is typically in early adulthood.

Symptoms:

- ❑ **Excessive anxiety or worry** involving multiple events or activities occurring more days **for at least 6 months**.
- **Anxiety and worry associated with at least three of the following:**
 - Restlessness , Easily fatigued
 - Poor concentration or mind going blank
 - Irritability, Muscle tension
 - Insomnia or unsatisfying sleep

Nonpharmacologic Therapy

Nonpharmacologic therapy includes:

- ☐ **Psychoeducation:** Patients should be instructed to **avoid stimulating agents**, eg, **caffeine**, amphetamine, **decongestants**, diet pills. **Why ?**
- ☐ **Exercise,**
- ☐ **stress management, and**
- ☐ **psychotherapy.**
 - Cognitive-behavioral therapy (CBT) is the most effective psychological therapy for GAD patients.
- **Combination of CBT and medication** is **superior** to either treatment alone.

Pharmacologic Therapy

- Pharmacologic alternatives:
 - Antidepressants, benzodiazepines, pregabalin, buspirone, hydroxyzine (atarax), and the second-generation antipsychotics (SGAs) have controlled clinical trial data supporting their use in GAD.
- Antidepressants are the drugs of choice for chronic GAD because of:
 - a tolerable side-effect profile;
 - no risk for dependency; and
 - efficacy in common comorbid conditions, including depression, panic, obsessive-compulsive disorder (OCD), and SAD.

Pharmacologic Therapy...

Benzodiazepines

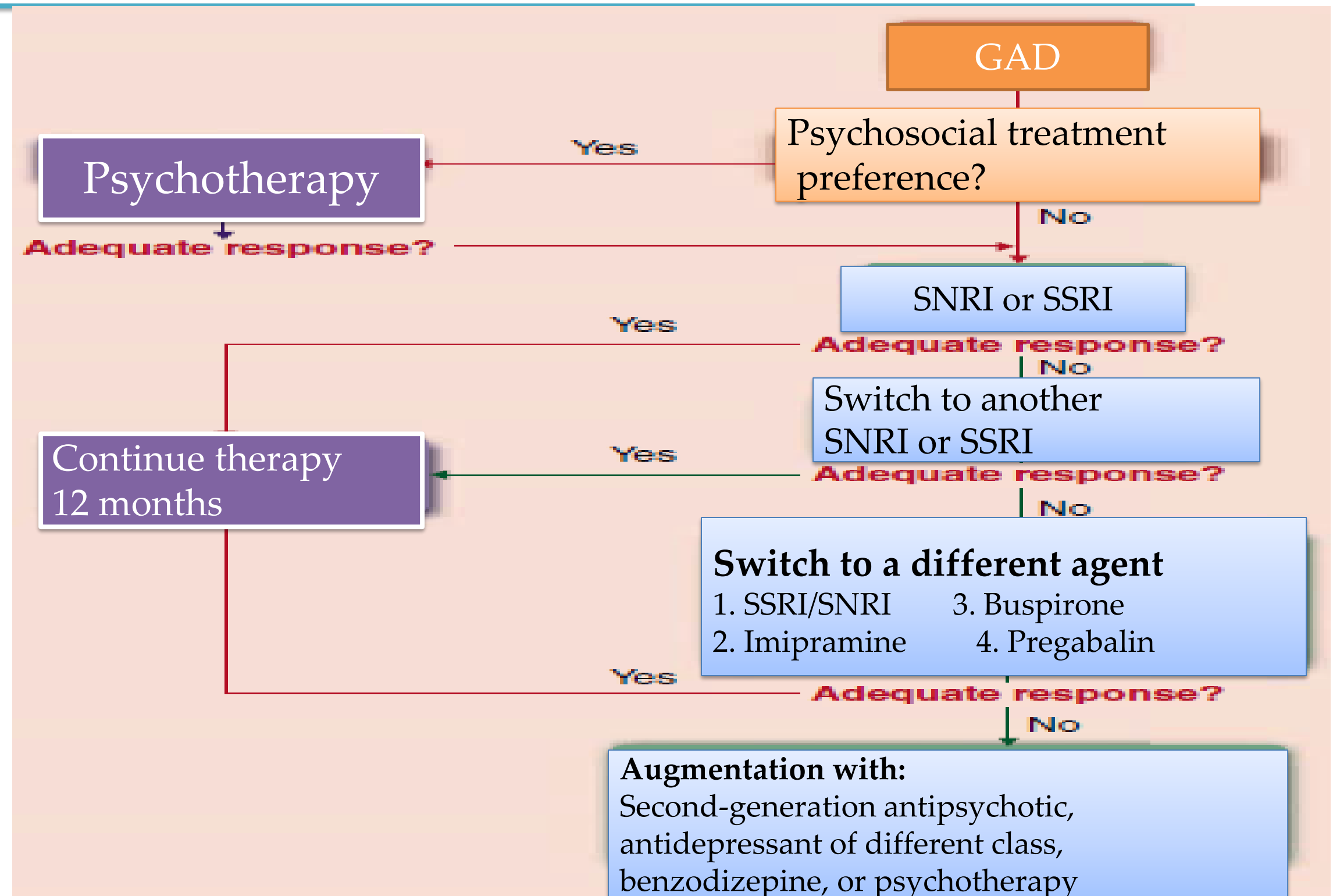
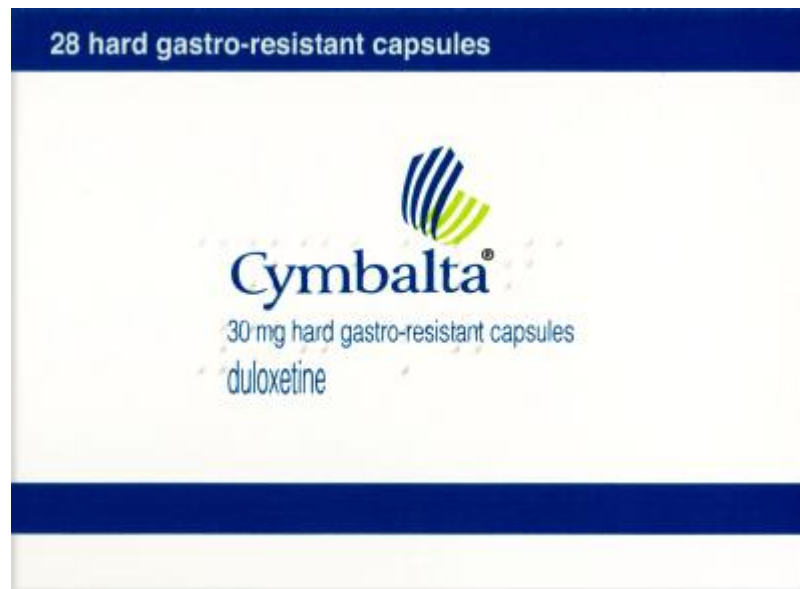
- **Benzodiazepines** remain the most effective and commonly used treatment for short-term management of anxiety when immediate relief of symptoms is desired.
- They are also recommended for intermittent or adjunctive use during GAD exacerbation or for sleep disturbance during the initiation of antidepressant treatment.

Pharmacologic Therapy...

▶ *Alternative Agents*

- Hydroxyzine, **Buspirone** and **pregabalin** are **alternative agents** for patients with **GAD without depression**.
- The SGA quetiapine XR has demonstrated benefit in GAD.
- Patients with GAD should be treated to symptom remission. **Recent guidelines recommend continuing treatment for 1 year** to decrease the risk of relapse.

Treatment algorithm for GAD



Antidepressants

- Antidepressants reduce the psychic symptoms (eg, worry and apprehension) of anxiety with a modest effect on autonomic or somatic symptoms (eg, tremor, rapid heart rate, and/or sweating).
- All antidepressants evaluated provide a similar degree of anxiety reduction. The onset of antianxiety effect is delayed 2 to 4 weeks.
- Selective serotonin reuptake inhibitors (SSRIs) or serotonin-norepinephrine reuptake inhibitors (SNRIs) are usually preferred over tricyclic antidepressants (TCAs) because of improved safety and tolerability.

Antidepressants...

SNRIs:

- **Venlafaxine** and **duloxetine** are approved by **FDA** for the treatment of GAD.
- **The most common side effects reported** in patients with GAD are **nausea, somnolence, dry mouth, dizziness, sweating**, constipation, and **anorexia**.

SSRIs:

- **SSRI** therapy is better tolerated than **TCAs**, and **tolerability** is similar to that of **venlafaxine**.
- **Citalopram** is efficacious in the treatment of **GAD in the elderly**. The SSRIs, **sertraline, fluoxetine**, and **fluvoxamine** have demonstrated **benefits** in **children and adolescents** with GAD

Antidepressants...



Tricyclic Antidepressants:

- **Imipramine** treatment of GAD results in a **higher rate of remission of anxiety symptoms** than treatment with **trazodone or diazepam**.
- TCA use is limited by bothersome adverse effects (eg, **sedation**, **orthostatic hypotension**, **anticholinergic** effects, and **weight gain**).
- TCAs have a **narrow therapeutic index** and are **lethal in overdose** because of **atrioventricular block**.

Benzodiazepines

- **Benzodiazepines** are recommended for **acute treatment** of GAD when short-term(2-4wks) relief is needed, as an **adjunct** during initiation of **antidepressant therapy**, or to **improve sleep**.
- They are **more effective** for **somatic symptoms** (insomnia, restlessness) than **psychic symptoms**.
- Major benzodiazepine disadvantages are :
 - **lack of effectiveness for depression**;
 - **risk for dependency and abuse**; and
 - **potential rebound anxiety**, especially with short-acting benzodiazepines.
- Because **lorazepam** and **oxazepam** **bypass hepatic oxidation**, they are preferred agents for patients **with reduced hepatic function** secondary to aging or disease (eg, **cirrhosis**; **hepatitis B or C** from intravenous drug use).

Table 40–6

Antidepressants Used in the Treatment of Panic and Social Anxiety Disorder^{18,23,42}

Medication Class	Recommended Starting Dose (mg/day)	Usual Therapeutic Dosage Range (mg/day)	Advantages	Disadvantages
SSRIs/SNRIs			SSRIs (in General) Antidepressant activity; antianxiety activity; single daily dosing (all but fluvoxamine); low toxicity; available in generic	SSRIs (in General) Activation; delayed onset of action; may precipitate mania; sexual side effects; GI side effects
Citalopram	10	20–40		
Escitalopram ^b	5–10	10–20		
Fluoxetine ^a	5–10	20–60		
Fluvoxamine	25	100–300		
Paroxetine ^{a,b}	10	20–60		
Sertraline ^{a,b}	25	50–200		
Venlafaxine XR ^{a,b}	37.5	75–225		
TCAs			TCAs (in General) Established efficacy; available in generic	TCAs (in General) Activation; sedation; anticholinergic effects; cardiovascular effects; delayed onset of action; may precipitate mania; sexual side effects; toxic in overdose; weight gain
Clomipramine	25 mg (twice a day)	75–250		
Imipramine ^a	10–25	75–250		
MAOI				
Phenelzine	15	45–90	Antidepressant effects; available in generic	Dietary restrictions; drug interactions; weight gain; orthostasis; may precipitate mania

^aFood and Drug Administration approved for use in panic disorder.^bFood and Drug Administration approved for use in social anxiety disorder.

Table 40–4

Comparison of Benzodiazepines

Drug Name (Brand Name)	Metabolite	Time to Peak Concentration (hours)	Half-Life Range (hours)	Approved Dosage Range (mg/day)	Dose Equivalent (mg)
Alprazolam ^{a,b} (Xanax)		1–2	12–15	1–4 (GAD) 1–10 (PD)	0.5
Lorazepam ^a (Ativan)		2–4	10–20	0.5–10	0.75–1
Oxazepam ^a (Serax)		2–4	5–15	30–120	15
Clonazepam ^b (Klonopin)		1–4	18–50	1–4	0.25
Chlordiazepoxide ^a (Librium)	<i>Desmethyldiazepam</i> <i>Desmethychlordiazepoxide</i> <i>Demoxepam</i> <i>Oxazepam</i>	1–4	5–30 40–120 18 14–95 5–15	25–100	10
Clorazepate ^a (Tranxene)	<i>Desmethyldiazepam</i> <i>Oxazepam</i>	1–2	40–120 5–15	7.5–60	7.5
Diazepam ^a (Valium)	<i>Desmethyldiazepam</i> <i>Oxazepam</i> <i>Temazepam</i>	0.5–2	20–80 40–120 5–15 8–15	2–40	5

^aFood and Drug Administration (FDA) approved for use in generalized anxiety disorder.

PANIC DISORDER

Clinical Presentation and Diagnosis of PD

Recurrent, unexpected panic attacks. Panic attack is an **abrupt surge of intense fear or discomfort peaking within minutes**, and **with four or more** of the following symptoms:

- Palpitations or rapid heart rate
- Sweating
- Trembling or shaking
- Sensation of shortness of breath
- Feeling of choking
- Chest pain or discomfort
- Nausea or abdominal distress
- Feeling dizzy or lightheaded
- Chills or hot flushes
- Paresthesias
- Derealization or depersonalization
- Fear of dying/
- Fear of losing control or “going crazy”

TREATMENT: PANIC DISORDER

General Approach to Treatment:

- Treatment options include **medication**, **psychotherapy**, or a **combination of both**.
- **The acute phase of PD** treatment **lasts about 12 weeks**.
- **Treatment should be continued** to prevent relapse for an additional **12 to 24 months** before attempting discontinuation.
- ...
- Patients with PD **should avoid stimulant agents** (eg, **decongestants**, **diet pills**, and **caffeine**) **that may precipitate a panic attack**.
- CBT generally includes :
 - ❖ **psychoeducation, self-monitoring,**
 - ❖ **countering anxious beliefs, and**
 - ❖ **modification of anxiety-maintaining behaviors.**
- CBT is considered a **first-line treatment of PD**, with **efficacy similar to that of pharmacotherapy**.

Pharmacologic Therapy

- Patients with PD may be treated with SSRIs, SNRIs, TCAs, or MAOIs, as well as benzodiazepines with similar effectiveness, but SSRIs have become the treatment of choice.
- Benzodiazepines often are used concomitantly with antidepressants, especially early in treatment, or as monotherapy to acutely reduce panic symptoms.
- Benzodiazepines are not preferred for long-term treatment but may be used when patients fail several antidepressant trials.

Pharmacotherapy of PD

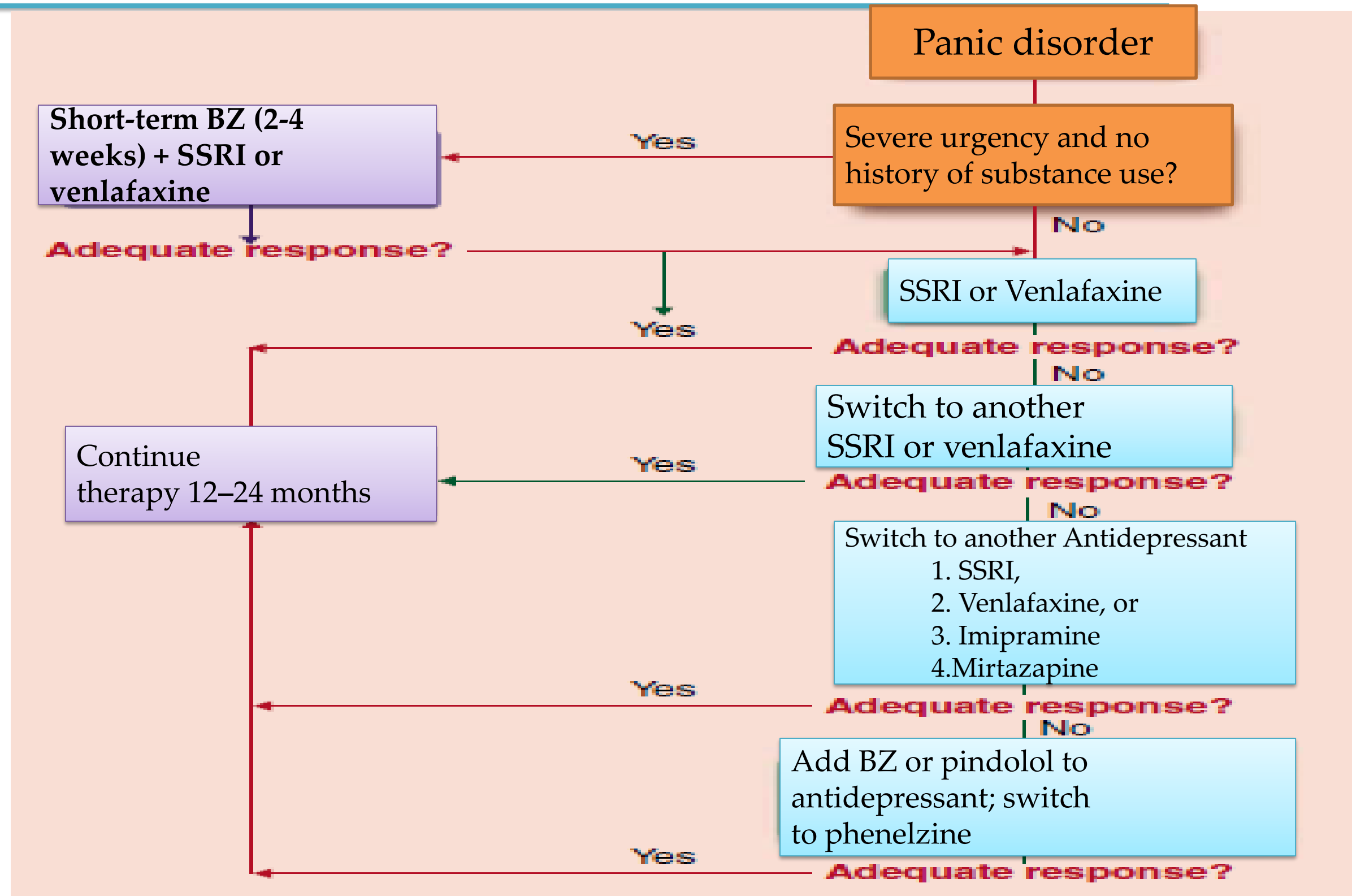


Table 40–6

Antidepressants Used in the Treatment of Panic Disorder^{18,23,42}

Medication Class	Recommended Starting Dose (mg/day)	Usual Therapeutic Dosage Range (mg/day)	Advantages	Disadvantages
SSRIs/SNRIs			SSRIs (in general) Antidepressant activity; antianxiety activity; single daily dosing (all but fluvoxamine); low toxicity; available in generic	SSRIs (in general) Activation; delayed onset of action; may precipitate mania; sexual side effects; GI side effects
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Imipramine ^a	10–25	75–250		
MAOI				
Phenelzine	15	45–90	Antidepressant effects; available in generic	Dietary restrictions; drug interactions; weight gain; orthostasis; may precipitate mania

SOCIAL ANXIETY DISORDER (SAD)

Clinical Presentation of SAD

- Individuals have marked fear or anxiety about one or more **social situations** where they are exposed to .
- **The individual fears** acting in a way or showing anxiety that will be negatively evaluated (ie, embarrassing).
- **Social situations almost always provoke fear or anxiety** and are avoided or undergone with intense fear or anxiety.

Clinical Presentation of SAD

- The fear or anxiety is:
 - ✓ out of proportion to the actual threat posed by the social situation;
 - ✓ persistent, typically lasting for 6 months or more;
 - ✓ causes clinically significant distress or impairment in social, occupational.
 - ✓ not attributable to medication or disease.

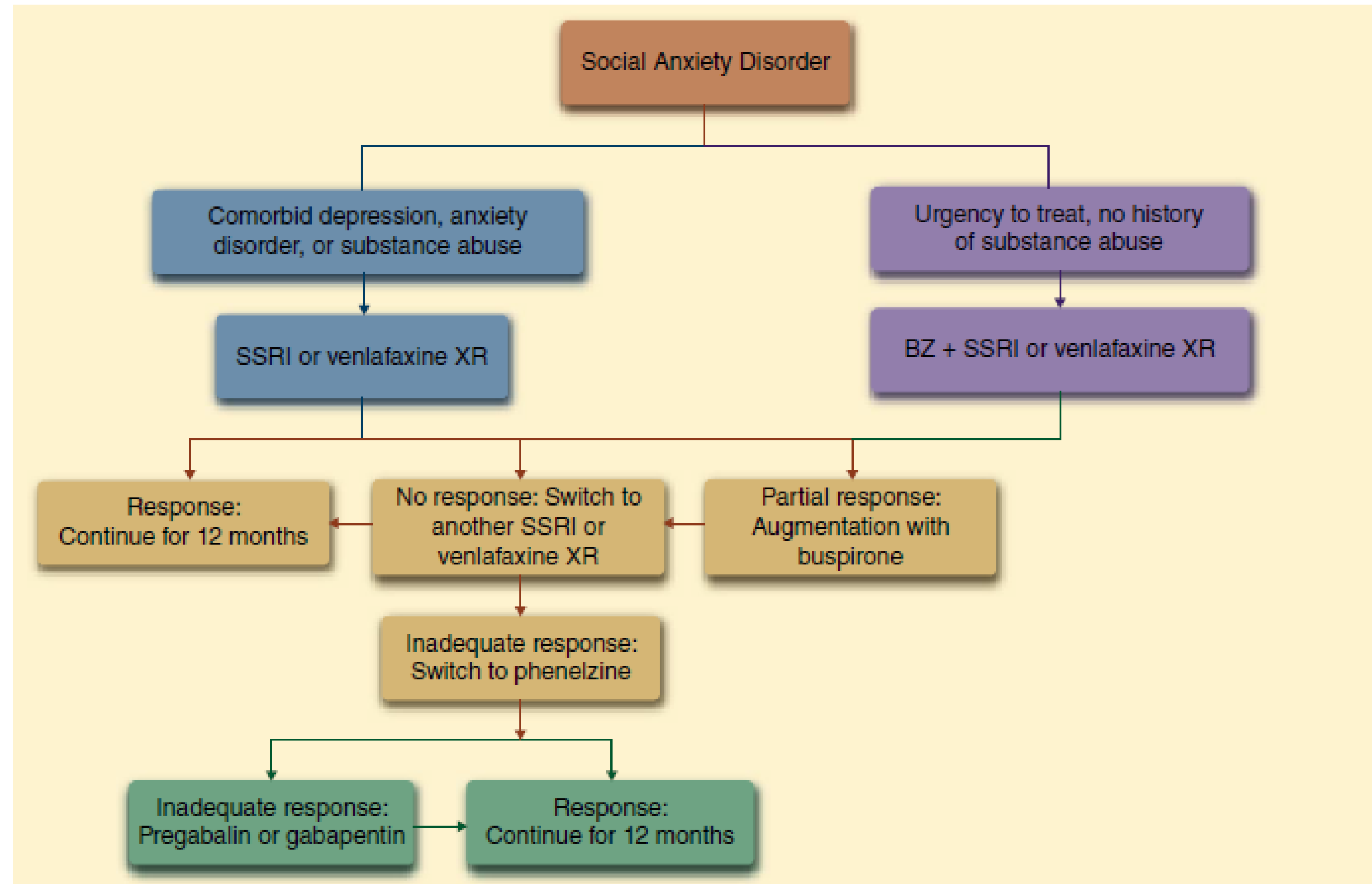
General Approach to Treatment

- Patients with SAD may be managed with pharmacotherapy or psychotherapy.
- Children with SAD should be offered psychotherapy first.
- Pharmacotherapy often is the first choice of treatment owing to relative greater access and reduced cost compared with psychotherapy.

Pharmacologic Therapy

- Several pharmacologic agents have demonstrated effectiveness in SAD, including the SSRIs, venlafaxine, phenelzine, benzodiazepines, gabapentin, and pregabalin, and β -Blockers (propranolol, atenolol; 1 hour before a performance situation).
- SSRIs are considered the drugs of choice based on their tolerability and efficacy for SAD and comorbid depression if present.
- The onset of response for antidepressants may be as long as 8 to 12 weeks. Patients responding to medication should be continued on treatment for at least 1 year.

Algorithm for the pharmacotherapy of SAD



Posttraumatic stress disorder (PTSD)

- Individuals have exposure to a traumatic event (actual or threatened death, serious injury, sexual violence).

Symptoms:

- •• Recurrent, distressing memories of the trauma
- •• Recurrent, disturbing dreams related to the trauma
- •• Reliving the traumatic event
- Reminders of the trauma result in a physiologic reaction and/or psychological distress
 - Irritability, Self-destructive behavior, Hypervigilance, Difficulty concentrating, Sleep disturbances, Isolating from others, loss of interest, negative emotions.

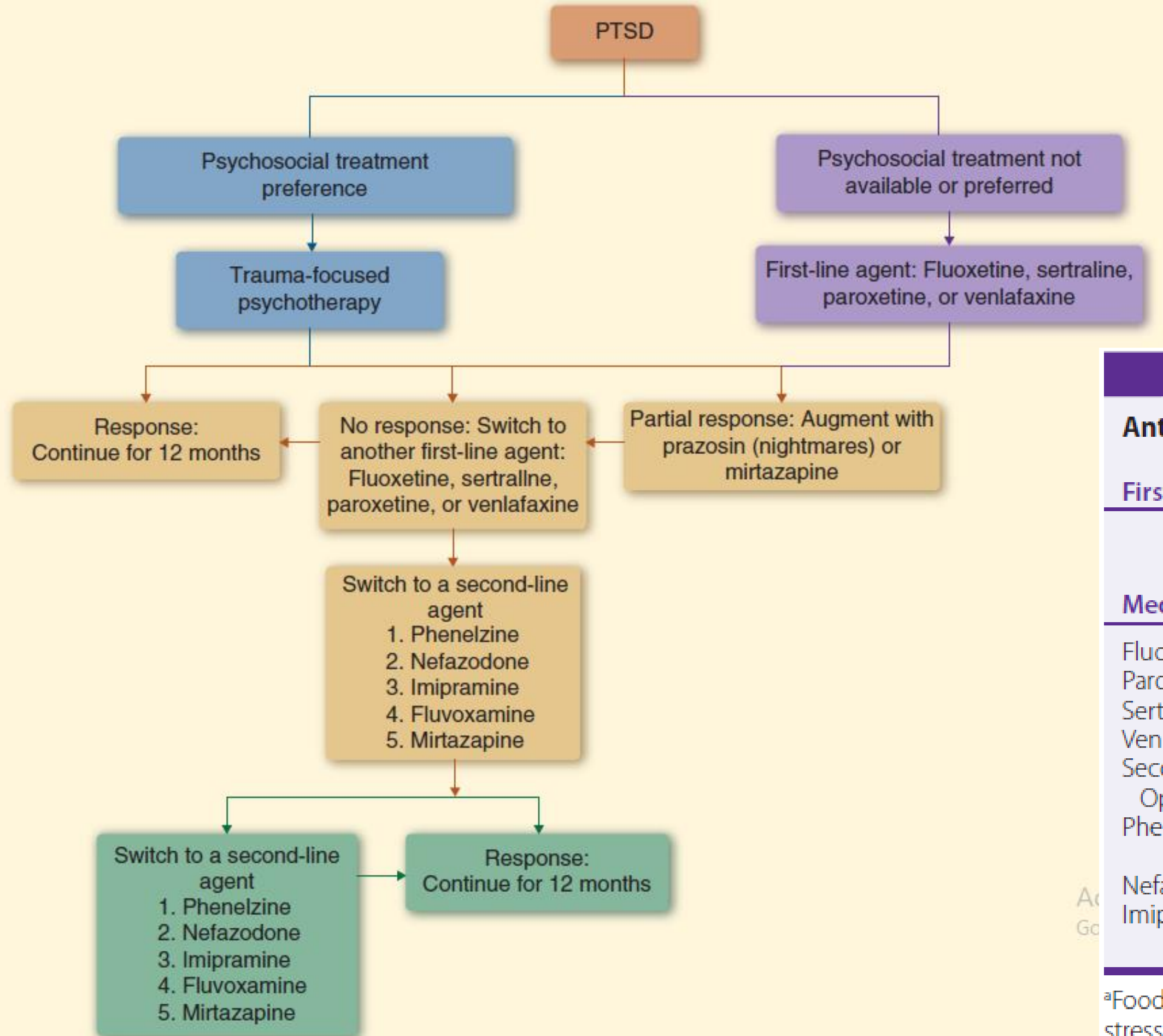


Table 41–6		
Antidepressants for Posttraumatic Stress Disorder ^{2,12,45}		
First-Line Options		
Medication	Recommended Starting Dose (mg/day)	Usual Therapeutic Dosage Range (mg/day)
Fluoxetine	10–20	20–80
Paroxetine ^a	10–20	20–60
Sertraline ^a	25	50–200
Venlafaxine XR	37.5	75–225
Second-Line Options		
Phenelzine	15 three times daily	15 mg daily; 60–90 in divided doses
Nefazodone	25–100 twice daily	150–600 in 2 divided doses
Imipramine	25–75	100–300 in 1 or 2 divided doses

^aFood and Drug Administration approved for use in posttraumatic stress disorder. XR=extended release