EFFEXOR XR is available in different dosage strengths (37.5 mg, 75 mg, and 150 mg).

**Indications**

EFFEXOR XR Extended-Release Capsules are prescription medicine indicated for the treatment, in adults, of Depression, Generalized Anxiety Disorder (GAD), Social Anxiety Disorder (SAD), and Panic Disorder (PD) with or without agoraphobia.

**Important Safety Information**

**Suicidality and Antidepressant Drugs**

Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, teens, and young adults. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. EFFEXOR XR is not approved for use in children and teens.

- Do not take EFFEXOR XR if you currently take, or have taken within the last 14 days, any medicine known as an MAOI such as linezolid or methylene blue. Do not take an MAOI within 7 days of stopping EFFEXOR XR. Ask your doctor or pharmacist if you are not sure if your medicine is an MAOI.
- All patients taking antidepressants should be watched closely for signs that their condition is getting worse or that they are becoming suicidal, especially when they first start therapy, or when their dose is increased or decreased. Patients should also be watched for becoming agitated, irritable, hostile, aggressive, impulsive, or restless. Such symptoms should be reported to the patient's doctor right away.
- Before starting EFFEXOR XR, tell your doctor if you’re taking or plan to take any prescription or over-the-counter drugs, including migraine headache medication, herbal preparations, and nutritional supplements, to avoid a potentially life-threatening condition.
- EFFEXOR XR may raise blood pressure in some patients. Your blood pressure should be controlled before starting treatment and should be monitored regularly.

Please see Important Safety Information on page 5 and accompanying Full Prescribing Information, including BOXED WARNING, and Medication Guide.
Your Personal Experience With EFFEXOR XR

This diary is a place to keep track of your experience while taking EFFEXOR XR. The information you record will help you see how you are doing with your treatment plan over time. Use it to write down your thoughts, any side effects you might be experiencing, or any questions you may have for your doctor.

Remember, it’s important that you take your medication as directed. Do not stop taking your medication without speaking to your doctor first.

### MONTH 1

Sticking with your treatment plan may help with your symptoms.

<table>
<thead>
<tr>
<th>The week of</th>
<th>Learn more about your treatment at <a href="http://www.EffexorXR.com">www.EffexorXR.com</a>.</th>
</tr>
</thead>
<tbody>
<tr>
<td>The week of</td>
<td>It may be time to refill your prescription.</td>
</tr>
<tr>
<td></td>
<td>Do you have your Choice Card for valuable monthly savings?</td>
</tr>
</tbody>
</table>

Select Important Safety Information (continued)

- Taking EFFEXOR XR with aspirin, nonsteroidal anti-inflammatory drugs, warfarin, or other drugs that affect coagulation may increase the risk of bleeding events.

- Some people are at risk for visual problems such as eye pain, changes in vision, or swelling or redness around the eye. You may want to undergo an eye examination to see if you are at risk and get preventative treatment if you are.

Please see Important Safety Information on page 5 and accompanying Full Prescribing Information, including BOXED WARNING, and Medication Guide.
### MONTH 2

Make sure you tell your doctor about any new prescription medications, over-the-counter medications, or herbal remedies you may be taking.

<table>
<thead>
<tr>
<th>The week of</th>
<th>Ensure your doctor is writing brand-name EFFEXOR XR to take advantage of the Choice Card. Visit EffexorXR.com/resources to download a tip sheet on how to request EFFEXOR XR.</th>
</tr>
</thead>
<tbody>
<tr>
<td>The week of</td>
<td></td>
</tr>
<tr>
<td>The week of</td>
<td></td>
</tr>
<tr>
<td>The week of</td>
<td>Is it time for another refill? To get the most from your treatment, always take your medicine as prescribed.</td>
</tr>
</tbody>
</table>

#### Select Important Safety Information (continued)

- When people suddenly stop using or quickly lower their daily dose of EFFEXOR XR, discontinuation symptoms may occur. Talk to your doctor before discontinuing or reducing your dose of EFFEXOR XR.
- Pregnant or nursing women shouldn’t take any antidepressant without consulting their doctor.
- Until you see how EFFEXOR XR affects you, be careful doing such activities as driving a car or operating machinery. Avoid drinking alcohol while taking EFFEXOR XR.

Please see Important Safety Information on page 5 and accompanying Full Prescribing Information, including BOXED WARNING, and Medication Guide.
MONTH 3

Get the most out of your therapy by keeping the lines of communication open with your doctor. During your next appointment, discuss any questions you’ve written down.

<table>
<thead>
<tr>
<th>The week of</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>☐ SUN ☐ MON ☐ TUE ☐ WED ☐ THU ☐ FRI ☐ SAT</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>The week of</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>☐ SUN ☐ MON ☐ TUE ☐ WED ☐ THU ☐ FRI ☐ SAT</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>The week of</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>☐ SUN ☐ MON ☐ TUE ☐ WED ☐ THU ☐ FRI ☐ SAT</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>The week of</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>☐ SUN ☐ MON ☐ TUE ☐ WED ☐ THU ☐ FRI ☐ SAT</td>
</tr>
</tbody>
</table>

Learn more about your therapy and take an active role in your treatment!
Visit EffexorXR.com/resources to find other useful tools, like a Doctor Discussion Guide, that may help you.

**Select Important Safety Information (continued)**

- In clinical studies, the most common side effects with EFFEXOR XR (reported in at least 10% of patients and at least twice as often as with placebo) were constipation, dizziness, dry mouth, insomnia, loss of appetite, nausea, nervousness, sexual side effects, sleepiness, sweating, and weakness.

Please see Important Safety Information on page 5 and accompanying Full Prescribing Information, including BOXED WARNING, and Medication Guide.
Indications

EFFEXOR XR Extended-Release Capsules are prescription medicine indicated for the treatment, in adults, of Depression, Generalized Anxiety Disorder (GAD), Social Anxiety Disorder (SAD), and Panic Disorder (PD) with or without agoraphobia.

Important Safety Information

Suicidality and Antidepressant Drugs
Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, teens, and young adults. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. EFFEXOR XR is not approved for use in children and teens.

- Do not take EFFEXOR XR if you currently take, or have taken within the last 14 days, any medicine known as an MAOI such as linezolid or methylene blue. Do not take an MAOI within 7 days of stopping EFFEXOR XR. Ask your doctor or pharmacist if you are not sure if your medicine is an MAOI.
- All patients taking antidepressants should be watched closely for signs that their condition is getting worse or that they are becoming suicidal, especially when they first start therapy, or when their dose is increased or decreased. Patients should also be watched for becoming agitated, irritable, hostile, aggressive, impulsive, or restless. Such symptoms should be reported to the patient's doctor right away.
- Before starting EFFEXOR XR, tell your doctor if you're taking or plan to take any prescription or over-the-counter drugs, including migraine headache medication, herbal preparations, and nutritional supplements, to avoid a potentially life-threatening condition.
- EFFEXOR XR may raise blood pressure in some patients. Your blood pressure should be controlled before starting treatment and should be monitored regularly.
- Taking EFFEXOR XR with aspirin, nonsteroidal anti-inflammatory drugs, warfarin, or other drugs that affect coagulation may increase the risk of bleeding events.
- Some people are at risk for visual problems such as eye pain, changes in vision, or swelling or redness around the eye. You may want to undergo an eye examination to see if you are at risk and get preventative treatment if you are.
- When people suddenly stop using or quickly lower their daily dose of EFFEXOR XR, discontinuation symptoms may occur. Talk to your doctor before discontinuing or reducing your dose of EFFEXOR XR.
- Pregnant or nursing women shouldn't take any antidepressant without consulting their doctor.
- Until you see how EFFEXOR XR affects you, be careful doing such activities as driving a car or operating machinery. Avoid drinking alcohol while taking EFFEXOR XR.
- In clinical studies, the most common side effects with EFFEXOR XR (reported in at least 10% of patients and at least twice as often as with placebo) were constipation, dizziness, dry mouth, insomnia, loss of appetite, nausea, nervousness, sexual side effects, sleepiness, sweating, and weakness.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.
START SAVING ON YOUR MEDICATION*:

- If you do not already have an EFFEXOR XR Choice Card, request one by visiting www.EffexorXR.com or calling 1-855-488-0749
- If you request your EFFEXOR XR Choice Card online, you will be able to print a temporary card and start saving right away. Otherwise, you will receive your card by mail within 7 to 10 business days
- Take your brand-name EFFEXOR XR prescription and EFFEXOR XR Choice Card to any participating pharmacy
- Use your card to continue saving on brand-name EFFEXOR XR through December 31, 2016

Terms and Conditions

By using the EFFEXOR XR Choice Card (the “Card”), you attest that you meet the eligibility criteria and will comply with the Terms and Conditions described below:

You will pay $4 for a 30-day supply (30 tablets) if:
- you use commercial/private insurance and your out-of-pocket expense for a 30-day supply of brand-name EFFEXOR XR is $130 or less.

You will pay $30 for a 30-day supply (30 tablets) if:
- you do not use prescription health coverage to purchase your brand-name EFFEXOR XR under this program or you use commercial/private insurance and your out-of-pocket expense for a 30-day supply of brand-name EFFEXOR XR is $130 or more. In addition:
  a) Medicare Part D patients may participate in this Card Program, but cannot use any part of their Medicare Part D prescription benefit for EFFEXOR XR during the term of this offer
  b) Out-of-pocket expenditures under this Card Program cannot be applied towards a patient’s Medicare Part D true out of pocket (TrOOP) expenses
  c) Patients participating in this category cannot seek reimbursement for a purchase of EFFEXOR XR from any third party insurance entity during the term of this offer

This offer is not valid for prescriptions that are eligible to be reimbursed, in whole or in part, by Medicaid or other federal or state healthcare programs (including any state prescription drug assistance programs and the Government Health Insurance Plan available in Puerto Rico [formerly known as “La Reforma de Salud”]).

For all eligible patients, you can only qualify for up to $2500 of savings per calendar year. After a maximum of $2500, you will pay usual monthly out-of-pocket costs.

This Card cannot be combined with any other rebate/coupon, free trial, discount, prescription savings card, or similar offer for the specified prescription.

The Card will be accepted only at participating pharmacies.

This Card is not health insurance.

Offer valid only in the U.S. and Puerto Rico, but not for Massachusetts residents or where otherwise prohibited by law.

The Card is limited to 1 use per person per month during this offering period and is not transferable. It is illegal to sell, purchase, trade, or counterfeit, or offer to sell, purchase, trade, or counterfeit this Card.

Pfizer reserves the right to rescind, revoke or amend the Card Program without notice at any time.

You must be 18 or older to participate in this Program.

Card Program expires December 31, 2016.

No membership fees.

For questions about this card, please call 1-855-488-0749, visit EffexorXR.com or write to the address below.

For reimbursement when using mail order, mail copy of original pharmacy receipt (cash register receipt NOT valid) with product name, date and amount circled to:

EFFEXOR XR Choice Card
14001 Weston Parkway, Suite 103
Cary, NC 27513-9967

Be sure to include a copy of the front of your Choice Card, your name and mailing address.

If you do not wish to receive any more information about EFFEXOR XR, please call 1-877-777-3543 or write to: Pfizer, Attn: EFFEXOR XR, PO Box 29387, Mission, KS 66201-9619

*Terms and conditions apply. See below for details.
**Effexor XR**

**(venlafaxine hydrochloride)**

**Extended-Release Capsules**

Rx only

---

**DESCRIPTION**

**Suicidality and Antidepressant Drugs**

Suicidality and antidepressant drugs increased the risk compared to placebo of suicidal thinking and behavior (suicidal ideation, suicide attempt, and suicide) in short-term studies of children, adolescents, and young adults with major depressive disorder and other psychiatric disorders. Anyone considering the use of Effexor XR or any other antidepressant in a child, adolescent, or young adult must balance this risk with the clinical need. Short-term studies did not show an increase in the risk of suicidality with antidepressant use compared to placebo. However, Effexor XR is not approved for use in pediatric patients. (See WARNINGS: Clinical Worsening and Suicide Risk, PRECAUTIONS: Information for Patients, and PRECAUTIONS: Pediatric Use)

---

**CLINICAL PHARMACOLOGY**

**Pharmacodynamics**

The mechanism of the antidepressant action of venlafaxine in humans is believed to be associated with its potent, rapid-acting inhibition of neuronal reuptake of serotonin and norepinephrine. Effexor XR is a potent inhibitor of serotonin and norepinephrine transporters and the only extensively metabolized compound. O-desmethylvenlafaxine (ODV) is the only active metabolite. Venlafaxine, venlafaxine O-desmethyl metabolites, and ODV have virtually equivalent plasma protein binding (approximately 99%) and venlafaxine has the empirical formula of C_{19}H_{25}NO_{4}Cl. Its molecular weight is 313.17. The structural formula is shown below:

![Venlafaxine hydrochloride](attachment:image)

Venlafaxine hydrochloride is a white to off-white crystalline solid with a solubility of 572 mg/mL in water (adjusted to pH 3.0 with sodium chloride). Its octanol-water (0.2 mM sodium chloride) partition coefficient coefficient is 0.43.

Effexor XR is formulated as an extended-release capsule for once-a-day oral administration. Drug release is controlled by diffusion through a semipermeable chloride ion-concentration driven ion-exchange fiber. Effexor XR contains venlafaxine hydrochloride equivalent to 75 mg, 150 mg, or 225 mg venlafaxine. Inactive ingredients consist of cellulose, titanium dioxide, red iron oxide, and silicon dioxide.

---

**PHARMACOKINETICS**

**Pharmacoynamics**

The pharmacokinetics of venlafaxine are linear, predictable, and dose proportional over the range of 75 to 450 mg. Mean steady-state plasma clearance of venlafaxine and ODV is 1.5±0.6 L/h/kg, respectively; apparent elimination half-lives are 5±3±3 h and 5.7±1.8 h, respectively. Venlafaxine and ODV are minimally bound at therapeutic concentrations to plasma proteins (27% and 30%, respectively).

---

**Absorption**

Venlafaxine is well absorbed and extensively metabolized in the liver. O-desmethylvenlafaxine (ODV) is the only major active metabolite. On the basis of mass balance studies, at least 92% of a single oral dose of venlafaxine is absorbed. The absolute bioavailability of ODV is about 45%. Administration of Effexor XR (150 mg q4h) generally resulted in lower Cmax (150 mg/mL for venlafaxine and 260 mg/mL for ODV) and later Tmax (5.5 hours for venlafaxine and 9 hours for ODV) than for Effexor (immediate release) (Cmax = 4.2 for immediate release 75 mg 12 hours 225 mg/mL for venlafaxine, and 290 mg/mL for ODV, Tmax = 3 hours for venlafaxine and 3 hours for ODV). ODV, LDV, and their more active metabolites, however, are not expected to be clinically important because the sum of venlafaxine and ODV is similar in the two groups and venlafaxine and ODV are pharmacologically approximately equivalent potent antidepressants.

---

Approximately 87% of a venlafaxine dose is recovered in the urine within 48 hours as unchanged venlafaxine (5%), unconjugated ODV (29%), conjugated ODV (28%), or other minor inactive metabolites (27%). Renal elimination of venlafaxine and its metabolites is thus the primary route of excretion.

---

**Special Populations**

Age and Gender: A population pharmacokinetic analysis of 404 venlafaxine-treated patients from two studies indicated that gender did not influence Cmax or T1/2 and that Cmax and T1/2 increased with age. The mean Cmax and T1/2 in patients with low CYP2D6 levels (“poor metabolizers”) had increased levels of venlafaxine and reduced levels of ODV compared to people with normal CYP2D6 (“extensive metabolizers”). The differences between the CYP2D6 poor and extensive metabolizers, however, are not expected to be clinically important because the sum of venlafaxine and ODV is similar in the two groups and venlafaxine and ODV are pharmacologically approximately equivalent potent antidepressants.

---

**Dosage and Administration**

**Pharmacodynamics**

**Pharmacokinetics**

In a 2-week period: depressed mood, markedly diminished interest or pleasure in usual activities, significant change in weight and/or appetite, insomnia or hypersomnia, psychomotor agitation or retardation, increased fatigue, decreased sex drive or sexual dysfunction, anorexia, unexplained aches, dizziness, weakness, nervousness, and problems. Effexor XR is significantly more effective than placebo in the treatment of major depressive disorder (MDD). The efficacy of Effexor XR in the treatment of major depressive disorder was established in controlled trials in adult outpatients meeting DSM-III-R or DSM-IV criteria for major depressive disorder.

A 12-week utilizing Effexor XR doses in a range of 75 to 225 mg/day (mean dose for completers was 150 mg/day). A 12-week study utilizing Effexor XR doses in a range of 75 to 225 mg/day (mean dose for completers was 177 mg/day) both demonstrated superiority of Effexor XR over placebo on the HAM-D total score, HAM-D-24 total score, HAM-D-17 total score, and the CGI Improvement item, and the CGI Global Improvement item. In both studies, Effexor XR was also significantly better than placebo for certain factors of the HAM-D, including the anxiety/somatization factor, the cognitive disturbance factor, and the retardation factor, as well as for the primary factor, a 4-week of treatment in patients meeting DSM-III-R criteria for major depressive disorder with melancholia utilizing Effexor XR (immediate release) in a range of 150 to 375 mg/day (1.5-dose) demonstrated superiority of Effexor over placebo on the HAM-D total score.

**Examination of subsets of the population studied did not reveal any differential responsiveness on the basis of gender.**

In a longer-term trial, adult outpatients meeting DSM-IV criteria for major depressive disorder who had responded during an 8-week open trial on Effexor XR (75, 150, or 225 mg, qAM) were randomized to continuation of their Effexor XR dose or to placebo, for up to 26 weeks of observation for relapse. Response during the open phase was defined as a ≥ 50% reduction in the HAM-D total score at the day 58 evaluation. Relapse during the double-blind phase was defined as: (1) a reappearance of major depressive disorder; or (2) in a subset of patients, the HAM-D total score ≥ 20. In those patients, the CGI Severity of Illness items were rated “4” by the investigator or “5” by the patient. Patients who received Effexor XR were significantly less likely to relapse than those receiving placebo. In a second longer-term trial, adult outpatients meeting DSM-IV criteria for major depressive disorder, relapse rate was reduced by about 40% although clearance was unchanged in patients with renal impairment (GR=10 to 70 mL/min) compared to normal subjects. In dialysis patients, ODV elimination half-life was prolonged by about 142% and clearance was reduced by about 56% compared to normal subjects. A large degree of interindividual variability was noted. Dosage adjustment is necessary in these patients (see DOSAGE AND ADMINISTRATION).

**Clinical Trials**

**Major Depressive Disorder**

The efficacy of Effexor XR (venlafaxine hydrochloride) extended-release capsules as a treatment for major depressive disorder was established in 8- and 12-week double-blind, randomized placebo-controlled, flexible-dose studies in adult outpatients meeting DSM-III-R or DSM-IV criteria for major depressive disorder.

In a 12-week study utilizing Effexor XR doses in a range of 75 to 225 mg/day (mean dose for completers was 150 mg/day). A 12-week study utilizing Effexor XR doses in a range of 75 to 225 mg/day (mean dose for completers was 177 mg/day) both demonstrated superiority of Effexor XR over placebo on the HAM-D total score, HAM-D-24 total score, HAM-D-17 total score, and the CGI Improvement item, and the CGI Global Improvement item. In both studies, Effexor XR was also significantly better than placebo for certain factors of the HAM-D, including the anxiety/somatization factor, the cognitive disturbance factor, and the retardation factor, as well as for the primary factor, a 4-week of treatment in patients meeting DSM-III-R criteria for major depressive disorder with melancholia utilizing Effexor XR (immediate release) in a range of 150 to 375 mg/day (1.5-dose) demonstrated superiority of Effexor over placebo on the HAM-D total score.
The efficacy of Effexor XR (immediate release) in the treatment of major depressive disorder in adult inpatients meeting diagnostic criteria for major depressive disorder with melancholia was established in a 4-week controlled trial (see Clinical Trials). The safety and efficacy of Effexor XR in hospitalized depressed patients have not been adequately studied.

The efficacy of Effexor XR in maintaining a response in major depressive disorder for up to 26 weeks following 8 weeks of acute treatment was demonstrated in a placebo-controlled trial. The efficacy of Effexor XR (immediate release) was re-evaluated in a 6-month extension trial (one of several) with recurrent major depressive disorder (MDD) patients who had been evaluated in the 8-week controlled trial and continued to be improved during an initial 26 weeks of treatment and were then followed for a period of up to 52 weeks (referred to as the 6-month extension in Clinical Trials). Nevertheless, the physician who elects to use Effexor/Effexor XR for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient (see DOSAGE AND ADMINISTRATION).

Generalized Anxiety Disorder Effexor XR is indicated for the treatment of Generalized Anxiety Disorder (GAD) as defined in DSM-IV. Anxiety or tension associated with the stress of everyday life usually does not require treatment with an anxiolytic. Exposure to the feared situation almost invariably provokes anxiety, which may approach the intensity of a panic attack. The feared situations are avoided or endured with intense anxiety or distress. The avoidance, avoidance anticipation, or distress in the feared situation(s) interferes significantly with the person's normal routine occupational or academic functioning, or social activities or relationships, or there is a marked distress about having the phobia. Lesser degrees of performance anxiety or shyness generally do not require psychopharmacological treatment.

The efficacy of Effexor XR in the treatment of Generalized Anxiety Disorder was established in four 12-week and one 6-month placebo-controlled trials with adult outpatients (see Clinical Trials). Although the effectiveness of Effexor XR has been demonstrated in a 6-month clinical trial in patients with GAD, the physician who elects to use Effexor XR for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient (see DOSAGE AND ADMINISTRATION).

Social Anxiety Disorder Effexor XR is indicated for the treatment of Social Anxiety Disorder, also known as Social Phobia, as defined in DSM-IV (295.89).

Panic Disorder Effexor XR is indicated for the treatment of panic disorder, with or without agoraphobia, as defined in DSM-IV. Panic disorder is characterized by the occurrence of discrete periods of intense fear or discomfort in which 4 or more of the following symptoms develop abruptly and reach a peak within 10 minutes: palpitations, pounding heart, or accelerated heart rate; sweating; trembling or shaking; sensations of shortness of breath or smothering; sensations of chills or warmth;feelings of impending doom; sensations of loss of control or unreality; fear of dying; nausea; vomiting; diarrhea; attacks of irritability, unusual changes in behavior, and the other symptoms described above, as well as the emergence of serotonin syndrome. The feared situations are avoided or endured with intense anxiety or distress. The avoidance, avoidance anticipation, or distress in the feared situation(s) interferes significantly with the person's normal routine occupational or academic functioning, or social activities or relationships, or there is a marked distress about having the phobia. Lesser degrees of performance anxiety or shyness generally do not require psychopharmacological treatment.

Panic disorder (DSM-IV) is characterized by the occurrence of recurrent, unexpected panic attacks, i.e., a discrete period of intense fear or discomfort, in which 4 or more of the following symptoms develop abruptly and reach a peak within 10 minutes: palpitations, pounding heart, or accelerated heart rate; sweating; trembling or shaking; sensations of shortness of breath or smothering; sensations of chills or warmth; feelings of impending doom; sensations of loss of control or unreality; fear of dying; nausea; vomiting; diarrhea; attacks of irritability, unusual changes in behavior, and the other symptoms described above, as well as the emergence of serotonin syndrome. The feared situations are avoided or endured with intense anxiety or distress. The avoidance, avoidance anticipation, or distress in the feared situation(s) interferes significantly with the person's normal routine occupational or academic functioning, or social activities or relationships, or there is a marked distress about having the phobia. Lesser degrees of performance anxiety or shyness generally do not require psychopharmacological treatment.

The concomitant use of Effexor XR with MAO Is intended to treat psychiatric disorders is contraindicated. Effexor XR should not be used concomitantly with MAO Is. Effexor XR should be discontinued at least 14 days before initiating treatment with MAO Is, and MAO Is should be discontinued at least 14 days before initiating treatment with Effexor XR. (see CONTRAINDICATIONS AND DOSAGE AND ADMINISTRATION).

Screening Patients for Bipolar Disorder A complete initial psychiatric examination, including a thorough psychiatric, physical, and drug history, and the use of an initial brief screening tool, should be used to identify patients who are at risk for bipolar disorder. Additional screening should be used in high-risk populations, such as those with a family history of bipolar disorder or a history of substance abuse. Screening may also be useful as part of ongoing risk assessment and management in the treatment of psychiatric disorders. In patients with suspected bipolar disorder, the symptoms should be monitored carefully. The diagnosis of bipolar disorder should be confirmed by longitudinal assessment of symptoms, and other illnesses that may present with similar symptoms, especially if these symptoms are severe, abrupt in onset, or not part of the patient's presenting symptoms. If the decision has been made not to continue treatment, medication should be tapered, as rapidly as is feasible, but with careful consideration of the potential for discontinuation reactions. (see DOSAGE AND ADMINISTRATION, Discontinuation of Treatment with Effexor XR, for a description of the risks of discontinuation of Effexor XR).

SSRIs should not be used as a monotherapy for the treatment of major depressive disorder in pediatric patients under the age of 18. When concomitant antidepressants are used with SSRIs in pediatric patients, the risk of suicidality is a concern (see CONTRAINDICATIONS AND DOSAGE AND ADMINISTRATION). Concomitant use of Effexor XR with other antidepressants or mood stabilizing agents that are known to increase suicidality is not recommended. For patients taking Effexor XR with other antidepressants or mood stabilizing agents, the patient should be monitored carefully. Efficacy and safety of Effexor XR in the treatment of major depressive disorder in pediatric patients have not been established.

The efficacy of Effexor XR in the treatment of Major Depressive Disorder (MDD) was established in a total of 295 short-term trials (median duration of 2 months) of 11 antidepressant drugs in children, adolescents, adults, and elderly patients. The use of MAO Is intended to treat psychiatric disorders with Effexor XR or within 7 days of stopping treatment with Effexor XR is contraindicated. (see CONTRAINDICATIONS AND DOSAGE AND ADMINISTRATION). Effexor XR should not be used concomitantly with MAO Is. Effexor XR should be discontinued at least 14 days before initiating treatment with MAO Is, and MAO Is should be discontinued at least 14 days before initiating treatment with Effexor XR.

Sustained increases of SDBP could have adverse consequences. Cases of elevated blood pressure requiring therapy have been reported in clinical trials. In premarketing panic disorder studies up to 12 weeks, 0.5% (5/1001) of the Effexor XR-treated patients and 0.4% (4/980) of the placebo-treated patients discontinued treatment because of elevated blood pressure. In these patients, the blood pressure increases were modest (1-24 mm Hg, SDBP).

Panic disorder (DSM-IV) is characterized by recurrent, unexpected panic attacks, i.e., a discrete period of intense fear or discomfort, in which 4 or more of the following symptoms develop abruptly and reach a peak within 10 minutes: palpitations, pounding heart, or accelerated heart rate; sweating; trembling or shaking; sensations of shortness of breath or smothering; sensations of chills or warmth; feelings of impending doom; sensations of loss of control or unreality; fear of dying; nausea; vomiting; diarrhea; attacks of irritability, unusual changes in behavior, and the other symptoms described above, as well as the emergence of serotonin syndrome. The feared situations are avoided or endured with intense anxiety or distress. The avoidance, avoidance anticipation, or distress in the feared situation(s) interferes significantly with the person's normal routine occupational or academic functioning, or social activities or relationships, or there is a marked distress about having the phobia. Lesser degrees of performance anxiety or shyness generally do not require psychopharmacological treatment.

Sustained Hypertension The use of MAO Is intended to treat psychiatric disorders with Effexor XR or within 7 days of stopping treatment with Effexor XR is contraindicated. (see CONTRAINDICATIONS AND DOSAGE AND ADMINISTRATION). Effexor XR should not be used concomitantly with MAO Is. Effexor XR should be discontinued at least 14 days before initiating treatment with MAO Is, and MAO Is should be discontinued at least 14 days before initiating treatment with Effexor XR.

The efficacy of Effexor XR in the treatment of panic disorder was established in two 12-week placebo-controlled trials with adult outpatients (see Clinical Trials). The efficacy of Effexor XR in the treatment of panic disorder was established in two 12-week placebo-controlled trials with adult outpatients (see Clinical Trials). The efficacy of Effexor XR in the treatment of panic disorder was established in two 12-week placebo-controlled trials with adult outpatients (see Clinical Trials). The efficacy of Effexor XR in the treatment of panic disorder was established in two 12-week placebo-controlled trials with adult outpatients (see Clinical Trials). The efficacy of Effexor XR in the treatment of panic disorder was established in two 12-week placebo-controlled trials with adult outpatients (see Clinical Trials). All patients being treated with antidepressants should be monitored carefully. Efficacy and safety of Effexor XR in the treatment of Major Depressive Disorder in pediatric patients have not been established.

In placebo-controlled premarketing studies, there were changes in mean blood pressure (see Table 2 for mean changes in supine systolic and supine diastolic blood pressure). Across most indications, a dose-related increase in supine systolic and diastolic blood pressure was evident in Effexor XR-treated patients.
**Major Depressive Disorder**

- 8-12 weeks: SSBP 0.28, SDBP 0.27, Placebo 0.28
- 12-24 weeks: SSBP 1.02, SDBP 1.01, Placebo 1.02

**Social Anxiety Disorder**

- 8-12 weeks: SSBP 0.12, SDBP 0.11, Placebo 0.12
- 12-24 weeks: SSBP 0.46, SDBP 0.45, Placebo 0.46

**Panic Disorder**

- 8-12 weeks: SSBP 0.13, SDBP 0.12, Placebo 0.13
- 12-24 weeks: SSBP 0.47, SDBP 0.46, Placebo 0.47

**Incidence of Insomnia and Nervousness**

- Placebo-Controlled Major Depressive Disorder, GAD, Social Anxiety Disorder, and Panic Disorder Trials

**Signs and Symptoms**

- Discontinuation or dose reduction of venlafaxine at various doses has been associated with the appearance of new symptoms, the frequency of which increased with increased dose level and with longer duration of treatment. Reported symptoms include agitation, anxiety, confusion, impaired coordination and balance, diarrhea, dizziness, dry mouth, dysphoric mood, fatigue, flu symptoms, headaches, hypomania, insomnia, nausea, nervousness, nightmares, sensory disturbances (including shock-like electrical sensations), somnolence, sweating, tremor, vertigo, and vomiting.

**Treatment of Adverse Events**

- Treatment-emergent insomnia and nervousness were more commonly reported in patients treated with Effexor XR (venlafaxine hydrochloride) extended-release capsules than with placebo in pooled analyses of short-term major depressive disorder, GAD, Social Anxiety Disorder, and panic disorder studies, as shown in Table 5.
Evaluation of the electrocardiograms for 769 patients who received Effexor (immediate release) in 4- to 6-week double-blind, placebo-controlled trials showed that the incidence of trial-emergent conduction abnormalities did not differ from that with placebo.

In patients with renal impairment (GFR = 10 to 70 mL/min) or cirrhosis of the liver, the clearances of venlafaxine and its active metabolites were decreased. Thus prolonging the elimination half-lives of these substances. A lower dose may be necessary (see DOSAGE AND ADMINISTRATION). Effexor XR, all drugs effective in the treatment of major depressive disorders, should be used with caution in such patients.

Information for Patients

Prescribers or other health professionals should inform patients, their families, and their caregivers about the benefits and risks associated with treatment with Effexor XR and should counsel them in its appropriate use.

A patient Medication Guide about “Antidepressant Medicines, Depression and Other Serious Mental Illness, and Suicide: Educational Tools for Patients” is provided. The prescriber or health professional should instruct patients, their families, and their caregivers to read the Medication Guide and should assist them in understanding its contents. Patients should be given the opportunity to discuss the contents of the Medication Guide and to ask questions as any questions they may have. The complete text of the Medication Guide is reprinted at the end of this document.

Patients should be advised of the following issues and asked to alert their prescriber if these occur while taking Effexor XR.

Clinical Warning and Suicide Risk: Patients, their families, and their caregivers should be encouraged to be alert for the emergence of anxiety, agitation, panic attacks, insomnia, irritability, hostility, hypervigilance, impulsivity, akathisia, dizziness, and mood changes, including symptoms suggestive of a serious clinical syndrome known as serotonin syndrome and/or the emergence of suicidal thoughts or behaviors. Families and caregivers should be advised to report such symptoms immediately and consider discontinuation of Effexor XR and/or other medications.

Drug Interactions: Drugs that inhibit CYP3A4 inhibitors and venlafaxine may increase levels of venlafaxine and ODV. Therefore, caution is advised if a patient’s therapy includes a CYP3A4 inhibitor and venlafaxine concomitantly.

Drugs Metabolized by Cytochrome P450 Isoenzymes

Venlafaxine is a substrate of the CYP 2D6 isoenzyme. Venlafaxine and the major human metabolite, O-desmethylvenlafaxine (ODV), were not mutagenic in the Ames test. However, O-amino-ODV, a minor metabolite, was mutagenic in the in vitro chromosomal aberration assay, but elicited a clastogenic response in the in vivo chromosomal aberration assay.

Carcinogenesis

Venlafaxine and the major human metabolite, O-desmethylvenlafaxine (ODV), were not carcinogenic in the 2-year bioassays in rats and mice, and were negative in the standard test battery of genotoxicity tests. The results of the in vivo chromosomal aberration assay, but not the in vitro chromosomal aberration assay, suggest that venlafaxine and its metabolite, ODV, may be potential clastogens in vivo. The significance of these findings is not known, and potentially could be more pronounced. Therefore, caution is advised if patients have congenital malformations.

Mutagenesis

Venlafaxine and the major human metabolite, O-desmethylvenlafaxine (ODV), were not mutagenic in the Ames test, and were negative in the standard test battery of genotoxicity tests. Therefore, the potential for a drug interaction between drugs that inhibit CYP3A4-mediated, reducing venlafaxine and ODV, resulting in increased plasma concentrations of venlafaxine and decreased concentrations of the active metabolite, CYP2D6 inhibitors such as paroxetine (see CLINICAL PHARMACOLOGY, DRUG INTERACTIONS). CYP2D6 inhibitors: In vitro and in vivo studies indicate that venlafaxine is metabolized to its active metabolite, ODV, by CYP2D6. The isoenzyme that is responsible for the genetic polymorphism seen in the metabolism of many antidepressants, therefore, the potential exists for a drug interaction between drugs that inhibit CYP3A4-mediated, reducing the metabolism of venlafaxine to ODV, resulting in increased plasma concentrations of venlafaxine and decreased concentrations of the active metabolite, CYP2D6 inhibitors such as paroxetine (see CLINICAL PHARMACOLOGY, DRUG INTERACTIONS).
PHARMACOLOGY

The information included in the Adverse Findings Observed in Short-Term, Placebo-Controlled Studies with Effexor XR subsection is based on data from a pool of three 8- and 12-week controlled clinical trials in major depressive disorder (three placebo-controlled two U.S., one international), on data from five controlled clinical trials in GAD with Effexor XR, on data up to 12 weeks from a pool of five controlled clinical trials in Social Anxiety Disorder, and on data up to 12 weeks from the placebo-controlled clinical trial in panic disorder. Information on adverse events added in additional adverse events added in Effexor XR in the-package insert and with a non-drug discontinuation syndrome. It should be noted that, in some cases, the clinical picture is consistent with serotonin syndrome (see CLINICAL PHARMACOLOGY, General, Changes in Height and Changes in Weight). Should the decision be made to treat a pediatric patient with Effexor XR, regular monitoring of weight and height is recommended during treatment, particularly if it is to be continued long term. The safety of Effexor XR treatment for pediatric patients has not been systematically assessed for chronic treatment longer than six months in duration. In the studies conducted in pediatric patients (ages 6-17), the occurrence of blood pressure and cholesterol increases was less clinically relevant in pediatric patients was similar to that observed in adults patients. Consequently, the precautions for adults apply to pediatric patients (see PRECAUTIONS, General; Serum Cholesterol Levels).

Adverse Findings Observed in Short-Term, Placebo-Controlled Studies with Effexor XR

Adverse Events Associated with Discontinuation of Treatment

Approximately 11% of the 375 patients who received Effexor XR (valtinoxal hydrochloride) extended-release capsules in placebo-controlled clinical trials for major depressive disorder discontinued treatment due to an adverse experience, compared with 6% of the 285 placebo-treated patients in those studies. Approximately 18% of the 1381 patients who received Effexor XR capsules in placebo-controlled clinical trials for Social Anxiety Disorder discontinued treatment due to an adverse experience, compared with 12% of the 555 placebo-treated patients in those studies. Approximately 15% of the 819 patients who received Effexor XR capsules in placebo-controlled clinical trials for Social Anxiety Disorder or Discontinuation due to an adverse experience, compared with 6% of the 662 placebo-treated patients in those studies. The most common events leading to discontinuation and considered to be drug-related (ie, leading to discontinuation in at least 1% of the Effexor XR-treated patients at a rate at least twice that of placebo for any indication) are shown in Table 6.

Table 6

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Body as a Whole</th>
<th>Effexor XR (n = 285)</th>
<th>Placebo (n = 285)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Body as a Whole</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthenia</td>
<td>--</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>Nausea</td>
<td>4%</td>
<td>6%</td>
<td>8%</td>
</tr>
<tr>
<td>Dry Mouth</td>
<td>0%</td>
<td>0%</td>
<td>1%</td>
</tr>
<tr>
<td>Nervous System</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dizziness</td>
<td>2%</td>
<td>1%</td>
<td>--</td>
</tr>
<tr>
<td>Insomnia</td>
<td>2%</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Tremor</td>
<td>1%</td>
<td>1%</td>
<td>2%</td>
</tr>
<tr>
<td>Skin</td>
<td>2%</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td><strong>Unrelated Gastrointestinal Impeachment</strong></td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>

1. In long-term placebo-controlled trials for GAD, the following was also a common event leading to discontinuation and was considered to be drug-related for Effexor XR-treated patients (% Effexor XR = [n = 278], 1%): Placebo (% = [n = 278]):

2. In a 6-month placebo-controlled trial for Social Anxiety Disorder, the following was also a common event leading to discontinuation and was considered to be drug-related for Effexor XR-treated patients (% Effexor XR = [n = 278], 1%); Placebo (% = [n = 278]): depression (5%, 0%); libido decreased (1%, 0%); and abnormal vision (3%, 0%).

3. Incidence is based on the number of male patients.

4. Incidence is based on the number of female patients.

Non-teratogenic Effects

Neonates exposed to Effexor XR, other SNRIs (Serotonin and Norepinephrine Reuptake Inhibitors), or SSRIs (Selective Serotonin Reuptake Inhibitors), late in the third trimester have developed complications requiring hospitalization, respiratory support, and feeding. Such complications can arise immediately upon delivery. Reported clinical findings have included respiratory distress, cyanosis, apnea, seizures, temperature instability, feeding difficulty, vomiting, hypoglycemia, hypernatremia, hyperthermia, hyperreflexia, tachy or bradycardia, irritability, and constant crying. These features are consistent with a direct toxic effect of SNRIs and SSRIs or, possibly, a drug discontinuation syndrome. It should be noted that, in some cases, the clinical picture is consistent with serotonin syndrome. (See also CLINICAL PHARMACOLOGY, General, Changes in Height and Changes in Weight).

Labor and Delivery

The effect of venlafaxine on labor and delivery in humans is unknown.

Nursing Mothers

Venlafaxine and Oxyd have been reported to be excreted in human milk. Because of the potential for serious adverse reactions in nursing infants from Effexor XR, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use

Safety and effectiveness in the pediatric population have not been established (see BOX WARNING and WARNINGS, Clinical Worsening and Suicide Risk). Two placebo-controlled trials in 766 pediatric patients with MDD and two placebo-controlled trials in 735 pediatric patients with GAD have been conducted with Effexor XR, and the data were not sufficient to support a claim for use in pediatric patients. Anyone considering the use of Effexor XR in a child or adolescent must balance the potential risks with the clinical need.

Although no studies have been designed to primarily assess Effexor XR’s impact on the growth, development, and maturation of children and adolescents, the studies that have been done suggest that Effexor XR may adversely affect height and weight (see PRECAUTIONS, General; Changes in Height and Changes in Weight). Should the decision be made to treat a pediatric patient with Effexor XR, regular monitoring of weight and height is recommended during treatment, particularly if it is to be continued long term. The safety of Effexor XR treatment for pediatric patients has not been systematically assessed for chronic treatment longer than six months in duration.

In the studies conducted in pediatric patients (ages 6-17), the occurrence of blood pressure and cholesterol increases was less clinically relevant in pediatric patients was similar to that observed in adults patients. Consequently, the precautions for adults apply to pediatric patients (see PRECAUTIONS, General; Serum Cholesterol Levels).

Generalized Anxiety Disorder

Note in particular the following adverse events that occurred in at least 5% of the Effexor XR patients and at a rate at least twice that of the placebo group for all placebo-controlled trials for the major depressive disorder indication (Table 7): Abnormal ejaculation, gastrointestinal complaints (nausea, dry mouth, and anorexia), CNS complaints (dizziness, somnolence, and abnormal dreams), and sweating. In the two U.S. placebo-controlled trials, the following additional events occurred in at least 5% of Effexor XR-treated patients (n = 192) and at a rate at least twice that of the placebo group: Abnormalities of sexual function (impotence in men, anorgasmia in women, and libido decreased), gastrointestinal complaints (constipation and flatulence), CNS complaints (insomnia, nervousness, and tremor), problems of special senses (abnormal vision), cardiovascular effects (hypertension and vasodilation), and yawning.

Contraindications

Effexor XR capsules in placebo-controlled clinical trials for major depressive disorder discontinued treatment due to an adverse experience, compared with 6% of the 285 placebo-treated patients in those studies. Approximately 18% of the 1381 patients who received Effexor XR capsules in placebo-controlled clinical trials for Social Anxiety Disorder discontinued treatment due to an adverse experience, compared with 12% of the 555 placebo-treated patients in those studies. Approximately 15% of the 819 patients who received Effexor XR capsules in placebo-controlled clinical trials for Social Anxiety Disorder discontinued treatment due to an adverse experience, compared with 6% of the 662 placebo-treated patients in those studies. The most common events leading to discontinuation and considered to be drug-related (ie, leading to discontinuation in at least 1% of the Effexor XR-treated patients at a rate at least twice that of placebo for any indication) are shown in Table 6.

Table 6

| Common Adverse Events Leading to Discontinuation in Treatment in Placebo-Controlled Trials
<table>
<thead>
<tr>
<th>Major Depressive Disorder Indication</th>
<th>Social Anxiety Disorder Indication</th>
<th>Panic Disorder Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effexor XR (n = 285)</td>
<td>Placebo (n = 285)</td>
<td>Placebo (n = 285)</td>
</tr>
<tr>
<td>Asthenia</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Nausea</td>
<td>4%</td>
<td>6%</td>
</tr>
<tr>
<td>Constipation</td>
<td>8%</td>
<td>8%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>4%</td>
<td>2%</td>
</tr>
<tr>
<td>Somnolence</td>
<td>4%</td>
<td>3%</td>
</tr>
<tr>
<td>Metabolic/Nutritional Weight Loss</td>
<td>3%</td>
<td>0%</td>
</tr>
<tr>
<td>ANOREXIC SYMPTOMS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dry Mouth</td>
<td>2%</td>
<td>1%</td>
</tr>
<tr>
<td>Constipation</td>
<td>0%</td>
<td>1%</td>
</tr>
<tr>
<td>Anorexia</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>Constipation</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>Nervous System</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dizziness</td>
<td>2%</td>
<td>1%</td>
</tr>
<tr>
<td>Insomnia</td>
<td>2%</td>
<td>1%</td>
</tr>
<tr>
<td>Nervousness</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>Tremor</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>Skin</td>
<td>2%</td>
<td>1%</td>
</tr>
<tr>
<td><strong>Unrelated Gastrointestinal Impeachment</strong></td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>

1. Incidence, rounded to the nearest %, for events reported by at least 2% of patients treated with Effexor XR, except for the following events which had an incidence equal to or less than placebo: abdominal pain, accidental injury, anxiety, arthralgia, chest pain, chills, dizziness, diplopia, dysmenorrhea, dysuria, ey strain, headache, infection, pain, palpitation, rinitis, and sinusitis.

2. Incidence greater than or equal to 10% in the placebo group for 4 placebo-controlled trials for the panic disorder indication (Table 10): gastrointestinal complaints (anorexia, constipation, dry mouth), CNS complaints (somnolence, tremor), abnormalities of sexual function (abnormal ejaculation), and sweating.

3. In long-term placebo-controlled trials for GAD, the following was also a common event leading to discontinuation and was considered to be drug-related for Effexor XR-treated patients (% Effexor XR = [n = 278], 1%): Placebo (% = [n = 278]): depression (5%, 0%); libido decreased (1%, 0%); and abnormal vision (3%, 0%).

4. In a 6-month placebo-controlled trial for Social Anxiety Disorder, the following was also a common event leading to discontinuation and was considered to be drug-related for Effexor XR-treated patients (% Effexor XR = [n = 278], 1%); Placebo (% = [n = 278]): depression (5%, 0%); libido decreased (1%, 0%); and abnormal vision (3%, 0%).

5. Incidence is based on the number of male patients.

6. Incidence is based on the number of female patients.

7. Incidence is based on the number of male patients.

8. Incidence is based on the number of female patients.

9. Incidence is based on the number of female patients.
Table 8: Treatment-Emergent Adverse Event Incidence in Short-Term Placebo-Controlled Effexor XR Clinical Trials in GAD Patients 1,2

<table>
<thead>
<tr>
<th>Body System</th>
<th>Preferred Term</th>
<th>Effexor XR (n = 1381)</th>
<th>% Reporting Event</th>
<th>Placebo (n = 556)</th>
<th>% Reporting Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body as a Whole</td>
<td>Asthenia</td>
<td>12%</td>
<td>8%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular System</td>
<td>Hypertension</td>
<td>3%</td>
<td>3%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Digestive System</td>
<td>Nausea</td>
<td>35%</td>
<td>12%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nervous System</td>
<td>Dry Mouth</td>
<td>16%</td>
<td>6%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory System</td>
<td>Yawn</td>
<td>3%</td>
<td>1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin</td>
<td>Sweating</td>
<td>10%</td>
<td>2%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Special Senses</td>
<td>Abnormal Vision 5</td>
<td>4%</td>
<td>2%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin</td>
<td>Weight Loss</td>
<td>2%</td>
<td>3%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Special Senses</td>
<td>Sexual Dysfunction</td>
<td>2%</td>
<td>1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Special Senses</td>
<td>Impotence 1</td>
<td>1%</td>
<td>1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal System</td>
<td>Nausea 9</td>
<td>9%</td>
<td>8%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal System</td>
<td>Diarrhea</td>
<td>6%</td>
<td>5%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal System</td>
<td>Abnormal EJ/A 7,8</td>
<td>3%</td>
<td>2%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal System</td>
<td>Constipation 4</td>
<td>3%</td>
<td>2%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>Headache</td>
<td>1%</td>
<td>1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>Anosmia</td>
<td>1%</td>
<td>1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>Somnolence</td>
<td>1%</td>
<td>1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>Apnea 5</td>
<td>1%</td>
<td>1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>Dry mouth</td>
<td>1%</td>
<td>1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>Yawn</td>
<td>1%</td>
<td>1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>Impotence</td>
<td>1%</td>
<td>1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>Organic Dysfunction 5,10</td>
<td>1%</td>
<td>1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>Hypertension 6</td>
<td>1%</td>
<td>1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>Anxiety</td>
<td>1%</td>
<td>1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>Asthenia</td>
<td>1%</td>
<td>1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>Dry mouth</td>
<td>1%</td>
<td>1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>Fatigue</td>
<td>1%</td>
<td>1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>Dizziness</td>
<td>1%</td>
<td>1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>Fatigue</td>
<td>1%</td>
<td>1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>Anxiety</td>
<td>1%</td>
<td>1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>Yawn</td>
<td>1%</td>
<td>1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>Impotence</td>
<td>1%</td>
<td>1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>Organic Dysfunction 5,10</td>
<td>1%</td>
<td>1%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Adverse events for which the Effexor XR reporting rate was less than or equal to the placebo rate are not included. These events are: abdominal pain, accidental injury, anxiety, back pain, diarrhea, dysmenorrhea, dysuria, flu syndrome, headache, injection, infection, nervousness, pain, paresthesia, pharyngitis, rash, rhinitis, and vomiting. 3, 4

1 Adverse events for which the Effexor XR reporting rate was less than or equal to the placebo rate are not included. These events are: abdominal pain, accidental injury, anxiety, back pain, diarrhea, dysmenorrhea, dysuria, flu syndrome, headache, injection, infection, nervousness, pain, paresthesia, pharyngitis, rash, rhinitis, and vomiting. 3, 4

2 < 1% means greater than zero but less than 1%. 3

3 Mostly "hot flashes." 4 Mostly "decreased appetite" and "loss of appetite." 5 Mostly "vivid dreams," "nightmares," and "increased dreaming." 6 Mostly "blurred vision." 7 Includes "delayed ejaculation" and "anorgasmia." 8 Percentage based on the number of males (Effexor XR = 454, placebo = 357). 9 Includes "abnormal orgasm" and "anorgasmia." 10 Includes "abnormal orgasm" and "anorgasmia." 11 Percentage based on the number of females (Effexor XR = 365, placebo = 338).
There have been reports of elevated clozapine levels that were temporally associated with adverse events, including seizures following electroconvulsive therapy. There have been reports of increased prothrombin time, partial thromboplatin time, or INR when Effexor XR was given to patients receiving warfarin therapy.

DRUG ABUSE AND DEPENDENCE

Controlled Substance Class

Effexor XR (venlafaxine hydrochloride) extended-release capsules is not a controlled substance.

Drug Interactions

Venlafaxine was not found to have any significant CNS stimulant activity in rodents. In primates drug discrimination tests, venlafaxine significantly increased licking and grooming behavior. In a rat brain imaging study, venlafaxine increased regional brain uptake of dopamine and serotonin.

VNS, peripheral vascular disease (mainly cold feet and/or cold hands), postural hypotension, and urinary retention. Cardiovascular system -

Digestive system -

Hem ic and lym phatic system -

Gastrointestinal system -

Psychiatric system -

Urogenital system -


cough, cold, flu, fever, headache, malaise, myalgia, pain, pyrexia; sores in the mouth, mouth or pharynx pain, sore throat; sweating, tachycardia, tremulousness, vomiting.

Frequent:

Infrequent:

Rare:


cough, dizziness, dysuria, fever, headache, hoarseness, infection, pharyngitis, rhinitis, sinusitis, sore throat; sneezing, teething, upper respiratory tract infection, upper respiratory tract infection with cough, upper respiratory tract infection with fever; urticaria; sinusitis.

Gastrointestinal system -

Hematologic system -

Cardiovascular system -

Respiratory system -

Urogenital system -

Psychiatric system -


cough, sneezing, runny nose, rhinitis, sore throat; fever, headache; sneezing, rhinitis, sinus congestion, sinusitis.

Eye -

Ear, Nose, Throat -

Musculoskeletal system -

Skin and Appendages -

Frequent:

Infrequent:

Rare:


cramping, diarrhea, dyspepsia, flatulence, heartburn, indigestion, nausea, vomiting; belching, halitosis, anorexia, weight gain, weight loss, dry mouth, taste perversion, mouth dry.

Psychiatric system -


colitis, gastroenteritis, gastritis, gastritis with hemorrhage, ileus, irritable bowel syndrome, inflammatory bowel disease, hemorrhoids, dysentry, constipation, diarrhea, enterocolitis, enteritis, esophagitis, esophageal ulcer, enteritis, esophagitis, gastritis, gastroparesis, inflammatory bowel disease, irritable bowel syndrome, inflammatory bowel disease, hemorrhoids, dysentry, constipation, diarrhea, enterocolitis, enteritis, esophagitis, gastritis, gastroparesis, inflammatory bowel disease, irritable bowel syndrome, inflammatory bowel disease, hemorrhoids, dysentry, constipation, diarrhea, enterocolitis, enteritis, esophagitis, gastritis, gastroparesis.

Psychiatric system -

Physical and Psychological Dependence

Effexor XR (venlafaxine hydrochloride) extended-release capsules is not a controlled substance.

Drug Interactions

Venlafaxine was not found to have any significant CNS stimulant activity in rodents. In primates drug discrimination tests, venlafaxine significantly increased licking and grooming behavior. In a rat brain imaging study, venlafaxine increased regional brain uptake of dopamine and serotonin.

VNS, peripheral vascular disease (mainly cold feet and/or cold hands), postural hypotension, and urinary retention. Cardiovascular system -

Digestive system -

Hem ic and lym phatic system -

Gastrointestinal system -

Psychiatric system -

Urogenital system -

Psychiatric system -


cough, dizziness, dysuria, fever, headache, hoarseness, infection, pharyngitis, rhinitis, sinusitis, sore throat; sweating, tachycardia, tremulousness, vomiting.

Gastrointestinal system -

Hematologic system -

Cardiovascular system -

Respiratory system -

Urogenital system -

Psychiatric system -


cramping, diarrhea, dyspepsia, heartburn, indigestion, nausea, vomiting; belching, halitosis, anorexia, weight gain, weight loss, dry mouth, taste perversion, mouth dry.

Psychiatric system -


colitis, gastroenteritis, gastritis, gastritis with hemorrhage, ileus, irritable bowel syndrome, inflammatory bowel disease, hemorrhoids, dysentry, constipation, diarrhea, enterocolitis, enteritis, esophagitis, esophageal ulcer, enteritis, esophagitis, gastritis, gastroparesis, inflammatory bowel disease, irritable bowel syndrome, inflammatory bowel disease, hemorrhoids, dysentry, constipation, diarrhea, enterocolitis, enteritis, esophagitis, gastritis, gastroparesis.

Psychiatric system -

Physical and Psychological Dependence

Effexor XR (venlafaxine hydrochloride) extended-release capsules is not a controlled substance.

Drug Interactions

Venlafaxine was not found to have any significant CNS stimulant activity in rodents. In primates drug discrimination tests, venlafaxine significantly increased licking and grooming behavior. In a rat brain imaging study, venlafaxine increased regional brain uptake of dopamine and serotonin.

VNS, peripheral vascular disease (mainly cold feet and/or cold hands), postural hypotension, and urinary retention. Cardiovascular system -

Digestive system -

Hem ic and lym phatic system -

Gastrointestinal system -

Psychiatric system -

Urogenital system -

Psychiatric system -


cramping, diarrhea, dyspepsia, heartburn, indigestion, nausea, vomiting; belching, halitosis, anorexia, weight gain, weight loss, dry mouth, taste perversion, mouth dry.

Psychiatric system -


colitis, gastroenteritis, gastritis, gastritis with hemorrhage, ileus, irritable bowel syndrome, inflammatory bowel disease, hemorrhoids, dysentry, constipation, diarrhea, enterocolitis, enteritis, esophagitis, esophageal ulcer, enteritis, esophagitis, gastritis, gastroparesis, inflammatory bowel disease, irritable bowel syndrome, inflammatory bowel disease, hemorrhoids, dysentry, constipation, diarrhea, enterocolitis, enteritis, esophagitis, gastritis, gastroparesis.

Psychiatric system -

Physical and Psychological Dependence

Effexor XR (venlafaxine hydrochloride) extended-release capsules is not a controlled substance.

Drug Interactions

Venlafaxine was not found to have any significant CNS stimulant activity in rodents. In primates drug discrimination tests, venlafaxine significantly increased licking and grooming behavior. In a rat brain imaging study, venlafaxine increased regional brain uptake of dopamine and serotonin.

VNS, peripheral vascular disease (mainly cold feet and/or cold hands), postural hypotension, and urinary retention. Cardiovascular system -

Digestive system -

Hem ic and lym phatic system -

Gastrointestinal system -

Psychiatric system -

Urogenital system -

Psychiatric system -


cramping, diarrhea, dyspepsia, heartburn, indigestion, nausea, vomiting; belching, halitosis, anorexia, weight gain, weight loss, dry mouth, taste perversion, mouth dry.

Psychiatric system -


colitis, gastroenteritis, gastritis, gastritis with hemorrhage, ileus, irritable bowel syndrome, inflammatory bowel disease, hemorrhoids, dysentry, constipation, diarrhea, enterocolitis, enteritis, esophagitis, esophageal ulcer, enteritis, esophagitis, gastritis, gastroparesis, inflammatory bowel disease, irritable bowel syndrome, inflammatory bowel disease, hemorrhoids, dysentry, constipation, diarrhea, enterocolitis, enteritis, esophagitis, gastritis, gastroparesis.

Psychiatric system -

Physical and Psychological Dependence

Effexor XR (venlafaxine hydrochloride) extended-release capsules is not a controlled substance.

Drug Interactions

Venlafaxine was not found to have any significant CNS stimulant activity in rodents. In primates drug discrimination tests, venlafaxine significantly increased licking and grooming behavior. In a rat brain imaging study, venlafaxine increased regional brain uptake of dopamine and serotonin.

VNS, peripheral vascular disease (mainly cold feet and/or cold hands), postural hypotension, and urinary retention. Cardiovascular system -

Digestive system -

Hem ic and lym phatic system -

Gastrointestinal system -

Psychiatric system -

Urogenital system -

Psychiatric system -


cramping, diarrhea, dyspepsia, heartburn, indigestion, nausea, vomiting; belching, halitosis, anorexia, weight gain, weight loss, dry mouth, taste perversion, mouth dry.

Psychiatric system -


colitis, gastroenteritis, gastritis, gastritis with hemorrhage, ileus, irritable bowel syndrome, inflammatory bowel disease, hemorrhoids, dysentry, constipation, diarrhea, enterocolitis, enteritis, esophagitis, esophageal ulcer, enteritis, esophagitis, gastritis, gastroparesis, inflammatory bowel disease, irritable bowel syndrome, inflammatory bowel disease, hemorrhoids, dysentry, constipation, diarrhea, enterocolitis, enteritis, esophagitis, gastritis, gastroparesis.
The risk of administering methylene blue by non-intravenous routes (such as oral tablets or by local injection) or in intravenous doses much lower than 1 mg/kg with Effexor XR is unclear. The clinician should, nevertheless, be aware of the possibility of emergent symptoms of serotonin syndrome with such use (see WARNINGS).

**Special Populations**

**Treatment of Pregnant Women During the Third Trimester**

Neonates exposed to Effexor XR, other SNRIs, or SSRIs, late in the third trimester have developed complications requiring prolonged hospitalization, respiratory support, and tube feeding (see PRECAUTIONS). When treating pregnant women with Effexor XR during the third trimester, the physician should carefully consider the potential risks and benefits of treatment.

**Patients with Hepatic Impairment**

Given the decrease in clearance and increase in elimination half-life for both venlafaxine and ODV that is observed in patients with hepatic cirrhosis and mild and moderate hepatic impairment compared with normal subjects (see CLINICAL PHARMACOLOGY), it is recommended that the total daily dose be reduced by 50% in patients with mild to moderate hepatic impairment. Since there was much individual variability in clearance between subjects with cirrhosis, it may be necessary to reduce the dose even more than 50%, and individualization of dosing may be desirable in some patients.

**Patients with Renal Impairment**

Given the decrease in clearance for venlafaxine and the increase in elimination half-life for both venlafaxine and ODV that is observed in patients with renal impairment (GFR = 10 to 70 mL/min) compared with normal subjects (see CLINICAL PHARMACOLOGY), it is recommended that the total daily dose be reduced by 25% to 50%. In patients undergoing hemodialysis, it is recommended that the total daily dose be reduced by 50%. Because there was much individual variability in clearance between patients with renal impairment, individualization of dosage may be desirable in some patients.

**Elderly Patients**

No dose adjustment is recommended for elderly patients solely on the basis of age. As with any drug for the treatment of major depressive disorder, Generalized Anxiety Disorder, Social Anxiety Disorder, or panic disorder, however, caution should be exercised in treating the elderly. When individualizing the dosage, extra care should be taken when increasing the dose.

**Maintenance Treatment**

There is no body of evidence available from controlled trials to indicate how long patients with major depressive disorder, Generalized Anxiety Disorder, Social Anxiety Disorder, or panic disorder, should be treated with Effexor XR. It is generally agreed that acute episodes of major depressive disorder require several months or longer of sustained pharmacological therapy beyond response to the acute episode. In one study, in which patients responding during 8 weeks of acute treatment with Effexor XR were assigned randomly to placebo or to the same dose of Effexor XR (75, 150, or 225 mg/day) during 26 weeks of maintenance treatment as they had received during the acute stabilization phase, longer-term efficacy was demonstrated. A second longer-term study has demonstrated the efficacy of Effexor in maintaining a response in patients with recurrent major depressive disorder who had responded and continued to be improved during an initial 26 weeks of treatment and were then randomly assigned to placebo or Effexor for periods of up to 52 weeks on the same dose (100 to 200 mg/day, on a b.i.d. schedule) (see Clinical Trials under CLINICAL PHARMACOLOGY). Based on these limited data, it is not known whether or not the dose of Effexor XR needed for maintenance treatment is identical to the dose needed to achieve an initial response. Patients should be periodically reassessed to determine the need for maintenance treatment and the appropriate dose for such treatment.

In patients with Generalized Anxiety Disorder, Effexor XR has been shown to be effective in 6-month clinical trials. The need for continuing medication in patients with GAD who improve with Effexor XR treatment should be periodically reassessed.

In patients with Social Anxiety Disorder, Effexor XR has been shown to be effective in a 6-month clinical trial. The need for continuing medication in patients with Social Anxiety Disorder who improve with Effexor XR treatment should be periodically reassessed.

**Discontinuing Effexor XR**

Symptoms associated with discontinuation of Effexor XR, other SNRIs, and SSRIs, have been reported (see PRECAUTIONS). Patients should be monitored for these symptoms when discontinuing treatment. A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible. If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered. Subsequently, the physician may consider decreasing the dose but at a more gradual rate. In clinical trials with Effexor XR, tapering was achieved by reducing the daily dose by 75 mg at 1 week intervals. Individualization of tapering may be necessary.

**HOW SUPPLIED**

Effexor XR® (venlafaxine hydrochloride) extended-release capsules are available as follows:

- 37.5 mg, grey cap/peach body with "W" and “Effexor XR®” on the cap and “37.5” on the body.
- NDC 0008-0837-20, bottle of 15 capsules in unit of use package.
- NDC 0008-0837-21, bottle of 30 capsules in unit of use package.
- NDC 0008-0837-22, bottle of 90 capsules in unit of use package.
- NDC 0008-0837-03, carton of 10 Redipak® blister strips of 10 capsules each.

- 75 mg, peach cap and body with "W" and “Effexor XR®” on the cap and “75” on the body.
- NDC 0008-0833-20, bottle of 15 capsules in unit of use package.
- NDC 0008-0833-21, bottle of 30 capsules in unit of use package.
- NDC 0008-0833-22, bottle of 90 capsules in unit of use package.
- NDC 0008-0833-03, carton of 10 Redipak® blister strips of 10 capsules each.

- 150 mg, dark orange cap and body with "W" and “Effexor XR®” on the cap and “150” on the body.
- NDC 0008-0836-00, bottle of 15 capsules in unit of use package.
- NDC 0008-0836-21, bottle of 30 capsules in unit of use package.
- NDC 0008-0836-22, bottle of 90 capsules in unit of use package.
- NDC 0008-0836-03, carton of 10 Redipak® blister strips of 10 capsules each.

Store at controlled room temperature, 20° to 25°C (68° to 77°F).
The unit of use package is intended to be dispensed as a unit.

The appearance of these capsules is a trademark of Wyeth Pharmaceuticals.
Read the Medication Guide that comes with EFFEXOR XR before you start taking it and each time you get a refill. There may be new information. This Medication Guide does not take the place of talking to your healthcare provider about your medical condition or treatment. Talk with your healthcare provider if there is something you do not understand or want to learn more about.

What is the most important information I should know about EFFEXOR XR?

EFFEXOR XR and other antidepressant medicines may cause serious side effects, including:

1. Suicidal thoughts or actions:
   • EFFEXOR XR and other antidepressant medicines may increase suicidal thoughts or actions in some children, teenagers, or young adults within the first few months of treatment or when the dose is changed.
   • Depression or other serious mental illnesses are the most important causes of suicidal thoughts or actions.
   • Watch for these changes and call your healthcare provider right away if you notice:
     New or sudden changes in mood, behavior, actions, thoughts, or feelings, especially if severe.
   • Pay particular attention to such changes when EFFEXOR XR is started or when the dose is changed.

2. Serotonin Syndrome
   • Fainting
   • Stiffness or rigidity in muscles
   • Rapid change in heart rate or blood pressure
   • High body temperature
   • Loss of consciousness (pass out)

3. Changes in blood pressure. EFFEXOR XR may:
   • increase your blood pressure. Control high blood pressure before starting treatment and monitor blood pressure regularly.

4. Enlarged pupils (mydriasis).

5. Anxiety and insomnia.

6. Changes in appetite or weight.

7. Manic/hypomanic episodes:
   • greatly increased energy
   • severe trouble sleeping
   • racing thoughts
   • reckless behavior
   • unusually grand ideas
   • excessive happiness or irritability
   • talking more or faster than usual

8. Low salt (sodium) levels in the blood.
   Elderly people may be at greater risk for this. Symptoms may include:
   • headache
   • weakness or feeling unsteady
   • confusion, problems concentrating or thinking or memory problems

9. Seizures or convulsions.

10. Abnormal bleeding: EFFEXOR XR and other antidepressant medicines may increase your risk of bleeding or bruising, especially if you take the blood thinner warfarin (Coumadin®), Jantoven®, a non-steroidal anti-inflammatory drug (NSAIDs, like ibuprofen or naproxen), or aspirin.

11. Elevated cholesterol.

12. Lung disease and pneumonia:
   EFFEXOR XR may cause rare lung problems. Symptoms include:
   • worsening shortness of breath
   • cough
   • chest discomfort

13. Severe allergic reactions:
   • trouble breathing
   • swelling of the face, tongue, eyes or mouth
   • rash, itchy welts (hives) or blisters, alone or with fever or joint pain.

Do not stop EFFEXOR XR without first talking to your healthcare provider. Stopping EFFEXOR XR too quickly or changing from another antidepressant too quickly may cause serious symptoms including:
   • anxiety, irritability
   • feeling tired, restless or problems sleeping
   • headache, sweating, dizziness
   • electric shock-like sensations, shaking, confusion, nightmares
   • vomiting, nausea, diarrhea

What is EFFEXOR XR?
EFFEXOR XR is a prescription medicine used to treat depression. It is important to talk with your healthcare provider about the risks of treating depression and also the risks of not treating it. You should discuss all treatment choices with your healthcare provider. EFFEXOR XR is also used to treat:
   • Generalized Anxiety Disorder (GAD)
   • Social Anxiety Disorder (SAD)
   • Panic Disorder (PD)

Talk to your healthcare provider if you do not think that your condition is getting better with EFFEXOR XR treatment.

Who should not take EFFEXOR XR?
Do not take EFFEXOR XR if you:
   • are allergic to EFFEXOR XR or any of the ingredients in EFFEXOR XR. See the end of this Medication Guide for a complete list of ingredients in EFFEXOR XR.
   • have uncontrolled angle-closure glaucoma
   • take a Monoamine Oxidase Inhibitor (MAOI). Ask your healthcare provider or pharmacist if you are not sure if you take an MAOI, including the antibiotic linezolid.
   • Do not take an MAOI within 7 days of stopping EFFEXOR XR unless directed to do so by your physician.
   • Do not start EFFEXOR XR if you stopped taking an MAOI in the last 2 weeks unless directed to do so by your physician.

People who take EFFEXOR XR close in time to an MAOI may have serious or even life-threatening side effects. Get medical help right away if you have any of these symptoms:
   • high fever
   • uncontrolled muscle spasms
   • stiff muscles
   • rapid changes in heart rate or blood pressure
   • confusion
   • loss of consciousness (pass out)

What should I tell my healthcare provider before taking EFFEXOR XR? Ask if you are not sure.
Before starting EFFEXOR XR, tell your healthcare provider if you:
   • Are taking certain drugs such as:
     • Medicines used to treat migraine headaches such as:
       • triptans
     • Medicines used to treat mood, anxiety, psychotic or thought disorders, such as:
       • tricyclic antidepressants
       • lithium
       • SSRIs
       • SNRIs
       • antipsychotic drugs
• Medicines used to treat pain such as:
  - tramadol
• Medicines used to thin your blood such as:
  - warfarin
• Medicines used to treat heartburn such as:
  - Cimetidine
• Over-the-counter medicines or supplements such as:
  - Aspirin or other NSAIDs
  - Tryptophan
  - St. John’s Wort
• have heart problems
• have diabetes
• have liver problems
• have kidney problems
• have thyroid problems
• have or had seizures or convulsions
• have bipolar disorder or mania
• have low sodium levels in your blood
• have high blood pressure
• have high cholesterol
• have or had bleeding problems
• are pregnant or plan to become pregnant. It is not known if EFFEXOR XR will harm your unborn baby. Talk to your healthcare provider about the benefits and risks of treating depression during pregnancy
• are breastfeeding or plan to breast-feed. Some EFFEXOR XR may pass into your breast milk. Talk to your healthcare provider about the best way to feed your baby while taking EFFEXOR XR.

Tell your healthcare provider about all the medicines that you take, including prescription and non-prescription medicines, vitamins, and herbal supplements. EFFEXOR XR and some medicines may interact with each other, may not work as well, or may cause serious side effects.

Your healthcare provider or pharmacist can tell you if it is safe to take EFFEXOR XR with your other medicines. Do not start or stop any medicine while taking EFFEXOR XR without talking to your healthcare provider first.

If you take EFFEXOR XR, you should not take any other medicines that contain (venlafaxine) including: venlafaxine HCl.

How should I take EFFEXOR XR?
• Take EFFEXOR XR exactly as prescribed. Your healthcare provider may need to change the dose of EFFEXOR XR until it is the right dose for you.
• EFFEXOR XR is to be taken with food.
• If you miss a dose of EFFEXOR XR, take the missed dose as soon as you remember. If it is almost time for the next dose, skip the missed dose and take your next dose at the regular time. Do not take two doses of EFFEXOR XR at the same time.
• If you take too much EFFEXOR XR, call your healthcare provider or poison control center right away, or get emergency treatment.
• When switching from another antidepressant to EFFEXOR XR your doctor may want to lower the dose of the initial antidepressant first to avoid side effects.

What should I avoid while taking EFFEXOR XR?
EFFEXOR XR can cause sleepiness or may affect your ability to make decisions, think clearly, or react quickly. You should not drive, operate heavy machinery, or do other dangerous activities until you know how EFFEXOR XR affects you. Do not drink alcohol while using EFFEXOR XR.

What are the possible side effects of EFFEXOR XR?
EFFEXOR XR may cause serious side effects, including:
• See “What is the most important information I should know about EFFEXOR XR?”
• Increased cholesterol- have your cholesterol checked regularly
• Newborns whose mothers take EFFEXOR XR in the third trimester may have problems right after birth including:
  • problems feeding and breathing
  • seizures
  • shaking, jitteriness or constant crying
  • Angle-closure glaucoma

Common possible side effects in people who take EFFEXOR XR include:
• unusual dreams
• sexual problems
• loss of appetite, constipation, diarrhea, nausea or vomiting, or dry mouth
• feeling tired, fatigued or overly sleepy
• change in sleep habits, problems sleeping
• yawning
• tremor or shaking
• dizziness, blurred vision
• sweating
• feeling anxious, nervous or jittery
• headache
• increase in heart rate

Tell your healthcare provider if you have any side effect that bothers you or that does not go away. These are not all the possible side effects of EFFEXOR XR. For more information, ask your healthcare provider or pharmacist.

CALL YOUR DOCTOR FOR MEDICAL ADVICE ABOUT SIDE EFFECTS. YOU MAY REPORT SIDE EFFECTS TO THE FDA AT 1-800-FDA-1088.

How should I store EFFEXOR XR?
• Store EFFEXOR XR at room temperature between 68°F and 77°F (20°C to 25°C).
• Keep EFFEXOR XR in a dry place.

Keep EFFEXOR XR and all medicines out of the reach of children.

General information about EFFEXOR
Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use EFFEXOR XR for a condition for which it was not prescribed. Do not give EFFEXOR XR to other people, even if they have the same condition. It may harm them.

This Medication Guide summarizes the most important information about EFFEXOR XR. If you would like more information, talk with your healthcare provider. You may ask your healthcare provider or pharmacist for information about EFFEXOR XR that is written for healthcare professionals.

For more information about EFFEXOR XR call 1-800-934-5556 or go to www.EFFEXORXR.com.

What are the ingredients in EFFEXOR XR?
Active ingredient: (venlafaxine)
Inactive ingredients:
• Extended-Release Capsules: cellulose, ethylcellulose, gelatin, hypromellose, iron oxides, and titanium dioxide.

This Medication Guide has been approved by the U.S. Food and Drug Administration for all antidepressants.
This product’s label may have been updated. For current full prescribing information, please visit www.pfizer.com

Distributed by
Wyeth Pharmaceuticals Inc
A subsidiary of Pfizer Inc, Philadelphia, PA 19101
LAB-0542-4.0
Revised May 2014