An Analysis of Major Depressive Disorder and the Effectivity of Effexor XR® (Venlafaxine Hydrochloride) in its Treatment

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Abstract

Major depressive disorder is characterized as the second leading cause of disability in developed nations. Common antidepressants like selective serotonin reuptake inhibitors (SSRIs) are often not effective in treating major depressive disorder in certain individuals. This has led to the rapid development of newer types of antidepressants like venlafaxine hydrochloride, which is sold under the brand name Effexor. Venlafaxine undergoes metabolism in the liver, with its main metabolite being O-desmethylvenlafaxine (ODV). Venlafaxine and ODV function in the inhibition of neuronal 5-hydroxytryptamine and norepinephrine reuptake, along with a much weaker inhibition of dopamine reuptake. This inhibitory effect results in venlafaxine's function as an antidepressant. Studies report that venlafaxine hydrochloride has a higher degree of efficacy than SSRIs and that it also demonstrates greater safety than tricyclic antidepressants. However, venlafaxine's success may also result in lower tolerability; in a double-blind clinical trial, various participants experienced nausea and vomiting following the use of venlafaxine, but these side effects proved to be early onset and gradually dissipated over the course of the trial. The research findings show that the advance of venlafaxine's dual function, as both an SSRI and a selective norepinephrine reuptake inhibitor, is critical to its usefulness in relieving depressive disorders that could previously not be properly treated by the leading antidepressants.

Introduction

Major depressive disorder (MDD) is the leading type of illness among mental and neurological disorders.[1] It has been reported that MDD is the main cause of worldwide disability, chiefly in middle- and high-income countries, which are equipped with extensive healthcare facilities that can lead to the proper diagnosis of MDD.[1] Depression affects approximately 121 million individuals worldwide, with major depression affecting 15 million Americans.[2] It has been predicted that depression will be the second most common health problem in the world by 2020.[2] Treatment for major depression varies, with pharmacological and psychological methods being employed.[2] The use of antidepressant medication still remains the primary method to treat major depression.[2]

Antidepressants contribute to the improvement of symptoms of major depression in approximately 65% to 70% of patients, but these medications also have side effects that discourage many patients from using them.[3] This has resulted in the development of several new types of antidepressants, intended to improve both efficacy and tolerability.[3] Research shows that patients who take Effexor (venlafaxine hydrochloride), a more recent pharmaceutical formulation, have often previously used another type of antidepressant, such as tricyclic antidepressants, selective serotonin reuptake inhibitors, and monoamine oxidase inhibitors.[4] These patients are also likely to have a more severe type of depression and have experienced thoughts of suicide prior to taking venlafaxine.[4,5] The main motive of the present work is to comprehensively study the progress that has been made in MDD diagnosis and treatment over time, as well as to establish how a pharmaceutical innovation like Effexor can yield better outcomes for MDD patients. The effectivity of Effexor in the management of MDD will be detailed through an analysis of its distinctive chemical structure, its mechanism of action following ingestion, and the positive results attained by those prescribed Effexor in multiple clinical trials.

History of Depression

Depression is currently defined as a mental condition characterized by emotional dejection, feelings of sadness greater than can be justified by reason, gloominess, constant feelings of inadequacy, lack of self-worth, and the inability to properly concentrate.[6] The first written account of a depressive state of mind, termed "melancholia," can be traced to ancient Mesopotamian texts dated 2000 B.C., when the general population believed that any mental illness was caused by the possession of one's soul by demons.[6] Individuals exhibiting melancholia were often treated through rather brutal techniques, such as starvation and beatings.[6] In about 400 B.C., the Greek physician Hippocrates attributed melancholia to an excess of black bile in the spleen, which he treated by bloodletting to cleanse the bodily fluids.[6] The standards of mental healthcare did not improve much as time passed. In the European Middle Ages, individuals suffering from depression were forced to live in the horrid conditions of mental asylums.[6] With the advancement of medicine and science, many doctors sought to identify the root of depression.[6] In 1917, Sigmund Freud proposed a form of treatment called psychoanalysis; he asserted that patients could settle inner conflicts through this type of "talking cure."[6] Lobotomies also became increasingly prevalent in the early 1900s, the notion being that the severing of connections in the prefrontal cortex of the frontal lobes of the brain would aid in the treatment of severe depression by producing a calming effect.[6] Most of these surgical procedures resulted in undesirable personality changes or coma, and occasionally proved fatal.[6] The 1950s were the turning point in the treatment of depression, with the use of medications to combat mental illness.[6] This progress in the treatment of depression has not only led to changes in the perception of mental illness but also provided individuals with the hope of being cured.[6]

Antidepressants

The first generation of antidepressants included tricyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MOAIs), which first appeared in the 1950s.[7] TCAs function by binding to 5-hydroxytriptamine (5-HT) and noradrenaline reuptake inhibitors

to prevent the reuptake of serotonin and noradrenaline from the synaptic cleft.[7] The MAOIs work by inhibiting the enzyme monoamine oxidase from breaking down monoamines, which allows for greater monoamine availability.[7] Although MAOIs are effective, they have numerous unfavorable side effects, such as liver dysfunction, low blood pressure, erectile dysfunction, and problems with urination.[7] Various undesirable side effects are also attributed to TCAs, inspiring scientists to research other methods of treating depression.[7]

The second-generation antidepressants were the selective serotonin reuptake inhibitors (SSRIs), which gained prominence in the 1970s and 1980s.[7] The use of SSRIs emerged as a form of first-line medication for MDD because of their effectiveness, tolerability, and safety as antidepressants.[7] SSRIs function by blocking the reuptake of serotonin and increasing its extracellular concentration in the brain.[7] While SSRIs remain the most widely prescribed form of antidepressants, they may not prove effective in treating patients with more severe forms of depression.[7]

The shortcomings of SSRIs have led to the generation of newer forms of antidepressants like serotonin-norepinephrine reuptake inhibitors (SNRIs).[7] Venlafaxine hydrochloride is the first SNRI to be used as an antidepressant, with studies reporting increased efficacy compared to SSRIs.[7] SNRIs function through the dual inhibition of serotonin and norepinephrine reuptake, allowing for an increase in the concentration of these neurotransmitters in the synaptic cleft.[7]

Diagnosis

Depression is characterized as a multifaceted disorder that can be attributed to various etiologies.[8] While multiple classification systems have been developed in the diagnosis of depression, there is still no single reliable method of classification that can be used in primary care.[8] The criteria for the diagnosis of depression articulated in the tenth revision of the *International Statistical Classification of Diseases and Related Health Problems* (ICD-10) and in the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV) share numerous similarities but also have subtle differences, which are shown in Table 1.[8] In the ICD-10 method of diagnosis, a patient must exhibit two of the first three listed symptoms, which include a depressed mood, loss of interest in everyday activities, and a reduction in energy, as well as two of the remaining seven symptoms.[8] In the DSM-IV method of diagnosis, a patient must have either a depressed mood or loss of interest, and at least five of the remaining eight symptoms.[8] These two methods of diagnosis require the symptoms to be present for at least two weeks before proper diagnosis can be made.[8] The ICD-10 and DSM-IV utilize a classification system that categorizes depressive episodes as mild, moderate, or severe based on the number and severity of the symptoms.[8] A recent modification to the diagnosis of depression has led to the addition of a type of depressive state that is referred to as subthreshold, which is evident when a patient exhibits fewer than five of the symptoms outlined by the DSM-IV.[8] The intensity of the symptoms and the level of impairment in function are used to differentiate between mild depression, moderate depression, and severe depression.[8]

Table 1. Comparison of symptoms required for diagnosis according to the ICD-10 and DSM-IV methods. Core symptoms are marked with an asterisk (*). Adapted from source.[8]

ICD–10	DSM–IV major/minor depressive disorder
Depressed mood*	Depressed mood by self-report or observation made by others*
Loss of interest*	Loss of interest or pleasure*
Reduction in energy*	Fatigue/loss of energy
Loss of confidence or self-esteem	Worthlessness/excessive or inappropriate guilt
Unreasonable feelings of self-reproach or inappropriate guilt	
Recurrent thoughts of death or suicide	Recurrent thoughts of death, suicidal thoughts or actual suicide attempts
Diminished ability to think/ concentrate or indecisiveness	Diminished ability to think/concentrate or indecisiveness
Change in psychomotor activity with agitation or retardation	Psychomotor agitation or retardation
Sleep disturbance	Insomnia/hypersomnia
Change in appetite with weight change	Significant appetite and/or weight loss

Following the diagnosis of MDD, treatment proceeds in three stages: the acute phase, the continuation phase, and the maintenance phase.[8] During the acute phase, depression symptoms improve; the continuation phase represents the absence of symptoms for a period of four to six months.[8] The maintenance phase is indicative of recovery; the main goal is prevention of the recurrence of depression symptoms.[8]

The Guideline Development Group has prepared a diagnostic tool based on a condensed set of DSM-IV symptoms to make diagnosis less complicated for primary care specialists.[8] Those symptoms include a depressed mood, diminished interest, feelings of worthlessness or guilt, impaired concentration, and recurrent thoughts of death or suicide.[8] Another method of diagnosis is the Hamilton Rating Scale for Depression (HRSD), which is an assessment scale that uses questions to gather information on the patient's depressive symptoms.[9] Atypical symptoms like hypersomnia (excessive sleepiness) and hyperphagia (excessive hunger) are not properly assessed by the HRSD.[9] A score of 0 to 7 on the HRSD is considered normal, meaning the patient is in the state of clinical remission.[9] A score of 20 or higher on the HRSD, which is typically required for participating in clinical trials, is indicative of the presence of moderate to severe depression.[9]

Causes

The serotonin hypothesis, which links depression to serotonin levels, was initially expressed in a paper by Alec Coppen in 1967.[6] He stated that MDD is caused by abnormal operation of the 5-HT system.[6] He proposed that the activity of the 5-HT system be enhanced by antidepressant strategies that restore euthymia, i.e., a tranquil mental state.[6] An association between specific symptoms based on the deficiency of a

select group of neurotransmitters has also been proposed.[6] It has recently been hypothesized that a 5-HT deficiency is related to anxiety and obsessions; that reduced norepinephrine neurotransmission is characterized by decreased alertness, low energy, and problems with concentration; and that dysfunctional dopamine activity is related to the lack of motivation or pleasure.[6] Scientists believe that depression is caused by multiple factors attributed to biological, psychological, and social causes.[6] It is critical to note that depression can be treated in various ways, based on the individual patient and the severity of symptoms.[6]

Synthesis of Venlafaxine Hydrochloride

Effexor (venlafaxine hydrochloride) has a chemical structure that was recently synthesized to serve as an antidepressant.[10] Unlike other antidepressants, venlafaxine hydrochloride lacks the tricyclic or tetracyclic structure.[10] Venlafaxine hydrochloride, as depicted in Figure 1, has the chemical designation of (R/S)-1-[2-(dimethylamino)-1-(4-methoxyphenyl)ethyl] cyclohexanol hydrochloride or (±)-1-[α-[(dimethyl-amino)methyl]-p-methoxybenzyl] cyclohexanol hydrochloride, and has the empirical formula of $C_{17}H_{27}NO_2HCl$. It has a molecular weight of 313.87 g/mol.[10]

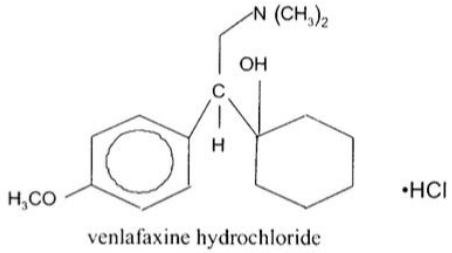

Figure 1. The chemical structure of venlafaxine hydrochloride. Adapted from source.[10]

Venlafaxine was initially synthesized through the nucleophilic addition of 4-methoxyphenyl acetonitrile (7.5.30) with cyclohexanone (7.5.31), using lithium diisopropylamide or butyllithium to generate (RS)-1-[cyano-(4methoxyphenyl) methyl] cyclohexanol (7.5.32).[7] The catalytic hydrogenation of (RS)-1-[cyano-(4methoxyphenyl) methyl] cyclohexanol through the use of the rhodium over alumina catalyst (Rh/Al_2O_3) generates (RS)-1-[2-amino-1-(4-methoxypheny) ethyl]-cyclohexanol (7.5.33).[7] This product undergoes dimethylation using a reductive amination Eschweiler-Clarke procedure in order to produce venlafaxine.[7] The overall yield of the process outlined in Figure 2 is approximately 25%, which led to efforts to improve the chemical synthesis of venlafaxine in order to procure a higher yield.[7] The pyrophoric reagents used in the reaction, n-butyllithium (n-BuLi) and lithium diisopropylamide (LDA), were replaced with sodium methoxide (CH_3NaO).[7] In addition, the costly Rh/Al_2O_3 catalyst was replaced with Raney nickel, which is a solid catalyst composed of a nickel-aluminum alloy, to further simplify the process.[7] These adjustments to the previous method of synthesis increased the overall yield to 55%.[7] The addition of a hydrochloride (HCl) salt to venlafaxine aids in the solubility of Effexor when it is orally administered.[7]

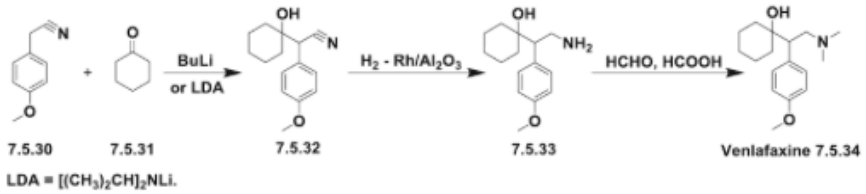

Figure 2. This reaction represents the chemical synthesis of venlafaxine, the active ingredient in Effexor. Adapted from source.[7]

Several other methods for the synthesis of venlafaxine have also been proposed to further expedite the process in a cost-effective manner.[7] While it has been suggested that both enantiomers of venlafaxine serve as antidepressants, it was previously hypothesized that the (+)-enantiomer functions in the inhibition of serotonin reuptake and the (-)-enantiomer functions in the inhibition of norepinephrine reuptake.[7]

Drug Development

Pharmacokinetics

Following the oral administration of venlafaxine hydrochloride, venlafaxine is rapidly absorbed and metabolized in the liver into O-desmethylvenlafaxine (ODV), which is its main metabolite.[10] Mass balance studies indicate that approximately 92% of a single dose of venlafaxine is absorbed and that 87% is excreted through the urine after 48 hours.[10] The composition of venlafaxine recovered in the urine is 5% unchanged venlafaxine, 29% unconjugated ODV, 26% conjugated ODV, and 27% minor inactive metabolites.[10] The bioavailability of venlafaxine is 45%.[10] Approximately 27%$\pm$2% of venlafaxine binds to human blood plasma at concentrations of 2.5 ng/mL to 2215 ng/mL, with 30%$\pm$12% of ODV binding to human blood plasma at concentrations of 100 ng/mL to 500 ng/mL.[10] In patients suffering from cirrhosis, a chronic condition leading to liver damage, the elimination half-life of venlafaxine was increased by 30% and that of ODV was prolonged by 60%.[10] In dialysis patients, the venlafaxine elimination half-life was increased by 180%, and the ODV elimination half-life also increased by 142%.[10]

Pharmacodynamics

The mechanism of action for venlafaxine hydrochloride involves the increase in potentiation of the neurotransmitters serotonin and norepinephrine in the central nervous system.[10] Venlafaxine and its main active metabolite, ODV, function in the inhibition of neuronal serotonin and norepinephrine reuptake.[10] Both venlafaxine and ODV also partake in the weak inhibition of dopamine reuptake.[10] In vitro studies have shown that venlafaxine and ODV do not have an affinity for α-1 adrenergic, muscarinic, and histaminergic receptors.[10] A recent study showed that venlafaxine has a higher affinity for the inhibition of the reuptake of serotonin compared to norepinephrine.[11] The reuptake of serotonin is initially inhibited, then followed by the inhibition of

norepinephrine reuptake.[11] Also, venlafaxine hydrochloride reportedly functions as an SSRI at lower doses, such as at 75 mg.[11]

Metabolites

In both in vitro and in vivo studies, venlafaxine was metabolized to its active metabolite, ODV, by Cytochrome P450 2D6 (CYP2D6).[10] Venlafaxine is also metabolized to N-desmethylvenlafaxine, N,O-didesmethylvenlafaxine, and other minor metabolites.[10]

Manufacture and Clinical Trials of Effexor

Manufacture

In 1993, Wyeth introduced venlafaxine hydrochloride immediate release (Effexor IR) tablets.[12] Effexor IR was available in doses ranging from 25 mg to 100 mg, with patients being required to take two tablets of Effexor IR each day.[12] The microencapsulated extended release version of Effexor (Effexor XR) was released in 1997.[12] Patients were prescribed only one capsule each day.[12] The clinical advantage of Effexor XR was that it reduced the main side effects of nausea and dizziness through its gradual release of the active ingredient.[12] In 2009, Pfizer purchased Wyeth and decide to manufacture only Effexor XR capsules.[12]

Composition, Dosage, and Administration

Effexor XR is a capsule that should be taken once daily with food.[13] Venlafaxine is a white to off-white crystalline solid, which has a solubility of 572 mg/mL in water.[10] The active ingredient in Effexor XR is venlafaxine; the inactive ingredients are cellulose, ethyl cellulose, gelatin, hypromellose, iron oxides, and titanium dioxide.[10] Capsules should be stored in a dry place at temperatures that range from 20°C to 25°C.[10] The recommended dose for a patient taking Effexor XR for the first time is 75 mg each day, as shown in Figure 3.[10] The Effexor XR capsules are available in dosages of 37.5 mg, 75 mg, 150 mg, and 225 mg.[10] Depending both on tolerability and on the severity of the depression symptoms, the dose can be increased up to 375 mg/day; however, increases in dosage by more than 75 mg should take place over a period greater than four days.[10] The high doses of Effexor XR are divided into three doses each day, to prevent possible irritability or other side effects from taking an excessive amount of the active ingredient.[10] The total daily dose should be reduced by up to 50% in patients with hepatic or renal impairment.[10] For individuals over the age of 18, the prescribed dose does not need to be adjusted based on the patient's age or gender.[10] Effexor is not currently approved for use in children.[10] A randomized, double-blind, placebo-controlled study that compared the extended release and immediate release formulations of venlafaxine hydrochloride concluded that patients experienced greater tolerability taking venlafaxine hydrochloride XR.[13] Generic venlafaxine hydrochloride is available in both extended release and immediate release forms.[13]

Figure 3. The 75 mg and 150 mg Effexor XR capsules. Adapted from source.[14]

Side Effects

The most commonly reported side effects encountered by patients taking Effexor XR are unusual dreams, sexual problems, loss of appetite, constipation, diarrhea, nausea, vomiting, dry mouth, fatigue, tremors, dizziness, blurred vision, sweating, headache, and an increased heart rate.[10] Most studies report that nausea is the most common side effect, especially during the initial weeks of taking the prescription.[10]

According to a study that analyzed the side effects of three doses of venlafaxine (75 mg, 225 mg, and 375 mg per day), along with a placebo, a mean increase in supine diastolic blood pressure (SDBP) of 7.2 mm Hg was evident in the group taking the 375 mg dosage of venlafaxine tablets during the sixth week of trials.[10] No significant changes in SDBP were recorded for participants taking the 75 mg or 225 mg venlafaxine tablets.[10] The elevation in SDBP levels was dose-dependent, and the researchers urged physicians to continuously monitor the blood pressure of patients taking Effexor XR at higher doses.[10]

In premarketing tests of Effexor XR, 0.26%, or 8 out of 3082 patients, reported having seizures.[10] These participants were taking doses of 150 mg/day or less.[10] A double-blind randomized clinical trial examining the efficacy of venlafaxine hydrochloride and citalopram, a SSRI, reported that twelve participants on venlafaxine hydrochloride stopped receiving treatment as a result of nausea and vomiting.[3] These side effects occurred during the first two weeks of treatment, and the participants who continued the trial did not report nausea or vomiting during the six remaining weeks of the eight-week trial.[3] It was determined that these side effects are an early onset type; a different study compared venlafaxine and fluoxetine, and reported similar findings.[3]

A study was also conducted to compare venlafaxine to other antidepressants, including fluoxetine, citalopram, and dosulepin, to determine the likelihood that the drugs put patients at risk of sudden cardiac death.[4] While both fluoxetine and citalopram are SSRIs, dosulepin is a TCA.[4] The final study focused on the reactions of the 207,384 patients taking one of the four antidepressants.[4] The results showed that venlafaxine, when compared to other antidepressants, was not associated with an increase in the risk of sudden cardiac death.[4] It was also reported that venlafaxine's association with increased fatal overdoses was related to other factors, such as the prescription of venlafaxine to patients who were at higher risk of suicide.[4] In response to an increase of

suicidal thinking in young adults ages 18-24 during trials of antidepressants, all antidepressants now carry a "black box" warning to alert both physicians and patients to the risk.[2]

Clinical Trials

A clinical trial examining the efficacy and remission rates for a select group of antidepressants was conducted by the Clinical Research and Development Department at Wyeth-Ayerst Laboratories.[15] The trial analyzed three SSRIs—fluoxetine, paroxetine, and fluvoxamine—along with venlafaxine XR, venlafaxine IR, and a placebo control group.[15] Patients in the clinical trial met the criteria outlined by the DSM-IV for at least 1 month and had minimum scores of 20 on the HRSD.[15] Participants included 68 inpatients and 1977 outpatients.[15] The doses employed were as follows: 25-100 mg/day of venlafaxine IR, 75-225 mg/day of venlafaxine XR, 20-80 mg/day of fluoxetine, 20-40 mg/day of paroxetine, and 100-200 mg/day of fluvoxamine.[15] This study defined remission as a total score that was less than or equal to 7 on the first seventeen items on the HRSD.[15]

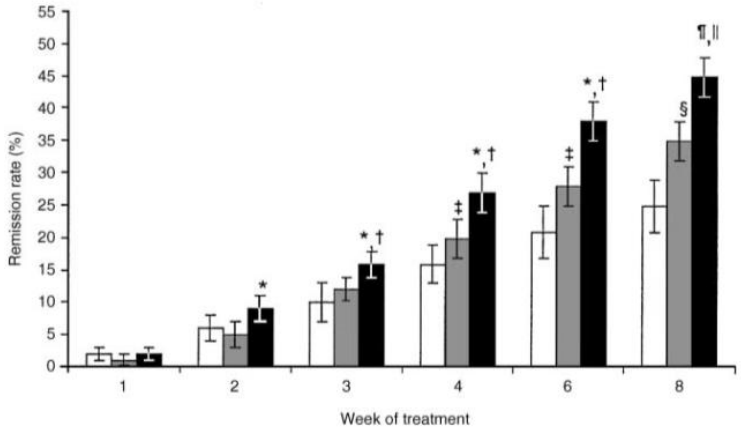

Figure 4. The remission rates of patients involved in the clinical trial examining venlafaxine, fluoxetine, paroxetine, and fluvoxamine. The black bar represents the venlafaxine; the gray bar represents the SSRIs; and the white bar represents the placebo. Adapted from source.[15]

After eight weeks of treatment, it was concluded that the final remission rates were 45% for venlafaxine, 35% for SSRIs, and 25% for the placebo control group, as displayed in Figure 4.[15] The difference in these rates was statistically significant.[15] Venlafaxine was statistically more effective than the SSRIs after the second week of treatment and more effective than the placebo after the third week of treatment.[15] Most physicians recommend that patients continue taking antidepressants for at least one year, even after their symptoms begin to ease.[15]

Another clinical trial was conducted on 123 patients with major depression, classified based on a score that was greater than or equal to 18 on the HRSD.[16] The patients received two antidepressants: one group took venlafaxine with doses starting at 75 mg/day, then increasing to 200-300 mg/day by the tenth day, and the other group was

assigned paroxetine with doses starting at 20 mg/day, then increasing to 30-40 mg/day by the eighth day.[16] Treatment response was measured by a decrease of greater than 50% on the HRSD, and remission was measured by a HRSD score of less than 10.[16] The results showed that, after a period of 28 days, a higher percentage of patients achieved remission while on venlafaxine, with a remission rate of 42%, than the patients who were taking paroxetine, which had a remission rate of 20%, as seen in Table 2.[16] The patients taking venlafaxine also experienced a greater therapeutic response, 52% compared to 33% for paroxetine. [16]

Table 2. The outcomes for patients treated with venlafaxine and paroxetine in a randomized, double-blind trial. Adapted from the source.[16]

Outcomes at 28 days	Venlafaxine	Paroxetine
Therapeutic response	52%	33%
Remission	42%	20%

Cost and Generic Alternatives

Cost

The cost of Effexor XR varies depending on the patient's insurance plan and the patient's eligibility for an Effexor XR choice card. The cost of Effexor XR for patients without insurance is shown in Table 3.

Table 3. The prices of Effexor XR for a 30-day supply based on the most commonly prescribed dosages for individuals without insurance.[17]

Dosage	Effexor XR (Without Insurance)
37.5 mg	$294.24
75 mg	$328.73
150 mg	$357.37

To make Effexor XR more affordable, Pfizer created an Effexor XR choice card program.[18] Patients who have insurance and pay an out-of-pocket expense of $130.00 or less for a 30-day supply of Effexor XR qualify to pay only $4.00 for a 30-day supply with the card.[18] The choice card covers the $75.00 co-pay for these individuals.[18] Patients who do not have health insurance and pay $130.00 or more for a 30-day supply of Effexor XR are eligible to receive a 30-day supply for $30 with the card program.[18] The choice card is accepted at selected pharmacies, such as Rite Aid, Walmart, and Food Lion.[18] The manufacturers of Effexor XR also have a website that enables patients to easily apply for the choice card and to locate pharmacies that participate in this savings program.[18] Through the program, patients are eligible to save up to $2,500.00 each year.[18]

Generic Alternatives

In August 2006, generic venlafaxine hydrochloride immediate-release tablets were made available by Teva Pharmaceuticals.[2] In 2008, Osmotica Pharmaceutical Corp. launched venlafaxine hydrochloride extended-release tablets.[2] Later, in July 2010, Teva also released venlafaxine hydrochloride extended-release capsules.[2] Now many other pharmaceutical companies also manufacture generic venlafaxine hydrochloride, including Cobalt Pharmaceuticals Inc., Pharmascience Inc., Ratiopharm, Sandoz, and Cipla Medpro.[2] While these generic alternatives aim to be less costly than the name-brand version, patients are advised to continue taking the antidepressant that is currently effective for them rather than change to a generic version.[2] A study comparing the pharmacokinetics of brand-name to generic formulations of venlafaxine was conducted in which healthy male volunteers took either Effexor XR or the generic Novo-venlafaxine XR for four days.[19] Participants were given four additional days to allow the drug to be fully excreted from their systems before taking the other venlafaxine formulation for another four days.[19] The results showed that the concentration of the active metabolite ODV was approximately 43% higher in the generic group at 3 hours and 48% higher at 5 hours.[19] Participants also reported three times more side effects while taking the Novo-venlafaxine than the brand-name Effexor XR.[19] These findings reflect how the generic form of venlafaxine is not bioequivalent to Effexor XR, with the generic formulation releasing its active ingredients at a much faster rate.[19]

Future Research

While the efficacy of Effexor has been studied in several scientific trials, studies of the impact of Effexor on pregnant patients and on individuals younger than 18 years of age have not occurred.[10] In one study, 120 mg/kg of venlafaxine was administered to rats each day during a period of 18 months, and the results did not show any teratogenic effects on the rats' reproduction or fertility.[10] Thus, additional studies should be geared toward Effexor's ability to aid minors and pregnant women, as the drug has the potential to benefit a great number of people who otherwise may continue to suffer from MDD.

Conclusion

Effexor XR or venlafaxine hydrochloride XR is type of antidepressant that functions as a dual reuptake inhibitor of norepinephrine and serotonin. This mechanism is often necessary to treat patients with severe depression and those who may not have responded adequately to SSRIs or other antidepressants. Multiple studies have shown that patients achieve higher rates of remission when taking Effexor than other SSRIs. The extended release formulation of Effexor alleviates the main side effects of Effexor immediate release, such as nausea and vomiting. The implementation of Pfizer's choice card program to make Effexor XR more affordable enables patients to receive name-brand treatment at much lower prices. The numerous positive implications associated with venlafaxine hydrochloride XR, such as its increased tolerability and efficacy, confirm the drug as an effective treatment for MDD patients.

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