Anafranil®
clomipramine hydrochloride capsules, USP
(25 mg, 50 mg, 75 mg)
Rx only
DESCRIPTION
Anafranil® (clomipramine hydrochloride capsules, USP) is an antidepressant that belongs to the class (dibenz[b,f]azepine) of pharmacologic agents known as tricyclic antidepressants. Anafranil is available as capsules of 25, 50, and 75 mg for oral administration.
Pharmacology
Anafranil is presumed to influence obsessive and compulsive behaviors through its effects on serotonergic neuronal transmission. The actual biochemical activity of the drug metabolizing enzymes is unknown, but CMI's capacity to inhibit the reuptake of serotonin (5-HT) is thought to be the principal mechanism of action.
INDICATIONS AND USAGE
Anafranil® (clomipramine hydrochloride capsules, USP) is indicated for the treatment of obsessive and compulsive compulsions in patients with Obsessive-Compulsive Disorder (OCD). The observed efficacy of Anafranil in patients with obsessive-compulsive disorder was demonstrated primarily in a double-blind, placebo-controlled, multicenter study of 31 adult patients who met the DSM-IV criteria for OCD (see CLINICAL TRIALS). Anafranil is contraindicated in patients with severe liver disease, but it is not clear whether this contraindication also applies to patients with mild to moderate liver disease.
Pharmacokinetics
Anafranil hydrochloride is a white to off-white crystalline powder. It is freely soluble in water, in methanol, and in methylene chloride, and insoluble in other solvents. Inactive Ingredients.
Clomipramine (CMI) is presumed to influence obsessive and compulsive behaviors through its effects on serotonergic neuronal transmission. The actual biochemical activity of the drug metabolizing enzymes is unknown, but CMI's capacity to inhibit the reuptake of serotonin (5-HT) is thought to be the principal mechanism of action.
Warnings
Surgery:
Prior to elective surgery with general anesthetics, therapy with Anafranil should be discontinued at least 14 days prior to surgery. Treatment with Anafranil should be resumed postoperatively when the patient has returned to a stable condition and when it is determined that surgery will not exacerbate patient symptoms.
Contra indication:
Anafranil is contraindicated in patients with severe liver disease, but it is not clear whether this contraindication also applies to patients with mild to moderate liver disease.
Clomipramine hydrochloride is a white to off-white crystalline powder. It is freely soluble in water, in methanol, and in methylene chloride, and insoluble in other solvents. Anafranil is available as capsules of 25, 50, and 75 mg for oral administration.
that are substrates for P450 2D6 (many other antidepressants, phenothiazines, and the Type 1, 2, and 3 monoamine oxidase inhibitors). In vitro studies have shown that Anafranil is a substrate for the CYP2D6 isoenzyme that is highly expressed in human liver. In vivo studies have shown that Anafranil may be metabolized by the CYP2D6 isoenzyme. Because Anafranil is highly lipid soluble, the administration of Anafranil to patients taking other drugs that are highly protein bound (e.g., warfarin, digoxin) may alter the plasma levels of Anafranil. Conversely, alterations in the levels of protein binding may result in changes in the plasma levels of Anafranil. Anafranil is highly protein bound, with a binding capacity of approximately 99%. The binding is non-specific and does not involve any specific anafranil interaction. Anafranil is stored in the liver of adult and adolescents and is metabolized in the liver by the CYP2D6 isoenzyme. The CYP2D6 isoenzyme is highly expressed in human liver and is highly dependent on the administration of Anafranil to patients with severe liver disease, but it is not clear whether this contraindication also applies to patients with mild to moderate liver disease.
Warnings
Surgery:
Prior to elective surgery with general anesthetics, therapy with Anafranil should be discontinued at least 14 days prior to surgery. Treatment with Anafranil should be resumed postoperatively when the patient has returned to a stable condition and when it is determined that surgery will not exacerbate patient symptoms.
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Incidence of Treatment-emergent Adverse Events in Placebo-Controlled Trials

Body System/Adverse Events

<table>
<thead>
<tr>
<th>Adults</th>
<th>Placebo</th>
<th>Anafranil</th>
<th>Placebo</th>
<th>Anafranil</th>
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<tr>
<td>Accidents</td>
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<td>Abnormal ECG</td>
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| Other Events Observed During the Premarketing Evaluation of Anafranil

During clinical testing in the U.S., multiple doses of Anafranil (clomipramine hydrochloride) capsules have been administered to more than 1,100 patients. Adverse events associated with the drug were recorded for nearly all patients, and the frequency with which adverse events were observed was not increased in patients receiving multiple doses of Anafranil. The following is a list of adverse events that have been observed in patients receiving multiple doses of Anafranil. Some adverse events occurring in patients taking multiple doses of Anafranil have not been included in the listing that follows because they have been considered to be mild and transient, have occurred infrequently, or have been considered to be events that are not drug-related. The following list is not all possible adverse events.

Body as a Whole

- Adverse events in patients taking multiple doses of Anafranil have been classified according to body system and listed in order of decreasing frequency. The frequency of adverse events is based on the percentage of patients reporting adverse events and on the severity of adverse events. Fewer than 10 patients may be included in some body system categories.

- In an 18-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.

- In a 52-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.

- In a 12-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.

- In a 24-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.

- In a 36-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.

- In a 48-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.

- In a 60-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.

- In a 72-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.

- In a 96-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.

- In a 120-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.

- In a 156-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.

- In a 180-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.

- In a 216-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.

- In a 252-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.

- In a 288-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.

- In a 324-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.

- In a 360-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.

- In a 396-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.

- In a 432-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.

- In a 468-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.

- In a 504-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.

- In a 540-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.

- In a 576-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.

- In a 600-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.

- In a 636-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.

- In a 672-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.

- In a 708-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.

- In a 744-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.

- In a 780-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.

- In a 816-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.

- In a 852-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.

- In a 888-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.

- In a 924-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.

- In a 960-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.

- In a 996-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.

- In a 1032-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.

- In a 1068-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.

- In a 1104-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.

- In a 1140-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.

- In a 1176-week trial, patients treated with multiple doses of Anafranil experienced a greater frequency of adverse events than those treated with a single dose.