PRESCRIBING INFORMATION

NAVANE* (thiothixene) CAPSULES

2 MG, 5 MG, 10 MG

Antipsychotic Agent

ERFA
Canada 2012 Inc.

8250 Décarie Blvd, suite 110
Montréal, QC
Canada, H4P 2P5

DATE OF REVISION:
December 19, 2012

Control number : 160699

ACTIONS

NAVANE (thiothixene) is an antipsychotic agent of the thioxanthene series. NAVANE possesses certain chemical and pharmacologic similarities to the piperazine phenothiazines and differences from the aliphatic group of phenothiazines. The mode of action of NAVANE has not been clearly established.

INDICATIONS AND CLINICAL USE

Thiothixene is an antipsychotic agent useful in the management of schizophrenia and other psychotic disorders.

As with other antipsychotic agents, some patients resistant to previous medication have responded favorably to NAVANE. It may also be of value in the management of withdrawn, apathetic schizophrenic patients.

Where more rapid control of acute behavior is desirable or oral administration is not possible, the intramuscular form of NAVANE may be indicated.

NAVANE is not recommended for the treatment of non-psychotic mental and emotional disorders.

CONTRAINDICATIONS

The use of NAVANE (thiothixene) in children under 12 years of age is not recommended, as safety and efficacy data for its use have not yet been accumulated in sufficient quantities.

NAVANE is contraindicated in patients with circulatory collapse, comatose states, central nervous system depression due to any cause and blood dyscrasias.

NAVANE is contraindicated in individuals who have shown hypersensitivity to the drug. It is not known whether there is a cross sensitivity between the thioxanthenes and the phenothiazine derivatives, but this possibility should be considered.

WARNINGS

As is true with many CNS drugs, NAVANE (thiothixene) may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery, especially during the first few days of therapy. Therefore, the patient should be cautioned accordingly.

As in the case of other CNS-acting drugs, patients receiving NAVANE should be cautioned about the possible additive effects (which may include hypotension) with CNS depressants and with alcohol. Potentiation of central nervous system depressants (sedatives, tranquilizers, narcotic analgesics, antihistamines, anaesthetics, and alcohol), atropine and organophosphorus insecticides, and reversal of epinephrine effect, have been observed with related drugs.

Neuroleptic Malignant Syndrome (NMS): Neuroleptic malignant syndrome is a potentially fatal symptom complex that has been reported in association with antipsychotic drugs, including NAVANE. The clinical manifestations of NMS are hyperpyrexia, muscle rigidity, altered mental status and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmias).

The management of NMS should include 1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy, 2) intensive symptomatic treatment and medical monitoring, and 3) treatment of any concomitant serious medical problems for which specific treatments are available. There is no general agreement about specific pharmacological treatment regimens for uncomplicated NMS.

If a patient required antipsychotic drug treatment after recovery from NMS, the potential reintroduction of drug therapy should be carefully considered. The patient should be carefully monitored, since recurrences of NMS have been reported.

Tardive Dyskinesia: Tardive dyskinesia, a syndrome consisting of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with neuroleptic (antipsychotic) drugs, including NAVANE. Although the prevalence of the syndrome appears to be highest among the elderly, especially elderly women, it is impossible to rely upon prevalence estimates to predict, at the inception of neuroleptic treatment, which patients are likely to develop the syndrome. Whether neuroleptic drug products differ in their potential to cause tardive dyskinesia is unknown.

Both the risk of developing the syndrome and the likelihood that it will become irreversible are believed to increase as the duration of treatment and the total cumulative dose of neuroleptic administered increase. However, the syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses.

There is no known treatment for established cases of tardive dyskinesia, although the syndrome may remit, partially or completely, if neuroleptic treatment is withdrawn. Neuroleptic treatment itself, however, may suppress (or partially suppress) the signs and symptoms of the syndrome. What effect suppression has upon the long-term course of the syndrome is unknown.

Use in Pregnancy: Safe use of NAVANE in pregnancy has not been established. It should, therefore, not be used in women of child-bearing potential unless, in the opinion of the physician, the expected benefits of the drug outweigh the potential hazard to the fetus.

PRECAUTIONS

In consideration of the known capability of NAVANE (thiothixene) and certain other antipsychotic drugs to precipitate convulsions, extreme caution should be used in patients with a history of convulsive disorders or those in a state of alcohol withdrawal, since it may lower the convulsive threshold. Although NAVANE potentiates the actions of the barbiturates, the dosage of the anticonvulsant therapy should not be reduced when NAVANE is administered concurrently.

Production or aggravation of EKG changes has occurred with thiothixene and therefore caution should be observed when there is increased risk to the patient (see “ADVERSE REACTIONS” section).

Though exhibiting rather weak anticholinergic properties, NAVANE should be used with caution in patients who are known or are suspected to have glaucoma, and in those who might be exposed to extreme heat or who are receiving atropine or related drugs.

Undue exposure to sunlight should be avoided. Photosensitive reactions have been reported in patients on NAVANE.

Rare cases of priapism have been reported with antipsychotic use, such as NAVANE. This adverse reaction, as with other psychotropic drugs, did not appear to be dose-dependent and did not correlate with the duration of treatment.

Hyperglycemia: Diabetic ketoacidosis (DKA) has occurred in patients with no reported history of hyperglycemia. Patients should have baseline and periodic monitoring of blood glucose and body weight.

Long-standing hyperprolactinemia when associated with hypogonadism may lead to decreased bone mineral density in both female and male subjects.

Hematologic:
Venous Thromboembolism

Venous thromboembolism (VTE), including fatal pulmonary embolism, has been reported with antipsychotic drugs, including NAVANE, in case reports and/or observational studies. When prescribing NAVANE all potential risk factors for VTE should be identified and preventive measures undertaken.
Neutropenia, granulocytopenia and agranulocytosis have been reported during antipsychotic use. Therefore, it is recommended that patients have their complete blood count (CBC) tested prior to starting NAVANE and then periodically throughout treatment.

Neuroleptic drugs, including NAVANE, may elevate prolactin levels in humans; the elevation persists during chronic administration. Although disturbances such as galactorrhea, amenorrhea, gynecomastia, and impotence have been reported, the clinical significance of elevated serum prolactin levels is unknown for most patients.

Careful observation should be made for pigmentary retinopathy, and lenticular pigmentation (fine lenticular pigmentation has been noted in a small number of patients treated with NAVANE for prolonged periods. Blood dyscrasias (agranulocytosis, pancytopenia, thrombocytopenic purpura), and liver damage (jaundice, biliary stasis), have been reported with related drugs.

Caution as well as careful adjustment of the dosages is indicated when NAVANE is used in conjunction with other CNS depressants.

Hepatic microsomal enzyme inducing agents, such as carbamazepine, were found to significantly increase the clearance of thiothixene. Patients receiving these drugs should be observed for signs of reduced effectiveness of NAVANE.

Due to a possible additive effect with hypotensive agents, patients receiving these drugs should be observed closely for signs of excessive hypotension when thiothixene is added to their drug regimen.

An antiemetic effect observed in animal studies with thiothixene may also occur in man; therefore, it is possible that NAVANE may mask signs of overdosage of toxic drugs and it may obscure conditions such as intestinal obstruction and brain tumor.

To lessen the likelihood of adverse reactions related to drug accumulation, patients on long-term therapy, particularly on high doses, should be evaluated periodically to decide whether the maintenance dosage could be lowered or drug therapy discontinued. Periodic blood counts and liver function tests should be performed. Sudden onset of severe central nervous system or vasomotor symptoms should be kept in mind.

Non-Teratogenic Effects:
Neonates exposed to antipsychotic drugs (including NAVANE) during the third trimester of pregnancy are at risk for extrapyramidal and/or withdrawal symptoms following delivery. There have been reports of agitation, hypertonia, hypotonia, tremor, somnolence, respiratory distress and feeding disorder in these neonates. These complications have varied in severity, while in some cases symptoms have been self-limited, in other cases neonates have required intensive care unit support and prolonged hospitalization.
NAVANE should not be used during pregnancy unless the expected benefits to the mother markedly outweigh the potential risks of the fetus.

ADVERSE REACTIONS

Since NAVANE (thiothixene) has pharmacologic properties similar to those of the phenothiazine, all the known adverse reactions of that class of drugs should be borne in mind when NAVANE is used.

Behavioral: The most common side-effects are initial and transient drowsiness, restlessness and agitation, and insomnia. (The incidence of sedation appears to be similar to that of the piperazine group of phenothiazine, but less than that of certain aliphatic phenothiazine).

Other adverse reactions reported less frequently are weakness or fatigue, excitement, depression and headache.

Hyperactivity, both psychic and motor, should be considered a pharmacologic effect of the drug which may be desirable, except in the patient who is already agitated and excited. Activation of psychotic symptomatology has been observed, but it usually responds to reduction of dosage or temporary discontinuation of the drug. Toxic confusional states may occur on rare occasions.

Neurological: The incidence and nature of extrapyramidal symptoms, including akathisia, pseudo-Parkinsonism and dystonic reactions, are similar to those encountered with the piperazine phenothiazine, but thiothixene is more likely to produce akathisia. They are usually controlled by reduction of dosage and/or administration of antiparkinson drugs depending on the type and severity of symptoms. Cerebral seizures have been reported (see PRECAUTIONS). Phenothiazine derivatives have been associated with cerebral edema and cerebrospinal fluid abnormalities.

Hyperreflexia has been reported in infants delivered from mothers having received structurally related drugs.

Tardive Dyskinesias: Since early detection of tardive dyskinesia is important, patients should be monitored on an ongoing basis. It has been reported that fine vermicular movement of the tongue may be an early sign of the syndrome. If this or any other

presentation of the syndrome is observed, the clinician should consider possible discontinuation of neuroleptic medication (see WARNINGS).

Neuroleptic Malignant Syndrome (NMS): (See WARNINGS)

Autonomic: Dry mouth, blurred vision, nasal congestion, constipation, increased sweating, increased salivation, and impotence have occurred infrequently with NAVANE therapy. Phenothiazines have been associated with miosis, mydriasis, and adynamic ileus.

Cardiovascular: Tachycardia, hypotension, lightheadedness, and syncope. In the event hypotension occurs, epinephrine should not be used as a pressor agent since, a paradoxical further lowering of blood pressure may result. Nonspecific EKG changes have been observed in some patients receiving thiothixene. These changes are usually reversible and frequently disappear on continued thiothixene therapy. The clinical significance of these changes is not known. Cardiac arrhythmias, including A-V block, paroxysmal tachycardia and ventricular fibrillation have been observed with some phenothiazines.

NOTE: Sudden deaths have occasionally been reported in patients who have received certain phenothiazine derivatives. In some cases the cause of death was apparently cardiac arrest or asphyxia due to failure of the cough reflex. In others, the cause could not be determined nor could it be established that death was due to phenothiazine administration.

Endocrine; Hyperprolactinemia, lactation, menstrual irregularities, moderate breast enlargement and amenorrhea have occurred in a small percentage of females receiving thiothixene. If persistent, this may necessitate a reduction in dosage or the discontinuation of therapy. Phenothiazines have been associated with false positive pregnancy tests, gynecomastia, hypoglycemia, hyperglycemia, and glycosuria.

Allergic: Rash, pruritus, urticaria, and rare cases of anaphylaxis have been reported with thiothixene. Undue exposure to sunlight should be avoided. Although not experienced with NAVANE, exfoliative dermatitis, contact dermatitis (in nursing personnel), have been reported with certain phenothiazines.

Hematologic: As is true with certain other antipsychotic drugs, leukopenia and leucocytosis, which are usually transient, can occur occasionally with thiothixene. Other

antipsychotic drugs have been associated with agranulocytosis, eosinophilia, hemolytic anemia, thrombocytopenia and pancytopenia.

Hepatic: Elevations of serum transaminase and alkaline phosphatase, usually transient, have been infrequently observed in some patients. No clinically confirmed cases of jaundice attributable to thiothixene have been reported.

Ophthalmologic: Fine lenticular pigmentation has been noted after prolonged therapy.

Other: Hyperpyrexia, anorexia, nausea, vomiting, diarrhea, increase in appetite and weight, weakness or fatigue, polydipsia and peripheral edema. Although not reported with thiothixene, evidence indicates there is a relationship between phenothiazine therapy and the occurrence of a systemic lupus erythematosus-like syndrome.

Patients should be advised of the risk of severe constipation during NAVANE treatment, and that they should tell their doctor if constipation occurs or worsens, as they may need laxatives.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

Symptoms: Manifestations include muscular twitching, drowsiness, and dizziness. Symptoms of gross overdosage may include CNS depression, rigidity, weakness, torticollis, tremor, salivation, dysphagia, hypotension, disturbances of gait, or coma.

Treatment: Essentially symptomatic and supportive. Early gastric lavage may be helpful. Keep patient under careful observation and maintain an open airway, since involvement of the extrapyramidal system may produce dysphagia and respiratory difficulty in severe overdosage. If hypotension occurs, the standard measures for managing circulatory shock should be used (I.V. fluids and/or vasoconstrictors).

If a vasoconstrictor is needed, levarterenol and phenylephrine are the most suitable drugs. Other pressor agents, including epinephrine, are not recommended, since phenothiazine derivatives may reverse the usual pressor elevating action of these agents and cause further lowering of blood pressure.

If CNS depression is present, recommended stimulants include caffeine and sodium benzoate. Picrotoxin or pentylenetetrazol should be avoided. Extrapyramidal symptoms may be treated with antiparkinson drugs.

There are no data on the use of peritoneal or hemodialysis, but they are known to be of little value in phenothiazine intoxication.

DOSAGE AND ADMINISTRATION

The use of NAVANE (thiothixene) in children under 12 years of age is not recommended, as safety and efficacy data for its use have not yet been accumulated in sufficient quantities. (See CONTRAINDICATIONS).

Oral: The usual optimal dosage of NAVANE is in the range of 15 to 30 mg daily. In most conditions, the initial dosage should be 5-10 mg daily. The dosage should be gradually increased to the optimally effective level based on patient response. An increase to 60 mg/day may be necessary; however, exceeding a total daily dosage of 60 mg/day rarely increases beneficial response. Patients on the average therapeutic dosage may be maintained on once-a-day therapy. Higher dosage can be given in two or three equally

divided doses. The dosage should be reduced to the lowest possible maintenance level as soon as possible.

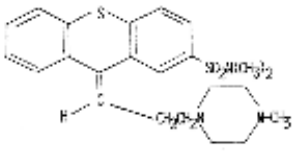
Intramuscular: For control of acute symptomatology or in patients unable to take oral medication, the usual dose is 4 mg of NAVANE intramuscular solution administered two or four times daily. Most patients are controlled on a total daily dose of 16 to 20 mg but effective doses have ranged from 6 to 30 mg daily. Dosage may be increased or decreased depending upon response. NAVANE should be administered by deep intramuscular injection preferably in the upper outer quadrant of the buttock (i.e., gluteus maximus) or the mid-lateral thigh and preferably at four-hour intervals. The deltoid area should be used only if well developed, such as in certain adults and older children, and then only with caution to avoid radial nerve injury. Intramuscular injections should not be made into the lower and mid-thirds of the upper arm. As with all intramuscular injections, aspiration is necessary to help avoid inadvertent injection into a blood vessel. Once satisfactory control of severe symptoms has been achieved, therapy should be continued with one of the oral forms of NAVANE.

AVAILABILITY

2 mg (white) capsules, bottles of 100; 5 mg (orange and white) capsules, bottles of 100; 10 mg (orange) capsules, bottles of 100.

CHEMISTRY AND PHARMACOLOGY

NAVANE (thiothixene) is an antipsychotic drug. Specifically, it is the cis isomer of N,N-dimethyl-9-[3-(4-methyl-1-piperazinyl)-propylidene]thioxanthene-2-sulfonamide.



Psychopharmacologic studies of thiothixene in animals reveal that it exerts several actions generally considered characteristic of antipsychotic drugs. It blocks conditioned

avoidance behavior in rats and monkeys, various central stimulant actions of amphetamine in mice and rats, and apomorphine-induced emesis in dogs.

Thiothixene suppresses conditioned avoidance behavior in rats at intraperitoneal doses of about 3.2 mg/kg. Escape behavior, however, is virtually unimpaired, even at 32 mg/kg. Similarly, thiothixene blocks the motor stimulation, mortality and characteristic stereotypy produced by amphetamine. Thermoregulation is virtually unaffected.

Like many phenothiazine derivatives thiothixene induces catalepsy in rats and both catalepsy and tremors in dogs and monkeys. Thiothixene does not cause loss of righting reflex at sublethal doses, nor does it induce skeletal muscle flaccidity. The hypnotic potentiating effect of thiothixene is relatively low.

Thiothixene causes only a slight hypotensive effect in unanesthetized dogs, even after 10 mg/kg orally. In anesthetized dogs, even after intravenous doses of 4 mg/kg, thiothixene also exerts only a mild hypotensive effect. At this same dose thiothixene reduces the pressor effects of epinephrine, norepinephrine and histamine without affecting the response of acetylcholine or angiotensin.

Thiothixene is essentially ineffective as an anticonvulsant, analgesic or diuretic. Its smooth-muscle spasmolytic effects against contractions elicited by acetylcholine, serotonin and especially histamine are relatively weak. The cortical evoked response of cats to thiothixene was similar to their response to other psychotropic drugs.

The overall pattern of effects produced by thiothixene in experimental animals appears to resemble closely that of thioproperazine.

Absorption and Distribution: Studies on excreta and bile in animals indicate that thiothixene is rapidly metabolized to a wide variety of compounds. Very little unchanged drug is recovered. It must therefore be noted that, from a time soon after absorption, the compounds being measured are primarily the metabolites of thiothixene rather than the parent drug. Thiothixene, like other tricyclic psychotherapeutic agents, appears to be well absorbed orally. Accordingly, although a number of metabolites are seen, very little unchanged drug is found in the feces after oral dosing and 65% of the orally administered radioactivity is recovered in the bile of a rat carrying a bile fistula. Thus the liver plays a dominant role in the disposal of the drug.

The high initial drug levels in the stomach of rats after oral administration of thiothixene are reminiscent of results obtained with chlorpromazine in mice. The high drug concentrations in the lung reported for chlorpromazine, thioridazine, perphenazine and prochlorperazine, however were not found with thiothixene. Brain tissue also contained relatively little S^{35} thiothixene. Low levels of drug in the brain have also been noted with trifluoperazine, chlorpromazine and thioridazine. Thiothixene and its metabolites are rapidly cleared from all tissues with the exception of the liver. Low peak serum concentrations are reached shortly after thiothixene administration and decline rapidly, but detectable amounts are still present 5 days after administration. The absorption, distribution and metabolism of thiothixene administered orally or parenterally are not significantly different.

TOXICOLOGY

Extensive animal toxicologic studies of NAVANE (thiothixene) have been completed. The LD_{50}"s (mg/kg) were: Oral, mice, male 820, female 2090; rats, male 1300, female 1980; dogs 500; IP, mice 530, rats 900. The LD_{50} (mg/kg) of NAVANE Oral Concentrate was: Oral, mice, male 203. Death could not be produced in male rats at maximally tolerated fluid volumes of 20 ml/kg (equivalent to 100 mg/kg thiothixene base). The intravenous LD_{50} of NAVANE Intramuscular Solution in male mice and rats was 25.4 and approximately 28 mg/kg respectively. Transient anemia and/or leukopenia have occurred in dogs at doses of 12.5 mg/kg and greater. This was not seen in rats and monkeys. Daily doses of 12.5 mg/kg or more over a prolonged period in the dog have produced elevations of alkaline phosphatase and transaminases and microscopic changes in the liver. Similar microscopic changes in the liver were also seen in rats after prolonged dosage of 50 mg/kg. There were no effects on liver function tests and no microscopic changes in the liver in monkeys. All these effects occurred at dosages 25 to 100 times higher than the usual optimal clinical dose. No ocular toxicity was noted in any of the animal studies with NAVANE even after administration of the drug at doses up to 100 mg/kg/day for periods up to 18 months. Lactation was noted in the rat (in males and females at doses of 5 mg/kg/day and above), the dog (one female at 6 mg/kg/day), and the monkey (one female at 25 mg/kg/day). These effects have been described with other psychotherapeutic agents.

Two dogs receiving intravenous injections of 15 mg/kg/day for 12 days showed severe venous and local irritation, making further injections impossible. Histopathologically,

focal areas of acute hepatocellular necrosis were observed in both dogs, and suppression of spermatogenesis was seen in the male. In another study, 15 mg/kg/day i.v. could only be given for 6 days due to the appearance of venous irritation and thrombus formation. Lower doses of 0.5 and 2 mg/kg/day for 30 days produced, with less frequency, similar, but less severe changes.

A vehicle control group showed minimal local irritation. In two additional studies in dogs, intravenous doses of 0.5-5 mg/kg/day for 15 days also produced some local irritation, including thrombus formation. Tremors, decreased activity and respiration, circling, biting, ataxia and prostration were noted following the injection of 5 mg/kg in one of the studies. These effects, however, were reversible and completely regressed within 30 minutes.

In rats, intramuscular injection of thiothixene parenteral solution, given at doses of 50, 25 or 5 mg/kg/day for five days, is irritating, producing muscle necrosis with localized swelling. Intramuscular injections for more than 5 days were not feasible because of irritation greatly magnified because of the large volumes involved.

In the animal reproductive studies with NAVANE, there was some decrease in conception rate, litter size, and the resorption rate in rats and rabbits which has been commonly reported with other psychotherapeutic agents. After repeated oral administration of NAVANE to rats (5 to 15, mg/kg/day), rabbits (3 to 50 mg/kg/day), and monkeys (1 to 3 mg/kg/day) before and during gestation, no teratogenic effects were seen.

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PART III: CONSUMER INFORMATION

Navane
Thiothixene

This leaflet is part III of a three-part "Product Monograph" published when Navane was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about Navane. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

NAVANE is used to treat schizophrenia and other psychotic disorders.

What it does:

Navane is an antipsychotic medication which affects chemicals in the brain that allow communication between nerve cells (neurotransmitters). These chemicals are called dopamine and serotonin. Exactly how Navane works is unknown. However, it seems to readjust the balance of dopamine and serotonin.

When it should not be used:

You should not use Navane if you have:

- **An allergy to thiothixene, to any of its ingredients or to phenothiazines**
- **A medical condition known as pheochromocytoma (a tumor of the adrenal gland)**
- **A severe heart or blood vessel disorder**
- **Severe kidney problems**
- **Had brain damage**
- **Liver disease**
- **A blood cell disorder such as anemia, low white blood cell counts, or low platelets**
- **Drowsiness, slow breathing, weak pulse**
- **Decreased alertness caused by taking certain medications or drinking alcohol**
- **You are going to receive anesthesia in the spine or for a region (such as an arm, leg or the lower part of your body)**
- **You are under 12 years old**

What the medicinal ingredient is:

Thiothixene

What the nonmedicinal ingredients are:

Corn starch, gelatin (bovine), lactose, magnesium stearate, silicon dioxide, sodium lauryl sulphate, titanium dioxide. The 5mg and 10mg capsules also contain FD&C yellow #6 and FD&C red # 3.

What dosage forms it comes in:

Capsules: 2mg, 5mg and 10mg

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

Studies with various medicines of the group to which NAVANE belongs, when used in the elderly patients with dementia, have been associated with an increased rate of death. NAVANE is not indicated in elderly patients with dementia.

BEFORE you use Navane talk to your doctor or pharmacist if:

- **You have heart disease, glaucoma or prostatic hypertrophy**
- **You are addicted to alcohol. You should not take Navane if you are under the effects of alcohol.**
- **You have risk factors for developing blood clots such as: a family history of blood clots, age over 65, smoking, obesity, recent major surgery (such as hip or knee replacement), immobility due to air travel or other reason, or take oral contraceptives ("The Pill").**
- **You are pregnant. Navane should not be used during pregnancy unless your doctor considers the benefits to you markedly outweigh the potential risks to the fetus**
- **You are taking barbiturates, painkillers , narcotics or, antihistamines or other drugs that make you drowsy.**
- **You have any allergies to this drug or its ingredients**
- **You have or ever had a blackout or seizure**
- **You are breast feeding.**

Navane may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery, especially during the first few days of therapy. You should be cautious when performing potentially hazardous tasks.

Effects on Newborns:

In some cases babies born to a mother taking Navane during pregnancy have experienced symptoms that are severe and require the newborn to be hospitalized. Sometimes, the symptoms may resolve on their own. Be prepared to seek immediate emergency medical attention for your newborn if they have difficulty breathing, are overly sleepy, have muscle stiffness, or floppy muscles (like a rag doll), are shaking, or are having difficulty feeding.

People who take Navane are cautioned:

- **Against exposure to extreme heat**
- **That drugs such as Navane increase the toxicity of certain types of insecticides ("organophosphorous" insecticides) including insecticides for agriculture (farming), treating animals (flea and tick control) and for treating pests around the house and garden. Be cautious if you must use these products while taking Navane.**
- **To avoid unnecessary exposure to sunlight**

INTERACTIONS WITH THIS MEDICATION

Navane can add to the effects of alcohol. You should avoid consuming alcoholic beverages while on Navane therapy.

Tell your doctor about all your prescription and over-the-counter medications, vitamins, minerals, herbal products (such as St. John's Wort), and drugs prescribed by other doctors. Do not start a new medication without telling your doctor.

Before using Navane, tell your doctor if you regularly use other medicines that make you sleepy (such as cold or allergy medicine, narcotic pain medicine, sleeping pills, muscle relaxants, and medicine for seizures, depression, or anxiety). You should not take Navane if you have drowsiness caused by other medications.

Drugs that may interact with Navane include:
anti-anxiety agents, antidepressants, muscle relaxants, anti-seizure medicine, high blood pressure medicine, cabergoline, metrizamide, guanethidine, guanadrel, grepafloxacin, sparfloxacin, lithium, cisapride, atropine-like drugs, narcotic pain relievers (e.g., codeine), drugs used to aid sleep, drowsiness-causing antihistamines (e.g., diphenhydramine), other drugs that may make you drowsy and carbamazepine.

Many cough-and-cold products contain ingredients that may add a drowsiness effect. Before using cough-and-cold medications, ask your doctor or pharmacist about the safe use of those products. Do not start or stop any medicine without doctor or pharmacist approval.

This list is not complete and there may be other drugs that can interact with Navane.

PROPER USE OF THIS MEDICATION

Take this medication by mouth exactly as prescribed. During the first few days your doctor may gradually increase your dose to allow your body to adjust to the medication. Do not take this more often or increase your dose without consulting your doctor. Your condition will not improve any faster but the risk of serious side effects will be increased. Do not stop taking this drug suddenly without your doctor's approval.

Your doctor will decide which dose is best for you.

Usual dose:

Usual Adult Initial dose: 5 to 10 mg once a day.

Usual adult optimal dose: 15 to 30 mg once a day. This dose could be increased by your physician.

Doses up to 60 mg a day can be divided in equal doses and given twice or three times a day.

Overdose:

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

Overdose symptoms may include agitation, and confusion, drowsiness, dizziness, muscle stiffness or twitching, increased salivation, trouble swallowing, weakness, loss of balance or coordination, and fainting.

Missed Dose:

Take the missed dose as soon as you remember. If it is almost time for your next dose, wait until then to take the medicine and skip the missed dose. Do not double your dose to make up the missed dose.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like other medications, Navane may cause some side effects. These side effects may be minor and temporary. However, some may be serious and need medical attention.

Side effects may include: sweating, urinary incontinence, dizziness, drowsiness, restlessness, agitation, depression, cramps, seizures, dry mouth, drooling, nasal congestion, nausea and vomiting, headache, menstrual changes, change in libido, impotence, swelling of the breasts and milk production in both men and women, weight changes and blurred vision, your skin may become more sensitive to sunburn, or you may have difficulty sleeping.

If any of these affects you severely, tell your doctor.

Your doctor should check your body weight before starting Navane and continue to monitor it for as long as you are being treated.

Your doctor should take blood tests before starting Navane. They will monitor blood sugar, your liver and the number of infection fighting white blood cells. Your doctor should continue to monitor your blood for as long as you are being treated.

If you have high levels of prolactin (measured with a blood test) and a condition called hypogonadism you may be at increased risk of breaking a bone due to osteoporosis. This occurs in both men and women.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM				
Symptom / effect		**Talk with your doctor or pharmacist**		**Stop taking drug and seek immediate emergency medical attention**
		Only if severe	**In all cases**	
Unknown	**Allergic Reaction:** rash, hives, swelling of the face, lips, tongue or throat, difficulty swallowing or breathing			✓
	Neuroleptic Malignant Syndrome: any group of symptoms which may include high fever, sweating, stiff muscles, fast heartbeat, fast breathing and feeling confused, drowsy or agitated			✓
	Extrapyramidal Symptoms: muscle stiffness, body spasms, upward eye rolling, exaggeration of reflexes, drooling, difficulty moving how and when you want.			✓
	Fast or irregular heartbeat		✓	
	Seizures or fits			✓
	Long-lasting (greater than 4 hours in duration) and painful erection of penis			✓

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM				
Symptom / effect		**Talk with your doctor or pharmacist**		**Stop taking drug and seek immediate emergency medical attention**
		Only if severe	**In all cases**	
	Tardive Dyskinesia: uncontrollable movements or twitches of the body, face, eyes or tongue, stretching the neck and body		✓	
	Low Blood Pressure: feeling of Lightheadedness or fainting especially when getting up from a lying or sitting position		✓	
	High Blood Pressure: headaches, vision disorders, nausea and vomiting		✓	
	Decreased sweating		✓	
	Jaundice: yellow colour to skin and eyes, dark urine		✓	
	Respiratory Infection: fever, flu-like symptoms, coughing, difficult or fast breathing		✓	
	New or worsening constipation		✓	
	Akathisia: a feeling of restlessness, inability to remain motionless		✓	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and seek immediate emergency medical attention
		Only if severe	In all cases	
	Vision Changes: blurred vision, glaucoma or other eye disorder		✓	
	Increased Blood Sugar: frequent urination, thirst and hunger	✓		
Uncommon	Blood clots: swelling, pain and redness in an arm or leg that can be warm to touch. You may develop sudden chest pain, difficulty breathing and heart palpitations.		✓	

This is not a complete list of side effects. For any unexpected effects while taking Navane, contact your doctor or pharmacist.

HOW TO STORE IT

Store this medication at room temperature between 15 and 30 oC away from heat and light. Do not store in the bathroom. Keep this and all medications out of the reach and sight of children.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- **Report online at www.healthcanada.gc.ca/medeffect**
- **Call toll-free at 1-866-234-2345**
- **Complete a Canada Vigilance Reporting Form and:**
  - **Fax toll-free to 1-866-678-6789, or**
  - **Mail to: Canada Vigilance Program**
    Health Canada
    Postal Locator 0701E
    Ottawa, Ontario
    K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at:
http://www.ECI2012.net
or by contacting the sponsor, ERFA Canada 2012 Inc., at:
1-800-922-3133

This leaflet was prepared by ERFA Canada Inc.

Last revised: December 19, 2012.