PATIENT's INFORMED CONSENT - INFORMATION SHEET

Limited access protocol for the use of oral cisapride in the treatment of refractory gastroesophageal reflux disease and other gastrointestinal motility disorders. - CIS-USA-154

DESCRIPTION AND PURPOSE

The purpose of this investigational limited access program is to allow the use of cisapride by patients with gastroesophageal reflux disease (a flow of stomach and small intestinal contents into the feeding tube) and other gastrointestinal motility disorders (problems moving food through the digestive system), who have failed standard therapy and cannot be managed by any other available therapy.

Cisapride has not been approved by the Food and Drug Administration (FDA) for use in these conditions. Although there have been some studies related to the efficacy of cisapride in these conditions, results of these studies are not uniformly consistent. Consideration for entry into this program will be limited to patients whose medical conditions are likely to result in serious health problems.

Propulsid® (cisapride) was approved by the FDA in 1993 for the treatment of nighttime heartburn due to gastroesophageal reflux disease in adults. The drug is also used for many other ("off-label") treatments in adults and children. However, the FDA has no information on the effectiveness and safety of cisapride for these uses, and these uses are not approved by the FDA. Approximately 9.5 million patients have received this drug in the US.

Because of reports of serious heart rhythm abnormalities and death associated with the use of cisapride, the maker of the drug (Janssen Pharmaceutica Products, L.P.), in consultation with the FDA, decided to stop marketing the drug in the United States on July 14, 2000. However, the company will make it available in an investigational limited access program for selected patients with serious medical conditions for whom other treatments have not worked. Risks related to cisapride use are discussed in detail under the "RISKS AND POSSIBLE SIDE EFFECTS" section of this consent form.

You may be eligible to participate in this investigational limited access program. Your potential eligibility is based on your physicians assessment that you have a serious or severe motility related disorder and you have failed other usually prescribed therapies. Information will be collected on any problems you may have while taking cisapride. Limited information will also be collected on whether the drug is effective for the condition you are being treated for.

Before you decide to participate in this investigational limited access program, you should read the following carefully. Ask as many questions as necessary to be sure that you understand what your participation will involve and which drugs will be used for your care.

RISKS AND POSSIBLE SIDE EFFECTS

The use of cisapride has been associated with serious cardiac arrhythmias (serious disturbances of heart rhythm), in some cases resulting in death. Eighty five percent of these cases were associated with a risk factor. Risk factors include taking certain drugs at the same time as cisapride and some health disorders that predispose patients to arrhythmias. (See Disallowed Medical Conditions and Disallowed Medication Section of this consent)

From the time the drug was approved in 1993, through the end of April 2000, there have been 416 reported cases (52 of them in children up to age 16) of serious heart rhythm abnormalities. Of these 416 cases, 124 (14 of them in children up to age 16) resulted in death. In addition to the "spontaneous reports", there have been reports of death and heart rhythm abnormalities in two controlled studies of cisapride in infants. In one study, in which 50 infants were treated with cisapride, one 9½ month old male receiving cisapride in combination with cimetidine (a drug which may increase the toxicity of cisapride) died suddenly. In the other study, 2 out of 35 children receiving cisapride with antibiotics known to increase the toxicity of cisapride, developed a serious heart arrhythmia (Torsades de pointes) that can lead to death. In this study

up to one third of the patients on cisapride developed ECG changes, which could lead to heart rhythm abnormalities.

Pediatric deaths have been associated with seizures and there has been at least one case of unexplained death in a 3-month old infant.There have been rare cases of sinus tachycardia (an abnormal rapid heart rhythm that is usually not life-threatening) reported.

PARTICIPATION

To be eligible for this program, you must be age 18 or older. Your program doctor will determine if you are eligible to participate in this program.

Participation in this program is voluntary. You may refuse to participate or withdraw from the program at any time. Your refusal to participate or wish to withdraw from the program will have no effect on your future medical care. If you decide to withdraw from the program, please contact your program doctor immediately.

PROCEDURES

Your program doctor, or associates, will thoroughly review your medical history records to determine if you are eligible to participate. If so, you will undergo a complete physical examination, an ECG (a graph of the electrical action of the heart), and routine laboratory blood tests. The ECG consists of placing pieces of sticky plastic on your arms and legs. These will stay in place and are attached to wires connected to a machine. Electrical activity readings of your heartbeat will be recorded on a paper printout from the machine. For laboratory tests, approximately 3 teaspoons of blood will be drawn from your arm.

Your program doctor will also decide if other diagnostic tests (such as X-rays) are appropriate. You should ask your program doctor to explain the other tests he/she will perform.

If you are a female of childbearing potential, you must have a negative urine pregnancy test to qualify for this program, and pregnancy testing must be repeated at specified visits throughout your participation in this program when other safety laboratory tests are performed. Also, you will not be able to participate if you are a nursing mother. Because the risk to the unborn child is unknown, females of childbearing potential must agree to use an effective form of birth control during participation in this program. Acceptable methods of birth control, include, but are not limited to oral contraceptives ("the pill"), NORPLANT®, DEPO-PROVERA®, IUD, diaphragm with spermicide, or condom with spermicide. Female patients who believe they may have become pregnant during the program must inform the program doctor immediately and stop taking the cisapride. Your program doctor must report the outcome of the pregnancy to the program sponsor.

If your test results are acceptable, and you are eligible to participate, you will receive the program medication, cisapride, which is to be taken 4 times a day: 15 minutes before meals and at bedtime. Cisapride is available in both tablet and liquid form.

You will be given a two-month supply of the program medication initially, a one month supply at week 6, and a 3 month supply thereafter. The program medication must be taken only by you, the person for whom it has been prescribed, and it must be kept out of the reach of children. Despite the child-resistant packaging, if you have children in your household that could gain access to it, open the medication and ingest it, the medication could be harmful. Please store the medication in a safe, non-accessible place. Please take care when handling glass bottles of liquid medication. All bottles of study medication, used or unused, must be returned to your physician.

An ECG will be performed four to six days after the start of cisapride treatment, three months after the start of cisapride treatment, and every six months thereafter.

At six weeks, your program doctor will assess whether the cisapride therapy is helping you. If cisapride is helping, you will be given an additional supply of medication. If cisapride has not improved your illness, your program doctor will either discontinue you from the program or, if he/she thinks an increased dose may benefit you, increase the dose of cisapride. If your program doctor increases your dose of cisapride, an ECG will be performed 4-6 days after the dose increase.

Three months after starting cisapride and every three months thereafter, you will be examined by your program doctor to ensure that there are no changes which might increase the risk of cisapride use. The examination will include a history, physical exam and reassessment of the risk and benefit of cisapride therapy. Three months after the start of cisapride treatment, and every six months thereafter, blood will be taken for testing (also, if applicable, a pregnancy test will be repeated). If there are no new risk factors and you continue to derive benefit from the drug, cisapride may be continued and you will be given additional cisapride supplies. There is no scheduled end point of this program.

If after one year of cisapride treatment within the Limited Access Program you have maintained a benefit and have not developed any risk factors to warrant discontinuation of treatment, the frequency of your office visits will decrease from every 3 months to every 6 months. ECG and laboratory testing will still be required every 6 months along with an updated History, Physical and Risk/Benefit Assessment. Thus, the interim 3 month visits in which no safety testing was required has been eliminated.

Additional supplies of cisapride will not be sent to your program doctor until your continued eligibility is verified. Therefore, it is important that you and your program doctor schedule and complete all visits and required testing before your supply of cisapride is depleted.

When you are discontinued from the program, a complete physical examination, ECG, and laboratory blood tests will be performed.

DISALLOWED MEDICAL CONDITIONS

To be eligible for this program, you **cannot** have any of the following medical conditions:

- kidney failure
- respiratory failure
- dehydration or vomiting
- malnutrition or eating disorders
- electrolyte disorders like decreased potassium, calcium, or magnesium
- **any** heart problems, including structural heart defects, abnormal heart rhythm, congestive heart failure, significant low heart rate
- **family** history of long QT syndrome (a heart condition related to the electrical activity of the heart)

These medical conditions may increase your risk for heart rhythm abnormalities and death when you take cisapride. You may not have these conditions now, but if your medical condition changes (for example, if you develop kidney disease) this may require that you stop taking cisapride. Please completely review the disallowed medical conditions list as well as the disallowed medications below. You must date and initial all pages of this consent after you have reviewed **both** lists.

You will also be provided a patient safety wallet card, cisapride product information, and the attached disallowed medication list each time you receive cisapride supplies from your program doctor. Please carry the wallet card at all times and show it to any other physician, pharmacist, or other health care provider who may change or add to your medical care.

DISALLOWED MEDICATIONS/SUBSTANCES

Certain medications/substances from the following categories must **not** be taken with cisapride. When taken together with cisapride, these drugs may increase the risk of cardiac arrhythmias or other side effects. Other drugs may elevate levels of cisapride in the blood. This may lead to a higher risk of side effects. Please verify that you are **not** taking any of these medications or substances:

- antibiotics such as clarithromycin, erythromycin, and troleandomycin
- antifungals such as fluconazole, itraconazole, ketoconazole
- antidepressants such as nefazodone, amitriptyline, or maprotiline
- protease inhibitors
- antiarrhythmics such as quinidine, procainamide and sotalol
- antipsychotic medications such as sertindole
- phenothiazine, such as prochlorperazine and promethazine

- other agents such as bepridil and sparfloxacin
- other gastromotility agents such as cimetidine or domperidone
- the administration of diuretics or insulin used in the acute setting
- grapefruit juice

A detailed list of medications (includes brand and generic names) follows.

If you require surgery while participating in the program, cisapride **must** be temporarily discontinued at least two (2) days prior to the surgery, because of possible drug interactions with certain anesthetics. Cisapride may be restarted after the surgery. Please contact your program doctor for further instruction.

ADDITIONAL RISKS AND SIDE EFFECTS

Other unlabeled, potentially serious illnesses which have been reported in pediatric patients taking cisapride include positive antinuclear antibody (a disease that affects cells in the body), reduction in the amount of certain types of cells in the blood (anemia and hemolytic anemia), reduction in the ability of blood to carry oxygen to body tissues (methemoglobinemia), high blood sugar (hyperglycemia), and low blood sugar (hypoglycemia) with abnormal accumulation of acids in the blood (acidosis), unexplained episodes of infants who stopped breathing (apnea), confusion, impaired concentration, depression, listlessness, visual changes accompanied by memory loss (amnesia), and rashes occurring with light exposure (severe photosensitivity reaction). The relationship to cisapride was not clear in these cases.

Those patients greater than 65 years of age may be at increased risk for cardiac arrhythmias because blood levels of cisapride are generally higher in the elderly. The rate of common adverse experiences in elderly patients was similar to that of younger adults.

In addition to the serious risks noted above, the most common side effects reported with the use of cisapride during clinical studies conducted in the United States (U.S.) were dizziness, vomiting, sore throat, chest pain, fatigue, back pain, depression, dehydration, muscular pain, diarrhea, abdominal pain, constipation, gas, and runny nose.

In other U.S. and international studies and in postmarketing experience, there have been rare reports of seizures and other extrapyramidal effects (the part of the nervous system involved in involuntary body movement, such as maintaining and adjusting posture, and large motor movements like those of your shoulder or thigh muscles). Also reported have been rapid heart rate, elevated liver enzymes, inflammation of the liver, reduction of the blood cells that help the blood to clot, reduction of a certain type of white blood cell (leukocyte), reduction of red blood cells due to bone marrow disorders (aplastic anemia), reduction of all types of cells in the blood (pancytopenia), and a reduction of granulocytes- a type of white blood cell (granulocytopenia). The relationship to cisapride was not clear in these cases.

There may be certain risks or side effects that exist but are currently unknown. Any new information obtained during the course of the program that might influence your desire to continue in the program will be provided to you as it becomes available.

Venipuncture is a routine procedure used for collecting blood samples. A needle is inserted into a vein in the arm and a small blood sample is withdrawn. Although one venipuncture is usually sufficient, a second one may be necessary if the first is not successful. Blood sampling may cause fainting and some pain and/or bruising at the site on your arm where the blood was taken. The laboratory blood tests will require approximately 15 ml (3 teaspoonfuls) of your blood to be drawn to test for abnormalities at screening, the first 3-month visit and then every six months.

You may have local irritation or rash from ECG skin attachments.

BENEFITS

It is possible that by participating in this program your condition may improve.

ALTERNATIVE TREATMENT

The majority of patients with GERD and nocturnal heartburn can be effectively managed with acid reduction by use of medications such as H2 antagonists or proton pump inhibitors. Patients with gastrointestinal motility disorders, such as gastroparesis, pseudo-obstruction or severe chronic constipation may be treated with metoclopramide. You should discuss these and any other methods of treatment with your program doctor.

TERMINATION

Participation in the program may be terminated by your program doctor without your consent if he/she thinks this is in your best interest. Janssen Pharmaceutica Products, L.P., the sponsor of this program, may also stop your participation at any time. Regardless of the reason for terminating the program, a final program visit will be performed, if possible.

Your participation may also be terminated without your agreement if your heart rhythm changes, you have other health problems due to taking cisapride, or if cisapride does not help your health problem.

PATIENT'S DECISION TO WITHDRAW

You have the right to withdraw from the study at anytime. This decision will not affect subsequent medical care. Because of the problems involved with taking cisapride, you will be asked to have an ECG and any other physical examination or lab tests necessary to make sure that you have no problems from taking cisapride.

COSTS

Certain procedures (e.g. laboratory blood tests, ECGs, and diagnostic tests) will be required throughout the program to monitor your safety. Since these tests are being done because of your participation in this investigational limited access program, your insurance company or other health care provider may not cover the costs of these procedures. You will be responsible for costs related to these procedures. The cost of travel to and from the hospital, your program doctor's fees, parking, childcare expenses (if applicable), and meals **will not** be covered. Cisapride will be provided at no cost to you or your program doctor.

PROGRAM RELATED INJURY

No compensation or medical treatment is available from the sponsor for any injuries arising from or related to participation in this program.

CONFIDENTIALITY

Your identity in this program will be treated as strictly confidential. However, in order to meet legal obligations, records identifying you will be inspected by individuals representing Janssen Pharmaceutica Products, L.P. and may also be inspected by the Food and Drug Administration (FDA) and/or the approving Institutional Review Board (IRB) the Mid*Lands Institutional Review Board. In addition, copies of your signed informed consent and hospital record(s) confirming your program eligibility will be provided to the program sponsor. Results of this program may be published in journals or presented at meetings, but you will not be identified by name, and every effort will be made to protect your identity. By signing this document, you consent to such inspection and disclosure.

QUESTIONS

If you have any questions at any time about the program or in the event of a drug side effect, you should contact Dr. Leonard Weinstock at 314-388-6578 (24-hour coverage).

This program has been reviewed by an Institutional Review Board (IRB) for the purpose of protecting your rights. If you have any questions concerning your rights as a program participant, you should call the Mid*Lands Institutional Review Board at (913) 385-1414 or 1-800-636-4445.

Patient Information - Disallowed Medications

NOTE: THIS IS A LIST OF DRUGS THAT HAVE THE POTENTIAL FOR INTERACTION WITH **CISAPRIDE. Formal studies have not proven the interaction of all of these drugs.**

All formulations (i.e., topical. oral, inhalant, IV) should be considered to have potential interaction with cisapride. This list was revised April 20, 2000.

THIS LIST IS NOT COMPREHENSIVE.

P450 3A4 INHIBITORS (This list is not comprehensive):

BRAND NAME	GENERIC NAME
ANTIDEPRESSANTS	
LUVOX	fluvoxamine
PAXIL	paroxetine
PROZAC	fluoxetine
SERZONE	nefazodone
ZOLOFT	sertraline
ANTI-INFECTIVE AGENTS	
AKNEMYCIN	erythromycin
BIAXIN	clarithromycin
CHIBROXIN	norfloxacin
E.E.S.	erythromycin
ERYDERM	erythromycin
ERYGEL	erythromycin
ERY-TAB	erythromycin
ERYTHROCIN	erythromycin
ERYTHROMYCIN BASE FILMTAB	erythromycin
ERYTHROSTATIN	erythromycin
NOROXIN	norfloxacin
QUININE SULFATE	quinine
SYNERCID	quinupristin and dalfopristin
TAO	troleandomycin
ANTIEMETICS	
MARINOL	dronabinol, THC
ANTIFUNGAL AGENTS	
DIFLUCAN	fluconazole
MICATIN	miconazole
MONISTAT	miconazole
NIZORAL	ketoconazole
SPORANOX	itraconazole
CARDIOVASCULAR AGENTS	
POSICOR	mibefradil
VIAGRA	sildenafil

P450 3A4 INHIBITORS (This list is not comprehensive):

BRAND NAME	GENERIC NAME
HEMATOLOGICAL AGENTS	
PLETAL	cilostazol
HIV PROTEASE INHIBITORS	
AGENERASE	amprenavir
CRIXIVAN	indinavir
NORVIR	ritonavir
RESPIRATORY AGENTS	
ACCOLATE	zafirlukast

MEDICATIONS KNOWN TO PROLONG THE QT INTERVAL AND INCREASE THE RISK OF ARRHYTHMIA (This list is not comprehensive):

BRAND NAME	GENERIC NAME
ANTIDEPRESSANTS	
ADAPIN	doxepin
ANAFRANIL	clomipramine
ASENDIN	amoxapine
DESYREL	trazodone
EFFEXOR	venlafaxine
ELAVIL	amitriptyline
ENDEP	amitriptyline
ETRAFON	amitriptyline
LIMBITROL	amitriptyline
LUDIOMIL	maprotiline
NORPRAMIN	desipramine
PAMELOR	nortriptyline
SINEQUAN	doxepin
SURMONTIL	trimipramine
TOFRANIL	imipramine
TRIAVIL	amitriptyline
VIVACTIL	protriptyline
ZONALON	doxepin
ANTIEMETICS	
PHENOTHIAZINE DERIVATIVES	
COMPAZINE	prochlorperazine
MELLARIL	thioridazine
PHENERGAN	promethazine
SERENTIL	mesoridazine
THORAZINE	chlorpromazine
TORECAN	thiethylperazine
TRILAFON	perphenazine
OTHER	
ANZEMET	dolasetron

MEDICATIONS KNOWN TO PROLONG THE QT INTERVAL AND INCREASE THE RISK OF ARRHYTHMIA (This list is not comprehensive):

BRAND NAME	GENERIC NAME
ANTIEPILEPTICS	
CEREBYX	fosphenytoin
FELBATROL	felbamate
ANTIHISTAMINES	
ASTELIN	azelastine
TAVIST	clemastine
HISMANAL	astemizole (withdrawn from market)
SELDANE	terfenadine (withdrawn from US market)
ANTI-INFECTIVE AGENTS	
AKNEMYCIN	erythromycin
BIAXIN	clarithromycin
E.E.S.	erythromycin
ERYDERM	erythromycin
ERYGEL	erythromycin
ERY-TAB	erythromycin
ERYTHROCIN	erythromycin
ERYTHROMYCIN BASE FILMTAB	erythromycin
ERYTHROSTATIN	erythromycin
NEBUPENT	pentamidine
PENTACARINAT	pentamidine
PENTAM	pentamidine
RAXAR	grepafloxacin
ZAGAM	sparfloxacin
ANTIMALARIAL	
	halofantrine
ANTIPSYCHOTICS	
HALDOL	haloperidol
ORAP	pimozide
SERLECT	sertindole
SEROQUEL	quetiapine
ANTIVIRAL AGENTS	
FOSCAVIR	foscarnet
BRONCHODILATORS	
SEREVENT	salmeterol
CANCER TREATMENT	
NOLVADEX	tamoxifen

MEDICATIONS KNOWN TO PROLONG THE QT INTERVAL AND INCREASE THE RISK OF ARRHYTHMIA (This list is not comprehensive):

BRAND NAME	GENERIC NAME
CARDIOVASCULAR AGENTS	
ANTIHYPERTENSIVE AGENTS	
CARDENE	nicardipine
DYNACIRC	isradipine
UNIRETIC	moexipril/HCTZ
CALCIUM CHANNEL BLOCKERS	
CALAN	verapamil
CARDIZEM	diltiazem
TARKA	verapamil/trandolapril
TECZEM	diltiazem/enalapril
TONOCARD	tocainide
VASCOR	bepridil
CERTAIN ANTIARRHYTHMICS	
Class I	
CARDIOQUIN	quinidine
DURAQUIN	quinidine
ENKAID	encainide
NORPACE	disopyramide
PROCAN	procainamide
PROCANBID	procainamide
PRONESTYL	procainamide
QUINIDEX	quinidine
QUINAGLUTE	quinidine
TAMBOCOR	flecainide
Class III	
BETAPACE	sotalol
BRETYLOL	bretylium
CORDARONE	amiodarone
CORVERT	ibutilide
TIKOSYN	dofetilide
ANTILIPEMICS	
LORELCO	probucol
DIARRHEA TREATMENT	
SANDOSTATIN	octreotide
MIGRAINE TREATMENT	
AMERGE	naratriptan
IMITREX	sumatriptan
ZOMIG	zolmitriptan
MUSCLE RELAXANTS	
ZANAFLEX	tizanidine
NARCOTIC DEPENDENCE	
ORLAAM	levomethadyl
NUTRITIONAL PRODUCTS	
HEARTCARE	hawthorn, crataegus laevigata

OTHER DISALLOWED MEDICATIONS: (included but not limited to):

BRAND NAME	GENERIC NAME
ANTIDIABETIC AGENTS - INTRAVENOUS (used in acute setting)	
various trade names	insulin
GASTROINTESTINAL AGENTS	
MOTILIUM	domperidone
TAGAMET	cimetidine
POTASSIUM WASTING DIURETICS - INTRAVENOUS (used in acute setting)	
LOOP DIURETICS	
BUMEX	bumetanide
LASIX	furosemide
DEMADEX	torsemide
EDECRIN	ethacrynic acid
THIAZIDES	
DIURIL	chlorothiazide
OTHER	
LOZOL	indapamide

ALSO DISALLOWED:

GRAPEFRUIT JUICE

ADDITIONAL DISALLLOWED MEDICATIONS

Update #2 – September 28, 2001

P450 3A4 INHIBITORS

Brand Name	Generic Name
Femstat 3	butoconazole
Sarafem	fluoxetine hydrochloride
Terazol	terconazole
Vagistat	ticonazole

MEDICATIONS KNOWN TO PROLONG THE QT INTERVAL AND INCREASE THE RISK OF ARRHYTHMIA

Brand Name	Generic Name
Dilantin	phenytoin
Geodon	ziprasidone
Inapsine	droperidol
Risperdal	risperidone
Zithromax	azithromycin
Floxin	ofloxacin
Levaquin	levofloxacin
Foradil Aerolizer	formoterol fumarate

PROPULSID CONTRAINDICATED DRUG LIST AS SPECIFIED IN PROPULSID LABELING

THE FOLLOWING TABLE IS NOT COMPREHENSIVE. This list contains the drugs that are specifically listed in PROPULSID labeling as contraindications

Generic Name	Brand Name(s)
Certain Macrolide Antibiotics	
Clarithromycin	Biaxin®
Erythromycin	E.E.S.®; E-mycin®; Pediazole®; My-E®; PCE®; Ery Ped®; Ery-Tab®; Erythrocin®; Ilosone®
Troleandomycin	TAO®
Certain Antifungals	
Fluconazole	Diflucan®
Itraconazole	Sporanox®
Ketoconazole	Nizoral® tablets
Class I Antiarrhythmics	
Disopyramide	Norpace®, Norpace CR®
Moricizine	Ethmozine®
Procainamide	Procanbid®; Procan SR®; Promine®; Pronestyl®; Pronestyl-SR®; Rhythmin®
Quinidine	Cardioquin®; Cin-Quin®; Duraquin®; Quinatime®; Quinaglute®; Dura-Tabs®; Quinalan®; Quinidex® Extentabs; Quinora®
Class III Antiarrhythmics	
Amiodarone	Cordarone®; Pacerone®
Bretylium	Bretylium® Tosylate; Bretylol®
Ibutilide	Corvert®
Sotalol	Betapace®
Dofetilide	Tikosyn® (currently not available on market)

Generic Name	Brand Name(s)
Tricyclic Antidepressants	
Amitriptyline	Elavil®; Endep®; Enovil®
Amitriptyline and Chlordiazepoxide	Limbitrol®
Amitriptyiline and Perphenazine	Etrafon®; Triavil®)
Amoxapine	Asendin®
Clomipramine	Anafranil®
Desipramine	Norpramine®
Doxepin	Adapin® Oral; Sinequin® Oral; Zonalon® Topical Cream
Imipramine	Janimine®; Tofranil®; Tofranil-PM®
Nortriptyline	Aventyl® Hydrochloride; Pamelor®
Protriptyline	Vivactil®
Trimipramine	Surmontil®
Phenothiazine Antipsychotics	
Chlorpromazine	Ormazine®; Thorazine®
Fluphenazine	Apo-Fluphenazine; Modecate Concentrate; Moditen; Permitil®; PMS-Fluphenazine; Prolixin®; Rho-Fluphenazine
Mesoridazine	Serentil®
Perphenazine	Trilafon®
Perphenazine and Amitriptyline	Etrafon®; Triavil®
Prochlorperazine	Compazine®
Promazine	Sparine®
Thiethylperazine Maleate	Norzine®; Torecan®
Thioridazine	Mellaril®; Mellaril-S®
Trifluoperazine	Stelazine®
Protease Inhibitors	
Amprenavir	Agenerase®
Indinavir	Crixivan®
Nelfinavir	Viracept®
Ritonavir	Norvir®
Saquinavir	Fortovase® Invirase™
Certain Antidepressants	
Nefazodone	Serzone®
Maprotiline	Ludiomil®
Certain Antipsychotic Medications	
Sertindole	
Other Agents	
Bepridil	Vascor®
Sparfloxacin	Zagam®
Grapefruit Juice	

INFORMED CONSENT - Patient

0. I,_____ _____ have read the above text and I agree to take part in the Cisapride (Propulsid®) Investigational Limited Access Program.

0. I was given a copy of this signed and dated Informed Consent Form and the corresponding Patient Information Sheet. I received an explanation of the nature, purpose, duration and foreseeable effects of the program and what I will be expected to do. The possible risks and benefits of the program and the alternative treatments available for my illness have been explained to me. I was given time and opportunity to inquire about the program and all my questions were answered to my satisfaction.

0. I agree to cooperate fully with the program doctor and will tell him/her if I suffer any unexpected or unusual symptoms. I confirm that I have informed the program doctor of any medication/drug, of whatever nature, I have taken in the month preceding the start of the program, or I am taking or plan to take, whether prescribed or not.

0. I understand that I am free to withdraw from the program at any time, without the need to justify my decision and without any disadvantage to my future medical treatment. Upon withdrawal, I will be asked to have an ECG and any other physical examination or lab tests necessary to make sure that no problems have developed from taking cisapride.

0. I have been informed that in the event of an illness or injury arising from or related to participation in this Investigational Limited Access Program, no compensation or medical treatment will be available from Janssen Pharmaceutica Products, L.P., the sponsor of this program.

0. I am aware that this program is subject to the review and approval of an Institutional Review Board (IRB).

0. I agree that results of the program may be passed on to the appropriate authorities and to the manufacturer of the drug under investigation.

0. I understand that representatives of the Sponsor, IRB or Regulatory Authorities may wish to inspect my medical records to verify the information collected. By signing this document I give permission for this review of my records.

I voluntarily ~~consent~~ to participate in the Cisapride Investigational Limited Access Program.

X _____ _____ _____

Patient's Signature *Date (mm/dd/yyyy)*

_____

Patient's Name in printing

I confirm that I have explained the nature, purpose and foreseeable effects of the program to the patient whose name is printed above. The patient consented to participate by his/her personally dated signature.

_____ _____ _____

Informed Consent Provider's Signature *Date (mm/dd/yyyy)*

Leonard Weinstock

Informed Consent Provider's Name in printing

Authorization to Use/Disclose Protected Health Information (PHI)

Protocol Title: **"Limited access protocol for the use of oral cisapride in the treatment of refractory gastroesophageal reflux disease and other gastrointestinal motility disorders"**

Protocol Number: **CIS-USA-154**

Sponsor: **Janssen Pharmaceutica Products, L.P.**

Permission To Release Personal Health Information

This document explains how personal health information collected about you during this treatment protocol may be used. Your personal health information includes, but is not limited to, information that was collected for your entry into the treatment protocol and information that is collected during the treatment protocol. The purpose of collecting this information is to allow the staff and the doctor to conduct the treatment protocol.

You may decide not to give permission for the release of your personal health information. In that case, you may not be able to participate in the treatment protocol. This is because the staff and/or the doctor would not be able to collect the information needed to conduct the treatment protocol.

The information the doctor sends to Janssen Pharmaceutica Products, L.P., does not include your name, address, or social security number except as identified on this document and the consent form. Instead, the doctor will use your initials and an assigned code number for the information that is sent to Janssen Pharmaceutica Products, L.P.

Your doctor may disclose your personal health information to the Institutional Review Board (IRB) and to Janssen Pharmaceutica Products, L.P., including people who work with Janssen Pharmaceutica Products, L.P. The people who work with Janssen Pharmaceutica Products, L.P. may include data monitoring committees, contract research organizations, and consultants who have contracts with the company to assist with the treatment protocol. An IRB is an independent body of individuals made up of medical/scientific professionals and nonmedical/nonscientific members, whose responsibility it is to ensure the protection of the rights, safety, and well-being of human subjects involved in a treatment protocol and to provide public assurance of that protection.

Your treatment records and also your entire medical record may be inspected at the doctor's office by Janssen Pharmaceutica Products, L.P. and/or people who work with Janssen Pharmaceutica Products, L.P. and by regulatory authorities in the United States, such as the Food and Drug Administration (FDA), or regulatory agencies from other countries. These reviews are done to check on the quality of the conduct of the treatment protocol. Safety information from the treatment protocol may be shared with the FDA.

You may ask the doctor to see and copy your personal health information related to the treatment protocol. You may also ask the doctor to correct any treatment protocol related information about you that is wrong.

This permission to share your personal health information for this treatment protocol does not have an expiration date. If you no longer want to share your personal health information, you may withdraw permission at any time by writing to the staff and/or the doctor at the address below:

Leonard Weinstock, M.D.
11525 Old Cabin Road
Creve Coeur, MO 63114

If you withdraw your permission after you have started in the treatment protocol, the staff and the doctor will stop collecting your personal health information. Although they will stop collecting new information about you, they will need to use the information they have already collected to evaluate the treatment protocol. If you start the treatment protocol and then you withdraw permission, you may not be able to continue to participate in the treatment protocol. This is because the staff and/or the doctor would not be able to collect the information needed to evaluate your participation in the treatment protocol.

Janssen Pharmaceutica Products, L.P. will make every effort to keep your personal health information private. But after the staff or the doctor share your personal health information from the treatment protocol, federal privacy laws may not keep it private. There might be laws in your state or other federal laws that would protect the privacy of this information.

You will receive a signed and dated copy of this form to keep with your consent form.

Printed Name of Participant

Signature of Participant Date

I certify that under state law I am the legally authorized representative of the Participant named above and that I am authorized to sign this form to release the Participant's medical records and health information as described above.

Printed Name of Legal Representative

Signature of Legal Representative Date

ADDITIONAL DISALLLOWED MEDICATIONS

NOTE: New additions to the list will be italicized.

P450 3A4 INHIBITORS

Brand Name	Generic Name
Femstat 3	butoconazole
Sarafem	fluoxetine hydrochloride
Terazol	terconazole
Vagistat	ticonazole

MEDICATIONS KNOWN TO PROLONG THE QT INTERVAL AND INCREASE THE RISK OF ARRHYTHMIA

Brand Name	Generic Name
Advair Diskus	fluticasone/salmeterol
Aloxi	***palonosetron***
Avelox	moxifloxacin
Dilantin	phenytoin
Dolophine	methadone
Flexeril	cyclobenzaprine
Floxin	ofloxacin
Foradil Aerolizer	formoterol fumarate
Geodon	ziprasidone
Inapsine	droperidol
Levaquin	levofloxacin
Risperdal	risperidone
Tequin	gatifloxacin
Zithromax	azithromycin
Zofran	ondansetron

ADDITIONAL DISALLOWED:

Zelnorm (tegaserod maleate) may NOT be taken with cisapride.

Precaution:

Caution should be exercised with the ingestion of red wine concomitant with cisapride therapy. Data from a recent clinical study (Clin Phar Ther Jul 2001) suggests that although the interaction of red wine and cisapride is minimal or not significant in most individuals, an elevation in plasma cisapride levels, similar in magnitude to that occurring with grapefruit juice, has been observed in some individuals. The clinical significance of this interaction has not been established.

Patient Information - Disallowed Medications by Brand Name

NOTE: THIS IS A LIST OF DRUGS THAT HAVE THE POTENTIAL FOR INTERACTION WITH CISAPRIDE. Formal studies have not proven the interaction of all of these drugs. All formulations (i.e., topical. oral, inhalant, IV) should be considered to have potential interaction with cisapride.

THIS LIST IS NOT COMPREHENSIVE AND IS SUBJECT TO REVISION AS ADDITIONAL INFORMATION BECOMES AVAILABLE.

BRAND NAME	GENERIC NAME
ACCOLATE®	Zafirlukast
ADAPIN®	Doxepin
ADVAIR DISKUS®	fluticasone/salmeterol
AGENERASE®	Amprenavir
AKNE-MYCIN®	Erythromycin
ALOXI®	Palonosetron
AMERGE®	Naratriptan
ANAFRANIL®	Clomipramine
ANZEMET®	Dolasetron
APO-FLUPHENAZINE	Fluphenazine
ASENDIN®	Amoxapine
ASTELIN®	Azelastine
AVELOX®	Moxifloxacin
AVENTYL® HYDROCHLORIDE	Nortriptyline
BETAPACE®	Sotalol
BIAXIN®	Clarithromycin
BRETYLIUM TOSYLATE	Bretylium
BRETYLOL	Bretylium
BUMEX® IV (in an acute setting)	Bumetanide
CALAN®	Verapamil
CARDENE®	Nicardipine
CARDIOQUIN®	Quinidine
CARDIZEM®	Diltiazem
CEREBYX®	Fosphenytoin
CHIBROXIN®	Norfloxacin
CIN-QUIN	Quinidine
COMPAZINE®	Prochlorperazine
CORDARONE®	Amiodarone
CORVERT®	Ibutilide
CRIXIVAN®	Indinavir
DEMADEX® IV (in an acute setting)	Torsemide
DESYREL®	Trazodone
DIFLUCAN®	Fluconazole
DILANTIN®	Phenytoin
DIURIL® IV (in an acute setting)	Chlorothiazide
DOLOPHINE®	Methadone
DURAQUIN	Quinidine
DURA-TABS®	Quinidine
DYNACIRC®	Isradipine
E.E.S.®	Erythromycin
EDECRIN® IV (in an acute setting)	ethacrynic acid

BRAND NAME	GENERIC NAME
EFFEXOR®	Venlafaxine
ELAVIL®	amitriptyline
E-MYCIN	erythromycin
ENDEP®	amitriptyline
ENKAID®	Encainide
ENOVIL	amitriptyline
ERY PED	erythromycin
ERYDERM®	erythromycin
ERYGEL®	erythromycin
ERY-TAB®	erythromycin
ERYTHROCIN®	erythromycin
ERYTHROMYCIN BASE FILMTAB®	erythromycin
ERYTHRO-STATIN	erythromycin
ETHMOZINE®	Moricizine
ETRAFON®	amitriptyline & perphenazine
FELBATOL®	Felbamate
FEMSTAT® 3	butoconazole
FLEXERIL®	cyclobenzaprine
FLOXIN®	Ofloxacin
FORADIL® AEROLIZER®	formoterol fumarate
FORTOVASE®	Saquinavir
FOSCAVIR®	Foscarnet
GEODON®	Ziprasidone
GRAPEFRUIT JUICE	grapefruit juice
HALDOL®	Haloperidol
HALFAN® (not listed in protocol or Informed Consent Form)	halofantrine
HEARTCARE®	hawthorn, crataegus laevigata
HISMANAL® (withdrawn from market)	astemizole
ILOSONE®	erythromycin
IMITREX®	sumatriptan
INAPSINE®	Droperidol
INSULIN (Various) IV (in an acute setting)	Insulin
INVIRASE®	Saquinavir
JANIMINE®	Imipramine
LASIX® IV (in an acute setting)	Furosemide
LEVAQUIN®	levofloxacin
LIMBITROL®	amitriptyline & chlordiazepoxide
LORELCO	Probucol
LOZOL® IV (in an acute setting)	Indapamide
LUDIOMIL®	Maprotiline
LUVOX®	fluvoxamine
MARINOL®	dronabinol, THC
MELLARIL®	Thioridazine
MELLARIL-S®	Thioridazine
MICATIN®	Miconazole
MODECATE CONCENTRATE	fluphenazine
MODITEN	fluphenazine
MONISTAT®	Miconazole

BRAND NAME	GENERIC NAME
MOTILIUM®	domperidone
MY-E	erythromycin
NEBUPENT®	pentamidine
NIZORAL®	ketoconazole
NOLVADEX®	Tamoxifen
NOROXIN®	Norfloxacin
NORPACE®	disopyramide
NORPACE® CR	disopyramide
NORPRAMIN®	desipramine
NORVIR®	Ritonavir
NORZINE	thiethylperazine maleate
ORAP®	Pimozide
ORLAAM®	levomethadyl
ORMAZINE	chlorpromazine
PACERONE®	amiodarone
PAMELOR®	Nortriptyline
PAXIL®	Paroxetine
PCE®	erythromycin
PEDIAZOLE®	erythromycin
PENTACARINAT®	pentamidine
PENTAM®	pentamidine
PERMITIL®	fluphenazine
PHENERGAN®	promethazine
PLETAL®	Cilostazol
PMS-FLUPHENAZINE	fluphenazine
POSICOR®	Mibefradil
PROCAN®	procainamide
PROCAN® SR	procainamide
PROCANBID®	procainamide
PROLIXIN®	fluphenazine
PROMINE®	procainamide
PRONESTYL®	procainamide
PRONESTYL-SR®	procainamide
PROZAC®	Fluoxetine
QUINAGLUTE®	Quinidine
QUINALAN	Quinidine
QUINATIME	Quinidine
QUINIDEX® EXTENTABS	Quinidine
QUININE SULFATE	Quinine
QUINORA®	Quinidine
RAXAR®	grepafloxacin
RHO-FLUPHENAZINE	fluphenazine
RHYTHMIN	procainamide
RISPERDAL®	Risperidone
SANDOSTATIN®	Octreotide
SARAFEM®	fluoxetine hydrochloride
SELDANE® (withdrawn from US market)	Terfenadine
SERENTIL®	mesoridazine

BRAND NAME	GENERIC NAME
SEREVENT®	Salmeterol
SERLECT	Sertindole
SEROQUEL®	Quetiapine
SERZONE®	nefazodone
SINEQUAN®	Doxepin
SPARINE	Promazine
SPORANOX®	itraconazole
STELAZINE®	trifluoperazine
SURMONTIL®	trimipramine
SYNERCID®	quinupristin and dalfopristin
TAGAMET®	Cimetidine
TAMBOCOR®	Flecainide
TAO®	troleandomycin
TARKA®	verapamil/trandolapril
TAVIST®	Clemastine
TECZEM	diltiazem/enalapril
TEQUIN®	gatifloxacin
TERAZOL®	terconazole
THORAZINE®	chlorpromazine
TIKOSYN® (currently not available on the market)	dofetilide
TOFRANIL®	imipramine
TOFRANIL-PM®	imipramine
TONOCARD®	Tocainide
TORECAN®	thiethylperazine maleate
TRIAVIL®	amitriptyline & perphenazine
TRILAFON®	perphenazine
UNIRETIC®	moexipril/hydroclorothiazide
VAGISTAT®	Ticonazole
VASCOR®	Bepridil
VIAGRA®	Sildenafil
VIRACEPT®	Nelfinavir
VIVACTIL®	protriptyline
ZAGAM®	sparfloxacin
ZANAFLEX®	Tizanidine
ZELNORM®	Tegaserod maleate
ZITHROMAX®	azithromycin
ZOFRAN®	ondansetron
ZOLOFT®	Sertraline
ZOMIG®	zolmitriptan
ZONALON® topical cream	Doxepin

PRECAUTION:

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Patient Information - Disallowed Medications by Generic Name

NOTE: THIS IS A LIST OF DRUGS THAT HAVE THE POTENTIAL FOR INTERACTION WITH CISAPRIDE. Formal studies have not proven the interaction of all of these drugs. All formulations (i.e., topical. oral, inhalant, IV) should be considered to have potential interaction with cisapride.

THIS LIST IS NOT COMPREHENSIVE AND IS SUBJECT TO REVISION AS ADDITIONAL INFORMATION BECOMES AVAILABLE.

GENERIC NAME	BRAND NAME
amiodarone	CORDARONE®
amiodarone	PACERONE®
amitriptyline	ELAVIL®
amitriptyline	ENDEP®
amitriptyline	ENOVIL
amitriptyline & chlordiazepoxide	LIMBITROL®
amitriptyline & perphenazine	ETRAFON®
amitriptyline & perphenazine	TRIAVIL®
amoxapine	ASENDIN®
amprenavir	AGENERASE®
astemizole	HISMANAL® (withdrawn from market)
azelastine	ASTELIN®
azithromycin	ZITHROMAX®
bepridil	VASCOR®
bretylium	BRETYLIUM TOSYLATE
bretylium	BRETYLOL
bumetanide	BUMEX® IV (in an acute setting)
butoconazole	FEMSTAT® 3
chlorothiazide	DIURIL® IV (in an acute setting)
chlorpromazine	ORMAZINE
chlorpromazine	THORAZINE®
cilostazol	PLETAL®
cimetidine	TAGAMET®
clarithromycin	BIAXIN®
clemastine	TAVIST®
clomipramine	ANAFRANIL®
cyclobenzaprine	FLEXERIL®
desipramine	NORPRAMIN®
diltiazem	CARDIZEM®
diltiazem/enalapril	TECZEM
disopyramide	NORPACE®
disopyramide	NORPACE® CR
dofetilide	TIKOSYN® (currently not available on the market)
dolasetron	ANZEMET®
domperidone	MOTILIUM®
doxepin	ADAPIN®
doxepin	SINEQUAN®
doxepin	ZONALON® topical cream
dronabinol, THC	MARINOL®
droperidol	INAPSINE®
encainide	ENKAID®

GENERIC NAME	BRAND NAME
erythromycin	AKNE-MYCIN®
erythromycin	E.E.S.®
erythromycin	E-MYCIN
erythromycin	ERY PED
erythromycin	ERYDERM®
erythromycin	ERYGEL®
erythromycin	ERY-TAB®
erythromycin	ERYTHROCIN®
erythromycin	ERYTHROMYCIN BASE FILMTAB®
erythromycin	ERYTHRO-STATIN
erythromycin	ILOSONE®
erythromycin	MY-E
erythromycin	PCE®
erythromycin	PEDIAZOLE®
ethacrynic acid	EDECRIN® IV (in an acute setting)
felbamate	FELBATOL®
flecainide	TAMBOCOR®
fluconazole	DIFLUCAN®
fluoxetine	PROZAC®
fluoxetine hydrochloride	SARAFEM®
fluphenazine	APO-FLUPHENAZINE
fluphenazine	MODECATE CONCENTRATE
fluphenazine	MODITEN
fluphenazine	PERMITIL®
fluphenazine	PMS-FLUPHENAZINE
fluphenazine	PROLIXIN®
fluphenazine	RHO-FLUPHENAZINE
fluticasone/salmeterol	ADVAIR DISKUS®
fluvoxamine	LUVOX®
formoterol fumarate	FORADIL® AEROLIZER®
foscarnet	FOSCAVIR®
fosphenytoin	CEREBYX®
furosemide	LASIX® IV (in an acute setting)
gatifloxacin	TEQUIN®
grapefruit juice	GRAPEFRUIT JUICE
grepafloxacin	RAXAR®
halofantrine	HALFAN® (not listed in protocol or Informed Consent Form)
haloperidol	HALDOL®
hawthorn, crataegus laevigata	HEARTCARE®
ibutilide	CORVERT®
imipramine	JANIMINE®
imipramine	TOFRANIL®
imipramine	TOFRANIL-PM®
indapamide	LOZOL® IV (in an acute setting)
indinavir	CRIXIVAN®
insulin	INSULIN (Various) IV (in an acute setting)
isradipine	DYNACIRC®
itraconazole	SPORANOX®

GENERIC NAME	BRAND NAME
ketoconazole	NIZORAL®
levofloxacin	LEVAQUIN®
levomethadyl	ORLAAM®
maprotiline	LUDIOMIL®
mesoridazine	SERENTIL®
methadone	DOLOPHINE®
mibefradil	POSICOR®
miconazole	MICATIN®
miconazole	MONISTAT®
moexipril/hydroclorothiazide	UNIRETIC®
moricizine	ETHMOZINE®
moxifloxacin	AVELOX®
naratriptan	AMERGE®
nefazodone	SERZONE®
nelfinavir	VIRACEPT®
nicardipine	CARDENE®
norfloxacin	CHIBROXIN®
norfloxacin	NOROXIN®
nortriptyline	AVENTYL® HYDROCHLORIDE
nortriptyline	PAMELOR®
octreotide	SANDOSTATIN®
ofloxacin	FLOXIN®
ondansetron	ZOFRAN®
palonosetron	ALOXI®
paroxetine	PAXIL®
pentamidine	NEBUPENT®
pentamidine	PENTACARINAT®
pentamidine	PENTAM®
perphenazine	TRILAFON®
phenytoin	DILANTIN®
pimozide	ORAP®
probucol	LORELCO
procainamide	PROCAN®
procainamide	PROCAN® SR
procainamide	PROCANBID®
procainamide	PROMINE®
procainamide	PRONESTYL®
procainamide	PRONESTYL-SR®
procainamide	RHYTHMIN
prochlorperazine	COMPAZINE®
promazine	SPARINE
promethazine	PHENERGAN®
protriptyline	VIVACTIL®
quetiapine	SEROQUEL®
quinidine	CARDIOQUIN®
quinidine	CIN-QUIN
quinidine	DURAQUIN
quinidine	DURA-TABS®

GENERIC NAME	BRAND NAME
quinidine	QUINAGLUTE®
quinidine	QUINALAN
quinidine	QUINATIME
quinidine	QUINIDEX® EXTENTABS
quinidine	QUINORA®
quinine	QUININE SULFATE
quinupristin and dalfopristin	SYNERCID®
risperidone	RISPERDAL®
ritonavir	NORVIR®
salmeterol	SEREVENT®
saquinavir	FORTOVASE®
saquinavir	INVIRASE®
sertindole	SERLECT
sertraline	ZOLOFT®
sildenafil	VIAGRA®
sotalol	BETAPACE®
sparfloxacin	ZAGAM®
sumatriptan	IMITREX®
tamoxifen	NOLVADEX®
Tegaserod maleate	ZELNORM®
terconazole	TERAZOL®
terfenadine	SELDANE® (withdrawn from US market)
thiethylperazine maleate	NORZINE
thiethylperazine maleate	TORECAN®
thioridazine	MELLARIL®
thioridazine	MELLARIL-S®
ticonazole	VAGISTAT®
tizanidine	ZANAFLEX®
tocainide	TONOCARD®
torsemide	DEMADEX® IV (in an acute setting)
trazodone	DESYREL®
trifluoperazine	STELAZINE®
trimipramine	SURMONTIL®
troleandomycin	TAO®
venlafaxine	EFFEXOR®
verapamil	CALAN®
verapamil/trandolapril	TARKA®
zafirlukast	ACCOLATE®
ziprasidone	GEODON®
zolmitriptan	ZOMIG®

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