SAFETY DATA SHEET

SECTION 1 - IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND OF THE COMPANY/UNDERTAKING

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Product identifier	Mifepristone - Drug Product (300 mg Tablets)
Synonyms	C-1073, RU-486, RU-38486
Trade names	Korlym®
Chemical family	Steroid
Relevant identified uses of the substance or mixture and uses advised against	Korlym is a cortisol receptor blocker indicated to treat the clinical and metabolic effects of hypercortisolism in patients with endogenous Cushing's syndrome.
Note	The ecological properties of this product/mixture and/or its ingredients have not been fully characterized. This SDS will be revisited as more data become available.
Issue Date	21 December 2011

SECTION 2 - HAZARDS IDENTIFICATION

Classification of the substance or mixture

Regulation (EC) 1272/2008 [GHS]	Target organ systemic toxicity (repeat exposure) - Category 2. Reproductive Toxicity - Category 1.
Directive 67/548/EEC or 1999/45/EC	T: R48/20/22. R60, R61 (Repr. Cat. 1).

Label elements

CLP/GHS hazard pictogram	
CLP/GHS signal word	Danger
CLP/GHS hazard statements	H360FD - May damage fertility. May damage the unborn child. H373 - May cause damage to liver, kidneys, thyroid, and endocrine system through prolonged or repeated exposure.
CLP/GHS precautionary statements	P201 - Obtain special instructions before use. P202 - Do not handle until all safety precautions have been read and understood. P260 - Do not breathe dust. P281 - Use personal protective equipment as required. P308 + P313 - If exposed or concerned: get medical advice/attention. P314 - Get medical advice/attention if you feel unwell. P405 - Store locked up. P501 - Dispose of contents/container to location in accordance with local/regional/national/international regulations.
Other hazards	Pharmacologically, mifepristone has anti-progestational and anti-glutocorticoid effects. In clinical trials, the most commonly reported adverse events were nausea, fatigue, headache, decreased blood potassium, arthralgia, vomiting, peripheral edema, hypertension, dizziness, decreased appetite, and endometrial hypertrophy.
US Signal word	Danger
US Hazard overview	Developmental hazard - can cause adverse effects on the developing fetus. Reproductive hazard - can cause adverse reproductive effects and damage fertility (affects male and female sex hormone levels). May cause damage to kidneys, liver, thyroid and endocrine system, based on animal data.
Note	This mixture is classified as hazardous according to Directive 67/548/EEC, Regulation EC No 1272/2008 (EU-CLP), and applicable US regulations. See Section 16 for full text of EU and GHS classifications. The GHS classifications are based on Regulation (EC) 1272/2008.

SECTION 3 - COMPOSITION/INFORMATION ON INGREDIENTS

Ingredient	CAS #	EINECS/ELINCS#	Amount	EU Classification	GHS Classification
Mifepristone	84371-65-3	N/A	60-70%	Toxic - T: R60, R61, R48/20/22	RT1A: H360FD; STOT-RE2: H373
Microcrystalline Cellulose	9004-34-6	232-674-9	15-25%	Not classified	Not classified

Note The ingredients listed above are considered hazardous. The remaining components are non-hazardous and/or present at amounts below reportable limits. See Section 16 for full text of EU and GHS classifications. The EU classification is based on Directive 67/548/EEC and the GHS classification is based on Regulation (EC) 1272/2008.

SECTION 4 - FIRST AID MEASURES

Description of first aid measures

Immediate Medical Attention Needed Yes

Eye Contact If easy to do, remove contact lenses, if worn. Immediately flush eyes with copious quantities of water for at least 15 minutes. If irritation occurs or persists, notify medical personnel and supervisor.

Skin Contact Wash exposed area with soap and water and remove contaminated clothing/shoes. If irritation occurs or persists, notify medical personnel and supervisor.

Inhalation Immediately move exposed subject to fresh air. If not breathing, give artificial respiration. If breathing is labored, administer oxygen. Immediately notify medical personnel and supervisor.

Ingestion If swallowed, call a physician immediately. Do not induce vomiting unless directed by medical personnel. Do not give anything to drink unless directed by medical personnel. Never give anything by mouth to an unconscious person. Notify medical personnel and supervisor.

Protection of first aid responders See Section 8 for Exposure Controls/Personal Protection recommendations.

Most important symptoms and effects, both acute and delayed See Sections 2 and 11

Indication of immediate medical attention and special treatment needed, if necessary Treat symptomatically and supportively. If accidental exposure occurs to an individual who is also taking one or more concomitant medications, consult the respective package or prescribing information for potential drug interactions.

SECTION 5 - FIREFIGHTING MEASURES

Extinguishing media	Use water spray (fog), foam, dry powder, or carbon dioxide, as appropriate for surrounding fire and materials.
Specific hazards arising from the substance or mixture	No information identified. May emit toxic fumes of carbon monoxide, carbon dioxide, oxides of nitrogen, and magnesium-containing compounds.
Flammability/Explosivity	No explosivity or flammability data identified. High concentrations of finely divided airborne organic particles can potentially explode if ignited.
Advice for firefighters	Wear full protective clothing and a self-contained breathing apparatus with a full facepiece operated in the pressure demand or other positive pressure mode. Decontaminate all equipment after use.

SECTION 6 - ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures	If product is released or spilled, take proper precautions to minimize exposure by using appropriate personal protective equipment (see Section 8). Area should be adequately ventilated.
Environmental precautions	Do not empty into drains. Avoid release to the environment.
Methods and material for containment and cleaning up	If tablets are spilled, scoop up and dispose of in a manner that is compliant with federal, state or local laws. If tablets are crushed/broken, do not raise dust. Clean up spill with HEPA-filtered vacuum if available. If not available, add water to allow for the material to enter solution. Collect material with absorbants. Place spill materials into a leak-proof container suitable for disposal. Decontaminate area a second time. Dispose of material in a manner that is compliant with federal, state and local laws.
Reference to other sections	See Sections 8 and 13 for more information.

SECTION 7 - HANDLING AND STORAGE

Precautions for safe handling	Avoid contact with eyes, skin and other mucous membranes. Wash thoroughly after handling. Use personal protective equipment. Do not eat, drink or smoke while handling this product. Avoid prolonged or repeated exposure. Provide sufficient air exchange and/or exhaust in workrooms. Take precautionary measures against static discharges. Use normal preventative fire protection measures.
Conditions for safe storage including any incompatibilities	Store at controlled room temperature 15 - 30°C (59 - 86°F).
Specific end use(s)	No information identified.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

Control Parameters/Occupational Exposure Limit Values

Compound	Issuer	Type	OEL
Mifepristone	Corcept, Inc.	TWA 8-HR	0.7 µg/m
Cellulose	ACGIH, Australia, Belgium, Estonia, France, Portugal, Romania, Singapore, Spain	TWA-8 HR	10 mg/m
	Ireland, United Kingdom	TWA-8 HR	10 mg/m (inhalable dust); 4 mg/m (respirable dust)
	Ireland	STEL	20 mg/m (total inhalable dust)
	Latvia	TWA-8 HR	2 mg/m
	Mexico	TWA-8 HR/STEL	10/20 mg/m
	NIOSH	TWA-8 HR	10 mg/m (total dust); 5 mg/m (respirable dust)
	OSHA	TWA-8 HR	15 mg/m (total dust); 5 mg/m (respirable fraction)
	United Kingdom	STEL	20 mg/m (inhalable dust); 12 mg/m (respirable dust)

DNELs/PNECs None identified.

Exposure/Engineering controls Selection and use of containment devices and personal protective equipment should be based on a risk assessment of exposure potential. Use local exhaust and/or enclosure at aerosol/dust-generating points. High-energy operations should be done within an approved emission control or containment system.

Respiratory protection Choice of respiratory protection should be appropriate to the task and the level of existing engineering controls. For routine powder handling tasks, an approved and properly worn powered air-purifying respirator equipped with HEPA filters or combination filters should provide ancillary protection based on the known or foreseeable limitations of existing engineering controls. Use a positive-pressure air- supplied respirator if there is any potential for an uncontrolled release, when exposure levels are not known, or in any other circumstances where air purifying respirators may not provide adequate protection.

Hand protection Should not be needed for normal handling of material. Impervious gloves are recommended if skin contact with product is possible and for bulk processing operations.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION …continued

Skin protection	Should not be needed during normal handling of packaged product. Wear gloves, lab coat, or other protective overgarment if skin contact is likely, e.g., during clean up of large spill. Base the choice of skin protection on the job activity and potential for skin contact.
Eye/face protection	Wear safety glasses with side shields, chemical splash goggles, or full face shield, if necessary. Base the choice of protection on the job activity and potential for contact with eyes or face. An emergency eye wash station should be available.
Environmental Exposure Controls	Avoid release to the environment and operate within closed systems wherever practicable. Air and liquid emissions should be directed to appropriate pollution control devices. In case of spill, do not release to drains. Implement appropriate and effective emergency response procedures to prevent release or spread of contamination and to prevent inadvertent contact by personnel.
Other protective measures	Wash hands in the event of contact with this product/mixture, especially before eating, drinking or smoking. Protective equipment is not to be worn outside the work area (e.g., in common areas or out-of-doors). Decontaminate all protective equipment following use.

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES

Information on basic physical and chemical properties

Appearance	Tablet
Color	Light yellow
Odor	No information identified.
Odor threshold	No information identified.
pH	Not applicable.
Melting point/freezing point	No information identified.
Initial boiling point and boiling range	Not applicable.
Flash point	No information identified.
Evaporation rate	No information identified.
Flammability (solid, gas)	No information identified.
Upper/lower flammability or explosive limits	No information identified.

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES …continued

Vapor pressure	No information identified
Vapor density	No information identified.
Relative density	No information identified.
Water solubility	Greatest solubility is in acidic media (~ 25mg/mL at pH 1.5); solubility declines rapidly as pH is increased. At pH values above 2.5, solubility of mifepristone is <1 mg/mL (mifepristone).
Solvent solubility	Very soluble in methanol, chloroform, acetone; poorly soluble in water, hexane, isopropyl ether (mifepristone).
Partition coefficient (*n-octanol/water*)	No information identified.
Auto-ignition temperature	No information identified.
Decomposition temperature	No information identified.
Viscosity	No information identified.
Explosive properties	No information identified.
Oxidizing properties	No information identified.

Other information

Molecular weight	429.60 (mifepristone)
Molecular formula	$C_{29}H_{35}NO_2$ (mifepristone)

SECTION 10 - STABILITY AND REACTIVITY

Reactivity	No information identified.
Chemical stability	No information identified.
Possibility of hazardous reactions	Not expected to occur.
Conditions to avoid	No information identified.
Incompatible materials	No information identified.
Hazardous decomposition products	No information identified.

SECTION 11 - TOXICOLOGICAL INFORMATION

Information on toxicological effects

Route of entry May be absorbed by inhalation, skin contact and ingestion.

Acute toxicity

Compound	Type	Route	Species	Dose
Mifepristone	--	--	--	--
Cellulose	LC_{50}	Inhalation	Rat	>5800 mg/m /4h
	LD_{50}	Oral	Rat	>5000 mg/kg
	LD_{50}	Dermal	Rabbit	>2000 mg/kg

Additional acute toxicity information Mifepristone has low acute oral toxicity. Mice, rats, and dogs were given 1000 mg/kg as a single oral dose and observed for 14-21 days. One male rat died. Toxicity in rodents included arched back, ambulatory difficulties and abdominal distention. In dogs, there was moderate diarrhea and vomiting.

Irritation/Corrosion No studies identified.

Sensitization No studies identified.

STOT-single exposure No studies identified.

STOT-repeated exposure/Repeat-dose toxicity In 6-month studies in both rats and monkeys, the observed effects were, in general, considered predictable consequences of the pharmacological suppression of glucocorticoid and progesterone activity, and included adverse effects on the following target organs: liver, kidneys, thyroid, and endocrine system.

The NOAEL in a 12-month study in dogs was considered to be 25 mg/kg/ day. Treatment related adverse effects in dogs included changes in red cell mass, liver and liver enzymes, testes and testosterone levels, epididymes, ovaries, and uterus at the high dose level. There was a small, but statistically significant, dose related prolongation of the QT and QTc intervals in the mid (25 mg/kg/day) and high dose groups (60/40 mg/kg/day). No QT effects were seen at 10 mg/kg/day.

Reproductive toxicity The pharmacological activity of mifepristone disrupts the estrus cycle of animals, precluding studies designed to assess effects on fertility during drug administration. A study was performed in rats to determine whether there were residual effects on reproductive function after termination of the drug exposure. Administration of the lowest oral dose of 0.3 mg/kg/day caused severe disruption of the estrus cycles for the three weeks of the treatment period. Following resumption of the estrus cycle, animals were mated and no effect on reproductive performance was observed.

SECTION 11 - TOXICOLOGICAL INFORMATION …continued

Developmental toxicity Mifepristone is a potent abortifacient. Studies conducted with rabbits suggest a teratogenic potential of mifepristone if pregnancy termination does not occur. Teratology studies have been conducted in mice, rats and rabbits at doses of 0.25 to 4.0 mg/kg/day. Because of the antiprogestational activity of mifepristone, fetal losses were much higher than in control animals. Skull deformities were detected in rabbit studies at approximately 1/6 the human exposure, although no teratogenic effects of mifepristone have been observed to date in rats or mice. These deformities were most likely due to the mechanical effects of uterine contractions resulting from decreased progesterone levels.

Genotoxicity Results from studies conducted in vitro and in animals have revealed no genotoxic potential for mifepristone.

Carcinogenicity Mifepristone is not listed by NTP, IARC, ACGIH or OSHA as a carcinogen. Rats and mice were evaluated for carcinogenicity potential. Rats were dosed for up to two years at doses of 5, 25, and 125 mg/kg of mifepristone. The high dose was the maximum tolerated dose, but exposure at all doses was below the human exposure at clinical doses based on AUC comparison. Rats had a statistically significant increase in thyroid and liver neoplasms. These tumors are common in rats exposed to drugs that induce enzyme metabolism, and are not considered to be clinically relevant. Mice were also tested for up to 2 years at mifepristone doses in females of 25 mg/kg, 100 mg/kg, and the maximum tolerated dose of 300 mg/kg, which was decreased to 125 mg/kg due to toxicity. The males were tested at mifepristone dose levels of 12.5, 65, and 125 mg/kg. All AUC levels were below the human AUC. No drug-related tumors were seen in mice.

Aspiration hazard No data available.

Human health data See "Section 2 - Other Hazards"

SECTION 12 - ECOLOGICAL INFORMATION

Toxicity

Compound	Type	Species	Concentration
Mifepristone	--	--	--
Cellulose	--	--	--

Additional toxicity information No data available.

Persistence and Degradability No data available.

Bioaccumulative potential Potential for bioconcentration in aquatic organisms is likely to be high.

Mobility in soil Mifepristone is expected to be immobile in soil, and adsorb to suspended solids and sediment.

Results of PBT and vPvB assessment No data available.

Other adverse effects No data available.

Note The environmental characteristics of this product/mixture have not been fully investigated. Releases to the environment should be avoided.

SECTION 13 - DISPOSAL CONSIDERATIONS

Waste treatment methods	Used product should be disposed of according to local, state, and federal regulations. Do not send down the drain or flush down the toilet. All wastes containing the material should be properly labeled. Dispose of wastes in accordance to prescribed federal, state, and local guidelines, e.g., appropriately permitted chemical waste incinerator. Rinse waters resulting from spill cleanups should be discharged in an environmentally safe manner, e.g., appropriately permitted municipal or on-site wastewater treatment facility.

SECTION 14 - TRANSPORT INFORMATION

Transport	Based on the available data, this product/mixture is not regulated as a hazardous material/dangerous good under EU ADR/RID, US DOT, Canada TDG, IATA, or IMDG.
UN number	None assigned.
UN proper shipping name	None assigned.
Transport hazard classes and packing group	None assigned.
Environmental hazards	Based on the available data, this product/mixture is not regulated as an environmental hazard or a marine pollutant.
Special precautions for users	Mixture not fully tested - avoid exposure.
Transport in bulk according to Annex II of MARPOL73/78 and the IBC Code	Not applicable.

SECTION 15 - REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture	This SDS complies with the requirements under US, EU and GHS (EU CLP - Regulation EC No 1272/2008) guidelines.
Chemical safety assessment	Not conducted.
OSHA Hazardous	Yes. Developmental hazard - can cause adverse effects on the developing fetus. Reproductive hazard - can cause adverse reproductive effects and damage fertility (affects male and female sex hormone levels). May cause damage to kidneys, liver, thyroid and endocrine system, based on animal data.
WHMIS classification	This product has been classified in accordance with the hazard criteria of the Controlled Products Regulations and the SDS contains all of the information required by those regulations.
TSCA status	Not listed
SARA section 313	Not listed.
California proposition 65	Not listed.

SECTION 16 - OTHER INFORMATION

Full text of R phrases and EU Classifications	T - Toxic. Repr. Cat. 1 - Toxic for reproduction Category 1. R60 - May impair fertility. R61 - May cause harm to the unborn child. R48/20/22 - Harmful: Danger of serious damage to health by prolonged exposure through inhalation and if swallowed.
Full text of H phrases, P phrases and GHS classification	RT1A - Reproductive toxicity Category 1A. STOT-RE2 - Specific Target Organ Toxicity Following Repeated Exposure Category 2. H360FD - May damage fertility. May damage the unborn child. H373 - May cause damage to liver, kidneys, thyroid, and endocrine system through prolonged or repeated exposure.
Sources of data	Information from published literature and internal company data.
Abbreviations	ACGIH - American Conference of Governmental Industrial Hygienists ADR/RID - European Agreement Concerning the International Carriage of Dangerous Goods by Road/Rail AIHA - American Industrial Hygiene Association CAS# - Chemical Abstract Services Number DNEL - Derived No Effect Level DOT - Department of Transportation EINECS - European Inventory of New and Existing Chemical Substances ELINCS - European List of Notified Chemical Substances EU - European Union GHS - Globally Harmonized System of Classification and Labelling of Chemicals IARC - International Agency for Research on Cancer

SECTION 16 - OTHER INFORMATION …continued

Abbreviations …continued

IDLH - Immediately Dangerous to Life or Health IATA - International Air Transport Association IMDG - International Maritime Dangerous Goods LOEL - Lowest Observed Effect Level LOAEL - Lowest Observed Adverse Effect Level NIOSH - The National Institute for Occupational Safety and Health NOEL - No Observed Effect Level NOAEL - No Observed Adverse Effect Level NTP - National Toxicology Program OEL - Occupational Exposure Limit OSHA - Occupational Safety and Health Administration PBT - Persistent, Bioaccumulative and Toxic PNEC - Predicted No Effect Concentration SARA - Superfund Amendments and Reauthorization Act STEL - Short Term Exposure Limit TDG - Transport Dangerous Goods TSCA - Toxic Substances Control Act TWA - Time Weighted Average WHMIS - Workplace Hazardous Materials Information System

Revisions

This is the first version of this SDS.

Disclaimer

The above information is based on data available to us and is believed to be correct. Since the information may be applied under conditions beyond our control and with which we may be unfamiliar, we do not assume any responsibility for the results of its use and all persons receiving it must make their own determination of the effects, properties and protections which pertain to their particular conditions. No representation, warranty, or guarantee, express or implied (including a warranty of fitness or merchantability for a particular purpose), is made with respect to the materials, the accuracy of this information, the results to be obtained from the use thereof, or the hazards connected with the use of the material. Caution should be used in the handling and use of the material because it is a pharmaceutical product. The above information is offered in good faith and with the belief that it is accurate. As of the date of issuance, we are providing all information relevant to the foreseeable handling of the material. However, in the event of an adverse incident associated with this product, this Safety Data Sheet is not, and is not intended to be, a substitute for consultation with appropriately trained personnel.