GlaxoSmithKline
PO Box 13398
5 Moore Drive
RTP, NC 27709

(919) 483-2100
(919) 483-2700 (24 hour contact)

Effective Date: 06/25/99

MATERIAL SAFETY DATA SHEET

SECTION 1: CHEMICAL SUBSTANCE

PRODUCT NAME: Lanoxin® (digoxin) Tablets

COMMON NAME: Digoxin

CHEMICAL NAME: (3β, 5β, 12β)-3-[(0-2,6-dideoxy-β-D-*ribo*-hexopyranosyl-(1→4)-*0*-2,6-dideoxy-β-D-ribo-hexopyranosyl-(1→4)-2,6-dideoxy-β-D-*ribo*- hexopyranosyl)oxy]-12,14-dihydroxycard-20(22)-enolide

SYNONYMS: Lanoxin® Tablets; Lanoxin Tablets; Lanoxin®; Lanoxin; digoxin; digoxinum; digoxosidum; 38U57

SUBSTANCE CLASS: Cardiac glycoside; cardiac failure

SECTION 2: HAZARDOUS INGREDIENTS

NAME	CAS/EINECS/ELINCS #	% w/v or w/w	GW LIMITS (mcg/m^3)	OTHER LIMITS (mcg/m^3)
Digoxin	20830-75-5 (CAS) EEC244-088-1 (EINECS)		1 mcg/m^3 (8 hour TWA) OEL (pure substance)	Not established

SECTION 3: HAZARDS IDENTIFICATION

THE RISK OF HEALTH HAZARDS MAY BE REDUCED WHEN LANOXIN® TABLETS ARE HANDLED IN UNIT DOSAGE FORM.

Digoxin is very toxic by inhalation and if swallowed in excess of the therapeutic dose.
Digoxin is readily absorbed from the gastrointestinal tract and is rapidly distributed throughout the body.
Contact with the eye can cause temporary visual disturbances.
Exposure in excess of the occupational exposure limit for digoxinmay cause symptoms including: nausea, vomiting, diarrhea, abdominal pain, yellow vision, low blood pressure, and irregular pulse; massive overdose may cause heart failure.
Detected in breast milk. May have adverse effect on nursing infant.

See also Section 11: "Toxicological Information".

TO THE BEST OF OUR KNOWLEDGE THE INFORMATION CONTAINED HEREIN IS ACCURATE AS OF THE DATE HEREOF. ANY DETERMINATION AS TO THE SUITABILITY OF THE PRODUCT FOR ANY PARTICULAR PURPOSE, ITS SAFE USE OR DISPOSAL SHALL BE THE RESPONSIBILITY OF THE USER. THE INFORMATION CONTAINED HEREIN IS IN NO WAY INTENDED TO SUPPLEMENT, MODIFY OR SUPERSEDE THE INFORMATION PROVIDED IN THE PRODUCT PACKAGE INSERT WITH RESPECT TO THE USE OF THE PRODUCT FOR MEDICAL PURPOSES. PLEASE REFER TO THE PRODUCT PACKAGE INSERT FOR INFORMATION REGARDING THE USE OF THE PRODUCT FOR MEDICAL PURPOSES.

SECTION 4: FIRST AID MEASURES

If in Eyes: Flush immediately with large quantities of water for 15 minutes. Obtain medical attention.

If on Skin: Remove contaminated clothing. Flush exposed skin with water and wash thoroughly with soap and water. Obtain medical attention.

If Inhaled: If not breathing, give artificial respiration or CPR. If breathing is difficult, give oxygen. Remove person to fresh air. Obtain medical attention.

If Ingested: If conscious, rinse mouth with water. Never give anything by mouth if unconscious. Obtain medical attention.

Notes to Physicians: Administer charcoal if within 1 hour of ingestion. Digibind is a specific antidote for digoxin toxicity and may be used to reverse adverse effects associated with known digoxin overdoses.

SECTION 5: FIRE / EXPLOSION HAZARDS & FIRE-FIGHTING MEASURES

FLASHPOINT/TEST METHOD:	Not applicable (powder).
LEL / UEL:	Not determined for Lanoxin® Tablets.
SPECIAL PROPERTIES RELATED TO FIRE HAZARD:	As packaged, Lanoxin® Tablets should be dust free. However, breakage of tablets, especially in bulk operations, could contribute to dust formation. As with any organic dust, there is potential for explosion when high concentrations are suspended in air. Combustible. Heating will give rise to toxic and irritant fumes.
STORAGE OR HANDLING CONDITIONS TO BE AVOIDED:	Store away from heat and moisture.
EXTINGUISHING MEDIA:	Water Spray, Multipurpose Dry Chemical.
FIRE-FIGHTING PROCEDURES:	Wear full protective clothing and use self-contained breathing apparatus (SCBA).

SECTION 6: SPILL AND LEAK PROCEDURES

SPILL RESPONSE PROCEDURES (Liquid, Solid, Gas/Vapor):

Protective equipment may be necessary for spills. (See Section 8, "Exposure Controls / Personal Protection" for guidance).

For small quantities associated with normal therapeutic use, collect spillage and transfer to a closed waste container for disposal. For large or bulk quantities, minimize dust generation. Collect spillage by HEPA vacuum or by carefully wet wiping with a suitable solvent and transfer to a labeled, sealed container for disposal. Wash spill area (floor or other contact surfaces) with a suitable cleaning solvent, such as an 80:20 ethanol/water solution or isopropyl alcohol, and then rinse area with soap and water.

SECTION 7: HANDLING AND STORAGE

HANDLING: Avoid exposure by any route. No open handling of powders or uncoated tablets unless precautions have been taken to prevent exposure. Aerosol-generating procedures should be conducted in a laboratory fume hood or with other suitable local exhaust ventilation. Handling of solids and solutions should be conducted in designated areas to minimize surface contamination. Clean surfaces that may be contaminated with the substance, such as hands, skin, and equipment surfaces, before leaving the work area. Properly identify (signage and labeling) potential hazards in designated work areas.

STORAGE: Store Lanoxin® Tablets in original container at 59° to 77°F (15° to 25°C) in a dry place and protect from light.

SECTION 8: EXPOSURE CONTROLS / PERSONAL PROTECTION

ENGINEERING CONTROLS: No special ventilation requirements for normal dosage and administration. For dusty processes, use process containment, local exhaust ventilation or other engineering controls to keep airborne concentrations below the occupational exposure limit (OEL) for digoxin.

PERSONAL PROTECTION:

Respiratory: Respiratory protective equipment may be necessary to provide additional protection for dusty processes and in the absence of sufficient local exhaust ventilation. Use NIOSH approved respiratory protection to control airborne levels below the OEL.

Eye: Workers should wear adequate eye protection to prevent eye contact.

Clothing: Adequate protective clothing should be worn to prevent occupational skin contact. Work uniform should not be worn outside designated chemical handling areas.

Gloves: Use impermeable (e.g., latex) gloves to prevent skin contact. Double glove as necessary and dispose of outer gloves according to federal, state, and local regulations.

WORK PRACTICES: Special care should be taken to ensure that contaminated clothing, equipment, and surfaces are properly cleaned or disposed of after use. Potentially contaminated clothing should be disposed of according to federal, state, and local regulations or packaged for laundering to prevent exposure of personnel.

Wash hands and other areas of skin contact thoroughly after handling this material.

SECTION 9: PHYSICAL / CHEMICAL PROPERTIES

APPEARANCE AND ODOR: Lanoxin ® Tablets are supplied as follows:
125 mcg scored, yellow tablets imprinted with LANOXIN and Y3B;
250 mcg scored, white tablets imprinted with LANOXIN and X3A.

PHYSICAL STATE (liquid/solid/gas): Solid.

MELTING POINT (deg. C): Not determined for Lanoxin® Tablets. The melting point for digoxin, the active ingredient in Lanoxin® Tablets, is decomposition above 230°C.

BOILING POINT (deg. C): Not determined for Lanoxin® Tablets.

SECTION 9: PHYSICAL / CHEMICAL PROPERTIES (cont'd)

SOLUBILITY/MISCIBILITY (% w/v): Not determined for Lanoxin® Tablets. Digoxin, the active ingredient in Lanoxin® Tablets, is practically insoluble in water and ether; slightly soluble in diluted (50%) alcohol and chloroform; and freely soluble in pyridine. Its solubility in 80:20 ethanol/water is approximately 8 mg/mL and approximately 3.6 mg/ml in isopropyl alcohol.

SECTION 10: STABILITY AND REACTIVITY

CHEMICAL STABILITY: Stable.

CONDITIONS TO AVOID: Not determined.

INCOMPATIBILITY WITH OTHER MATERIALS: Not determined for Lanoxin® Tablets. No known incompatibilities have been identified for digoxin, the active ingredient in Lanoxin® Tablets.

HAZARDOUS DECOMPOSITION PRODUCTS: Hazardous decomposition products of Lanoxin® Tablets have not been determined. Hazardous decomposition products of digoxin, the active ingredient in Lanoxin® Tablets, may include toxic oxides of carbon.

HAZARDOUS POLYMERIZATION: Not applicable.

SECTION 11: TOXICOLOGICAL INFORMATION

THE RISK OF HEALTH HAZARDS MAY BE REDUCED WHEN LANOXIN® TABLETS ARE HANDLED IN UNIT DOSAGE FORM.

PHARMACOLOGICAL ACTIVITY: Lanoxin® (digoxin) Tablets are indicated for the treatment of mild to moderate heart failure. Lanoxin® is also indicated for the control of ventricular response rale in patients with chronic atrial fibrillation. Digoxin, the active ingredient in Lanoxin® Tablets, inhibits sodium-potassium ATPase, an enzyme that regulates the quantity of sodium and potassium inside cells. Increased intracellular concentrations of sodium and calcium positively affects function of cardiac muscle.

OCCUPATIONAL EXPOSURE LIMITS: For digoxin, the active ingredient in Lanoxin® (digoxin) Tablets , the Glaxo Wellcome estimated safe working level is an eight hour time-weighted average (TWA) of 1 mcg/m^3.

ACUTE TOXICITY: Digoxin is very toxic by inhalation and if swallowed in excess of the therapeutic dose. It is readily absorbed from the gastrointestinal tract and is rapidly distributed throughout the body.

The acute toxicity of digoxin varies widely in different species. Lethal doses of digoxin following single oral administration were:

Oral LD_{50} (Mouse) = 17 mg/kg
Oral LD_{50} (Cat) = 200 mcg/kg

Acute occupational exposure to digoxin may cause symptoms similar to those reported in medicinal use of this drug substance including: vomiting, diarrhea, abdominal pain, yellow vision, hypotension (low blood pressure), and irregular pulse. Massive overdoses may cause heart failure.

SECTION 11: TOXICOLOGICAL INFORMATION (cont'd)

REPEAT DOSE TOXICITY: No repeat dose animal studies have been reported for digoxin. Repeated occupational exposure to digoxin may produce adverse effects similar to those observed during its therapeutic use including: vomiting, diarrhea, abdominal pain, yellow vision, hypotension (low blood pressure), and irregular pulse. (see also "Clinical Safety, below). Massive overdoses may cause heart failure.

IRRITATION: Digoxin is a severe irritant to the eyes. There are no data available on the skin irritation potential of this substance.

SENSITIZATION: There are no data available on the sensitization potential of this substance.

REPRODUCTIVE EFFECTS: Animal reproduction studies involving the therapeutic routes of administration for digoxin (oral and intravenous injection) have not been conducted. A single intramuscular injection study of digoxin conducted on domestic animals caused abnormalities of the blood and lymphatic systems.

For recommended dosage and administration, Lanoxin® Tablets are classified as "Pregnancy Category C". It is unknown whether Lanoxin® Tablets can cause fetal harm when administered to a pregnant woman or whether Lanoxin® can affect reproductive capacity. Digoxin, the active ingredient in Lanoxin® Tablets, is transferred both transplacentally and in breast milk. Because of the potential for serious adverse reactions in nursing infants, precautions should be taken to limit exposure to this substance while pregnant or nursing. Medical evaluation of exposure and attention to compliance with standard operating procedures and/or other workplace health and safety directives is advised.

GENOTOXICITY: There are no definitive data on the mutagenic potential of digoxin.

CARCINOGENICITY: There have been no long-term studies performed in animals to evaluate carcinogenic potential of digoxin.

CLINICAL SAFETY: In general, adverse reactions associated with therapeutic use of Lanoxin® Tablets are dose-dependent and occur at doses higher than those necessary to achieve a therapeutic effect. The most commonly cited adverse effects associated with therapeutic use of Lanoxin® Tablets are gastrointestinal disturbances (anorexia, nausea, vomiting, diarrhea, abdominal pain) and CNS disturbances (visual disturbances, headache, dizziness, apathy, confusion, anxiety, depression, and hallucination). Prolonged use of Lanoxin® Tablets, in rare instances, has resulted in swelling of the breasts (men), thrombocytopenia, and dermal abnormalities (rash).

Toxic effects associated with therapeutic use of Lanoxin® Tablets last longer in persons with impaired renal function since digoxin is excreted unmetabolized in urine. Absorption and resulting toxicity of digoxin may be significantly affected by interactions with other medicinal substances.

SECTION 12: ECOLOGICAL INFORMATION

ENVIRONMENTAL EFFECTS: Environmental effects testing is currently underway. Preliminary test suggest that digoxin may be toxic to aquatic organism at concentrations greater than 50mg/L. Until environmental effects have been fully determined, dispose of unused compound or process wastes by incineration.

SECTION 12: ECOLOGICAL INFORMATION (cont'd)

STUDY NAME	RESULTS	COMMENTS
Water Solubility:	0.0293 mg/ml	
Dissociation Constant:	No ionizable functional groups	
n-Octanol/Water Partition Coefficient:	Log P = 26.4	
UV/Visible Spectrum:	λ_{max} (0.1N NaOH)=223 nm λ_{max} (0.1N HCl)=220 nm λ_{max} (water)=220 nm	

SECTION 13: WASTE DISPOSAL

ROUTINE: Unused product should be disposed of at an approved facility in accordance with federal, state and local regulations.

ACCIDENTAL RELEASE: Clean up spills immediately, observing precautions in Section 8 - "Personal Protection". Remove or decontaminate all residues in accordance with federal, state and local regulations.

SECTION 14: TRANSPORTATION INFORMATION:

Component 1 or Formulation 1: Lanoxin® (digoxin) Tablets

US Department of Transportation
Proper Shipping Name: Not Regulated in transportation

IATA/ICAO
Proper Shipping Name: Not Regulated in transportation

IMDG
Proper Shipping Name: Not Regulated in transportation

RQ: None Marine Pollutant: No

SECTION 15: REGULATORY INFORMATION

EC PACKAGING AND LABELING FOR SUPPLY: Digoxin is not listed under the Chemicals (Hazard Information and Packaging for Supply) (Amendment) Regulations, 1997. However, suitable labeling would be:

Indication of Danger (Hazard Symbol): Very Toxic

R phrases: R26/28: Very toxic by inhalation and if swallowed.

S phrases: 22: Do not breathe dust.
S24/25: Avoid contact with skin and eyes.
S26: In case of contact with eyes, rinse immediately with plenty of water and seek medical advice.
S36/37/39: Wear suitable protective clothing, gloves and eye/face protection.

OTHER LEGISLATION: Not determined.

SECTION 16: OTHER INFORMATION

REVISION DATE: 06/25/99 SUPERSEDES: 10/31/94