PRODUCT MONOGRAPH

[Pr]DIGIBIND®

Digoxin Immune Fab (Ovine) for injection

sterile lyophilized powder

Specific Antibody for Digoxin

GlaxoSmithKline Inc.
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Table of Contents

[Pr]DIGIBIND®

Digoxin Immune Fab (Ovine)

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Clinically Relevant Nonmedicinal Ingredients
Intravenous	Sterile lyophilized powder/38 mg of digoxin-specific Fab fragments	sorbitol and sodium chloride.

INDICATIONS AND CLINICAL USE

DIGIBIND®, Digoxin Immune Fab (Ovine) is indicated for:

- treatment of potentially life-threatening digoxin toxicity. Although designed specifically to treat life-threatening digoxin toxicity, it has also been used successfully to treat life-threatening toxicity due to digitoxin. Since human experience is limited the consequences of repeated exposures are unknown, DIGIBIND® is not indicated for milder cases of digitalis toxicity.

Manifestations of life-threatening toxicity include severe ventricular arrhythmias such as ventricular tachycardia or ventricular fibrillation, or progressive bradyarrhythmias such as severe sinus bradycardia, or second- or third-degree heart block not responsive to atropine.

Ingestion of more than 10 mg of digoxin in previously healthy adults or 4 mg of digoxin in previously healthy children, or ingestion causing steady-state serum concentrations greater than 10 ng/mL, often results in cardiac arrest. Digitalis-induced progressive elevation of the serum potassium concentration also suggests imminent cardiac arrest. If the potassium concentration exceeds 5 mEq/L in the setting of severe digitalis intoxication, DIGIBIND® therapy is indicated.

CONTRAINDICATIONS

There are no known contraindications to the use of DIGIBIND®, Digoxin Immune Fab (Ovine).

WARNINGS AND PRECAUTIONS

General

Suicidal ingestion often involves more than one drug; thus, toxicity from other drugs should not be overlooked.

One should consider the possibility of anaphylactic, hypersensitivity or febrile reactions to DIGIBIND®, Digoxin Immune Fab (Ovine). If an anaphylactoid reaction occurs, the drug infusion should be discontinued and appropriate therapy initiated using aminophylline, oxygen, volume expansion, diphenhydramine, corticosteroids and airway management as indicated. The need for epinephrine should be balanced against its potential risk in the setting of digitalis toxicity.

Since the Fab fragment of the antibody lacks the antigenic determinants of the Fc fragment, it should pose less of an immunogenic threat to patients than does an intact immunoglobulin molecule. Patients with known allergies would be particularly at risk, as would individuals who have previously received antibodies or Fab fragments raised in sheep.

Papain is used to cleave the whole antibody into Fab and Fc fragments, and traces of papain or inactivated papain residues may be present in DIGIBIND®. Patients with allergies to papain, chymopapain, or other papaya extracts also may be particularly at risk.

Skin testing for allergy was performed during the clinical investigation of DIGIBIND®. Only one patient developed erythema at the site of skin testing, with no accompanying wheal reaction; this individual had no adverse reaction to systemic treatment with DIGIBIND®. Since allergy testing can delay urgently needed therapy, it is not routinely required before treatment of life-threatening digitalis toxicity with DIGIBIND®.

Skin Testing

Skin testing may be appropriate for high risk individuals, especially patients with known allergies or those previously treated with DIGIBIND®. The intradermal skin test can be performed by:

1. Diluting 0.1 mL of reconstituted DIGIBIND® (9.5 mg/mL) in 9.9 mL sterile isotonic saline (1:100 dilution, 95 μg/mL).

2. Injecting 0.1 mL of the 1:100 dilution (9.5 μg) intradermally and observing for an urticarial wheal surrounded by a zone of erythema. The test should be read at 20 minutes.

The scratch test procedure is performed by placing one drop of a 1:100 dilution of DIGIBIND® on the skin and then making a ¼ inch scratch through the drop with a sterile needle. The scratch site is inspected at 20 minutes for an urticarial wheal surrounded by erythema. If skin testing causes a systemic reaction, a tourniquet should be applied above the site of testing and measures to treat anaphylaxis should be instituted. Further administration of DIGIBIND® should be avoided unless its use is absolutely essential, in which case the patient should be pretreated with corticosteroids and diphenhydramine. The physician should be prepared to treat anaphylaxis.

Standard therapy for digitalis intoxication includes withdrawal of the drug and correction of factors that may contribute to toxicity, such as electrolyte disturbances, hypoxia, acid-base disturbances and agents such as catecholamines. Also, treatment of arrhythmias may include judicious potassium supplements, lidocaine, phenytoin, procainamide and/or propranolol; treatment of sinus bradycardia or atrioventricular block may involve atropine or pacemaker insertion.

Carcinogenesis and Mutagenesis

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

Reproductive Toxicology

Treatment of 5 pregnant baboons with digoxin-specific antibody Fab fragments by intravenous infusion daily for 60 days from approximate Gestation Day 113, which is equivalent to the third trimester in humans (duration of pregnancy in the baboon is approximately 180 days), resulted in no treatment-related adverse effects on tolerability, gestation, parturition or infant viability. Transient antibodies to digoxin-specific antibody Fab fragments were observed in 1 of 5 pregnant animals on Days 15 and 30 of the dosing period, but not later in gestation. Daily exposure to digoxin-specific antibody Fab fragments was at least 3 times higher than average human exposure, based on dose.

Cardiovascular

Patients with intrinsically poor cardiac function may deteriorate from withdrawal of the inotropic action of digoxin. Studies in animals have shown that the reversal of inotropic effect is relatively gradual, occurring over hours. When needed, additional support can be provided by use of intravenous inotropes, such as dopamine or dobutamine, or vasodilators. One must be careful in using catecholamines not to aggravate digitalis toxic rhythm disturbances. Clearly, other types of digitalis glycosides should not be used in this setting. Redigitalization should be postponed, if possible, until the Fab fragments have been eliminated from the body, which may require several days. Patients with impaired renal function may require a week or longer.

Endocrine and Metabolism

Massive digitalis intoxication can cause hyperkalemia; administration of potassium supplements in the setting of massive intoxication may be hazardous (see WARNINGS AND PRECAUTIONS; Monitoring and Laboratory Tests section). After treatment with DIGIBIND® Digoxin Immune Fab (Ovine), the serum potassium concentration may drop rapidly and must be monitored frequently, especially over the first several hours after DIGIBIND® is given (see WARNINGS AND PRECAUTIONS; Monitoring and Laboratory Tests section).

Renal

The elimination half-life in the setting of renal failure has not been clearly defined. Patients with renal dysfunction have been successfully treated with DIGIBIND®. There is no evidence to suggest the time-course of therapeutic effect is any different in these patients than in patients with normal renal function, but excretion of the Fab fragment-digoxin complex from the body is probably delayed. In patients who are functionally anephric, one would anticipate failure to clear the Fab fragment-digoxin complex from the blood by glomerular filtration and renal excretion. Whether failure to eliminate the Fab fragment-digoxin complex in severe renal failure can lead to reintoxication following release of newly unbound digoxin into the blood is uncertain. Such patients should be monitored for a prolonged period for possible recurrence of digitalis toxicity.

Special Populations

Pregnant Women

Treatment of pregnant baboons with digoxin-specific antibody Fab fragments during a period equivalent to the third trimester in humans showed no adverse effects on pregnancy or viability of offspring (see Non-clinical Information). There are no animal data to support use in the first and second trimester.

In the absence of adequate experience of administration of digoxin-specific antibody Fab fragments to pregnant women, the potential benefit to the mother must be weighed against the unknown risks to the fetus.

Nursing Women

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when DIGIBIND® is administered to a nursing woman.

Pediatrics

DIGIBIND® has been successfully used in infants with no apparent adverse sequelae. As in all other circumstances, use of this drug in infants should be based on careful consideration of the benefits of the drug balanced against the potential risks involved.

Monitoring and Laboratory Tests

DIGIBIND® will interfere with digitalis immunoassay measurements. Thus, the standard serum digoxin concentration measurement can be clinically misleading until the Fab fragment is eliminated from the body.

Serum digoxin or digitoxin concentration should be obtained before DIGIBIND® administration, if at all possible. These measurements may be difficult to interpret if drawn soon after the last digitalis dose, since at least 6 to 8 hours are required for equilibration of digoxin between serum and tissue. Patients should be closely monitored, including temperature, blood pressure, electrocardiogram and potassium concentration, during and after administration of DIGIBIND®. The total serum digoxin concentration may rise precipitously following administration of DIGIBIND®, but this will be almost entirely bound to the Fab fragment and therefore not able to react with receptors in the body.

Potassium concentrations should be followed carefully. Severe digitalis intoxication can cause life-threatening elevation in serum potassium concentration by shifting potassium from inside to outside the cell. The elevation in serum potassium concentration can lead to increased renal excretion of potassium. Thus, these patients may have hyperkalemia with total body deficit of potassium. When the effect of digitalis is reversed by DIGIBIND®, potassium shifts back inside the cell, with a resulting decline in serum potassium concentration. Hypokalemia may thus develop rapidly. For these reasons, serum potassium concentration should be monitored repeatedly, especially over the first several hours after DIGIBIND® is given, and cautiously treated when necessary.

ADVERSE REACTIONS

In general, the adverse reactions of DIGIBIND® Digoxin Immune Fab (Ovine) are dose-dependent and occur at doses higher than those needed to achieve a therapeutic effect.

Hence, adverse reactions are less common when DIGIBIND® is used within the recommended dose range or therapeutic serum concentration range and when there is careful attention to concurrent medications and conditions.

Allergic reactions to DIGIBIND® have been reported rarely. Patients with a history of allergy, especially to antibiotics, appear to be at particular risk (see WARNINGS AND PRECAUTIONS section). In a few instances, low cardiac output states and congestive heart failure could have been exacerbated by withdrawal of the inotropic effects of digitalis. Hypokalemia may occur from reactivation of (sodium, potassium) ATPase (see WARNINGS AND PRECAUTIONS; Monitoring and Laboratory Tests section). Patients with atrial fibrillation may develop a rapid ventricular response from withdrawal of the effects of digitalis on the atrioventricular node.

Very rarely, DIGIBIND® can cause thrombocytopenia.

DRUG INTERACTIONS

There are no known drug interactions to the use of DIGIBIND®, Digoxin Immune Fab (Ovine).

DOSAGE AND ADMINISTRATION

Dosing Considerations

General Guidelines
The dosage of DIGIBIND®, Digoxin Immune Fab (Ovine), varies according to the amount of digoxin (digitoxin) to be neutralized. The average dose used during clinical testing was 10 vials.

Recommended Dose and Dosage Adjustment

Dosage for Acute Ingestion of Unknown Amount: 20 vials (760 mg) of DIGIBIND® is adequate to treat most life-threatening ingestion in both adults and children. However, in children it is important to monitor for volume overload. The physician may consider administering 10 vials, observing the patient's response, and following with an additional 10 vials if indicated.

Dosage for Toxicity During Chronic Therapy: For **adults**, 6 vials (228 mg) usually is adequate to reverse most cases of toxicity. This dose can be used in patients who are in acute distress or for whom a serum digoxin or digitoxin concentration is not available. In **infants and small children** (≤ 20 kg) a single vial usually should suffice.

Methods for calculating the dose of DIGIBIND® required to neutralize the known or estimated amount of digoxin or digitoxin in the body are given below (see **Dosage Calculation** section).

When determining the dose for DIGIBIND®, the following guidelines should be considered:

- Erroneous calculations may result from inaccurate estimates of the amount of digitalis ingested or absorbed, or from nonsteady-state serum digitalis concentrations. Inaccurate serum digitalis concentration measurements are a possible source of error. Most serum digoxin assay kits are designed to measure values less than 5 ng/mL. Dilution of samples is required to obtain accurate measures above 5 ng/mL.

- Dosage calculations are based on a steady-state volume of distribution of approximately 5 L/kg for digoxin (0.5 L/kg for digitoxin) to convert serum digitalis concentration to the amount of digitalis in the body. The conversion is based on the

principle that body load equals drug steady-state serum concentration multiplied by volume of distribution. These volumes are population averages and vary widely among individuals. Many patients may require higher doses for complete neutralization. Doses should ordinarily be rounded up to the next whole vial.

- If toxicity has not adequately reversed after several hours or appears to recur, readministration of DIGIBIND® at a dose guided by clinical judgment may be required.

- Failure to respond to DIGIBIND® raises the possibility that the clinical problem is not caused by digitalis intoxication. If there is no response to an adequate dose of DIGIBIND®, the diagnosis of digitalis toxicity should be questioned.

Dosage Calculation

Acute Ingestion of Known Amount: Each vial of DIGIBIND® contains 38 mg of purified digoxin-specific Fab fragments which will bind approximately 0.5 mg of digoxin (or digitoxin). Thus, one can calculate the total number of vials required by dividing the total digitalis body load in mg by 0.5 mg/vial (see **Formula 1**).

For toxicity from an acute ingestion, total body load in milligrams will be approximately equal to the amount ingested in milligrams multiplied by 0.80 (to account for incomplete absorption) for digoxin tablets. For digitoxin, the total body load will be approximately equal to the amount ingested in milligrams.

Table 1 gives dosage estimates in number of vials for **adults and children** who have ingested a single large dose of digoxin and for whom the approximate number of tablets is known. The DIGIBIND® dose (in number of vials) represented in Table 1 can be approximated using the following formula:

Formula 1:

$$\text{Dose (in \# of vials)} = \frac{\text{Total digitalis body load in mg}}{\text{0.5 mg of digitalis bound/vial}}$$

Table 1: Approximate DIGIBIND® Dose for Reversal of a Single Large Digoxin Overdose

Number of Digoxin Tablets*	DIGIBIND® Dose # of Vials
25	10
50	20
75	30
100	40
150	60
200	80

* 0.25 mg tablets with 80% bioavailability

Calculations Based on Steady-State Serum Digoxin Concentrations: Table 2 gives dosage estimates in number of vials for **adult patients** for whom a steady-state serum digoxin concentration is known. The DIGIBIND® dose (in number of vials) represented in Table 2 can be approximated using the following formula:

Formula 2:

Calculation with digoxin in ng/mL:

$$\text{Dose (in \# of vials)} = \frac{\text{(Serum digoxin concentration in } \mathbf{ng/mL}\text{) x (weight in kg)}}{100}$$

Calculation with digoxin in nmol/L (S.I. units):

$$\text{Dose (in \# of vials)} = \frac{\text{(Serum digoxin concentration in } \mathbf{nmol}\text{/L) x 0.781 x (weight in kg)}}{100}$$

Table 2: Adult Dose Estimates of DIGIBIND® (in # of Vials) From Steady-State Serum Digoxin Concentration (nmol/L)

Patient Weight (kg)	Serum Digoxin Concentration (nmol/L)							
	1	**2**	**4**	**8**	**12**	**16**	**20**	**25**
40	0.5 v	1 v	2 v	3 v	4 v	5 v	7 v	8 v
60	0.5 v	1 v	2 v	4 v	6 v	8 v	10 v	12 v
70	1 v	2 v	3 v	5 v	7 v	9 v	11 v	14 v
80	1 v	2 v	3 v	5 v	8 v	10 v	13 v	16 v
100	1 v	2 v	4 v	7 v	10 v	13 v	16 v	20 v

v = vials

Table 3 gives dosage estimates in milligrams of DIGIBIND® for **infants and small children** based on the steady-state serum digoxin concentration. The DIGIBIND® dose represented in Table 3 can be estimated by multiplying the dose (in number of vials) calculated from Formula 2 by the amount of DIGIBIND® contained in a vial (38 mg/vial) (see **Formula 3**). Since infants and small children can have much smaller dosage requirements, it is recommended that the 38 mg vial be reconstituted as directed and administered with a tuberculin syringe. For very small doses, a reconstituted vial can be diluted with 34 mL of sterile isotonic saline to achieve a concentration of 1 mg/mL.

Formula 3: Dose (in mg) = [Dose (in # of vials)] x [38 mg/vial]

Table 3: Infants and Small Children Dose Estimates of DIGIBIND® (in mg) From Steady-State Serum Digoxin Concentration (nmol/L)

Patient Weight (kg)	Serum Digoxin Concentration (nmol/L)							
	1	**2**	**4**	**8**	**12**	**16**	**20**	**25**
1	0.3* mg	0.6* mg	1.2* mg	2.5* mg	4 mg	5 mg	6 mg	8 mg
3	1* mg	2* mg	4 mg	8 mg	11 mg	15 mg	18 mg	23 mg
5	1.5* mg	3* mg	6 mg	12 mg	18 mg	24 mg	30 mg	38 mg
10	3* mg	6 mg	12 mg	24 mg	36 mg	48 mg	60 mg	75 mg
20	6 mg	12 mg	24 mg	48 mg	72 mg	95 mg	119 mg	149 mg

* Dilution of reconstituted vial to 1 mg/mL may be desirable.

Calculation Based on Steady-State Digitoxin Concentration: The DIGIBIND® dose for digitoxin toxicity can be approximated using the following formula:

Formula 4:

Calculation with digitoxin in ng/mL:

$$\text{Dose (in \# of vials)} = \frac{\text{Serum digitoxin concentration in } \mathbf{ng/mL}) \times \text{(weight in kg)}}{1{,}000}$$

Calculation with digitoxin in nmol/L (S.I. units):

$$\text{Dose (in \# of vials)} = \frac{\text{(Serum digitoxin concentration in } \mathbf{nmol/L}) \times 0.765 \times \text{(weight in kg)}}{1{,}000}$$

If the dose based on ingested amount differs substantially from that calculated from the serum digoxin or digitoxin concentration, it may be preferable to use the higher dose.

Administration

DIGIBIND® is administered by intravenous route over 30 minutes. It is recommended that it be infused through a 0.22 micron membrane filter to ensure no undissolved particulate matter is administered. If cardiac arrest is imminent, it can be given as a bolus injection (see Overdosage section).

OVERDOSAGE

Not available.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

DIGIBIND®, Digoxin Immune Fab (Ovine), is a sterile lyophilized powder of antigen binding fragments (Fab) derived from specific antidigoxin antibodies raised in sheep. DIGIBIND® binds molecules of digoxin, making them unavailable for binding at their site of action on cells in the body. The Fab fragment-digoxin complex accumulates in the blood, from which it is excreted by the kidney. The net effect is to shift the equilibrium away from binding of digoxin to its receptors in the body, thereby, reversing its effects.

The affinity of digoxin for DIGIBIND® is in the range of 10^9 to 10^{11} M^{-1}, which is greater than the affinity of digoxin for (sodium, potassium) ATPase, the presumed receptor for its toxic effects. The affinity of DIGIBIND® for digitoxin is about ten times less than for digoxin (10^8 to 10^9 M^{-1}).

Pharmacokinetics

After intravenous injection of DIGIBIND® in the baboon, digoxin-specific Fab fragments are excreted in the urine with a biological half-life of about 9 to 13 hours. In humans with normal renal function the half-life appears to be 15 to 20 hours. Experimental

studies in animals indicate that these antibody fragments have a large volume of distribution in the extracellular space, unlike whole antibody which distributes in a space only about twice that of the plasma volume. Ordinarily, following administration of DIGIBIND®, improvement in signs and symptoms of digitalis intoxication begins within one-half hour or less.

STORAGE AND STABILITY

Store under refrigeration (2° to 8°C). Unreconstituted vials can be stored at up to 30°C for a total of 30 days.

Reconstituted Solutions

The contents in each vial should be dissolved with 4 mL of Sterile Water for Injection, by gentle mixing, to give a clear, colourless, approximately isosmotic solution with a protein concentration of 9.5 mg/mL. Reconstituted product should be used promptly. If it is not used immediately, it may be stored under refrigeration at 2° to 8°C for up to 4 hours. The reconstituted product may be diluted with sterile isotonic saline to a convenient volume. Parenteral drug products should be inspected visually for particulate matter and discolouration prior to administration, whenever solution and container permit.

SPECIAL HANDLING INSTRUCTIONS

Not applicable.

DOSAGE FORMS, COMPOSITION AND PACKAGING

Availability of Dosage Form

DIGIBIND® Digoxin Immune Fab (Ovine), is available as a sterile lyophilized powder supplied in boxes of one (1) vial containing 38 mg of purified lyophilized digoxin-specific Fab fragments.

Composition

Each vial contains 38 mg of digoxin-specific Fab fragments, 75 mg of sorbitol as a stabilizer, and 28 mg of sodium chloride. There are no preservatives added. Each vial will bind approximately 0.5 mg digoxin (or digitoxin).

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: Digoxin Immune Fab (Ovine)

Molecular weight: approximately 46,200

CLINICAL TRIALS

Not available.

DETAILED PHARMACOLOGY

Not available.

MICROBIOLOGY

Not available.

TOXICOLOGY

Not available.

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PART III: CONSUMER INFORMATION

PrDIGIBIND®
Digoxin Immune Fab (Ovine)

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

ABOUT THIS MEDICATION

What the medication is used for:
DIGIBIND®, Digoxin Immune Fab (Ovine) is used in the treatment of life-threatening digoxin intoxication. It has also been used successfully to treat life-threatening toxicity due to digitoxin.

What it does:
DIGIBIND®, Digoxin Immune Fab (Ovine) is a sterile freeze-dried powder of antigen binding fragments (Fab) derived from specific antidigoxin antibodies raised in sheep. DIGIBIND® binds molecules of digoxin, making them unavailable for binding at their site of action on cells in the body.

When it should not be used:
Do not use DIGIBIND®, Digoxin Immune Fab (Ovine) if:
- you are hypersensitive to any of the ingredients.
- you have allergies to papain, chymopain or other papaya extracts.
- you have previously received antibodies or Fab fragments raised in sheep.

What the medicinal ingredient is:
DIGIBIND®, Digoxin Immune Fab (Ovine) contains 38 mg of digoxin-specific Fab fragments.

What the important nonmedicinal ingredients are:
DIGIBIND®, Digoxin Immune Fab (Ovine) contains 28 mg of sodium chloride and 75 mg of sorbitol as a stabilizer. There are no preservatives added.

What dosage forms it comes in:
DIGIBIND®, Digoxin Immune Fab (Ovine) is available as a sterile freeze-dried powder supplied in boxes of one (1) vial containing 38 mg of purified freeze-dried digoxin-specific Fab fragments.

WARNINGS AND PRECAUTIONS

BEFORE you use DIGIBIND®, Digoxin Immune Fab (Ovine) talk to your doctor or pharmacist if:
- You have any allergies to this drug or its ingredients.
- You are pregnant or breastfeeding.

INTERACTIONS WITH THIS MEDICATION

There are no known drug interactions to the use of DIGIBIND® Digoxin Immune Fab (Ovine)

PROPER USE OF THIS MEDICATION

Usual dose:
The dosage of DIGIBIND®, Digoxin Immune Fab (Ovine) varies according to the amount of digoxin (digitoxin) to be neutralized. The average dose used during clinical testing was 10 vials.

Dosage for Acute Ingestion of Unknown Amount: 20 vials (760 mg) of DIGIBIND® is adequate to treat most life-threatening ingestions in both adults and children. However, in children it is important to monitor for volume overload, (fluid buildup in the body causing rapid heartbeat, shortness of breath, and swelling in the hands and feet). The physician may consider administering 10 vials, observing the patient's response, and follow with an additional 10 vials if necessary

Dosage for Toxicity During Chronic Therapy: For adults, 6 vials (228 mg) usually is adequate to reverse most cases of toxicity. This dose can be used in patients who are in acute distress for whom a serum digoxin concentration is not available. In infants and small children (≤ 20 kg) a single vial usually should suffice.

The methods for calculating the dose of DIGIBIND® required to neutralize a known or estimated amount of digoxin or digitoxin in the body is provided in Part I: DOSAGE AND ADMINISTRATION section.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Allergic reactions to DIGIBIND®, Digoxin Immune Fab (Ovine) have been reported rarely. Patients with a history of allergy, especially to antibiotics, appear to be at particular risk. In a few instances :
- low cardiac output states (low volume of blood being pumped by the heart) and,
- congestive heart failure,

allergic reactions could have been worsened by withdrawal of the inotropic (force of muscle contraction) effects of digitalis.

Low plasma potassium concentrations may occur from reactivation of (sodium, potassium) ATPase (a protein complex responsible for converting potential energy into ATP, the molecule the body uses for fuel). Patients with atrial fibrillation (an irregular heartbeat) may develop a rapid ventricular response to withdrawal of the effects of digitalis on the atrioventricular node.

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

One should consider the possibility of anaphylactic (a severe allergic reaction, that may be life threatening), hypersensitivity or febrile reactions (related to or characterised by fever) to DIGIBIND®, Digoxin Immune Fab (Ovine). If a severe allergic reaction occurs, the drug infusion should be discontinued and appropriate therapy initiated.

HOW TO STORE IT

Store under refrigeration (2° to 8°C). Unreconstituted vials can be stored at up to 30°C for a total of 30 days.

Reconstituted product should be used promptly. If it is not used immediately, it may be stored under refrigeration at 2° to 8°C for up to 4 hours.

REPORTING SUSPECTED SIDE EFFECTS

To monitor drug safety, Health Canada through the Canada Vigilance Program collects information on serious and unexpected effects of drugs. If you suspect you have had a serious or unexpected reaction to this drug you may notify Canada Vigilance:

By toll-free telephone: 866-234-2345
By toll-free fax: 866-678-6789
Online: www.healthcanada.gc.ca/medeffect
By email: CanadaVigilance@hc-sc.gc.ca

By regular mail:
Canada Vigilance National Office
Marketed Health Products Safety and Effectiveness Information Bureau
Marketed Health Products Directorate
Health Products and Food Branch
Health Canada
Tunney's Pasture, AL 0701C
Ottawa ON K1A 0K9

NOTE: Should you require information related to the management of the side effect, please contact your health care provider before notifying Canada Vigilance. 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.gsk.ca
or by contacting the sponsor,
GlaxoSmithKline Inc.
7333 Mississauga Road
Mississauga, Ontario
L5N 6L4
1-800-387-7374

This leaflet was prepared by GlaxoSmithKline Inc.

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