CARDIOPLEGIC- calcium chloride, magnesium chloride, potassium chloride and sodium chloride solution
Baxter Healthcare Corporation

CARDIOPLEGIC SOLUTION

FOR CARDIAC PERFUSION

NOT FOR INTRAVENOUS INJECTION

(PL 146 Plastic)

Rx only

DESCRIPTION

Baxter Cardioplegic Solution is a sterile, nonpyrogenic, essentially isotonic, formulation of electrolytes in Water for Injection, USP. It is a "core solution" intended for use ***only after addition of sodium bicarbonate*** to adjust pH prior to administration. After buffering with sodium bicarbonate it is suitable for cardiac instillation (usually with hypothermia) to induce arrest during open heart surgery. Other agents may be added to the solution prior to instillation. (See INSTRUCTIONS FOR USE.)

Each 100 mL of solution contains Calcium Chloride Dihydrate USP 17.6 mg, Magnesium Chloride, Hexahydrate USP 325.3 mg, Potassium Chloride USP 119.3 mg, and Sodium Chloride USP 643 mg, in Water for Injection, USP. May contain HCl and/or NaOH for pH adjustment. Electrolyte content per liter (not including ions for pH adjustment): Sodium (Na+) 110 mEq; Magnesium (Mg++) 32 mEq; Potassium (K+) 16 mEq; Calcium (Ca++) 2.4 mEq; Chloride (Cl-) 160 mEq. Osmolar concentration, 304 mOsmol/liter (calc.); pH 3.8 (3.5 to 3.9) prior to sodium bicarbonate addition.

It is required that 10 mL (840 mg) of 8.4% Sodium Bicarbonate Injection, USP (10 mEq each of sodium and bicarbonate) be added aseptically and thoroughly mixed with each 1000 mL of cardioplegic solution to adjust pH. **Use 10 mL of Hospira[1] List 4900, 8.4% Sodium Bicarbonate Injection, USP, to achieve the approximate pH of 7.8 when measured at room temperature. Use of any other Sodium Bicarbonate Injection may not achieve this pH due to the varying pH's of Sodium Bicarbonate Injections.** Due to its inherent instability with other components, sodium bicarbonate must be added just prior to administration. After this addition, the solution must be stored under refrigeration and be used within 24 hours. The buffered admixture contains the following electrolytes (per liter): Na+ 120 mEq, Mg++ 32 mEq, K+ 16 mEq, Ca++ 2.4 mEq, Cl- 160 mEq and bicarbonate (HCO_3^-) 10 mEq; osmolar concentration, 324 mOsmol/liter (calc.); pH 7.8 (approx.). If other agents are added, these values may be altered. The solution contains no bacteriostat, or antimicrobial agent and is intended only for use (after adjusting pH with sodium bicarbonate) in a single operative procedure. When smaller amounts are required, the unused portion should be discarded. Cardioplegic solution with added sodium bicarbonate used as a coronary artery infusate induces cardiac arrest, combats ischemic ionic disturbances, buffers ischemic acidosis and protects energy sources for functional recovery after ischemia.

Calcium Chloride, USP is chemically designated calcium chloride, dihydrate ($CaCl_2 \cdot 2\ H_2O$), white fragments or granules freely soluble in water.

Magnesium Chloride, USP is chemically designated magnesium chloride, hexahydrate ($MgCl_2 \cdot 6\ H_2O$), deliquescent flakes or crystals very soluble in water.

Potassium Chloride, USP is chemically designated KCl, a white granular powder freely soluble in water.

Sodium Chloride, USP is chemically designated NaCl, a white crystalline powder freely soluble in water.

Water for Injection, USP is chemically designated H_2O.

The flexible plastic container is fabricated from a specially formulated polyvinyl chloride. Water can permeate from inside the container into the overwrap but not in amounts sufficient to affect the solution significantly. Solutions in contact with the plastic container may leach out certain chemical components from the plastic in very small amounts; however, biological testing was supportive of the safety of the plastic container materials. Exposure to temperatures above 25°C/77°F during transport and storage will lead to minor losses in moisture content. Higher temperatures lead to greater losses. It is unlikely that these minor losses will lead to clinically significant changes within the expiration period.

CLINICAL PHARMACOLOGY

Cardioplegic solution with added sodium bicarbonate when cooled and instilled into the coronary artery vasculature, causes prompt arrest of cardiac electromechanical activity, combats intracellular ion losses and buffers ischemic acidosis. When used with hypothermia and ischemia, the action may be characterized as cold ischemic potassium-induced cardioplegia.

This is conducive to providing the surgeon with a quiet, relaxed heart and bloodless field of operation.

Calcium (Ca++) ion in low concentration is included in the solution to maintain integrity of cell membrane to ensure that there is no likelihood of calcium paradox during reperfusion.

Magnesium (Mg++) ion may help stabilize the myocardial membrane by inhibiting a myosin phosphorylase, which protects adenosine triphosphate (ATP) reserves for postischemic activity. The protective effects of magnesium and potassium have been shown to be additive.

Potassium (K+) ion concentration is responsible for prompt cessation of mechanical myocardial contractile activity. The immediacy of the arrest thus preserves energy supplies for postischemic contractile activity in diastole.

The chloride (Cl-) and sodium (Na+) ions have no specific role in the production of cardiac arrest. Sodium is essential to maintain ionic integrity of myocardial tissue. The chloride ions are present to maintain the electroneutrality of the solution.

Added bicarbonate (HCO_3^-) anion is included as a buffer to render the solution slightly alkaline and compensate for the metabolic acidosis that accompanies ischemia.

Extemporaneous alternative buffering to the described formulation of this solution is not recommended.

INDICATIONS AND USAGE

Baxter Cardioplegic Solution when suitably buffered in combination with ischemia and hypothermia is used to induce cardiac arrest during open heart surgery.

CONTRAINDICATIONS

Baxter Cardioplegic Solution must not be administered without the addition of 8.4% Sodium Bicarbonate Injection, USP, Hospira[1] List 4900.

NOT FOR INTRAVENOUS INJECTION.

This solution is only for instillation into cardiac vasculature after buffering with sodium bicarbonate.

WARNINGS

This solution should be used only by those trained to perform open heart surgery. This solution is intended only for use during cardiopulmonary bypass when the coronary circulation is isolated from the systemic circulation. (See INDICATIONS AND USAGE.)

Do not instill the solution into the coronary vasculature unless sodium bicarbonate has been added. If large volumes of cardioplegic solution are infused and allowed to return to the heart lung machine without any venting from the right heart, then plasma magnesium and potassium levels may rise. Development of severe hypotension and metabolic acidosis while on bypass has been reported when large volumes (8 to 10 liters) of solution are instilled and allowed to enter the pump and then the systemic circulation. Right heart venting is therefore recommended. The buffered solution with added sodium bicarbonate should be cooled to 4°C prior to administration and used within 24 hours of mixing.

PRECAUTIONS

Myocardial temperature should be monitored during surgery to maintain hypothermia.

Continuous electrocardiogram monitoring is essential to detect changes in myocardial activity during the procedure.

Appropriate equipment to defibrillate the heart following cardioplegia should be readily available.

Inotropic support drugs should be available during postoperative recovery.

Do not administer unless solution is clear and container is undamaged.

Discard unused portion.

Drug Interactions

Additives may be incompatible. Consult with pharmacist, if available. When introducing additives, use aseptic technique, mix thoroughly and do not store. (See INSTRUCTIONS FOR USE.)

Pregnancy

Category C

Animal reproduction studies have not been conducted with Cardioplegic Solution. It is also not known whether this solution can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity.

Cardioplegic Solution should be given to a pregnant woman only if clearly needed.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established. Because of differences in structure, function, and metabolism, clinical myocardial protection strategies and Cardioplegia solutions that are effective in adult hearts may be less effective in the immature heart.

Geriatric Use

Clinical studies of cardioplegic solution did not include sufficient numbers of subjects aged 65 and over to determine whether they responded differently from younger subjects. Other reported clinical experience has not identified differences in responses between older and younger patients.

In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosage range reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease.

This product is unique in that there is no hepatic or renal excretion and specific adjustments for dosing in the elderly are not known.

ADVERSE REACTIONS

Intraoperative and perioperative potential hazards of open heart surgery include myocardial infarction,

electrocardiographic abnormalities, and arrhythmias, including ventricular fibrillation. Spontaneous recovery after cardioplegic cardiac arrest may be delayed or absent when circulation is restored. Defibrillation by electric shock may be required to restore normal cardiac function.

OVERDOSAGE

Overzealous instillation of the solution may result in unnecessary dilatation of the myocardial vasculature and leakage into the perivascular myocardium, possibly causing tissue edema. (See WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.)

DOSAGE AND ADMINISTRATION

The following information is suggested as a guide and is subject to variation according to the preference and experience of the surgeon. It is required that 10 mL (840 mg) of 8.4% Sodium Bicarbonate Injection, USP (10 mEq each of sodium and bicarbonate) be added aseptically and thoroughly mixed with each 1000 mL of cardioplegic solution to adjust pH. **Use 10 mL of Hospira[1] List 4900, 8.4% Sodium Bicarbonate Injection, USP, to achieve the approximate pH of 7.8 when measured at room temperature. Use of any other Sodium Bicarbonate Injection may not achieve this pH due to the varying pH's of Sodium Bicarbonate Injections.** Due to its inherent instability with other components, sodium bicarbonate must be added just prior to administration. After this addition, the solution must be used within 24 hours. The solution should be cooled to 4°C prior to use. Following institution of cardiopulmonary bypass at perfusate temperatures of 28° to 30°C, and after cross-clamping of the ascending aorta, the buffered solution is administered by rapid infusion into the aortic root. The initial rate of infusion may be 300 mL/m2/minute (about 540 mL/min in a 5' 8", 70 kg adult with 1.8 square meters of surface area) given for a period of two to four minutes. Concurrent external cooling (regional hypothermia of the pericardium) may be accomplished by instilling a refrigerated (4°C) physiologic solution such as a Normosol®[2] -R (balanced electrolyte replacement solution) or Ringer's Injection into the chest cavity.

Should myocardial electromechanical activity persist or recur, the solution may be reinfused at a rate of 300 mL/m2/min for a period of two minutes. Reinfusion of the solution may be repeated every 20 to 30 minutes or sooner if myocardial temperature rises above 15° to 20°C or returning cardiac activity is observed. The regional hypothermia solution around the heart also may be replenished continuously or periodically in order to maintain adequate hypothermia. Suction may be used to remove warmed infusates. An implanted thermistor probe may be used to monitor myocardial temperature.

The volumes of solution instilled into the aortic root may vary depending on the duration or type of open heart surgical procedure.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. (See PRECAUTIONS.)

INSTRUCTIONS FOR USE

To Open

Tear outer wrap at notch and remove solution container. Visually inspect the container. If the outlet port protector is damaged, detached, or not present, discard container as solution path sterility may be impaired. If supplemental medication is desired, follow directions below before preparing for administration. Some opacity of the plastic due to moisture absorption during the sterilization process may be observed. This is normal and does not affect the solution quality or safety. The opacity will diminish gradually. To add 10 mL of 8.4% Sodium Bicarbonate Injection, USP, Hospira[1] List 4900, and other supplemental medication, follow directions below before preparing for administration.

To Add Medication

1. Prepare additive port.
2. Using aseptic technique and an additive delivery needle of appropriate length, puncture resealable additive port at target area, inner diaphragm and inject. Withdraw needle after injecting medication.
3. The additive port may be protected by covering with an additive cap.
4. Mix container contents thoroughly.

Preparation for Administration

(Use aseptic technique)

1. Close flow control clamp of administration set.
2. Remove cover from outlet port at bottom of container.
3. Insert piercing pin of administration set into port with a twisting motion until the set is firmly seated. **NOTE:** See full directions on administration set carton.
4. Suspend container from hanger.
5. Squeeze and release drip chamber to establish proper fluid level in chamber.
6. Attach aortic infusion device to set.
7. Open flow control clamp to expel air from set and aortic infusion device. Close clamp.
8. Position aortic infusion device to introduce solution into aortic root.
9. Regulate rate of administration with flow control clamp.

HOW SUPPLIED

Baxter Cardioplegic Solution is supplied (without sodium bicarbonate) in a single-dose 1000 mL flexible plastic container as follows:

2B1462 NDC 0338-0341-04

WARNING: Do not use flexible container in series connections.

Exposure of pharmaceutical products to heat should be minimized. Avoid excessive heat. Protect from freezing. It is recommended that the product be stored at room temperature (25°C); however, brief exposure up to 40°C does not adversely affect the product.

For Product Information
Call 1-800-933-0303

Baxter Healthcare Corporation
Deerfield, IL 60015 USA

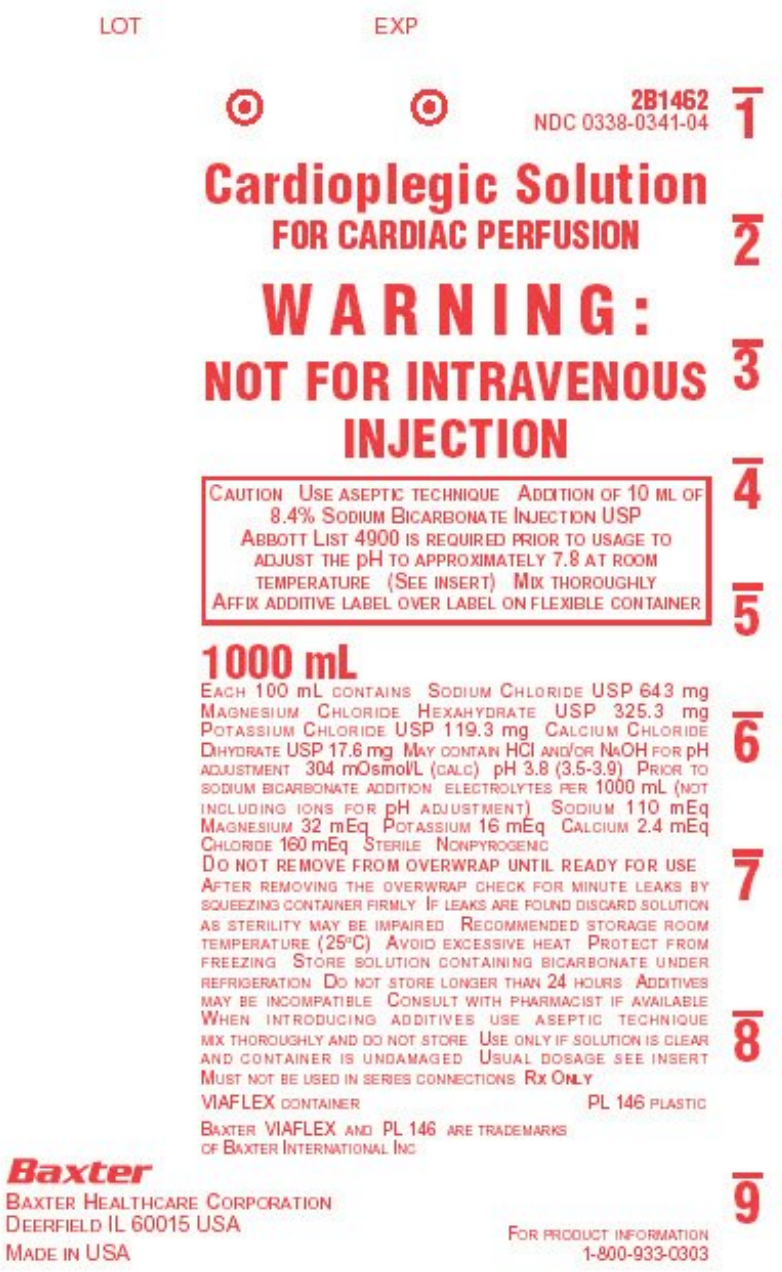
Printed in USA

07-19-73-074

Rev. June 2014

Baxter and PL146 are trademarks of Baxter International Inc.
[1]Hospira, Inc., Lake Forest, IL 60045 USA
[2]Normosol® is a trademark of Hospira, Inc.

PACKAGE LABELING - PRINCIPAL DISPLAY PANEL



Container Label

Container Label

LOT
EXP

2B1462

NDC 0338-0341-04

Cardioplegic Solution
FOR CARDIAC PERFUSION

W A R N I N G :
NOT FOR INTRAVENOUS
INJECTION

CAUTION USE ASEPTIC TECHNIQUE ADDITION OF 10 ML OF 8.4% SODIUM BICARBONATE INJECTION USP ABBOTT LIST 4900 IS REQUIRED PRIOR TO USAGE TO

ADJUST THE pH TO APPROXIMATELY 7.8 AT ROOM TEMPERATURE (SEE INSERT) MIX THOROUGHLY
AFFIX ADDITIVE LABEL OVER LABEL ON FLEXIBLE CONTAINER

1000 mL
EACH 100 mL CONTAINS SODIUM CHLORIDE USP 643 mg MAGNESIUM CHLORIDE HEXAHYDRATE USP 325.3 mg POTASSIUM CHLORIDE USP 119.3 mg CALCIUM CHLORIDE DIHYDRATE USP 17.6 mg MAY CONTAIN HCI AND/OR NAOH FOR pH ADJUSTMENT 304 mOsmol/L (CALC) pH 3.8 (3.5-3.9) PRIOR TO SODIUM BICARBONATE ADDITION ELECTROLYTES PER 1000 mL (NOT INCLUDING IONS FOR pH ADJUSTMENT) SODIUM 110 mEq MAGNESIUM 32 mEq POTASSIUM 16 mEq CALCIUM 2.4 mEq CHLORIDE 160 mEq STERILE NONPYROGENIC

DO NOT REMOVE FROM OVERWRAP UNTIL READY FOR USE

AFTER REMOVING THE OVERWRAP CHECK FOR MINUTE LEAKS BY SQUEEZING CONTAINER FIRMLY IF LEAKS ARE FOUND DISCARD SOLUTION AS STERILITY MAY BE IMPAIRED RECOMMENDED STORAGE ROOM TEMPERATURE (25°C) AVOID EXCESSIVE HEAT PROTECT FROM FREEZING STORE SOLUTION CONTAINING BICARBONATE UNDER REFRIGERATION DO NOT STORE LONGER THAN 24 HOURS ADDITIVES MAY BE INCOMPATIBLE CONSULT WITH PHARMACIST IF AVAILABLE WHEN INTRODUCING ADDITIVES USE ASEPTIC TECHNIQUE MIX THOROUGHLY AND DO NOT STORE USE ONLY IF SOLUTION IS CLEAR AND CONTAINER IS UNDAMAGED USUAL DOSAGE SEE INSERT MUST NOT BE USED IN SERIES CONNECTIONS

Rx ONLY

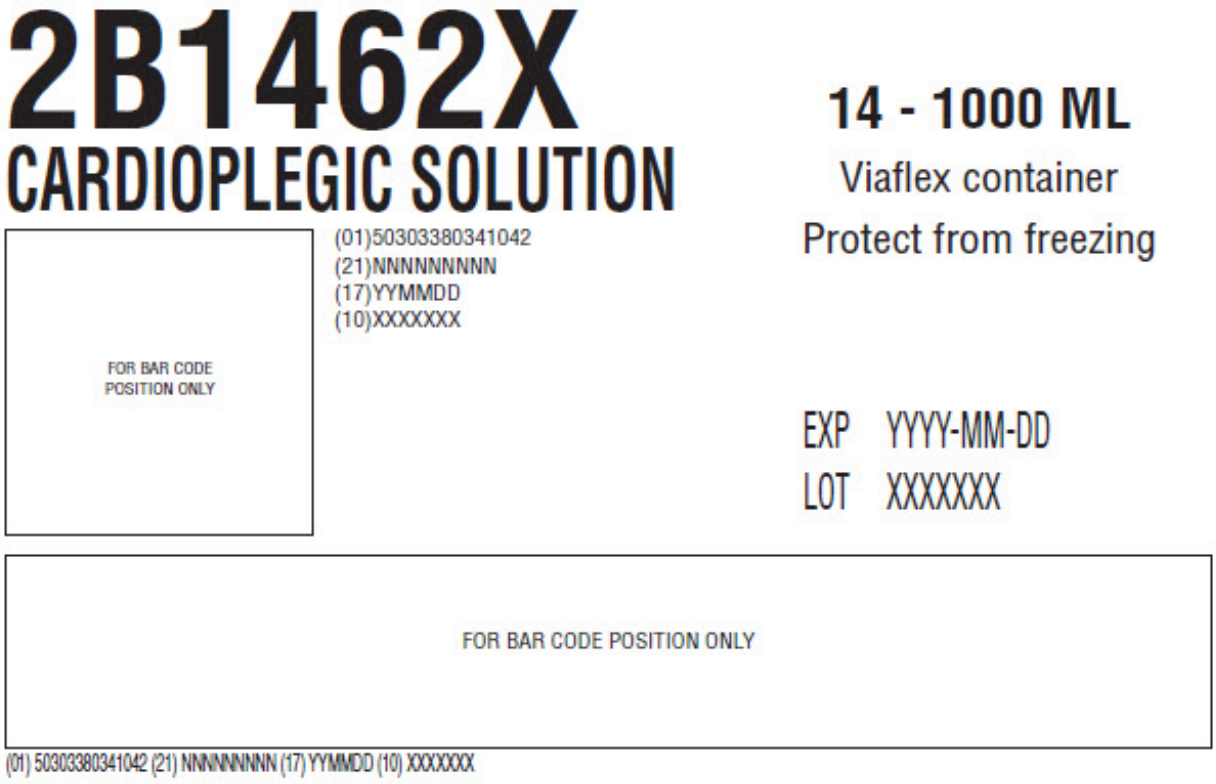
VIAFLEX CONTAINER PL 146 PLASTIC

Baxter logo
BAXTER HEALTHCARE CORPORATION
DEERFIELD IL 60015 USA

MADE IN USA

FOR PRODUCT INFORMATION

1-800-933-0303



Carton Label - panel 1

Carton Label - panel 1

2B1462X
CARDIOPLEGIC SOLUTION

14-1000 ML

Viaflex container
Protect from freezing

BAR CODE
(01)50303380341042
(21)NNNNNNNNN
(17)YYMMDD
(10)XXXXXXX

EXP YYYY-MM-DD
LOT XXXXXXX

BAR CODE
(01)50303380341042 (21)NNNNNNNNN (17)YYMMDD (10) XXXXXXX

Carton Label – panel 2

2B1462X
CARDIOPLEGIC SOLUTION

14 – 1000 ML

Viaflex container
Protect from freezing

EXP YYYY-MM-DD

CARDIOPLEGIC

calcium chloride, magnesium chloride, potassium chloride and sodium chloride solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0338-0341
Route of Administration	INTRA-ARTERIAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
CALCIUM CHLORIDE (UNII: M4I0D6VV5M) (CALCIUM CATION - UNII:2M83C4R6ZB, CHLORIDE ION - UNII:Q32ZN48698)	CALCIUM CHLORIDE	17.6 mg in 100 mL
MAGNESIUM CHLORIDE (UNII: 02F3473H9O) (MAGNESIUM CATION - UNII:T6V3LHY838, CHLORIDE ION - UNII:Q32ZN48698)	MAGNESIUM CHLORIDE	325.3 mg in 100 mL
POTASSIUM CHLORIDE (UNII: 660YQ98I10) (POTASSIUM CATION - UNII:295O53K152, CHLORIDE ION - UNII:Q32ZN48698)	POTASSIUM CHLORIDE	119.3 mg in 100 mL
SODIUM CHLORIDE (UNII: 451W47IQ8X) (SODIUM CATION - UNII:LYR4M0NH37, CHLORIDE ION - UNII:Q32ZN48698)	SODIUM CHLORIDE	643 mg in 100 mL

Inactive Ingredients	
Ingredient Name	**Strength**
WATER (UNII: 059QF0KO0R)	
HYDROCHLORIC ACID (UNII: QTT17582CB)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0338-0341-04	14 in 1 CARTON	04/21/2000	
1		1000 mL in 1 BAG; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA075323	04/21/2000	

Labeler - Baxter Healthcare Corporation (005083209)

Establishment

Name	Address	ID/FEI	Business Operations
Baxter Healthcare Corporation		059140764	ANALYSIS(0338-0341) , MANUFACTURE(0338-0341) , LABEL(0338-0341) , PACK(0338-0341) , STERILIZE(0338-0341)

Establishment

Name	Address	ID/FEI	Business Operations
Baxter Healthcare Corporation		194684502	ANALYSIS(0338-0341)

Revised: 7/2014 Baxter Healthcare Corporation