ISOPLATE- sodium chloride, sodium gluconate, sodium acetate, potassium chloride, magnesium chloride, sodium phosphate, dibasic, and potassium phosphate, monobasic solution Terumo BCT Ltd.

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use ISOPLATE SOLUTION - Platelet Additive Solution [PAS-F] safely and effectively. See full prescribing information for ISOPLATE SOLUTION - Platelet Additive Solution [PAS-F].

ISOPLATE SOLUTION

Platelet Additive Solution [PAS-F]
Sterile Fluid
Polyolefin Bag

Initial U.S. Approval: 2013

RECENT MAJOR CHANGES

Dosage and Administration (2.2)	5/2015

INDICATIONS AND USAGE

ISOPLATE SOLUTION - Platelet Additive Solution [PAS-F] is an isotonic solution to replace a portion of the plasma to store Platelets Pheresis Platelet Additive Solution (PAS) Added Leukocytes Reduced products collected using a hyperconcentrated collection on Terumo BCT's Trima Accel system. Platelets Pheresis PAS Added Leukocytes Reduced products are stored in a mix of 65% Isoplate and 35% plasma.
Platelets in ISOPLATE SOLUTION can be stored at a concentration range of 0.7 to 2.1 × 10^6/µL for up to 5 days at 20-24 °C with continuous agitation in the Terumo BCT ELP bag [citrated polyvinyl chloride (PVC)]. (1)

DOSAGE AND ADMINISTRATION

- ISOPLATE SOLUTION is added to hyperconcentrated platelets after the apheresis procedure is complete. (2)
- ISOPLATE SOLUTION may only be used with the Trima Accel system. For instructions on the use of the solution with the Trima Accel system, see the Trima Accel system operator's manual. (2.1)
- Follow the directions for connecting the ISOPLATE SOLUTION bag to the Trima Accel System. (2.2)

DOSAGE FORMS AND STRENGTHS

- 500 mL sterile fluid in polyolefin bag (3)

CONTRAINDICATIONS

- DO NOT INFUSE ISOPLATE SOLUTION DIRECTLY TO THE PATIENTS. (4)

WARNINGS AND PRECAUTIONS

- Verify that the ISOPLATE SOLUTION has been securely attached to the platelet additive solution line on the Trima Accel system tubing set using aseptic technique. (5)

ADVERSE REACTIONS

ISOPLATE SOLUTION is expected to cause adverse events that are seen with platelet transfusion. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Terumo BCT, Inc. at 1-877-339-4228 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

USE IN SPECIFIC POPULATIONS

ISOPLATE SOLUTION has not been studied in controlled clinical trials with specific populations.

Revised: 5/2015

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

ISOPLATE SOLUTION - Platelet Additive Solution [PAS-F] is an isotonic solution to replace a portion of the plasma to store Platelets Pheresis Platelet Additive Solution (PAS) Added Leukocytes Reduced products collected using a hyperconcentrated collection on Terumo BCT's Trima Accel system *[See Dosage and Administration (2).]*

Platelets Pheresis PAS Added Leukocytes Reduced products are stored in a mix of 65% ISOPLATE SOLUTION and 35% plasma. Platelets in the solution can be stored at a concentration range of 0.7 to $2.1 \times 10^6/\mu L$ for up to 5 days at 20-24 °C with continuous agitation in the Terumo BCT ELP bag [citrated polyvinyl chloride (PVC)] *[See Clinical Studies (14).]*

2 DOSAGE AND ADMINISTRATION

2.1 General Dosing Information

ISOPLATE SOLUTION is added to hyperconcentrated platelets after the apheresis procedure is complete. It is not intended for direct intravenous infusion.

ISOPLATE SOLUTION may only be used with the Trima Accel system for automated blood collection. For instructions on the use of the solution with the Trima Accel system, see the Trima Accel system operator's manual.

2.2 Administration

- Ensure solution is the ISOPLATE SOLUTION and is within the expiration date.
- Inspect the bag. Do not use if the container is damaged, leaking or if there is any visible sign of deterioration.
- Use only if solution is clear and free of particulate matter.
- Protect from sharp objects.

Directions for Connecting the ISOPLATE SOLUTION Bag to the Trima Accel System

At the prompt to connect the platelet additive solution to the Trima Accel system tubing set:

1. Remove the overwrap by pulling down at notch, and remove the ISOPLATE SOLUTION bag.
2. Before use, perform the following checks *[See Warnings and Precautions (5).]*:
   - Check for leaks by squeezing the bag. If leaks are found, discard bag.
   - Ensure the solution is the ISOPLATE SOLUTION and is within the expiration date.
   - Inspect the solution in good light. Bags showing cloudiness, haze, or particulate matter should not be used.
3. Remove the protective cap from the port on the bag.
4. Connect the bag to the Trima Accel system tubing set using aseptic technique and hang the solution.
5. Break the frangible connector. When you break frangible connectors, bend them in both directions to ensure that you break them completely. Failure to do so may result in restricted flow.
6. Proceed per the Trima Accel system operator's manual.

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

3 DOSAGE FORMS AND STRENGTHS

500 mL ISOPLATE SOLUTION - Platelet Additive Solution [PAS-F] is a sterile isotonic solution in a polyolefin bag. Each 100 mL contains: Sodium Chloride 0.53 g; Sodium Gluconate 0.5 g; Sodium Acetate Trihydrate 0.37 g; Potassium Chloride 0.037 g; Magnesium Chloride Hexahydrate 0.03 g; Dibasic Sodium Phosphate Dihydrate 0.008 g; Monobasic Potassium Phosphate 0.00082 g; in Water for Injection.

4 CONTRAINDICATIONS

DO NOT INFUSE ISOPLATE SOLUTION DIRECTLY TO THE PATIENTS.

5 WARNINGS AND PRECAUTIONS

- Verify that the solution bag has been securely attached to the platelet additive solution line on the Trima Accel system tubing set using aseptic technique.
- Do not reuse. Discard unused or partially used solution bags.

6 ADVERSE REACTIONS

ISOPLATE SOLUTION is added to platelets after the apheresis procedure is complete. It is not for direct intravenous infusion. It is expected to cause adverse events that are normally associated with platelet transfusion.

6.1 Clinical Trials Experience

No adverse reactions were reported in the subjects infused with < 10 mL of radiolabeled platelets stored for 5 days in 65% ISOPLATE SOLUTION, and rinsed prior to infusion *[See Clinical Studies (14).]*

8 SPECIAL POPULATIONS

ISOPLATE SOLUTION has not been adequately studied in controlled clinical trials with specific populations.

11 DESCRIPTION

ISOPLATE SOLUTION - Platelet Additive Solution [PAS-F] is an isotonic solution designed to replace a proportion of the plasma used in the storage of Platelet Pheresis, Leukocytes Reduced PAS products collected using a hyperconcentrated collection on Terumo BCT's Trima Accel system.

The solution is sterile, nonpyrogenic and contains no bacteriostatic or antimicrobial agents.

The formulas of the active ingredients are provided in Table 1.

Table 1: Active Ingredients

Ingredients	Molecular Formula	Molecular Weight
Sodium Chloride USP	NaCl	58.44
Sodium Acetate Trihydrate USP	CH3COONa·3H2O	136.08
Potassium Chloride USP	KCl	74.55
Magnesium Chloride Hexahydrate USP	MgCl2·6H2O	203.30
Dibasic Sodium Phosphate Dihydrate USP	Na2HPO4·2H2O	177.98
Monobasic Potassium Phosphate NF	KH2PO4	136.09
Sodium Gluconate USP	C6H11NaO7	218.14

Each 100 mL of ISOPLATE SOLUTION contains: Sodium Chloride USP 0.53 g; Sodium Gluconate USP 0.5 g; Sodium Acetate Trihydrate USP 0.37 g; Potassium Chloride USP 0.037 g; Magnesium Chloride Hexahydrate USP 0.03 g; Dibasic Sodium Phosphate Dihydrate USP 0.008 g; Monobasic Potassium Phosphate NF 0.00082 g; in Water for Injection USP.

pH may be adjusted with glacial Acetic Acid USP or Sodium Hydroxide NF pH: 7.4 (7.0-7.8).

Concentration of Electrolytes (mEq/liter): Sodium 141; Potassium 5; Magnesium 3; Chloride 98; Phosphate (HPO=4) 1 (0.5 mmole P/liter); Acetate (CH3COO–) 27; Gluconate (HOCH2(CHOH)4COO–) 23.

The polyolefin bag is not made with natural rubber latex or PVC. Di(2-ethylhexyl)phthalate (DEHP) is present only in sterile dock tube.

The bag is made from a multilayered film. It contains materials that have been tested to demonstrate the suitability of the container for storing pharmaceutical solutions. The solution contact layer is an elasticized polyolefin. The bag is nontoxic and biologically inert. The bag-solution unit is a closed system and is not dependent upon entry of external air during administration. The bag is overwrapped to provide protection from the physical environment and to provide an additional moisture barrier when necessary.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

ISOPLATE SOLUTION contains the following key components to maintain platelet function:

- Sodium chloride for osmolarity
- Acetate to fuel platelet metabolism
- Gluconate or phosphate for buffering
- Magnesium and potassium to reduce platelet activation[1,2]

This solution has no pharmacological effect; the solution provides the appropriate components for

platelet function while allowing for a lower volume of plasma in the platelet product during storage.

14 CLINICAL STUDIES

In Vivo radiolabeled recovery and survival

A paired study was completed to verify that *in vivo* radiolabeled recovery and survival of hyperconcentrated leukocyte reduced platelets collected by apheresis on the Trima Accel system, diluted in ISOPLATE SOLUTION, and stored for five days (Test) meet FDA acceptance criteria in comparison with fresh autologous platelets (Control). Table 2 summarizes the *in vivo* radiolabeled platelet recovery and survival data.

Table 2 – In Vivo Radiolabeled Platelet Recovery and Survival Data (N = 23)

	Recovery			**Survival**		
	Test	**Control**	**Test/Control**	**Test**	**Control**	**Test/Control**
	%	**%**	**%**	**Days**	**Days**	**%**
Average	**51.1**	**60.2**	**85**	**6.6**	**8.7**	**76**
St. Dev.	10.9	10.2	10	1.2	0.9	12
Min	32.6	40.4	66	4.5	6.4	52
Max	84.1	82.8	102	8.8	10.0	104

The primary outcomes for this study were:

Recovery: Test minus 66% Control is equal to or greater than zero with one-sided 97.5% confidence limit

Survival: Test minus 58% Control is equal to or greater than zero with one-sided 97.5% confidence limit

Both primary outcomes were met for hyperconcentrated leukocyte reduced platelets collected on the Trima Accel system and stored in ISOPLATE SOLUTION.

In Vitro Platelet Quality Study

A paired study was completed to verify that *in vitro* platelet quality (functional assays) of hyperconcentrated leukocyte reduced platelets collected by apheresis on the Trima Accel system, diluted in ISOPLATE SOLUTION, and stored for five days (Test) meet FDA acceptance criteria in comparison to plasma-stored platelets (Control). Table 3 summarizes the *in vitro* platelet quality data.

Table 3 – In Vitro Platelet Quality Data (N = 66)

Functional Assay	**Isoplate Stored Apheresis Platelets (Test) Average (Standard Deviation)**	**Plasma Stored Apheresis Platelets (Control) Average (Standard Deviation)**
pH	7.4 (0.2)	7.5 (0.1)
CD62 Expression; P-Selectin (%)	22.8 (15.6)	15.0 (9.8)
Morphology Score (Max Score 400)	289 (49)	292 (47)
Hypotonic Shock Response (%)	53.3 (12.4)	55.9 (10.9)
Extent of Shape Change	33.2 (5.9)	35.0 (6.0)

(%)	23.2 (5.0)	25.0 (6.0)

The primary outcome for this study was:

pH: 95% or more of test units will have a pH (22 °C) greater than 6.2 with a one-sided confidence interval of 95%

All 66 platelet products collected in this study had pH > 6.2 therefore the primary outcome for pH was met for hyperconcetrated platelets collected on the Trima Accel system and stored in ISOPLATE SOLUTION.

15 REFERENCES

1. Gulliksson H. Platelet storage media. Transfus Apher Sci 2001;24:241-4.
2. Ringwald J, Zimmermann R, Eckstein R. The new generation of platelet additive solution for storage at 22 degrees C: development and current experience. Transfus Med Rev 2006;20:158-64.

16 HOW SUPPLIED/STORAGE AND HANDLING

ISOPLATE SOLUTION - Platelet Additive Solution [PAS-F] is a clear solution supplied in sterile and nonpyrogenic polyolefin bags. The ISOPLATE SOLUTION bags are packaged 18 bags per case.

SIZE	CATALOG NUMBER	NDC NUMBER
500 mL	40850	14537-408-50

STORAGE

Store up to 25 °C [See USP Controlled Room Temperature].

Platelets Pheresis PAS Added Leukocytes Reduced products are stored in a mix of 65% ISOPLATE SOLUTION and 35% plasma. Platelets in the solution can be stored at a concentration range of 0.7 to 2.1 × 106/µL for up to 5 days at 20-24 °C with continuous agitation in the Terumo BCT ELP bag [citrated polyvinyl chloride (PVC)].

Issued: May 2015

Manufactured by
Terumo BCT, Inc.
Lakewood, CO 80215 USA

PRINCIPAL DISPLAY PANEL - 500 mL Bag Label

Isoplate Solution
Platelet Additive Solution [PAS-F]

Catalog # 40850
Polyolefin Bag
500 mL

NDC 14537-408-50

Sterile. Non-pyrogenic. Do not use unless the solution is clear and the container is intact. Rx only. Single use container.

Caution: Not for direct intravenous infusion.

Recommended storage: Store up to 25 °C (See USP Controlled Room Temperature).

Each 100 mL contains:
Sodium Chloride USP 0.53 g
Sodium Gluconate USP 0.5 g
Sodium Acetate Trihydrate USP 0.37 g
Potassium Chloride USP 0.037 g
Magnesium Chloride Hexahydrate USP 0.03 g
Dibasic Sodium Phosphate Dihydrate USP 0.008 g
Monobasic Potassium Phosphate NF 0.00082 g
In Water for Injection USP

Manufactured by Terumo BCT, Inc.
10811 W. Collins Ave., Lakewood CO 80215, USA

777969-551
TERUMOBCT

Lot
Expiry Date

Isoplate Solution
Platelet Additive Solution [PAS-F]

Catalog # 40850 **Polyolefin Bag** **500 mL**

NDC 14537-408-50

Sterile. Non-pyrogenic. Do not use unless the solution is clear and the container is intact. Rx only. Single use container.

Caution: Not for direct intravenous infusion.

Recommended storage: Store up to 25 °C (See USP Controlled Room Temperature).

Each 100 mL contains:

Sodium Chloride USP	0.53 g
Sodium Gluconate USP	0.5 g
Sodium Acetate Trihydrate USP	0.37 g
Potassium Chloride USP	0.037 g
Magnesium Chloride Hexahydrate USP	0.03 g
Dibasic Sodium Phosphate Dihydrate USP	0.008 g
Monobasic Potassium Phosphate NF	0.00082 g
In Water for Injection USP	

Manufactured by Terumo BCT, Inc.
10811 W. Collins Ave., Lakewood CO 80215, USA

777969-551

TERUMOBCT

Lot

Expiry Date

ISOPLATE

sodium chloride, sodium gluconate, sodium acetate, potassium chloride, magnesium chloride, sodium phosphate, dibasic, and potassium phosphate, monobasic solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:14537-408
Route of Administration	INTRAVENOUS		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
SODIUM CHLORIDE (UNII: 451W47IQ8X) (SODIUM CATION - UNII:LYR4M0NH37, CHLORIDE ION - UNII:Q32ZN48698)	SODIUM CHLORIDE	0.53 g in 100 mL
SODIUM GLUCONATE (UNII: R6Q3791S76) (GLUCONIC ACID - UNII:R4R8J0Q44B, SODIUM CATION - UNII:LYR4M0NH37)	SODIUM GLUCONATE	0.5 g in 100 mL
SODIUM ACETATE (UNII: 4550K0SC9B) (ACETATE ION - UNII:569DQM74SC, SODIUM CATION - UNII:LYR4M0NH37)	SODIUM ACETATE	0.37 g in 100 mL
POTASSIUM CHLORIDE (UNII: 660YQ98I10) (POTASSIUM CATION - UNII:295O53K152, CHLORIDE ION - UNII:Q32ZN48698)	POTASSIUM CHLORIDE	0.037 g in 100 mL
MAGNESIUM CHLORIDE (UNII: 02F3473H9O) (MAGNESIUM CATION - UNII:T6V3LHY838, CHLORIDE ION - UNII:Q32ZN48698)	MAGNESIUM CHLORIDE	0.03 g in 100 mL
SODIUM PHOSPHATE, DIBASIC, UNSPECIFIED FORM (UNII: GR686LBA74) (PHOSPHATE ION - UNII:NK08V8K8HR, SODIUM CATION - UNII:LYR4M0NH37)	SODIUM PHOSPHATE, DIBASIC, UNSPECIFIED FORM	0.008 g in 100 mL
POTASSIUM PHOSPHATE, MONOBASIC (UNII: 4J9FJ0HL51) (PHOSPHATE ION - UNII:NK08V8K8HR, POTASSIUM CATION - UNII:295O53K152)	POTASSIUM PHOSPHATE, MONOBASIC	0.00082 g in 100 mL

Inactive Ingredients	
Ingredient Name	**Strength**
WATER (UNII: 059QF0KO0R)	

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:14537-408-50	18 in 1 CASE		
1		500 mL in 1 CONTAINER; Type 9: Other Type of Part 3 Combination Product (e.g., Drug/Device/Biological Product)		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	BN090067	03/05/2013	

Labeler - Terumo BCT Ltd. (233649834)

Revised: 12/2018 Terumo BCT Ltd.