CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-910

LABELING

NORMOCARB HF™

(NORMOCARB HF™ 25
NORMOCARB HF™ 35)
Sterile Electrolyte Concentrate for Infusion

Dilute prior to use.

DESCRIPTION

NORMOCARB HF™ is a clear, sterile, nonpyrogenic, electrolyte concentrate used in Continuous Renal Replacement Therapy (CRRT) as a replacement solution in hemofiltration or hemodiafiltration .

Composition:

Undiluted NORMOCARB HF™ 25 contains 90.73 g/L sodium chloride (NaCl), 2.06 g/L magnesium chloride hexahydrate ($MgCl_2 \cdot 6H_2O$) and 28.35 g/L sodium bicarbonate ($NaHCO_3$) in water for injection.

Undiluted NORMOCARB HF™ 35 contains 82.84 g/L sodium chloride (NaCl), 2.06 g/L magnesium chloride hexahydrate ($MgCl_2 \cdot 6H_2O$) and 39.70 g/L sodium bicarbonate ($NaHCO_3$) in water for injection.

Diluted NORMOCARB HF™ 25 or NORMOCARB HF™ 35 solutions when prepared as directed, contain the following:

	Concentration Diluted NORMOCARB HF™ 25		Concentration Diluted NORMOCARB HF™ 35	
Component	**(mMol/L)**	**(mEq/L)**	**(mMol/L)**	**(mEq/L)**
Sodium (Na)	140.0	140.0	140.0	140.0
Magnesium (Mg)	0.75	1.5	0.75	1.5
Chloride (Cl)	116.5	116.5	106.5	106.5
Bicarbonate (HCO_3)	25.0	25.0	35.0	35.0
Total Anions	141.5 mEq/L		141.5 mEq/L	
Total Cations	141.5 mEq/L		141.5 mEq/L	
Theoretical Osmolarity	283 mOsm/L		283 mOsm/L	
pH	8.55 ± 0.25		8.55 ± 0.25	

NORMOCARB HF™ contains no bacteriostatic or antimicrobial agents.

CLINICAL PHARMACOLOGY

NORMOCARB HF™ is a pharmacologically inactive solution. The concentrations of electrolytes are chosen to help to restore plasma levels to physiological concentrations.

NORMOCARB HF™ is used as replacement solution to replace water and electrolytes removed during hemofiltration and hemodiafiltration.

Bicarbonate in the solution is used as an alkalinizing buffer to normalize acid-base balance.

INDICATIONS AND USAGE

NORMOCARB HF™, after dilution, is indicated in adults and children for use as a replacement solution in CRRT to replace water and to correct electrolytes and acid-base imbalance.

CONTRAINDICATIONS

None.

WARNINGS

NORMOCARB HF™ must be diluted only with Sterile Water for Injection before use. **DO NOT USE NORMAL SALINE, RINGERS LACTATE OR ANY OTHER DILUENT.**

PRECAUTIONS

Application of the solutions should only be under the direction of a physician competent in intensive care treatment including CRRT.

The patient's hemodynamic fluid, electrolyte and acid-base balance should be monitored throughout the procedure. Note that citrate, when used as an anticoagulant, contributes to the base load and can reduce plasma calcium levels.

After prolonged hemofiltration or hemodiafiltration, there are risks of hypokalemia, hypocalcemia, hypophosphatemia, and hypoglycemia.

ADVERSE REACTIONS

Adverse reactions can result from the solution or the CRRT procedure.

Improper use can lead to fluid imbalance and disturbances in electrolyte, acid-base and glucose balance.

DOSAGE AND ADMINISTRATION

NORMOCARB HF™ MUST BE DILUTED BEFORE USE. For dilution, one 240 mL vial of NORMOCARB HF™ should be added to 3 L of Sterile Water for Injection to make 3.24 L of infusate solution. See RECONSTITUTION below for detailed instructions.

NORMOCARB HF™ must not be used if a precipitate has been formed or if container seals have been damaged.

Individualization of Treatment:

Pre- or Post-Filter: The volume of solution (diluted NORMOCARB HF™) administered will depend upon the fluid balance of the individual patient, the target fluid balance to be achieved, the body weight and the amount of fluid removed from the patient's circulation during the hemofiltration process. When administered post-filter, the replacement rate should not be greater than one third of the

blood flow rate; e.g., for blood flow of 100 ml/min, equivalent to 6000 ml/hour, post-filter replacement rate should not exceed 2000 ml/hour. **Reconstitution (Preparation of Infusate Solution Using NORMOCARB HF™ and Sterile Water for Injection):**

Requirements:

- NORMOCARB HF™
- 1 vented intravenous (IV) transfer set, 1 20 G needle
- 3 L of Sterile Water for Injection
- Alcohol swabs

Important Considerations Before Reconstitution:

NORMOCARB HF™ must be diluted before use with Sterile Water for Injection only -- do not use normal saline, Ringers Lactate or any other diluent. D50W may be added to Sterile Water for Injection, if required by physician's orders, as described in the method below. Do not prepare more infusate solution than can be used in a 24-hour period.

Method:

1. Remove bag of Sterile Water for Injection from outer protective bag and wipe injection port on bag with alcohol swab.
2. Using aseptic technique:
    a. Assemble IV line, needle, and close clamp
    b. Spike vial
    c. Connect needle to bag
3. Using vial hanger, hang vial from IV pole.
4. Open clamp and empty contents of one 240 mL vial into a 3 L bag of Sterile Water for Injection to make 3.24 L of infusate.
5. Special Consideration: See Additions section below.
6. Clamp IV line.
7. Fill out required information on accompanying "Medication Added" sticker and apply to bag.
8. Disconnect needle and IV set.
9. Shake to mix by rocking or rolling the bag and contents thoroughly. When diluted, solution contains approximately (mEq/L):

Diluted Solutions	Na	Mg	Cl	HCO_3
Normocarb HF™ 25	140	1.5	116.5	25.0
Normocarb HF™ 35	140	1.5	106.5	35.0

10. If additives were introduced, check bag for precipitates.

11. Connect bag to CRRT hemofiltration circuit and institute hemofiltration.

Diluted NORMOCARB HF™ should be used within 24 hours. It may be stored at normal room temperature or refrigerated (2° - 30°C). Do not freeze infusate solution or expose to excessive heat.

Additions:
When introducing additives, use aseptic techniques.

Potassium: Potassium chloride up to 4 mEq/L may be added to the diluted solution.

Calcium: Calcium chloride up to 1.25 mMol/L (2.5 mEq/L) may be added to the diluted solution.

Glucose: Up to 12 mL of D50W may be added to the diluted solution to provide a concentration of up to 10.2 mMol/L of dextrose.

Phosphate: Potassium phosphate up to 1.2 mMol/L (2.4 mEq/L) may be added to the diluted solution. The total potassium concentration should not exceed 4 mEq/L.

Other drugs: Some drugs may be incompatible with NORMOCARB HF™. In general, other drugs should be administered through a different line.

HOW SUPPLIED

NORMOCARB HF™ is available as a clear, sterile, nonpyrogenic, bicarbonate infusate concentrate in single-use vials of 240 mL. NORMOCARB HF™ contains no bacteriostatic or antimicrobial agents.

240 mL vial	NDC
Normocarb HF™ 25	16951-0125-1
Normocarb HF™ 35	16951-0135-1

Undiluted NORMOCARB HF™ should be stored at 20° - 25°C (68° - 77°F) [See USP Controlled Room Temperature]. Do not freeze. Do not use if a precipitate has formed or if container seals have been damaged.

Rx only.

Manufactured by:

Apotex Inc.

Toronto, Ontario

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