RUSSIAN ACADEMY OF SCIENCES
SCIENTIFIC-PRODUCTION FIRM "PERFTORAN"

# PERFTORAN

## BLOOD SUBSTITUTE WITH GAS-TRANSPORTING FUNCTION

# DRUG CHARACTERISTICS

Perftoran is 10 vol.% submicronic perfluorocarbon emulsion based on perfluoroorganic compounds capable of transporting gases.
Perftoran improves gas exchange and metabolism in tissues;
Perftoran increases $O_2$-carrying capacity of blood;
Perftoran stabilizes the membranes;
Perftoran improves blood flow and peripheral microcirculation;
Perftoran restores the central hemodynamics;
Perftoran apparently protects myocardium;
Perftoran acts as diuretics;
Perftoran is calcium slow channel blocking agent.

# QUALITATIVE AND QUANTATIVE COMPOSITION

White emulsion with slightly blue tint.

## Reagents:

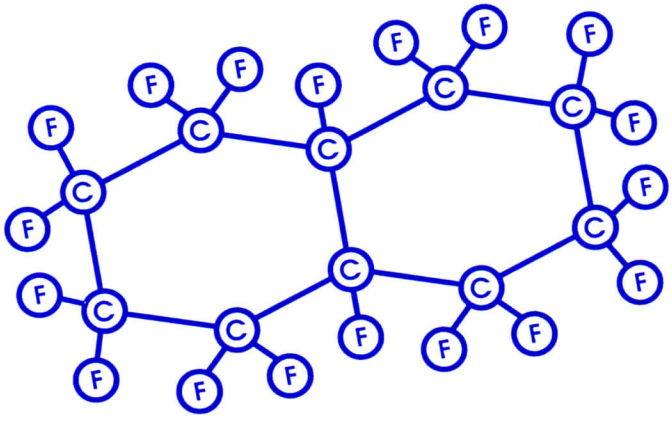
| | |
|---|---|
| $C_{10}F_{18}$ - perfluorodecalin (Mw=462 D) | 13 g |
| $C_{12}F_{23}N$ - perfluorometylcyclohexylpiperidin (Mw=595 D) | 6.5 g |
| SAA - proxanol - 268 (Mw ≈8000 D) | 4.0 g |
| NaCl - sodium chloride | 0.6 g |
| KCl - kalium chloride | 0.039 g |
| $MgCl_2$ - magnesium chloride | 0.019 g |
| $NaHCO_3$ - sodium hydrocarbonate | 0.065 g |
| $NaH_2PO_4$ - sodium hydrophosphate | 0.02 g |
| $C_6H_{12}O_6$ - glucose | 0.2 g |
| $H_2O$ - water for injection | 100 ml |

## Physical properties:

| | |
|---|---|
| F - content of fluorine | $<10^{-5}$ M |
| Average particle size | 0.03÷0.15 μm |
| Osmolality | 280÷340 mOsm |
| Viscosity | 2.5 sP |
| pH | 7.2÷7.8 |
| vol.% $O_2$ - $O_2$ solubility ($pO_2$=760 mm Hg., t=+20° C) | ~ 7.0 vol.% |
| vol.% $CO_2$ - $CO_2$ solubility ($pCO_2$=760 mm Hg., t=+20° C) | ~ 60 vol.% |

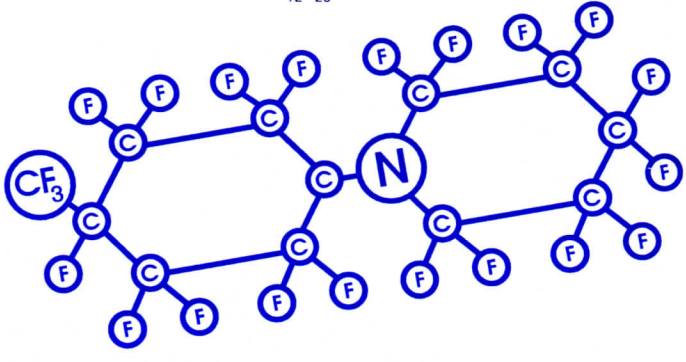
## Chemical and structural characteristics of Perftoran's main compounds:

Perfluorodecalin (PFD) - $C_{10}F_{18}$

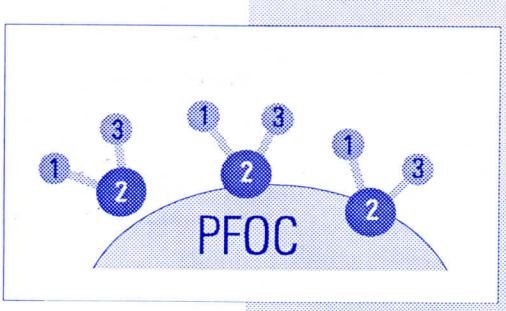


| | |
|---|---|
| Molecular weight | 462 D |
| Trans-isomer | 50-55% |
| Cis-isomer | 45-50% |
| Main ingredient (perfluoride admixture 7%) | 93% |

Perfluorometylcyclohexylpiperidin (PFMCP) - $C_{12}F_{23}N$



| | |
|---|---|
| Molecular weight | 595 D |
| It contains 3 isomers: | |
| $C_{12}F_{23}N$ Mw = 595 D | 62-71% |
| $C_{12}F_{23}N$ Mw = 595 D | 20-39% |
| $C_{12}F_{23}N$ Mw = 595 D | 4-9% |
| Main ingredient (perfluoride admixtures 0.5-3%) | 97% |




Sheme of Perftoran's particle.

## Proxanol is a surface-active agent (SAA)

It consists of 2 compounds:
oxyethylen and oxypropilen:
HO - $(C_2H_4O)_x$ - $(C_3H_6O)_y$ - $(C_2H_4O)_z$ - H
y(2) - number of oxypropilen chains,
x, z (1,3) - number of oxyethylen chains.

# Indications for administration

It is recommended to use Perftoran as a plasma substitute with $O_2$- and $CO_2$-carrying function.
It is used in conditions, such as the following:

acute and chronic hypovolemia (traumatic, posthemorrhagic shock from burns and septic shock, during or after operations);

alteration of microcirculation and peripheral blood flow (insufficient perfusion of tissues, septic shock, infections, fat embolism, cranial trauma);

anti-ischemic protection of transplants;

heart operations (in heart-lung apparatus);

local use (local perfusion, bronchopulmonary lavage).

# Contraindications

Perftoran is contraindicated in patients with hemophilia, allergic diseases and collagen vascular diseases.
It should not be used in pregnancy.

# Adverse effects

The injection of test-dose can cause allergic reactions, such as: hyperaemia, tachicardia, decrease in blood pressure, hypertermia, headache, chest pain and lumbal pain, difficulty in breathing, neutropenia, and anaphylactic reactions. The adverse reactions occur rarely and they disappear in 10-15 minutes without special treatment.
When adverse reactions occur the infusion of Perftoran should be stopped and corticosteroids should be used immediately.

# Drug interactions

Perftoran can be administered together with albumin, saline solutions, glucose, and antibiotics.
In contrast to colloid solutions saline solutions do not alter the biological, physical and chemical features of Perftoran.
Colloid solutions cause a significant increase in particle size and change the biological and chemical characteristics of Perftoran. Therefore colloid infusions should be used after administration of Perftoran or through other peripheral venous access.

# Dosage and administration

Perftoran is a broad-spectrum emulsion. The dose depends on the severity and character of disease.
Perfluorocarbon emulsion is administered as bolus or continuos infusion. Before use it is recommended to provide a biological test after the first 30 drops. The infusion should be started slowly.

Treatment of acute and chronic hypovolemia.
The dosage of Perftoran is 5 to 30 ml/kg. It is administered intravenous as short or continuous infusion. To achieve best results patient should receive adequate oxygenation with 40% to 60% inspired $O_2$ during 24 hours after the infusion of Perftoran.

Treatment of microcirculation and metabolism disorders.
The dosage of Perftoran is 4 to 8 ml/kg (max. single dose is 30 ml/kg). It is used as continuous infusion with an interval between administrations of 1-4 days. The total dose is 100 ml/kg. To achieve best results the patient should receive adequate oxygenation with 40% to 60% inspired $O_2$ during 24 hours after the infusion of Perftoran.

Anti-ischemic protection of transplants.
Perftoran is administered to donor and recipient at a dose of 20 ml/kg as short or continuous infusion 2 hours before operation.
Heart operations.
Perftoran is used as the main solution for artificial blood flow at a dose of 10 to 40 ml/kg.
Regional usage.
Perftoran is used as a solution for standard oxygenation apparatus for regional perfusion at a dose of 40 ml/kg.
Local usage.
(Bronchopulmonal lavage, etc.).
The administration of Perftoran is similar to administration of traditional treatment.

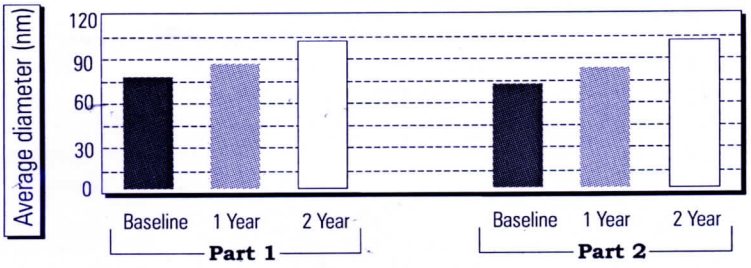



**Fig. 2.0. Change of fluorocarbon emulsion's average diameter (nm) after storage at - 18°C for 2 year.**

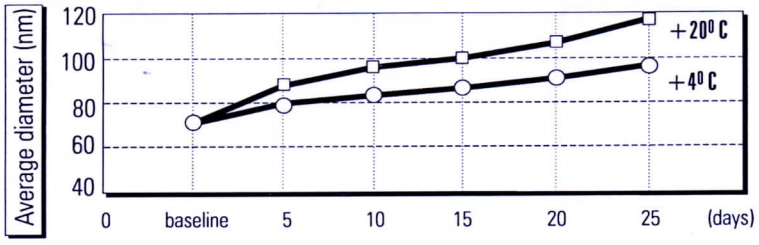



**Fig. 2.1. Change of fluorocarbon emulsion's average diameter (nm) after storage at + 4°C and at + 20°C for 1 month.**

# Precautions

Follow the storage and thawing instructions. Proper storage and thawing avoid the increase in particle size and appearance of sediment in the emulsion (free perfluorocarbon phase). If sediment appears emulsion should not be used.
Perftoran should not be mixed in one syringe or system with dextranes - polyglukin, reopolyglukin with molecular weight < 100 000. Use this solutions after the administration of Perftoran or through another peripheral venous access.

# Shelf life and storage

Perftoran should be stored at the temperature - 5°C to - 18°C.
The shelf life is 2 years (Fig 2.0).
After thawing emulsion can be stored at the temperature +4°C for 2 weeks (Fig.2.1).
Inappropriate storage or thawing leads to increase in particle size. Maximal average size should be 0,15 μm (or 150 nm). It is recommended to thaw Perftoran at room temperature. Perftoran may be thawed and refrozen 5 times.
After thawing the emulsion should be thoroughly shacked.
The emulsion should not be used in the following conditions:
stratification of emulsion (even after shaking);
opacity of emulsion (milky colour);
sediment in emulsion (transparent oily drops on the vial wall).
The perfluorocarbon emulsion should not be stored at temperatures below -18°C or thawed at temperatures above +30°C.

# Package

Glass vials, containing 100, 200, and 400 ml of perfluorocarbon emulsion.

# Firms and address

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