Patisiran: Compatibility with Commonly Used Infusion Components

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SUMMARY

- A compatibility and stability study was performed to evaluate the patisiran admixture with commonly used IV administration devices.[1]
  - The admixture was chemically and physically stable within the variables studied, and no chemical incompatibility or instability was expected for the admixture if exposed to the materials of construction of commonly available infusion components.[1]
- The decision to administer patisiran via devices other than those recommended in the US Prescribing Information should be determined on a case-by-case basis in accordance with established policies and guidelines set forth by the relevant administrative body or bodies for a given health care setting.

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DOSING AND PREPARATION INFORMATION

Compatibility Study Results

A compatibility and stability study was performed to evaluate the patisiran admixture with commonly used IV administration devices. Different configurations of the IV administration devices were tested with parameters including concentration of the admixture, residence time in the infusion components, temperature, and light exposure. The materials of construct are summarized in **Table 1**.[1]

All configurations of the IV administration devices passed the stability and compatibility evaluation with patisiran admixture. The evaluation of chemical and physical stability of the patisiran drug product admixture was performed by selecting commonly available infusion bags and administration components. The experiments were configured to evaluate commonly available configurations of the infusion bag and administration components as could be reasonably anticipated in a clinical or commercial setting.[1]

In no case did the prepared admixture exceed the allowable range from the initial concentration of siRNA or lipid content. Additionally, in no case did drug substance purity, pH, particle size, or percent encapsulation of the siRNA exceed the allowable ranges.[1]

These data thereby confirmed that the admixture was chemically and physically stable within the variables studied, and no chemical incompatibility or instability was expected for the admixture if exposed to the materials of construction of commonly available infusion components. The components utilized for the assessment and their materials of construction are summarized in **Table 1**.[1]

Due to the hydrophobic nature of the lipid nanoparticles, and an increased propensity for leaching of the plasticizer DEHP from PVC contact surfaces that contain this plasticizer, only DEHP-free PVC or non-PVC DEHP-free infusion components were selected for the analysis. Additionally, instructions to avoid the use of components containing this plasticizer are included on the product label.[1,2]

Compatibility with Other Infusion Components

The evaluation did not extend to devices other than the components tested in the study. The decision to administer patisiran via devices other than those recommended in the US Prescribing Information should be determined on a case-by-case basis in accordance with established policies and guidelines set forth by the relevant administrative body or bodies for a given health care setting.

Table 1. Materials of Construction by Component.[1]

Device Type	Manufacturer	Part #	Materials of Construction
0.45 µm PES Syringe Filter	Pall	HP4644	Acrylic Polyethersulfone membrane
	Millipore	SLHPM33RS	Acrylic Polyethersulfone membrane
Disposable Hypodermic Needle	BD	305195	Polypropylene Epoxy Silicone Stainless steel
Disposable Syringe	BD	309604	Polypropylene Latex-free elastomer Silicone
	BD	302830	
IV Infusion Bag	Baxter	UE1322D	Polypropylene Polyamide Polyethylene
	Hospira	0409-7983-25	Polyolefin
	Fresenius Kabi	FAH1322	Polypropylene
	B Braun	L8002	Ethylene Propylene
Solution Set	Baxter	2H8519	Polyvinyl chloride Acrylonitrile butadiene styrene Linear low-density polyethylene Acrylic Silicone High-molecular-weight polycarbonate Silicone Rubber Polypropylene Low-density polyethylene
	B Braun	352049	Acrylonitrile butadiene styrene Polyvinyl chloride Parylene Polycarbonate Silicone

Device Type	Manufacturer	Part #	Materials of Construction
Filtered Extension Set	Baxter	2C1103	Low-density polyethylene Polyester Polyvinyl chloride Acrylic Polyether sulfone membrane Acrylonitrile butadiene styrene Hot stamp foil Copolyester Synthetic polyisoprene
	B Braun	473994	Polycarbonate Polyvinyl chloride Acrylic Polyethersulfone Polytetrafluoroethylene Silicone Acrylonitrile butadiene styrene
IV Catheter	BD	381432	Proprietary polyether urethane Polypropylene Epoxy
	Smiths Medical	4050	Fluorinated ethylene propylene Radiopaque fillers
	B Braun	4251628-02	Polypropylene Stainless steel Polyurethane

Abbreviations: IV = intravenous; PES = polyethersulfone.

ONPATTRO PRESCRIBING INFORMATION – RELEVANT CONTENT

The DOSAGE AND ADMINISTRATION section provides the following information[2]:

Preparation Instructions

- *Filter ONPATTRO through a sterile 0.45 micron polyethersulfone (PES) syringe filter into a sterile container.*
- *Withdraw the required volume of filtered ONPATTRO from the sterile container using a sterile syringe.*
- *Dilute the required volume of filtered ONPATTRO into an infusion bag containing 0.9% Sodium Chloride Injection, USP for a total volume of 200 mL. Use infusion bags that are di(2-ethylhexyl)phthalate-free (DEHP-free).*

Infusion Instructions

- *Use a dedicated line with an infusion set containing a 1.2 micron polyethersulfone (PES) in-line infusion filter. Use infusion sets and lines that are DEHP-free.*

ABBREVIATIONS

DEHP = di-(2-ethylhexyl)-phthalate; IV = intravenous; PES = polyethersulfone; PVC = polyvinyl chloride; siRNA = small interfering ribonucleic acid; US = United States.

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REFERENCES

1. Alnylam Pharmaceuticals. Data on file. MED-ALL-TTR02-1900027.
2. ONPATTRO (patisiran) Prescribing Information. Cambridge, MA: Alnylam Pharmaceuticals, Inc.