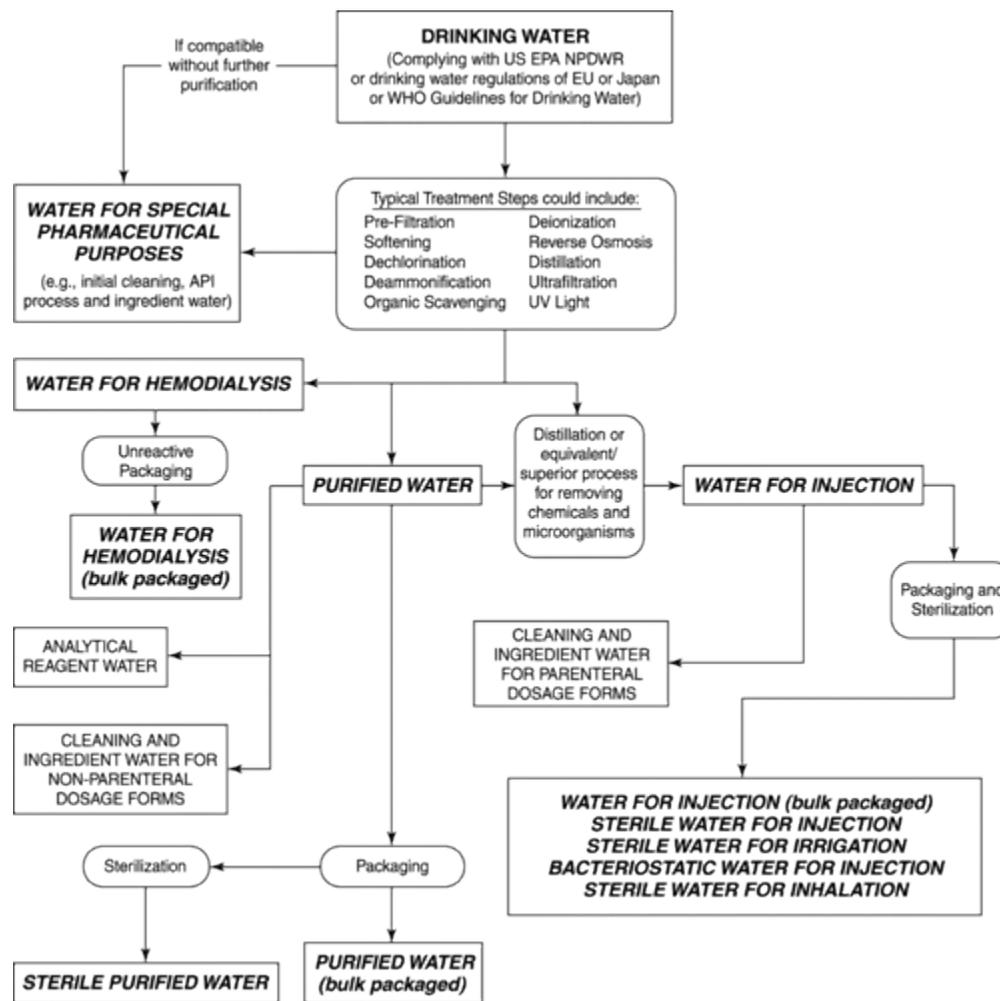


MEETING USP STANDARDS FOR WATER USED TO RECONSTITUTE MEDICATIONS

In the space of reconstitution and non-sterile compounding in the retail pharmacy world, water for use during reconstitution has been considered ‘water as an ingredient’ or more specifically ‘Water for Special Pharmaceutical Purposes’ as defined by USP <1231>. According to USP <<1231>>:

“Water is widely used as a raw material, ingredient, and solvent in the processing, formulation, and manufacture of pharmaceutical products, active pharmaceutical ingredients (APIs)...”

Therefore, water, when used in the process of reconstituting a manufactured medication, fell into the category of Water for Special Pharmaceutical Purposes, which encompass initial cleaning, API process, and ingredient water, as seen in the monograph below:



USP <<1231>>, Fig. 1. Water for pharmaceutical purposes

While labels on medications for reconstitution generally indicate to use a specified volume of water for reconstitution, it has never been clear the level of water quality required by a manufacturer. Therefore, best practice has generally accepted that water as an ingredient need only to meet standards outlined and described by USP <1231>.

However, recent guidance from USP in light of new revisions being made to the relevant chapters outlining best practices for sterile and nonsterile compounding, indicates that the use of ‘Purified Water’ is the requisite level of water quality to be used for all non-sterile compounding moving forward, including reconstitution.

As quoted from USP <795>, there are three categories of non-sterile compounding. As it relates to routine reconstitution, pharmacies are only concerned with the first category, Simple Non-Sterile compounding, performed every day at retail and independent pharmacies across the country:

“Simple: making a preparation that has a USP compounding monograph or that appears in a peer-reviewed scientific journal article that contains specific quantities of all components, compounding procedure and equipment, and stability data for that formulation with appropriate beyond-use dating; or reconstituting or manipulating commercial products that may require the addition of one or more ingredients as directed by the manufacturer.”

New language for USP <795>, being considered now and ratified in June of 2019, clarifies the water quality standard even further:

*“**Purified Water**, or an equivalent quality of water, must be used to reconstitute conventionally manufactured nonsterile products when water quality is not stated in the manufacturer’s labeling (See Water for Pharmaceutical Purposes <1231>).”*

Therefore, using water that has been ‘purified’ by previously acceptable methods or even bottled water that does not meet the stringent USP <795> definition of ‘purified water’ is not sufficient, unless that water meets the conductivity, TOC, and bacteria specifications as outlined in USP <645> and USP <643>, which are spelled out below.

USP Purified Water Standard

Purified Water (PW) v Highly Purified Water (HPW)

Parameter	Unit	PW	HPW
Total Organic Carbon (TOC)	ppb	<500	<500
Conductivity	µS/cm @ 25 °C	≤ 1.3	≤ 1.3
Endotoxin (EU/ml)	ppm	n/a	≤ 0.25 EU/ml
Aerobic Bacteria	CFU/ ml	≤ 100 cfu/ml	≤ 10 cfu/100ml

Suitable methods of meeting the guidelines for 'USP Purified Water' for reconstitution include using an RO system in conjunction with a deionizing (DI) filter that completely eliminates conductivity in water, sterile pharmaceutical grade bottled water, or installing water vapor distillation systems.

"In our opinion, a six-stage Reverse Osmosis water filtration system that includes a DI Resin Filter is the most economical, easily-maintained way for pharmacies to meet USP standards for purified water", said Dan Connor, FillPure Technical Director and Certified Water Specialist (CWS). "Sterile bottled water is expensive and wasteful for reconstitution. Vapor distillation is even more expensive and requires constant upkeep. A six-stage RO system is the best solution to keep pharmacies USP compliant".

The USP, FDA, Joint Commission, and Boards of Pharmacy collectively have reiterated that their top priority is ensuring public health. Their position is such that all patients have the right to safe and efficacious medication and the only way to accomplish this mission is for all stakeholders to focus on standardization.

Standards are developed and created by the consensus of experts across the industry including academia, healthcare professionals, industry partners, third party payers, and other stakeholders. The hope and promise of standardization is striking a balance between quality and safety, without overregulating or underregulating, while maintaining reasonable cost and accessibility to the patient.

As pharmacies navigate and understand the ever-changing regulatory landscape, they must be sure the products and services they offer to their customers evolve as well. FillPure's goal is to help pharmacies stay compliant with best practice industry standards and feel confident that they are offering their customers superior and appropriate water quality that is standardized across all stores.