HAYASHIBARA
NAGASE Group

May 7, 2020

TO: Signet

Specifications

TREHALOSE P

Trehalose USP-NF

Definition: A stable, non-reducing disaccharide with 2 glucose molecules linked in an α,α-1,1 configuration; dihydrate
Storage: Store at room temperature. Avoid direct sunlight, and high temperature and humidity.
Shelf Life: Three (3) years from the production date
Package: Carton box (Net 20 kg)

Variables	Specifications	Methods	Frequency
Color and clarity of solution	A_{720} : Not more than 0.050 $A_{420} - A_{720}$: Not more than 0.100	USP-NF method*1	Every lot
Identification			
(A) Infrared absorption	Both spectra exhibit maxima only at the same wavelengths.	USP-NF method*1	Every lot
(B) Sugars	A violet color develops at the interface between the two solutions.	USP-NF method*1	Every lot
(C) No reducing sugars	A brown color does not develop.	USP-NF method*1	Every lot
Optical rotation, *Specific rotation*	$[\alpha]_D^{20}$: +197° – +201°	USP-NF method*1	Every lot
Microbial enumeration tests and Tests for specified microorganisms			
(1) Total aerobic microbial count	Not more than 100 CFU/g	USP-NF method*1	Every lot
(2) Total combined molds and yeasts count	Not more than 50 CFU/g	USP-NF method*1	Every lot
(3) *Salmonella* species	Absence	USP-NF method*1	Every lot
(4) *Escherichia coli*	Absence	USP-NF method*1	Every lot
pH	4.5 – 6.5	USP-NF method*1	Every lot
Water	9.0% – 11.0%	USP-NF method*1	Every lot
Residue on ignition	Not more than 0.1%	USP-NF method*1	Every lot
Soluble starch	No blue color develops.	USP-NF method*1	Every lot
Chloride	Not more than 0.0125%	USP-NF method*1	Every lot
Sulfate	Not more than 0.0200%	USP-NF method*1	Every lot
Heavy metals	Not more than 5 ppm, as Pb	USP40-NF35 <231> *Method I**2	Every lot
Nitrogen content	Not more than 0.005%	USP-NF method*1	Every lot
Related substances	The areas of any peaks corresponding to maltotriose and other polysaccharides and eluting before trehalose are NMT half of the area of the peak corresponding to trehalose in the chromatogram of the *Standard solution* (0.5%). The areas of any peaks corresponding to glucose and eluting after trehalose are NMT half of the area of the peak corresponding to trehalose in the chromatogram of the *Standard solution* (0.5%).	USP-NF method*1	Every lot
Assay, % of Trehalose	99.0% – 101.0% on the anhydrous basis	USP-NF method*1	Every lot
Particle size	35% – 55% retained on 75 μm 5% – 18% retained on 150 μm	USP-NF <786>*3	Every lot

*1 According to each method specified in the TREHALOSE DIHYDRATE monograph in the current USP-NF
*2 According to the method specified in General Tests and Assays in USP40-NF35 – Numbers in brackets <###> refer to the test methods.
*3 According to the method specified in General Tests and Assays in the current USP-NF – Numbers in brackets <###> refer to the test methods.

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Trehalose Dihydrate Ph.Eur.

Definition: Non-reducing disaccharide with 2 glucose molecules linked in an α,α-1,1 configuration; dihydrate
Storage: Store at room temperature. Avoid direct sunlight, and high temperature and humidity.
Shelf Life: Three (3) years from the production date
Package: Carton box (Net 20 kg)

Variables	Specifications	Methods	Frequency
Identification			
(A) Infrared absorption spectrophotometry	The spectra exhibit similar intensities to *trehalose dihydrate CRS*.	*Ph.Eur.* method*1	Every lot
(B) Sugars	A violet colour develops at the interface.	*Ph.Eur.* method*1	Every lot
(C) No reducing sugars	No brown colour develops.	*Ph.Eur.* method*1	Every lot
Appearance of solution	Clear and colourless	*Ph.Eur.* method*1	Every lot
pH	4.5 to 6.5	*Ph.Eur.* method*1	Every lot
Specific optical rotation (Anhydrous substance)	$[\alpha]_D^{20}$: +197° to +201°.	*Ph.Eur.* method*1	Every lot
Related substances	- Impurities A (glucose), B (oligosaccharides): Not more than 0.5% for each impurity - Unspecified impurities: Not more than 0.2% for each impurity - Total: Not more than 1.0%	*Ph.Eur.* method*1	Every lot
Chlorides	Maximum 125 ppm	*Ph.Eur.* method*1	Every lot
Sulphates	Maximum 200 ppm	*Ph.Eur.* method*1	Every lot
Heavy metals	Maximum 5 ppm (as Pb)	*Ph.Eur.* method*1	Every lot
Soluble starch	No blue colour develops.	*Ph.Eur.* method*1	Every lot
Water	9.0% to 11.0%	*Ph.Eur.* method*1	Every lot
Sulphated ash	Maximum 0.1%	*Ph.Eur.* method*1	Every lot
Microbial contamination			
(1) Total aerobic microbial count	Not more than 10^2 CFU/g	*Ph.Eur.* method*1	Every lot
(2) Total combined yeasts and molds count	Not more than 50 CFU/g	*Ph.Eur.* method*1	Every lot
(3) *Escherichia coli*	Absence	*Ph.Eur.* method*1	Every lot
(4) *Salmonella*	Absence	*Ph.Eur.* method*1	Every lot
Assay, % of Trehalose	99.0% to 101.0% (on the anhydrous basis)	*Ph.Eur.* method*1	Every lot
Particle size	35% to 55% retained on 75 μm 5% to 18% retained on 150 μm	*Ph.Eur. <2.9.38>*2	Every lot

*1 According to each method specified in the TREHALOSE DIHYDRATE monograph in the current European Pharmacopoeia
*2 According to the method specified in GENERAL CHAPTERS in the current European Pharmacopoeia – Numbers in brackets <###> refer to the test methods.

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TREHALOSE P

Trehalose Hydrate JP

Definition: Non-reducing disaccharide with 2 glucose molecules linked in an α,α-1,1 configuration; dihydrate
Storage: Store at room temperature. Avoid direct sunlight, and high temperature and humidity.
Shelf Life: Three (3) years from the production date
Package: Carton box (Net 20 kg)
Compatible Specification: Japanese Pharmacopoeia

Variables	Specifications	Methods	Frequency
Description	White crystals or a white crystalline powder	JP method*1	Every lot
Identification			
(1)	A purple color appears at the zone of contact.	JP method*1	Every lot
(2)	No brown color appears.	JP method*1	Every lot
(3)	Both spectra exhibit similar intensities of absorption at the same wave numbers.	JP method*1	Every lot
Optical rotation	$[\alpha]_D^{20}$: +197– +201°	JP method*1	Every lot
pH	4.5 – 6.5	JP method*1	Every lot
Color and clarity of solution	A_{720} : Not more than 0.050 $A_{420} - A_{720}$: Not more than 0.100 (30 w/v%)	JP <2.24>*2	Every lot
Purity			
(1) Chloride	Prepare the control solution with 0.7 mL of 0.01 mol/L hydrochloric acid VS (not more than 0.0125%).	JP <1.03>*2 (2.0 g)	Every lot
(2) Sulfate	Prepare the control solution with 0.83 mL of 0.005 mol/L sulfuric acid VS (not more than 0.0200%).	JP <1.14>*2 (2.0 g)	Every lot
(3) Heavy metals	Not more than 5ppm, as Pb	JP method*1	Every lot
(4) Related substances	The total area of the peaks which are eluted before the peak of trehalose and the total area of the peaks which are eluted after the peak of trehalose obtained from the sample solution are both not larger than 1/2 times the peak area of trehalose from the standard solution.	JP method*1	Every lot
(5) Dextrin, soluble starch and sulfite	A yellow color appears, which is changed to blue on addition of 1 drop of starch TS.	JP method*1	Every lot
(6) Nitrogen	Not more than 0.005%.	JP method*1	Every lot
Water	9.0 – 11.0%	JP method*1	Every lot
Residue on ignition	Not more than 0.1%	JP method*1	Every lot
Assay, % of Trehalose	99.0 – 101.0% (Trehalose ($C_{12}H_{22}O_{11}$), calculated on the anhydrous basis)	JP method*1	Every lot
Microbial enumeration tests and tests for specified microorganisms			
(1) Total aerobic microbial count	Not more than 100 CFU/g	JP <4.05>*2	Every lot
(2) Total combined yeasts/molds count	Not more than 50 CFU/g	JP <4.05>*2	Every lot
(3) *Escherichia coli*	Absence	JP <4.05>*2	Every lot
(4) *Salmonella*	Absence	JP <4.05>*2	Every lot
Particle size	35－55% retained on 75 μm and 5－18% retained on 150μm (25 g, Antistatic agent 0.25 g, Method II, Mechanical agitation, 15 min)	JP <3.04>*2	Every lot

*1 According to each method specified in the Trehalose Hydrate monograph in the current Japanese Pharmacopoeia
*2 According to the method specified in GENERAL TESTS, PROCESSES AND APPARATUS in the current Japanese Pharmacopoeia – Numbers in brackets <###> refer to the test methods.

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