SODIUM STARCH GLYCOLATE
(NATRII AMYLA GLYCOLAS)

Draft proposal for inclusion for The International Pharmacopoeia
(August 2020)

DRAFT FOR COMMENTS

Please send any comments you may have on this draft working document to Dr Herbert Schmidt, Technical Officer, Norms and Standards for Pharmaceuticals, Technical Standards and Specifications (email: schmidt@who.int) by 31 October 2020.

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SCHEDULE FOR THE ADOPTION PROCESS OF DOCUMENT QAS/20.859:

SODIUM STARCH GLYCOLATE

(NATRII AMYLA GLYCOLAS)

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[Note from the Secretariat. It is proposed to include the monograph on Sodium starch glycolate in the The International Pharmacopoeia.

The monograph is based on the corresponding, internationally-harmonized text developed by the Pharmacopoeial Discussion Group (PDG). Editorial modifications have been made in order to be in line with the style used in The International Pharmacopoeia.]
SODIUM STARCH GLYCOLATE
(CARBOXYMETHYLAMYLUM NATRICUM)

This monograph is based on the corresponding, internationally-harmonized text developed by the Pharmacopoeial Discussion Group (PDG). Editorial modifications have been made in order to be in line with the style used in The International Pharmacopoeia.

Chemical name. Starch carboxymethyl ether, sodium salt. CAS Reg. No. 9063-38-1.

Description. White or almost white, fine, free-flowing powder.

Solubility. Practically insoluble in dichloromethane. It gives a translucent suspension in water.

Category. Disintegrant.

Storage. Sodium starch glycolate should be kept in an airtight container, protected from light.

Labelling. The designation on the container of Sodium starch glycolate should state its type.

Additional information. Sodium starch glycolate is very hygroscopic.

Requirements

Definition. Sodium starch glycolate is the sodium salt of a cross-linked partly O-carboxymethylated starch. Type A contains not less than 2.8% and not more than 4.2% of Na, and Type B contains not less than 2.0% and not more than 3.4% of Na, each calculated with reference to the substance washed with ethanol (80% v/v) TS and dried.
Identity tests

A. Prepare with shaking and without heating a mixture of 4.0 g of the substance to be examined and 20 mL of carbon-dioxide-free water R. The mixture has the appearance of a gel. Add 100 mL of carbon-dioxide-free water R and shake. A suspension forms that settles after standing.

B. To an acidified solution, add iodinated potassium iodide TS. The solution becomes blue or violet.

C. Place 2.5 g in a silica or platinum crucible and add 2 mL of sulfuric acid (~500 g/L) TS. Heat on a water-bath, then cautiously raise the temperature progressively over an open flame. Ignite, preferably in a muffle furnace, at 575 °C to 625 °C. Continue heating until all black particles have disappeared. Cool, add a few drops of a sulfuric acid (~100 g/L) TS, and heat and ignite as above. Add a few drops of ammonium carbonate (158 g/L) TS, evaporate to dryness, and ignite as above. Cool, dissolve the residue in 50 mL of water R and mix. The solution yields reaction B described under 2.1 General identification tests as characteristic of sodium.

Clarity and colour of solution. Centrifuge the suspension obtained in identity test A at 2500 g for 10 minutes. Collect carefully the supernatant. The supernatant is clear, when compared as described under 1.11.1 Colour of liquids and colourless, when compared as described under 1.11.2 Degree of coloration of liquids.

Sodium glycolate. Carry out the test protected from light.

Prepare the following solutions:

Test solution. Place 0.20 g in a beaker. Add 5 mL of acetic acid (~300 g/L) TS and 5 mL of water R. Stir until dissolution is complete (about 10 minutes). Add 50 mL of acetone R and 1 g of sodium chloride R. Filter through a fast filter paper impregnated
with acetone R, rinse the beaker and filter with acetone R. Combine the filtrate and washings and dilute to 100.0 mL with acetone R. Allow to stand for 24 hours without shaking. Use the clear supernatant.

Reference solution. Dissolve 0.310 g of glycolic acid R, previously dried in a desiccator (over about 100 g of molecular sieve R) at atmospheric pressure and at room temperature overnight, in water R and dilute to 500.0 mL with the same solvent. Place 5.0 mL of this solution in a beaker. Add 5 mL of acetic acid (~300 g/L) TS and allow to stand for about 30 minutes. Add 50 mL of acetone R and 1 g of sodium chloride R. Filter through a fast filter paper impregnated with acetone R, rinse the beaker and filter with acetone R. Combine the filtrate and washings and dilute to 100.0 mL with acetone R. Allow to stand for 24 hours without shaking. Use the clear supernatant.

Heat 2.0 mL of the test solution on a water-bath for 20 minutes. Cool to room temperature and add 20.0 mL of 2,7-dihydroxynaphthalene TS. Shake and heat in a water-bath for 20 minutes. Cool under running water, transfer to a volumetric flask and dilute to 25.0 mL with sulfuric acid (~1760 g/L) TS, maintaining the flask under running water. Within 10 minutes, measure the absorbance at 540 nm as described under 1.6 Spectrophotometry in the visible and ultraviolet regions using water R as the blank. The absorbance of the solution prepared with the test solution is not greater than that of a solution prepared at the same time and in the same manner with 2.0 mL of the reference solution (2.0%).

Sodium chloride. Place 0.500 g in a beaker and suspend in 100 mL of water R. Carefully add 1 mL of nitric acid (~1000 g/L) TS. Titrate with silver nitrate (0.1 mol/L) VS, determining the end-point potentiometrically, using a silver-based indicator electrode and a double-junction reference electrode containing a solution of potassium nitrate (100 g/L) TS in the outer jacket and a standard filling solution in the inner jacket. Each mL of silver nitrate (0.1 mol/L) VS is equivalent to 5.844 mg of NaCl. The content of NaCl is not greater than 7.0 %.
**pH value (1.13).** Disperse 1.0 g in 30 mL of carbon-dioxide-free water R; pH of the suspension, 5.5 to 7.5 for Type A and 3.0 to 5.0 for Type B.

**Iron.** Use 10 mL of the solution prepared for identity test C. Treat the solution as described in **2.2.4 Limit test for iron**, using 0.5 mL of iron standard FeTS; not more than 20 µg/g.

**Loss on drying.** Dry 1.000 g of the test substance at 130 °C for 1.5 hours; it loses not more than 100 mg/g.

**Microbial contamination.** It complies with the tests for *Escherichia coli* and *Salmonella (3.3.2).*

**Assay.** Shake about 1 g with 20 mL of ethanol (80% v/v) TS, stir for 10 minutes and filter. Repeat the operation until chloride has been completely extracted and verify the absence of chloride using silver nitrate (~0.1 mol/L) TS. Dry the residue at 105 °C to constant mass. To 0.700 g of the dried residue, add 80 mL of anhydrous acetic acid R and heat under a reflux condenser for 2 h. Cool the solution to room temperature. Titrate with perchloric acid (0.1 mol/L) VS, determining the end-point potentiometrically, as described under **2.6 Non-aqueous titration.** Carry out a blank titration. Each mL of perchloric acid (0.1 mol/L) VS is equivalent to 2.299 mg of Na.

**New reagents**

**Ethanol (80% v/v) TS**

*Procedure.* Dilute 831 mL of ethanol (~750 g/L) TS to 1000 mL with water R.

**Iodinated potassium iodide TS**

*Procedure.* Dissolve 500 mg of iodine R and 1.5 g of potassium iodide R in water R and dilute to 25 mL with the same solvent.
Ammonium carbonate (158 g/L) TS

A 158 g/L solution of ammonium carbonate R1.

Ammonium carbonate R1

A mixture of varying proportions of ammonium hydrogen carbonate (NH₄HCO₃) and ammonium carbamate (NH₂COONH₄). It liberates not less than 30 per cent m/m of NH₃.

Description. White or almost white translucent mass.

Solubility. Slowly soluble in about 4 parts of water. It is decomposed by boiling water.

Assay. Dissolve 2.00 g in 25 mL of water R. Slowly add 50.0 mL of hydrochloric acid (1 mol/L) VS, titrate with sodium hydroxide (1 mol/L) VS, using 0.1 mL of methyl orange ethanol TS1 as indicator. Each mL of hydrochloric acid (1 mol/L) VS is equivalent to 17.03 mg of NH₃.

Methyl orange ethanol TS1

Procedure. Dissolve 0.1 g of methyl orange R in 80 mL of water R and dilute to 100 mL with ethanol (~750 g/L) TS.

Test for sensitivity. A mixture of 0.1 mL of methyl orange ethanol TS1 and 100 mL of carbon-dioxide-free water R is yellow. Not more than 0.1 mL of hydrochloric acid (1 mol/L) VS is required to change the colour to red.

Colour change. pH 3.0 (red) to pH 4.4 (yellow).

Glycolic acid R

C₂H₄O₃. 2-Hydroxyacetic acid. CAS Reg. No. 79-14-1.

Description. Crystals.
Solubility. Soluble in water, in acetone, in ethanol (~750 g/L) TS and in methanol.

Melting point. About 80 °C.

Molecular sieve R

CAS Reg. No. 70955-01-0.

Molecular sieve composed of sodium aluminosilicate. It is available as beads or powder with a pore size of 0.4 nm.

When reused, it is recommended that the molecular sieve be regenerated according to the manufacturer’s instructions.

2,7-Dihydroxynaphthalene TS

Dissolve 10 mg of 2,7-dihydroxynaphthalene R in 100 mL of sulfuric acid (~1760 g/L) TS and allow to stand until decolorised.

Storage. Use within 2 days.

2,7-Dihydroxynaphthalene R

C_{10}H_8O_2. Naphthalene-2,7-diol. CAS Reg. No. 582-17-2

Description. Needles.

Solubility. Soluble in water and in ethanol (~750 g/L) TS.

Melting point. About 190 °C.

Silver nitrate (~0.1 mol/L) TS

A 17 g/L solution of silver nitrate R.