ZINC GLUCONATE
Draft proposal for *The International Pharmacopoeia*
(August 2012)

Draft for comment

This document was provided by a quality control expert. Should you have any comments thereon, please send these to Dr Herbert Schmidt, Medicines Quality Assurance Programme, Quality Assurance and Safety: Medicines, World Health Organization, 1211 Geneva 27, Switzerland; fax: (+41 22) 791 4730 or e-mail: schmidhh@who.int with a copy to gaspardm@who.int by 17 September 2012.

In order to speed up the process for receiving draft monographs and for sending comments, please let us have your e-mail address (to bonnyw@who.int) and we will add it to our electronic mailing list. Please specify if you wish to receive monographs.

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**SCHEDULE FOR THE ADOPTION PROCESS OF DOCUMENT QAS/12.490**

*Draft proposal for revision of a published monograph in*

*The International Pharmacopoeia*

**ZINC GLUCONATE**

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<tr>
<td>Discussion of preliminary draft revision at consultation on specifications for medicines and quality control laboratory issues</td>
<td>29-31 May 2012</td>
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<tr>
<td>Draft sent out for comments following discussion at consultation on specifications for medicines and quality control laboratory issues</td>
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<td>Discussion at forty-seventh meeting of the WHO Expert Committee on Specifications for Pharmaceutical Preparations</td>
<td>9-12 October 2012</td>
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<td>Further follow-up action as required</td>
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[Note from the secretariat:

Comments are sought whether to include in the monograph a specification on total aerobic microbial count (TAMC) and total combined yeasts/moulds count (TYMC).]

Zinci gluconas
Zinc gluconate

\[ \text{C}_{12}\text{H}_{22}\text{ZnO}_{14+x}\text{H}_2\text{O} \]

Relative molecular mass. 455.7 (anhydrous).

Chemical name. Zinc gluconate; CAS Reg. No. 4468-02-4.

Other names. Gluconic acid, zinc complex.

Description. White or almost white, hygroscopic, crystalline powder.

Solubility. Soluble in water; practically insoluble in anhydrous ethanol.

Category. Adjunct to oral rehydration salts in (prevention and) treatment of dehydration due to diarrhoea; astringent.

Storage. Zinc gluconate should be kept in a tightly closed container.

Additional information. Zinc gluconate is a hygroscopic material, and should be protected from atmospheric moisture.

Requirements

Definition. Zinc gluconate contains not less than 98.0% and not more than 102.0% of \( \text{C}_{12}\text{H}_{22}\text{ZnO}_{14} \) calculated with reference to the anhydrous substance.
Identity tests

A. Dissolve 0.1 g in 5 ml of water R. Add 0.5 ml of potassium ferrocyanide (~53 g/l) TS. A white precipitate is formed that does not dissolve upon the addition of 5 ml of hydrochloric acid (~330 g/l) TS.

B. Carry out the test as described under 1.14.1 Thin-layer chromatography, using silica gel R5 as the coating substance and a mixture of 10 volumes of ethyl acetate R, 50 volumes of water R and 40 volumes of ethanol (~750 g/l) TS as the mobile phase. Apply separately to the plate 1 µl of each of 2 solutions in water R containing (A) 10 mg of the test substance per ml and (B) 10 mg of calcium gluconate R per ml. After removing the plate from the chromatographic chamber, heat the plate for 10 minutes at 105 °C. Spray with ammonium molybdate/cerium sulfate/sulfuric acid TS. Heat the plate for 10 minutes at 105 °C. Examine the chromatogram in daylight. The principal spot obtained with solution A corresponds in position, appearance and intensity to that obtained with solution B.

Clarity and colour of solution. A solution of 0.2 g in 10 ml of water R is clear and colourless.

pH value (1.13). pH of a 0.01 g/ml solution, 5.5–7.5.

Water. Determine as described under 2.8 Determination of water by the Karl Fischer method, Method A. Use 0.250 g of the test substance. The water content is not more than 120 mg/g.

Cadmium. Determine by atomic absorption spectrophotometry 1.8 Atomic spectrometry: emission and absorption, Method 2, at a wavelength of 228.8 nm using a cadmium hollow cathode lamp, an air-acetylene flame, and a slit width of 0.5 nm. Dissolve 1.25 g in 25 ml of water R. As a reference solution use cadmium standard (1000 µg Cd/ml) TS; not more than 2 µg of Cd per g.

Chlorides. Dissolve 0.5 g in 25 ml of water R, and proceed as described under 2.2.1 Limit test for chlorides; the chloride content is not more than 500 µg/g.

Heavy metals. Use 1.0 g for the preparation of the test solution as described under 2.2.3 Limit test for heavy metals, Procedure 4, not more than 10 µg/g, substituting acetic acid (~60 g/l) PbTS with hydrochloric acid (~70 g/l) TS in all cases.

Reducing sugars. Dissolve 0. 5 g in a mixture of 2 ml of hydrochloric acid (~330 g/l) TS and 10 ml of water R. Boil for 5 minutes, allow to cool, add 10 ml of sodium carbonate (~10 g/l) TS and allow to stand for 10 minutes. Dilute to 25 ml with water R and filter. To 5 ml of the filtrate add 2 ml of cupri-tartaric TS and boil for 1 minute. Allow to stand for 2 minutes; no red-brown precipitate is formed.

Sulfates. Dissolve 0.96 g in 25 ml of water R, and proceed as described under 2.2.2 Limit test for sulfates; the sulfate content is not more than 500 µg/g.
Assay

Dissolve about 200 mg, accurately weighed, in 50 ml of acetic acid (~10 g/l) TS and proceed with the titration as described under 2.5 Complexometric titrations for zinc. Each ml of disodium edetate (0.05 mol/l) VS is equivalent to 22.78 mg of C_{12}H_{22}ZnO_{14}.

Reagents and test solutions to be added

Ammonium molybdate / cerium sulfate / sulfuric acid TS.
Procedure. Dissolve 2.5 g ammonium molybdate R and 1.0 g cerium sulfate R in sulfuric acid (~100 g/l) to produce 100 ml.

Cadmium R.
Cd
A commercially available reagent of suitable grade.

Cadmium standard (1000 µg Cd/ml) TS.
Procedure. Dissolve 0.100 g of cadmium R in sufficient amount of equal volumes of hydrochloric acid (~330 g/l) TS and water R and dilute to 100 ml with a 1 per cent V/V solution of hydrochloric acid (~330 g/l) TS.

Note. For the preparation of this test solution commercially available cadmium standard solution 1000 µg Cd/ml can also be used.

Calcium gluconate R.
C_{12}H_{22}CaO_{14}.H_{2}O.
A commercially available reagent of suitable grade.

Cerium sulfate R.
CeO_{8}S_{2}.
A commercially available reagent of suitable grade.

Cupri-tartaric TS.
Procedure. Dissolve 34.6 g copper (II) sulfate R in sufficient water to produce 100 ml. Separately dissolve 173 g of potassium sodium tartrate R and 50 g sodium hydroxide in 400 ml water R; heat to boiling, allow to cool and dilute to 500 ml with water R. Shortly before use, mix together equal volumes of both solutions.

Potassium ferrocyanide (~53 g/l) TS.
A solution of potassium ferrocyanide R containing about 53 g of K_{4}Fe(CN)_{6} per litre.

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