THE UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

PUBLIC ASSESSMENT REPORT FOR SUXAMETHONIUM CHLORIDE 50MG/ML SOLUTION FOR INJECTION/INFUSION

Version number 1.0
21 August, 2023

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1. Introduction

Suxamethonium chloride 50mg/ml solution for injection/infusion is a generic medicinal product containing the active substance Suxamethonium chloride. The reference product is “Anectine 50 mg/mL solution for injection or infusion (Aspen Pharma Trading Limited, Ireland)’. Suxamethonium is an ultra-short acting, depolarising, neuromuscular blocking agent. Suxamethonium, an analogue of acetylcholine, inhibits neuromuscular transmission by depolarising the motor end plates in skeletal muscle. The depolarisation may be observed as fasciculation. Subsequent neuromuscular transmission is inhibited as long as an adequate concentration of suxamethonium remains at the receptor site. Onset of flaccid paralysis occurs within 30-60 seconds of intravenous injection and with single administration persists for 2-6 minutes.

The paralysis following administration of suxamethonium is progressive, with differing sensitivities of different muscles. This initially involves consecutively the levator muscles of the face, muscles of the glottis and finally the intercostals and the diaphragm and all other skeletal muscles.

The short duration of suxamethonium is considered to be due to its rapid metabolism in the blood. Suxamethonium is rapidly hydrolysed by plasma cholinesterase to succinylcholine (which possesses clinically insignificant depolarising muscle relaxant properties) and then more slowly to succinic acid and choline. Suxamethonium chloride 50mg/ml solution for injection/infusion is approved in Tanzania for use in all ages.

Product details

Registration number	TAN 23 HM 0301
Brand name	N/A
Generic name, strength, and form	Each ml of solution for injection or infusion contains 50 mg of suxamethonium chloride dihydrate (equivalent to 36.55 mg of suxamethonium).
ATC classification	muscle relaxant ATC Code: M03AB01
Distribution category	POM
Country of origin	India
Associated product	N/A
Marketing Authorization Holder	Macarthys Laboratories T/A Martindale Pharma Address: Bampton Road, Harold Hill, Romford, RM3 8UG United Kingdom
Local Technical Representative	Laborex Tanzania Ltd. P O Box 70032, Dar es Salaam

1.1 Assessment procedure

The application for registration of Suxamethonium chloride 50mg/ml solution for injection/infusion was submitted on 25/08/2022. The product underwent full assessment. Assessment was completed in 3 (three) rounds of evaluation and the product was registered on 01/06/2023.

1.2 Information for users

Visual description of the finished product	Suxamethonium chloride injection is a clear, colourless solution practically free from particulates in a type I clear glass ampoule
Primary packing material	Type I clear glass ampoule
Secondary packing materials	Printed carton box
Shelf-life and storage condition	18 months, Store in a refrigerator, between 2 and 8°C. Do not freeze. Store in the original package to protect from light
Route of administration	Intravenous
Therapeutic indications	Used for muscle relaxation daring general anaesthesia

2. Labelling and product information

Summary of product characteristics
The SmPC included all the relevant information to ensure correct and safe use of the medicine by healthcare providers. The complete SmPC can be accessed here.

Package insert/leaflet
The package insert is confirmed to be derived from the SmPC and contains sufficient data for the end user. Since the product is POM, the package insert contains full prescribing information as per SmPC.

Container labels
The product label information is presented in English. Details in the secondary pack label include:

Brand name:

Composition:

Pack size:

Manufacturing details:

Storage conditions:

Manufacturer address:

Unique identifier:

Special warnings/precautions or instructions for use:
The details of the primary pack include:

Brand name and strength:

Manufacturing details:

Name of manufacturer:

The content of the primary and secondary labels was aligned to the requirements of the Part V of the Compendium: Guidelines on Format and Content of Product Labels for Medicinal products. The label contains sufficient information for proper identification of the medicine and post marketing follow up of the product.

Mock labels are appended as annex I.

3. Scientific discussion

Quality of Active Pharmaceutical Ingredient

Information on quality of the API was submitted in form of CEP.

General Information

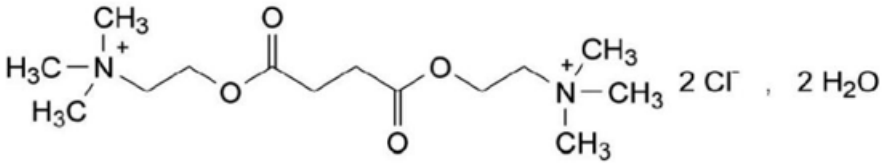
Suxamethonium chloride API is compendia in Ph.Eur., BP, USP.

Molecular formula: $C_{14}H_{30}Cl_2N_2O_4$, $2H_2O$

Chemical name:

2,2′-[butanedioylbis(oxy)]bis(N,N,N-trimethylethanaminium) dichloride

Structure:



General properties

Suxamethonium chloride is a white or almost white, crystalline powder, hygroscopic, freely soluble in water, slightly soluble in alcohol. It melts at about 160°C, determined without previous drying. No discussion on polymorphism has been confirmed. Nevertheless, as active is present in the drug product dissolved in water, hence the polymorphic form and particle size distribution are not considered as critical quality aspects.

Manufacture

Suxamethonium chloride API manufacturer is Mac-Chem Products India PvT Ltd, Plot No. N-211/2/10, Tarapur, MIDC, Boisar, District-Thane, Pin-401506, India and Solara Active Pharma Sciences Limited "Batra Centre" No. 28, Sardar Patel Road, Guindy, India-600 032 Chennai, Tamil Nadu. The manufacturing complies with GMP requirements as evidenced by the GMP certificates issued. Suxamethonium chloride API is manufactured by chemical synthesis using conventional techniques. Sufficient controls of quality of materials and in-process checks were employed throughout the manufacturing process.

Specifications

The API specifications were set as per Ph. Eur standards and ICHQ3A. The parameters monitored during quality control are: Appearance, identification, appearance of solution, pH, choline chloride, water, sulfated ash, assay, microbiological quality, related substances, residual solvents, and bacterial endotoxins. Compliance to these specifications were established via batch analysis data and stability studies.

Stability and container closure system

Mac-Chem Products India PvT Ltd:

The re-test period of Suxamethonium chloride API is 60 months when packed in double polyethylene bags in an aluminium laminated bag placed in a polyethylene drum with storage condition ‘Store below 25°C’.

Solara Active Pharma Sciences Limited:

The re-test period of Suxamethonium chloride API is 48 months when packed in double polyethylene bags (outer black), placed in polyethylene drums with storage condition ‘Store below 25°C’.

Quality of the Finished Pharmaceutical Product

Formulation

Suxamethonium chloride 50mg/ml solution for injection/infusion is a grey/pink “Size 0” coloured hard gelatin capsules containing white to off white powder.

Suxamethonium chloride 50mg/ml solution for injection/infusion contains the Suxamethonium chloride other ingredients listed here after: dilute hydrochloric acid, nitrogen, and water for injections. The quantities of all ingredients are confirmed to be in line with the recommendations of Handbook of Pharmaceutical Excipients, 8th Edition in terms of function and quantities.

Manufacture

The finished product manufacturer is Macarthys Laboratories Ltd, t/a Martindale Pharma, Bampton Road,Harold Hill,Romford, Essex, RM3 8UG, United Kingdom.. The compliance of the sites to TMDA GMP standards was confirmed through desk review on DD/MM/YYYY.

Specifications

The FPP is compendia. The manufacturer controls the quality of the finished product as per USP standards and ICH requirements. The parameters monitored during quality control are: Description, identification, pH, osmolality, assay, sub-visible particles, extractable volume, degradation products (provisional), succinylmonocholine chloride, choline chloride, other impurities (total), sterility, endotoxin. Compliance to the standard was established using batch analysis data and stability data.

Stability and container closure system

Stability studies were conducted on 3(three) batches of the finished product stored at 2-8°C for 18 months and 25℃±2℃ /60%±5%RH for 6 months. Based on the stability data presented, the approved shelf-life is 18 months when stored in Type 1 glass ampoules with storage condition ‘Store in a refrigerator, between 2 and 8°C. Do not freeze. Store in the original package to protect from’.

Safety and efficacy information

Suxamethonium chloride 50mg/ml solution for injection/infusion is a parenteral formulation and therefore fulfils the exemption mentioned in the part III: guidelines on therapeutic equivalence requirements, which states that a bioequivalence study is not required if the solutions for injection that contain the same active ingredients and excipients in the same concentrations as currently registered products and which are administered by the same route(s). The quantitative composition of Suxamethonium chloride 50mg/ml solution for injection/infusion is entirely the same as the reference products in the market. Therefore, it may be considered as therapeutic equivalent, with the same efficacy/safety profile as known for the active substance of the reference medicinal product. The current product can be used instead of its reference product

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4. Benefit-Risk Assessment and Conclusion

On basis of the data submitted, the current state of knowledge and compliance to Good Manufacturing Practice, the benefit of the product outweighs the risks associated with its use when used in accordance to the summary of product characteristics. Suxamethonium chloride 50mg/ml solution for injection/infusion is recommended for registration.

5. Post-approval updates

Variation applications

Reference number	Date submitted	Change requested	Recommendation	Granting date

Feedback from pharmacovigilance, post marketing surveillance and enforcement activities

Type of feedback	Impact	Response

Re-registration applications

Application for renewal of registration was submitted on <DDMMYYYY>. The application was finalized in <number> rounds of evaluation. The product was confirmed to still be compliant to the standards of quality, safety and efficacy, hence registration was renewed on <DDMMYYYY>.

PART 5: CHANGE HISTORY

Version number	Date	Description of update	Section(s) Modified	Approval date

Annex I: Mock up labels;

Primary pack label;

Secondary pack label: