THE UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

PUBLIC ASSESSMENT REPORT FOR THYMOGAM (ANTITHYMOCYTE GLOBULIN (EQUINE)250 MG/ 5 ML) SOLUTION

Version number 1.0
7 November 2023

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1. Introduction

Thymogam is a generic medicine of Antithymocyte globulin (equine). Thymogam is an immunosuppressant medicine belonging to L04AA03 – selective immunosuppressants group. Thymogam exerts is activity by altering the function of the T lymphocytes, which are responsible in part for cell-mediated immunity and are involved in humoral immunity. Thymogam is approved in Tanzania for use in adults and children.

1.1 Product details

Registration number	TAN 20 HM 0384
Brand name	Thymogam
Generic name, strength and form	Antithymocyte globulin (equine) 250 mg
ATC classification	L04AA03 – selective immunosuppressants
Distribution category	POM
Country of origin	India
Associated product	None
Marketing Authorization Holder	Bharat Serums & Vaccines Ltd. Address: 17th Floor, Hoechst House, Nariman Point, Mumbai – 400 021. Country: India E-Mail:corporate@bharatserums.com
Local Technical Representative	Salama Pharmaceuticals Limited, 13/19 Uhuru/ Nyamwezi Street, Kariakoo P. O. Box 65235 Dar es Salaam TANZANIA

1.2 Assessment procedure

The application for registration of Thymogam 250 was submitted on 23/08/2016. The product underwent full assessment. Assessment was completed in 5 rounds of evaluation. Thymogam was registered on 25/09/2020.

1.3 Information for users

Visual description of the finished product	Clear or slightly opalescent and colourless or pale yellow coloured liquid free from suspended particles in 5 ml vial
Primary packing material	USP type 1, glass vial
Secondary packing materials	
Shelf-life and storage condition	24 Months Store between 2°C and 8°C
Route of administration	Intravenous (IV) Only

Therapeutic indications	Renal transplantation: THYMOGAM is indicated for the management of allograft rejection, including delay of onset of first rejection episode, in patients who have undergone renal transplantation. It is also given as an adjunct along with the conventional therapy to delay the onset of 1st rejection episode. Aplastic Anaemia: THYMOGAM is indicated in the treatment of moderate to severe aplastic anaemia in patients not suitable for bone marrow transplant.

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 simplified information for patients.

Container labels

The product label information is presented in English. Details in the secondary pack label include:
Brand name: Thymogam
Composition: Antithymocyte globulin – Equine
Pack size: 5 ml
Manufacturing details: batch number, manufacturing date, expiry date
Storage conditions: Store between 2°C and 8°C.Do not freeze.
Manufacturer address: Bharat Serums and Vaccines Ltd, Plot No. K – 27, Additional M.I.D. C., Ambernath (E)
Unique identifier: Not applicable
Special warnings/precautions or instructions for use: None

The details of the primary pack include:
Brand name and strength: Thymogam 250 mg
Manufacturing details: batch number, manufacturing date, expiry date
Name of manufacturer: Bharat Serums and Vaccines Ltd

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.
Describe any approved deviation to the requirements and the justification for the deviation.

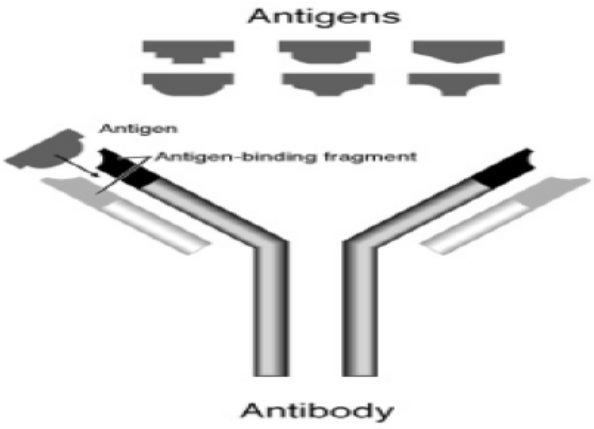
3. Scientific discussion

Quality of Immunogenic substance(s)

Information on quality of the API was submitted in form of Full details.

General properties
Antithymocyte Globulin (Equine) API is non-compendia.

Molecular formula:
Chemical name: Fab2 (Fragment, antigen binding)/Immunoglobulin G Fragment
Structure:



Critical physico-chemical properties of the API were <solubility, particle size, polymorphism>.

Manufacture
The API manufacturing site, Bharat Serums & Vaccines Ltd. Plot No. K – 27, Jambivili Village, Anand Nagar, Additional M.I.D.C., Ambernath (East), India was noted to comply with WHO GMP requirements as evidenced by the GMP certificate issued by <state the issuing authority>. Antithymocyte Globulin (Equine) is manufactured from animals antisera 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 in-house standards and ICHQ6B. The parameters monitored during quality control are: characters, protein, assay-cytotoxicity, pH, osmolality. Compliance to these specifications were established via batch analysis data and stability studies.

Stability and container closure system

The re-test period of Antithymocyte Globulin (Equine) API is 6 months when packed in stainless container with an airtight lid and stored at 2 ºC – 8 ºC.

Quality of the Finished Immunogenic Product

Formulation

Thymogam is a clear or slightly opalescent and colourless or pale yellow coloured liquid, free from suspended particles. Thymogam contains Antithymocyte Globulin (Equine) and other ingredients listed hereafter glycine , sodium chloride , water for injection. The quantities of all ingredients are confirmed to be in line with the recommendations of Handbook of Pharmaceutical Excipients, Edition number in terms of function and quantities. Ingredient, <excipient> is of safety concern therefore appropriate warnings were included in the product label.

Manufacture

The finished product was manufactured at Bharat Serums & Vaccines Ltd., Plot No. K – 27, Jambivili Village,Anand Nagar, Additional M.I.D.C., Ambernath (East), India. The compliance of the site to TMDA GMP standards was confirmed through site inspection on 16 and 18 December 2017.

Specifications

The FPP is non-compendia. The manufacturer controls the quality of the finished product as per in-house and ICHQ6B requirements. The parameters monitored during quality control are: characters, precipitation test, immunoelectrophoresis, extractable volume, pH, osmolality, proteins, stabilizer, distribution of molecular size, purity, anti-A and anti-B haemagglutinins, haemolysins, sterility , pyrogens, assay – cytotoxicity assay ED50, abnormal toxicity, anti-thrombocyte antibodies and anti-human serum proteins assay-immunodiffusion. Compliance to the standard was established using batch analysis data and stability data.

Stability and container closure system

Stability studies were conducted on 3 batches of the finished product stored at 2° - 8°C for 24 months and 25 °C ±2°C/60%±5%RH for 6 months. Based on the stability data presented, the approved shelf-life is 24 months when stored in 5 ml USP Type I moulded, narrow mouth, transparent, colourless flint glass vial with rubber bung and Aluminium Flip Off seal 20 mm Bio Green at 2ºC to 8°C.

Safety and efficacy information

Safety and efficacy of Thymogam was established through reliance on the innovator product and product use in the country of origin.

4. Benefit-Risk Assessment and Conclusion

On basis ofthe 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. Thymogam 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

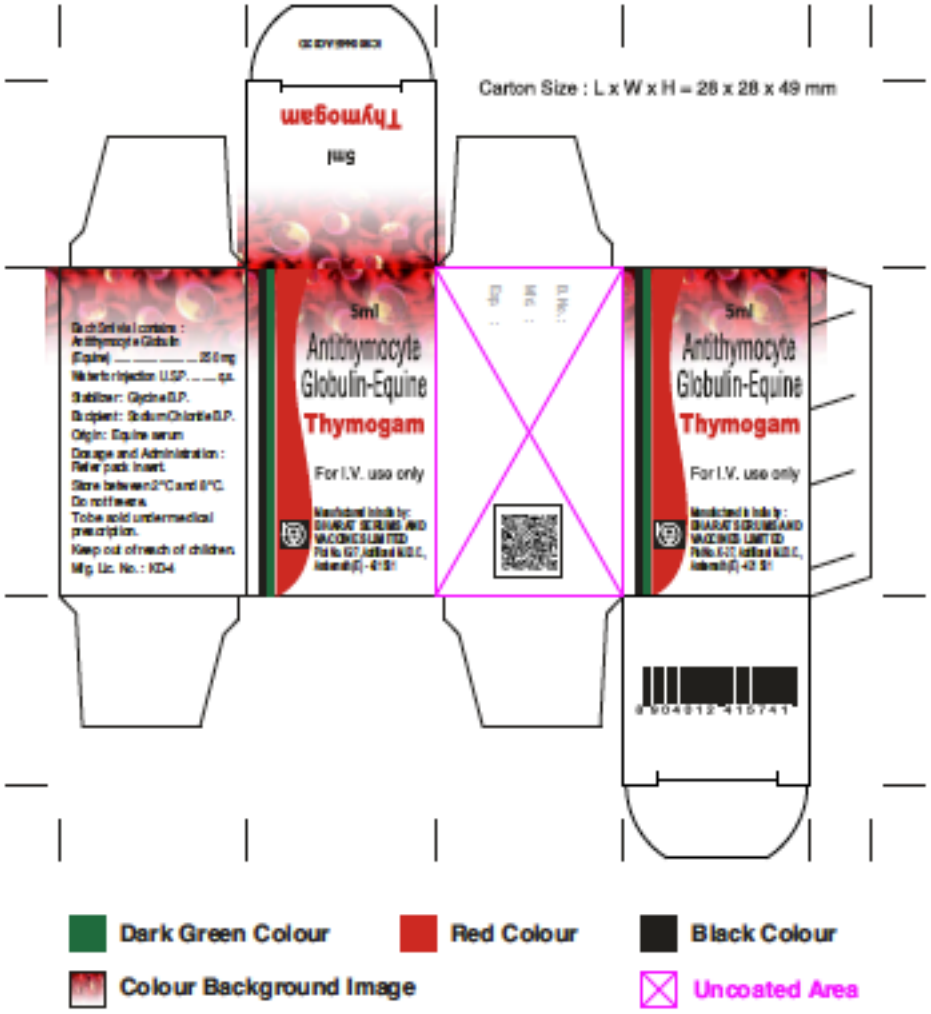
Re-registration applications

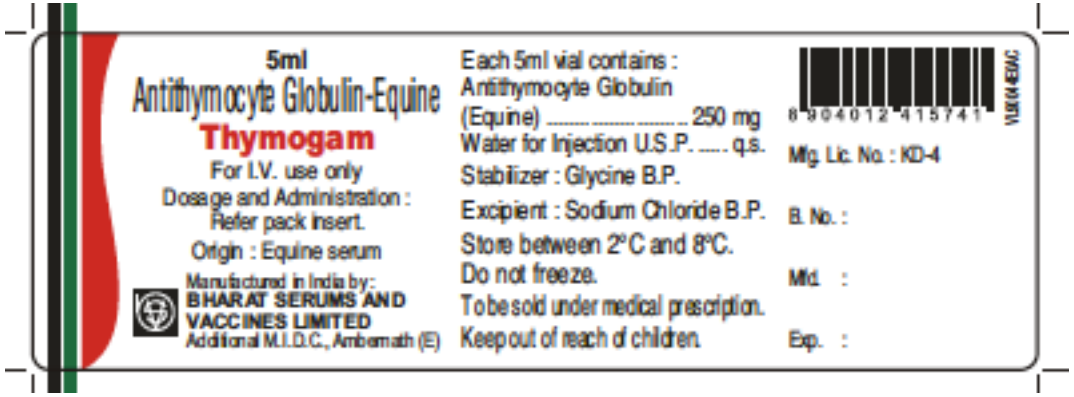
Application for renewal of registration was submitted on <DDMMYYYY>. The application was finalized in <number> rounds of evaluation. The product was confirmed to still be compliant to the standards of quality, safety and efficacy, hence registration was renewed on <DDMMYYYY>.

PART 5: CHANGE HISTORY

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

Annex I: Mock up label




5ml
Antithymocyte Globulin-Equine
Thymogam
For I.V. use only
Dosage and Administration :
Refer pack insert.
Origin : Equine serum
Manufactured in India by:
BHARAT SERUMS AND
VACCINES LIMITED
Additional M.I.D.C., Ambernath (E)
Each 5ml vial contains :
Antithymocyte Globulin
(Equine) ..... 250 mg
Water for Injection U.S.P. ..... q.s.
Stabilizer : Glycine B.P.
Excipient : Sodium Chloride B.P.
Store between 2°C and 8°C.
Do not freeze.
To be sold under medical prescription.
Keep out of reach of children.
8 904012 415741
Mfg. Lic. No. : KD-4
B. No. :
Mfd. :
Exp. :