Concerned Member State Comments on Day 70 Preliminary Assessment Report to be sent at Day 100 at the latest

1. This document is sent by:

CMS	France
Contact point, project team leader (name) phone email	[redacted] Email: [redacted]
Assessors, if applicable (name e-mail, phone)	
Date/Day of procedure	13-09-2021 – Day 100

2. This document concerns:

Procedure number	DE/H/6691//DC
Name of the medicinal product in the RMS	TRIENTINE WAYMADE 200 mg, gélule
Name of the active substance	Trientine
Applicant	Waymade B.V
Deadline for comments	

3. Comments, general

3.1 Assessment of the RMS

We endorse the RMS assessment, but also have additional comments ☒

We do not fully endorse the RMS assessment, and have other comments ☐

3.2 Conclusions on the product
Our conclusion is that the product is:

Approvable, provided that satisfactory responses are given to the list of questions and/or the SmPC/PL/labelling is changed according to the comments ☐

Non-approvable ☐

3.3. List of Questions/Proposed conditions for marketing authorisation
We have grounds of potential serious risks to public health on the following part of the assessment report not already raised by the RMS as major objections

Quality ☐

Non-Clinical ☐

Clinical ☐

Risk Management Plan ☐

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SmPC ☐

PL ☐

Labelling ☐

We have additional other concerns on the following part of the assessment report

Quality ☐

Non-Clinical ☐

Clinical ☒

Risk Management Plan ☐

SmPC ☐

PL ☐

Labelling ☐

Module 1 – Application related comments (including product name) ☐

4. Potential serious risk to public health

Quality

Rationale

Non-clinical

Potential serious risk to public health not already raised by the RMS as major objection
Rationale

Clinical

Potential serious risk to public health not already raised by the RMS as major objection
Rationale

Risk management plan

Potential serious risk to public health not already raised by the RMS as major objection
Rationale

SmPC

PL

Potential serious risk to public health not already raised by the RMS as major objection
Rationale

Labelling

Potential serious risk to public health not already raised by the RMS as major objection
Rationale

5. Additional other concerns

Quality

Other concerns not already raised by the RMS
Rationale

Non-clinical

Other concerns not already raised by the RMS
Rationale

Clinical

Other concerns not already raised by the RMS FR's CMS endorses RMS concerns and would like add the following : 1/ Test certificate of analysis is not complete. Indeed, expiry date is missing. The applicant should provide a complete analysis certificate for the test product with the expiry date. 2/ The concentration points used to calculate the terminal slope were not found. The applicant should mentioned which concentration points were used to calculate the terminal slope (number of concentrations points, time related to the first and last concentration points used).
Rationale

Risk Management Plan

Other concerns not already raised by the RMS
Rationale

SmPC

Other concerns not already raised by the RMS **4.1;** The indication treatment of gall reflux gastritis should be deleted as it is not authorised in France. **6.1 List of excipients** The E numbers should be given when the excipient is listed in the Guideline on the excipients in the label and package leaflet of medicinal products for humanuse as having recognised action or effect. Capsule content: Stearic acid Capsule shell: Gelatin Titanium dioxide (E171)

Printing ink:
Shellac ~~(E904)~~
Propylene Glycol ~~(E1520)~~
Black Iron Oxide (E172)
Potassium Hydroxide ~~(E525)~~

Rationale

PL

Other concerns not already raised by the RMS

Please note that the name authorised in France is
TRIENTINE WAYMADE 200 mg, gélule
Please add: Trientine Dihydrochloride

5. HOW TO STORE X

6. FURTHER INFORMATION

What Trientine Waymade capsules contain
The active substance is trientine.
Each hard capsule contains 300 mg trientine dihydrochloride, equivalent to 200 mg trientine.

The other ingredients are
Capsule content: Stearic acid
Capsule shell: Gelatin, titanium dioxide (E171)
Printing ink: Shellac ~~(E904),~~ propylene glycol ~~(E1520),~~ black iron oxide (E172), potassium hydroxide ~~(E525)~~

What Trientine Waymade capsules look like and contents of the pack
Each hard capsule is a cylindrical size “1” hard gelatin capsule with an opaque, white coloured-cap, printed with “Waymade” in black ink and an opaque white coloured body, printed with “Trientine 300 mg” in black ink. The capsule is filled with white to off-white powder.
White, high density polyethylene (HDPE) round bottles, containing a silica gel desiccant in the bottle, and closed with a polypropylene closure.
Pack size: A bottle of 100 hard capsules in a carton.

Rationale

Labelling

Other concerns not already raised by the RMS **PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING** **{Carton and Bottle}**
1. NAME OF THE MEDICINAL PRODUCT
Please note that the name authorised in France is **TRIENTINE WAYMADE 200 mg, gélule** Please add: Trientine Dihydrochloride
Rationale

Module I – Application related comments (including product name)[1]

Other concerns not already raised by the RMS - The following proposed operators: the release site, the batch control testing site are located in the UK. Furthermore, we note that a site responsible for secondary packaging is located in UK, but no finished product importation site in the EU27 is proposed. The United Kingdom has become a third country. In this regard we would like to remind about the published guidance concerning the impact of UK's withdrawal from the EU (please refer to this page: http://www.hma.eu/535.html) which indicates that such entities need to be changed to EU27/EEA entities. Please propose the required changes in response to this validation check list. Please note a marketing authorisation can only been issued if your application complies with the applicable legal requirements. - For the **manufacturing site APOTHECON PHARMACEUTICALS PRIVATE LIMITED – PLOT N°1134 to 1137, 1138-A1B, 1143-B, 1144 A1B – Padra Jambusar Highway – Tal.Padra, P.O. Dabhasa, Vadodara, Gujarat 391 440 INDE**: A new GMP certificate issued from a European competent authority and specifying active substance TRIENTINE DIHYDROCHLORIDE should be provided. **NAME OF THE MEDICINAL PRODUCT** Please note that the name authorised in France is **TRIENTINE WAYMADE 200 mg, gélule**
Rationale

6. Additional information for the Applicant

[1] Please note that for 10.1 and 10.3 applications with a centrally authorised product as reference product, the product name in RMS and all CMS must be the same. It is therefore important that comments on the product name are sent early in the procedure in order to reach agreement before day 210/90.

Response document:

Please note that any response document submitted by email should be sent to the following email addresses:
[redacted]