Premier Consulting Insight 203

Expediting Regulatory Decisions:
Coordinating Dual Active Substance Master File (ASMF) Submissions

Background

The Marketing Authorization (MA) holder for a treatment for onychomycosis (a fungal infection of the nail), having previously secured regulatory approval in several markets, including the U.S. and Canada, sought to introduce the product to the European market.

The MA holder intended to use the decentralized procedure, a mechanism for authorizing medicines in more than one EU Member State in parallel, particularly for medicines that do not need to be authorized via the EU-wide centralized procedure and have not already been authorized in any Member State.[1]

Completion of the Marketing Authorization Application (MAA) required utilization of the Active Substance Master File (ASMF) procedure, which is designed to facilitate evaluation of the suitability of the use of the active substance in the medicinal product.[2] (See our recent blog post for more information about the ASMF process.)

Objective

The ASMF holder engaged Premier Consulting to coordinate the submission of two separate ASMFs, which were required because the active substance was manufactured in two sites by different manufacturers. .

Challenges

1. The dual ASMF submission process required the request of two separate EU ASMF reference numbers and the preparation of two separate application forms, as well as the concurrent submission of both ASMFs. concurrent submission of both ASMFs.
2. The project also required close coordination between Premier Consulting's chemistry, manufacturing, and controls (CMC); regulatory affairs; and regulatory operations functions – as well as with the ASMF holder – in order to complete the concurrent ASMF submissions.
3. Each ASMF required multiple versions of Module 1 (M1), including separate cover letters, letters of access and submission, and administrative details, each tailored to the needs of the relevant National Competent Authorities (NCAs) and submission channels.
4. Lacking any prior ASMF experience, the client was uncertain of timelines or the requisite steps of the submission process.
5. Except for a handful of sample website documents, very little regulatory guidance on the ASMF procedure was available from the European Medicine Agency (EMA).

Strategy

- Premier Consulting streamlined the process by using the client's previous submissions in the U.S. and Canada as a template and by repurposing much of Modules 2 (M2, Quality Overall Summary) and 3 (M3, Quality).
- The repurposing of M2 and M3 allowed Premier Consulting's CMC experts to focus primarily on updating M1, which required more substantive changes to conform with European requirements and the Common European Submission Portal.

Solutions

- Selected a "worksharing ASMF" submission procedure to avoid unnecessary duplication, harmonize the assessment process, and reduce the resource and regulatory burden on the NCAs, ASMF holder, and MA holder
- Coordinated the submission process with full transparency to the client regarding expectations, scope of work, challenges, and delays
- Helped the ASMF holder navigate a delay on the MA holder's side in compiling pertinent data to populate the relevant modules
- Strictly adhered to each NCA's submission guidelines, while ensuring sufficient time for CMC, regulatory affairs, and regulatory operations to complete their respective tasks

Results

Premier Consulting coordinated and successfully delivered the submissions for both ASMFs, which were key components of the MA application. As of this writing, the application awaits review by the German and Italian health authorities.

More broadly, Premier Consulting secured the ASMF holder's full trust and confidence in this highly specialized regulatory area, ensuring seamless engagement for any future updates to the ASMF documents or other submissions as needed.

Lessons Learned

Determining the feasibility of repurposing much of the M2 and M3 modules was key to the project's success, and a valuable lesson for ASMF and/or MA holders seeking to conduct business in Europe after having already secured approval in another market. The repurposing allowed Premier Consulting to focus our energies on addressing the intricacies of M1.

From a publishing perspective, familiarity with the Common European Submission channel is crucial, as the uploading and transmission processes are more intricate than the FDA's Electronic Submissions Gateway, which requires less organization.

Finally, regardless of the type of application, it is best practice to designate an ASMF lead point of contact. In this case, the main contact was one of Premier Consulting's CMC experts, who oversaw the review of M2 and M3 along with preparation of all M1 documentation, and who assumed ownership of communication with all departments and functions involved in the project.

References

1. Decentralised procedure. Glossary of Regulatory Terms, European Medicines Agency (EMA); 2022. https://www.ema.europa.eu/en/glossary/decentralised-procedure.
2. Guideline on Active Substance Master File Procedure – Final.

Project Description

To coordinate the submission of two separate ASMFs for an active substance being manufactured in two sites by different manufacturers

Therapeutic Area

Dermatology

Therapeutic

A treatment for onychomycosis that was already approved in several markets and being introduced into the European market

Outcome

Premier Consulting coordinated and successfully delivered the submissions for both ASMFs and secured the ASMF holder's full trust and confidence.

services@premierconsulting.com | premierconsulting.com