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Committee for Human Medicinal Products (CHMP)

Closing report on assessment of a supply shortage of a medicinal product due to manufacturing and quality problems.

This template aims to provide guidance on the evaluation of the end of a shortage supply due to manufacturing and quality problems. The assessment of a product shortage due to manufacturing or quality problem may require a cross-functional team of clinical, quality and pharmacovigilance experts. The level of information and the subsequent assessment will vary on a case by case basis.

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Table of Contents

1. Introduction

1.1. Description of the defect or GMP/manufacturing problem

Briefly summarise the quality or GMP issue that led to the shortage and include a chronology of events (reference initial assessment report, as applicable):

- *Start and cause of the supply shortages and affected pharmaceutical forms or strengths of the medicinal product(s).*
- *Duration of the shortage*
- *Geographical impact of the shortage*

Mention any other medicinal products whose supply was affected by the shortage.

2. Discussion

2.1. Quality

Discuss any actions taken by the supervisory authorities to verify the corrective and preventive measures taken, e.g. inspections, sampling and testing.

Discuss the adequacy of the root cause analysis, corrective and preventative actions identified by the MAH to restore appropriate product quality as described by the marketing authorisation and/or by the manufacturer to restore compliance with GMP.

Discuss the appropriateness of any quality variations that have been submitted to implement the corrective actions and/or normalise the supply situation.

Discuss whether there is an outstanding need for recall of any affected batches.

2.2. Clinical

The Clinical impact of the use of the defective product should be summarised.

Clinical impact of the use of the alternative treatment, e.g. alternate formulations, lower strength, other medicinal product or procedures should be summarised.

Evaluation of any possible impact on the use of the concomitant medications prescribed with the medicinal product as part of the normal treatment regimen should be described.

Impact on vulnerable populations, emergent specific adverse events, withdrawal symptoms, off-label use or other potential indications should be discussed, as identified during the use of the product under shortage conditions.

If there was a switch to another product, discuss:

- *Ease of identifying treatment alternates (of the same or a different product).*
- *Experience with "switching" patients to alternative strengths, formulations, dosages of the same medicinal product, if relevant.*

- *Experience with "switching" patients to alternative strengths, formulations, dosages of a different medicinal product, if relevant.*

Consideration for patients remaining on the alternate therapy versus those switching back to the original medicinal product recommended once shortage is resolved should be discussed. Effectiveness of the original treatment recommendations should be considered.

Discussion on the need to update the PI and the EPAR based on the clinical use of the product under shortage (i.e. with temporary treatment recommendations) shall be included.

2.3. Pharmacovigilance

If supply of defective product was maintained, discuss the results of the overall enhanced pharmacovigilance monitoring and reporting during the period, taking into account the adequacy of actions taken, e.g. frequency of monitoring; relevant ADR terms; and mechanisms for rapidly collating data from different Member States.

New safety signals, spontaneous reports and any additional data provided by the MAH or other sources should be taken into account.

The compliance of the MAH and effectiveness of the temporary pharmacovigilance and risk minimisation measures should be summarised, e.g. educational material and DHPC.

If patients were switched to another treatment discuss any newly identified safety signals, potential medical errors.

Discuss the usefulness and effectiveness of communication channels and tools used to update the public on the shortage and on clinical recommendations.

3. Conclusions

Conclusion on the following should be stated:

- *End of a shortage of supply as the quality of the medicinal product has been restored and demand can be met.*
- *Effectiveness of the temporary treatment recommendations.*
- *Findings of the enhanced pharmacovigilance monitoring undertaken.*
- *Effectiveness of the risk minimisation actions taken.*
- *Effectiveness of public communication plan.*
- *Overall benefit-risk for the affected medicinal product following the end of a shortage in supply.*
- *Whether there are any lessons to be learned that could be applied in future cases (for industry, regulators, physicians, patients, public).*

4. Recommendations

Recommendations on the following should be stated:

- *The need for any further supervisory measures against the manufacturer of the medicinal product or active substance.*
- *The need for any further regulatory measure for the marketing authorisation, ASMF or CEP.*

- *Need to withdraw batches of affected/defective product*
- *Need to switch patients back from alternative treatment*
- *The need for any further patient follow up or monitoring.*
- *The responsibility (e.g. EMA, Rapporteur, NCA etc) for the follow up of any regulatory or procedural commitments and requests (e.g. submission of a variation, submission of additional reports)*
- *The need for any update on the existing public communication.*
- *The need for further action based on lessons learned.*