



**Evaluation of dependence at the European
Medicines Agency (EMA)**

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Outline

- Legal basis and Guidelines for Marketing Authorisation
- Pre-authorisation Evaluation
- Post-authorisation Phase
- Illicit use of substances
- Conclusion

Legal basis & Guidelines for MA (1)

- Directive 2001/83, as amended
 - Art. 71 (2) (special prescription)
 - Art. 102 (Pharmacovigilance)
- Annexe I to the Directive (CTD)
 - *Non-clinical*: dependence potential is part of toxicology requirements, if applicable (Part I, 4.1)
 - *Clinical*: observations in clinical trials should look for signs of dependence/addiction (Part I, 5.2, g(1))

Legal basis & Guidelines for MA

- Non-clinical Guideline on dependence potential (EMA/CHMP/SWP/94227/2004)
- Clinical: dependence studies are addressed in specific therapeutic guidelines

Pre-authorisation Evaluation (1)

- **Identification of dependence potential:**
 - UN classification of narcotic and psychotropic substances
 - Pharmacological classes:
 - CNS-active drugs (see non-clinical guideline)
 - Results from pharmacological studies

Pre-authorisation Evaluation (2)

- Conditions to MA
 - *Type of prescription*: special prescription (quantitative control of use/distribution)
 - *Product Information*: warnings in SPC (section 4.2, 4.4) and Package Leaflet
 - *Packaging*: e.g. limited content

Post-authorisation Phase (1)

- Monitoring of AEs including abuse/misuse
 - Passive surveillance (e.g. spontaneous reporting)
 - Active surveillance (clinical studies)
 - Post-marketing studies
 - Pharmaco-epidemiological studies etc.
- Risk Management Plan
 - safety profile,
 - specific safety monitoring,
 - risk minimisation measures (e.g. pharmaceutical form (color), education material etc.)

Post-authorisation Phase (2)

- Regulatory measures (CHMP) if significant alteration of the R/B balance
 - Restrictions or warnings in the SPC,
 - Change of legal status
 - Suspension/withdrawal of Marketing Authorisation

Illicit use of substances (1)

EU legal basis for controlling new psychoactive substances

Council Decision 2005/387/JHA, replacing the 1997 Joint (97/396/JHA)

- scope extended to substances of established medicinal value
- involves pharmaceutical legislation (pharmacovigilance systems)
- however no provisions for controlling a substance of medical value. If public health concerns, the CHMP should evaluate the impact on the R/B and propose adequate measures.

Illicit use of substances (2)

Cooperation EMEA-EMCDDA

- Scientific support of EMEA in the risk assessment of psychotropic substances in the frame of the Council Decision
- Exchange of information/ adverse effects on misuse of psychotropic substances

Conclusion

- Before any Marketing Authorisation, the dependence potential of a medicinal product will be evaluated and further monitored (pharmacovigilance)
- EU legislation do not provide a mechanism for controlling psychotropic substances
- Classifications of drugs is given only at International and/or National level
- EU coordination by EMCDDA of the information on drug abuse collected by the Member States (National networks).
- Strengthening of the cooperation between EMEA & EMCDDA to allow a rapid and reliable exchange of information with electronic tools (Eudravigilance) is ongoing.