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SCIENCE MEDICINES HEALTH

Improving and harmonising the Summary of Product Characteristics and the conditions for use of old antibacterials

current use of legal tools and future perspectives

Best use of medicines legislation to bring new antibiotics to patients and combat the resistance problem – EMA, London 8 November 2013

Presented by: Dr. Radu Botgros
Scientific Administrator-Office of Anti-infectives and Vaccines

An agency of the European Union





One European system: two procedures for approving medicines



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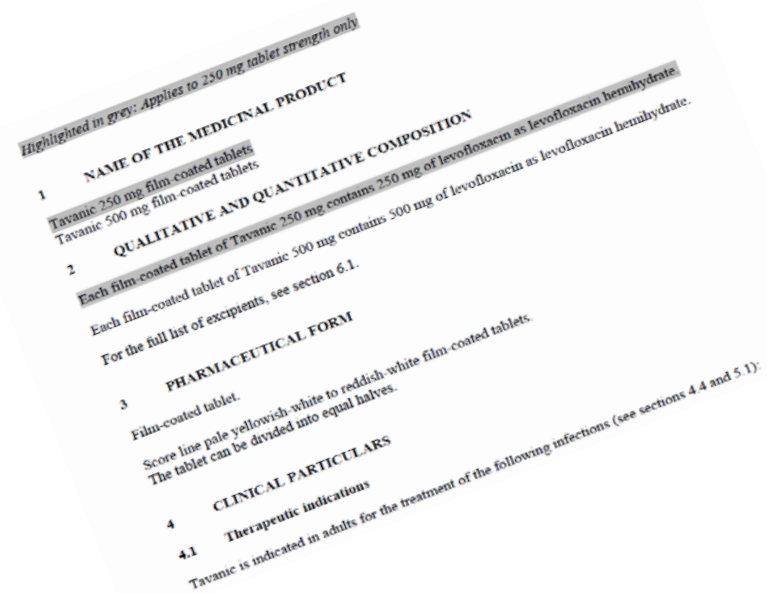
Centralised procedure



Mutual recognition and decentralised procedure



Summary of product characteristics (SmPC)



- Legal document approved as a part of the marketing authorisation
- Basis of information for healthcare professionals on how to use a medicine
- Information updated throughout the lifecycle of the product



Harmonisation of SmPCs of old antibacterials across the EU

Referral procedures

- Reg (EC) 726/2004
- Dir 2001/83/EC
- New PhV legislation:
 - Reg (EU) 1235/2010
 - Dir 2010/84/EU
- procedures used to resolve certain issues (such as concerns over the safety or benefit-risk balance) of a medicine/class of medicines and to harmonise SmPCs where necessary
- Different types:
 - "art 30" and "art 31" referrals of particular interest
 - "art 5(3)" for major tuberculostatics, art 107 (moxifloxacin)



other procedures: e.g. art 45 of the Paediatric Regulation, etc.



Article 30 of Directive 2001/83/EC ("Divergent decision referral")

- triggered when Member States have adopted different decisions over the years for some medicines (e.g. different indications, contraindications or posology) and there is a need to **harmonise** across the EU.
- article 30(1) referral: divergent decisions adopted by MSs concerning the authorisation, suspension or withdrawal of a particular medicinal product (e.g. different indications, contraindications or posology)
- *triggered by the EC, a MS, a MAH/Applicant.*
- article 30(2) referral: initiated for the same reasons when the medicinal product is on the list of the coordination group.



Article 30 triggered by European Commission

Proactive harmonisation

- Member States propose each year products for SmPC harmonisation
- CMD(h) lays down list and forwards to Commission
- Commission or MS, in agreement with EMA, may refer the product

CMD(h) subgroup (with participation of CMD(h), CHMP, EC, EMA) on SmPC harmonisation

- ➔ Mandate and criteria for selection agreed and published



Article 30 triggered by the Marketing Authorisation Holder

- ❑ voluntary triggering of a procedure by the MAH, to harmonise the Product Information of own products.
- ❑ the MAH defines the scope of the referral (which presentations, which indications to include).
- ❑ the procedure starts with a proposal for a harmonised Product Information submitted by the MAH, to be assessed by the CHMP.



Completed art. 30 referrals for antibacterials

Approved name	INN	Associated names	Opinion date	EC decision date
Augmentin	amoxicillin+clavulanic acid		19.01.2009	19.10.2009
Ciprofloxacin Bayer	ciprofloxacin		24.07.2008	07.10.2008
Tazocin	piperacillin/tazobactam	Tazobac, Tazocel, Tazonac	21.10.2010	21.02.2011
Fortum	ceftazidime	Cefortam, Glazidin, Panzim, Solvetan	21.10.2010	13.01.2011
Tienam	imipenem/cilastatin	Conet, Imipem, Primaxin, Tenacid, Zienam	06.12.2010	10.03.2011
Tavanic	levofloxacin	Tavanic and associated names	24.05.2012	31.07.2012
Zinacef	cefuroxime sodium	Curocef, Curoxim, Curoxim Monovial, Curoxima, Curoxime, Zinnat, Zinocep, Zinocep Vena	24.05.2012	10.09.2012
Zinnat	cefuroxime axetil	Cefuroxima Solasma, Cefuroxima Allen, Cefuroxima Duncan, Elobact, Nivador, Oraxim, Selan, Tilexim, Zinadol, Zipos, Zoref	24.05.2012	23.08.2012
Targocid	teicoplanin	Targocid, Teicomid	30.05.2013	pending



Example of finalised harmonisation: meropenem

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Summary **Key facts** **All documents**

The European Medicines Agency has completed a review of Meropenem and associated names. The Agency's Committee for Medicinal Products for Human Use (CHMP) has concluded that there is a need to harmonise the prescribing information for Meropenem and associated names in the European Union (EU).
The review was carried out under an 'Article 30' referral¹.
The European Commission issued a decision on 15 October 2009.

¹ Article 30 of Directive 2001/83/EC as amended, referral on the grounds of divergent decisions adopted by member States

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[What is Meropenem?](#)

[Why was Meropenem reviewed?](#)

[What are the conclusions of the CHMP?](#)

Name	Language	First published	Last updated
Questions and answers on the referral for Meropenem and associated names meropenem powder for solution for injection or infusion 500 mg and 1 g - Final	EN = English		11/12/2009

 Current status:
European
Commission final
decision

Harmonisation involves:

- ✓ review of evidence to support efficacy,
- ✓ replacement of older broad indications that are no longer used with more specific indications based on the available data and
- ✓ a review of the posology in all age groups.
- ✓ Section 5.1 (describing the microbiological properties) is also updated.

Areas harmonised:

- 4.1 therapeutic indications
- 4.2 posology and method of administration
- 4.3. contraindications
- 4.4 special warnings and precautions for use



Article 31 of Directive 2001/83/EC ("community interest referral")

- triggered when the public health interest of the Community is involved, following concerns relating to the **quality, safety or efficacy** of a medicine/class of medicines which is/are on the market in the EU.
- *triggered by the EC, a MS, a MAH/Applicant.*
- Scope can relate to a range of products or a therapeutic class.
- Referral type used for norfloxacin (completed) and colistin (ongoing)



Limitations of regulatory actions

- Number of procedures per year limited by the capacity of the EU regulatory network
- Different patterns of prevalence and resistance of infectious diseases
- Differences in clinical practice and use of certain antibiotics
- Harmonisation and modernisation of SmPC cannot and should not replace treatment guidelines and antibiotic stewardship



CHMP/IDWP proposal for prioritisation of harmonisation of old antibacterials SmPCs to CMDh (2011)

1. vancomycin	9. erithromycin
2. amoxicillin	10. clindamycin
3. ampicillin	11. rifampicin
4. phenoxymethylpenicillin	12. gentamicin
5. benzylpenicillin	13. tobramycin
6. cefotaxime	14. amikacin
7. azithromycin	15. trimethoprim/sulphamethoxazole
8. clarithromycin	16. metronidazole
17. doxycycline	



Conclusions

Improvement of SmPCs of „old“ antibacterials:

- Important regulatory tool which ensures the provision of the same updated information to all EU healthcare professionals
- Opportunity to modernise the product information
- Should not replace treatment guidelines/antibiotic stewardship
- Prioritisation of the exercise is key, in view of the limited resources.
- Harmonisation of SmPCs by referrals should continue and should be strengthened



BACK-UP SLIDES



Article 30

1. If *two or more applications* submitted in accordance with Articles 8, 10, 10a, 10b, 10c and 11 have been made for marketing authorisation for a particular medicinal product, and if Member States have adopted *divergent decisions* concerning the authorisation of the medicinal product or its suspension or revocation, a Member State, the Commission or the applicant or the marketing authorisation holder may refer the matter to the Committee for Medicinal Products for Human Use, hereinafter referred to as "the Committee", for the application of the procedure laid down in Articles 32, 33 and 34.



Article 30

2. In order to promote **harmonisation of authorisations for medicinal products authorised in the Community**, Member States shall, each year, forward to the coordination group **a list of medicinal products for which a harmonised summary of product characteristics should be drawn up**. The coordination group shall lay down a list taking into account the proposals from all Member States and shall forward this list to the Commission. The Commission or a Member State, in agreement with the Agency and taking into account the views of interested parties, may refer these products to the Committee in accordance with paragraph 1.



Article 31

1. The Member States or the Commission or the applicant or the marketing authorisation holder shall, in specific cases where the interests of the Community are involved, refer the matter to the Committee for application of the procedure laid down in Articles 32, 33 and 34 before any decision is reached on a request for a marketing authorisation or on the suspension or revocation of an authorisation, or on any other variation to the terms of a marketing authorisation which appears necessary, in particular to take account of the information collected in accordance with Title IX. The Member State concerned or the Commission shall clearly identify the question which is referred to the Committee for consideration and shall inform the applicant or the marketing authorisation holder. The Member States and the applicant or the marketing authorisation holder shall supply the Committee with all available information relating to the matter in question.



Article 31

2. Where the referral to the Committee concerns a range of medicinal products or a therapeutic class, the Agency may limit the procedure to certain specific parts of the authorisation. In that event, Article 35 shall apply to those medicinal products only if they were covered by the authorisation procedures referred to in this Chapter.