HARP
(Harmonisation of RMP Project)

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HaRP

- Potřeba HaRP- historické pozadí
- Co je HaRP
- Metodologie
- Role zástupců farmaceutického průmyslu
- Výhled do budoucna

Potřeba HaRP – historické pozadí

- Art 8 (3) (iaa) Directive 2001/83/EC - Povinnost předkládání RMP

- -> Leden 2014 tabulka obsahující **safety concerns** z RMP odsouhlasených v registračních procedurách

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safety concerns per approved Risk Management Plan (RMP) of active substances per pr

Doc. Ref: CMDh/330/2015, Rev.19 January 2019

Note: The green marked products concern dossiers authorised under Article 8.3 legal basis

Active substance	Brand name	MRP/DCP number	Legal basis	MAH	RMS or MS (in case of strictly nationally authorised product)	RMP
Testosterone	Testavan; Testarzon	NL/H/3958/001/DC	icle 8(3), full-mixed doss	Ferring BV	NL	Version 1.0 dated 15.12.2016
Tacrolimus	Tacrolimus Accord 0.1%	UK/H/5921/002/DC	Generic (Article 10(1))	Accord Healthcare Limited	UK	Version 5.0 dated 25.10.2017
Tadalafil	Tadalafil 2.5 mg, 5 mg, 10 mg, 20 mg Film-coated Tablets	UK/H/5902/001-004/DC	Generic (Article 10(1))	Accord Healthcare Limited	UK	Version 3.0 dated 19.02.2016
	Tadalafil-ratiopharm 5 mg;10mg;20mg	DE/H/4013/002-004/E001 DE/H/4574/001-004/DC DE/H/4575/001-004/DC DE/H/4629/001-003/DC	Generic (Article 10(1))	Teva Pharma B.V.	DE	Version 1.0 dated 09.06.2016 Version 2.1 dated 18.01.2017
	Tadalafil Farmaprojects (in RMS)	UK/H/6272/001-004/DC	Generic (Article 10(1))	Farmaprojects, S.A.U (in RMS)	UK	Version 2.0 dated 26.01.2017
	Tadagis	SI/H/0166/001-004/DC	Generic (Article 10(1))	Krka, d.d., Novo mesto	SI	Version 1.1 dated 17.08.2016
	N/A	UK/H/6186/001-004/DC	Generic (Article 10(1))	Bristol Laboratories Ltd.	UK	Version 1.1 dated 19.08.2016
	Tadalafil 2.5 mg, 5 mg, 10 mg, 20 mg Film-coated Tablets	UK/H/5902/001-004/E/0[illegible]	Generic (Article 10(1))	Accord Healthcare Limited	UK	Version 3.0 dated 19.02.2016
	Tadalafil Sandoz 2,5 mg, filmomhulde tabletten Tadalafil Sandoz 5 mg, filmomhulde tabletten Tadalafil Sandoz 10 mg, filmomhulde tabletten Tadalafil Sandoz 20 mg, filmomhulde tabletten	NL/H/3612/001-004	Generic (Article 10(1))	Sandoz B.V.	NL	Version 1.5 dated 27.10.2016
Quator		NL/H/3613/001-004	Generic (Article 10(1))	Sandoz B.V.	NL	Version 1.5 dated 27.10.2016

494 Léčivých látek
~ 1478 léčivých přípravků
(březen 2019)

Products overview | Abacavir | abacavir_lamivudine | Acebutolol | acetylcysteine | acetylsalicylic acid | acetylsalicyl acid_at(...

Potřeba HaRP

- Nekompletní tabulka na stránkách CMDh
- Nekonzistence mezi generiky i referenčními přípravky
- Rozdíly mezi LP v rámci EU
- GVP V rev. 2
- -> Pracovní zátěž přetrvává

HaRP Harmonisation of RMP Procedure/Project

Co je HaRP

- Projekt pro harmonizaci RMP (safety concerns)
  - ✓ LP s platným rozhodnutím o registraci
  - ✓ Stejné účinné látky
  - ✓ S různými RMP
- V současnosti 27 členů z 16 zemí, Předsedá NL

HARP: 2 domény

Doména 1

Příprava **list of safety concerns** generických přípravků pro léčivé látky, u nichž brzy vyprší ochrana dat

Doména 2

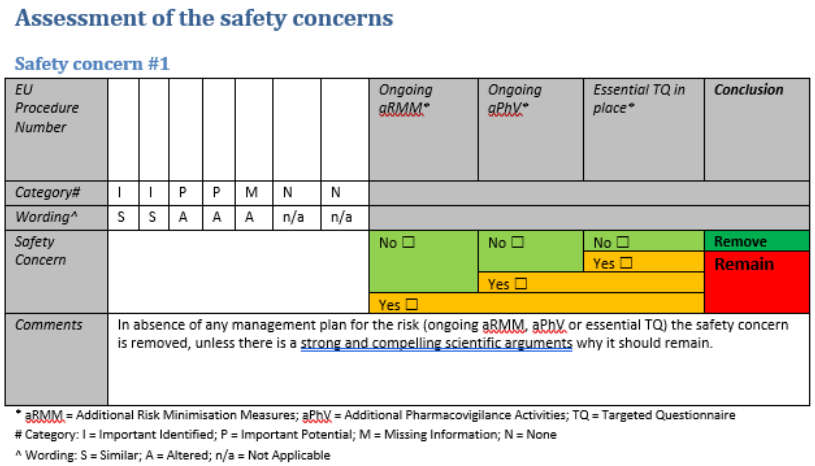
Revize již existující tabulky na stránkách CMDh

HaRP Doména 2

- Léčivé látky pro něž není inovativní přípravek na trhu, nebo nemá RMP
- Tabulka na stránkách CMDh je přezkoumávána a informace, které obsahuje, jsou základem pro hodnocení RMP HaRPem
- Do této domény nejsou zahrnuty látky, které nejsou v seznamu na stránkách CMDh

Metodologie hodnocení safety concerns

- Členové skupiny HaRP navrhují jednotlivé látky k hodnocení. Na pravidelných schůzkách jsou tyto návrhy schvalovány a poté hodnoceny.
- K hodnocení využívána šablona, vytvořena pro potřeby skupiny HaRP.



Assessment of the safety concerns

Safety concern #1

EU Procedure Number								*Ongoing aRMM**	*Ongoing aPhV**	*Essential TQ in place**	***Conclusion***
Category#	I	I	P	P	M	N	N				
*Wording^*	S	S	A	A	A	n/a	n/a				
Safety Concern								No ☐	No ☐	No ☐	**Remove**
										Yes ☐	**Remain**
									Yes ☐		
								Yes ☐			
Comments	In absence of any management plan for the risk (ongoing aRMM, aPhV or essential TQ) the safety concern is removed, unless there is a strong and compelling scientific arguments why it should remain.										

* aRMM = Additional Risk Minimisation Measures; aPhV = Additional Pharmacovigilance Activities; TQ = Targeted Questionnaire

Category: I = Important Identified; P = Important Potential; M = Missing Information; N = None

^ Wording: S = Similar; A = Altered; n/a = Not Applicable

Assessment of the safety concerns

Safety concern #1

EU Procedure Number								*Ongoing aRMM**	*Ongoing aPhV**	*Essential TQ in place**	*Conclusion*
Category#	I	I	P	P	M	N	N				
*Wording^*	S	S	A	A	A	n/a	n/a				
Safety Concern								No ☐	No ☐	No ☐	Remove
										Yes ☐	Remain
									Yes ☐		
								Yes ☐			
Comments	In absence of any management plan for the risk (ongoing aRMM, aPhV or essential TQ) the safety concern is removed, unless there is a strong and compelling scientific arguments why it should remain.										

* aRMM = Additional Risk Minimisation Measures; aPhV = Additional Pharmacovigilance Activities; TQ = Targeted Questionnaire

Category: I = Important Identified; P = Important Potential; M = Missing Information; N = None

^ Wording: S = Similar; A = Altered; n/a = Not Applicable

Prostate cancer

EU Procedure Number	NL/H/3958/001/DC	*Ongoing aRMM**	*Ongoing aPhV**	*Essential TQ in place**	***Conclusion***
Category#	P				
*Wording^*	S				
Safety Concern	Prostate cancer	No ☒ Yes ☐	No ☒ Yes ☐	No ☒ Yes ☐	**Remove**
Comments	**Remove** While testosterone replacement treatment may increase serum prostate-specific antigen levels in some men, it often remains within clinically acceptable ranges, and has not been shown to increase the risk of prostate cancer (PSUSA/00002908/201512). The topic is under routine monitoring and will be presented in the next PSURs. Prostate cancer is listed as contraindication and sufficient warnings/precautions are present in product information.				

* aRMM = Additional Risk Minimisation Measures; aPhV = Additional Pharmacovigilance Activities; TQ = Targeted Questionnaire

Category: I = Important Identified; P = Important Potential; M = Missing Information; N = None

^ Wording: S = Similar; A = Altered; n/a = Not Applicable

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Disturbances of liver function

EU Procedure Number	DE/H/4587/001/DC DE/H/4623/001/DC	DE/H/3103/001/DC	*Ongoing aRMM**	*Ongoing aPhV**	*Essential TQ in place**	***Conclusion***
Category#	I	I				
*Wording^*	S	A				
Altered wording	Disturbances of hepatobiliary function		No ☒ Yes ☐	No ☒ Yes ☐	No ☒ Yes ☐	**Remove**
Comments	**Remove** No aRMM is in place concerning this risk. The medicinal product is contraindicated in patients with severe hepatic impairment. In addition, an advice how to handle liver disturbances is included in section 4.4 of the originator SmPC. Routine PhV is considered sufficient to monitor these risks. -->Risks for which there are no additional pharmacovigilance activities and/or additional risk minimisation measures can be removed from the safety specification in line with the updated GVP V Rev. 2.0.					

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Venous thromboembolism

EU Procedure Number	DE/H/4587/001/DC DE/H/4623/001/DC	DE/H/3103/001/DC	*Ongoing aRMM**	*Ongoing aPhV**	*Essential TQ in place**	***Conclusion***
Category#	I	I				
*Wording^*	S	S				
Altered wording			No ☐ Yes ☒	No ☒ Yes ☐	No ☒ Yes ☐	**Remain**
Comments	**Remain** Additional risk minimisation measures (check-list for prescribers and patient information card) are in place, therefore venous thromboembolism should remain in the summary of safety concerns.					

* aRMM = Additional Risk Minimisation Measures; aPhV = Additional Pharmacovigilance Activities; TQ = Targeted Questionnaire

Category: I = Important Identified; P = Important Potential; M = Missing Information; N = None

^ Wording: S = Similar; A = Altered; n/a = Not Applicable

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Recommendation*

Safety specifications	Additional PhV activities	Additional Risk minimisation measures	Essential Targeted Questionnaires	specific clinical actions
Important Identified risk				
Venous thromboembolism		Checklist for prescribers; Patient information card		
Arterial thromboembolism		Checklist for prescribers; Patient information card		
Important potential risk				
None				
Missing information				
None				

Jednání se zástupci farmaceutického průmyslu

- Předložení prvních hodnotících zpráv AESGP (Association of the European Self-Medication Industry)

Hodnocené látky (25):

Almotriptan, alprazolam, amlodipine, bemiparin, bisoprolol, calcium carbonate, cetirizine, colchicine, donepezil, etoposide (for infusion), fluorouracil (systemic use), gemcitabine, haloperidol (oral solution), hyoschine butylbromide, macrogol 3350, sodium chloride, sodium hydrogen carbonate, potassium chloride, melphalan, menotrophin, montelukast, pantoprazole, rupatadine, testosterone (transdermal/topical), vilnorebine (for infusion).

Výhled do budoucna

- PhV WSP WP duben 2019

Pharmacovigilance Work Sharing Procedures Working /Party

- Schválení CMDh
- Publikace s cover note na stránkách CMDh.

  ~červen/červenec?
- Jednání s držiteli originálních léčivých přípravků

Užitečné odkazy

- RMP - Safety concerns na stránkách CMDh

http://www.hma.eu/464.html

Děkuji za pozornost

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