Prapassorn Thanaphollert, Thailand

- Former Director of Bureau of Drug Control, Advisor to Thai Food and Drug Administration, Ministry of Public Health Thailand

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20 January 2015, Sheraton Maria Isabel Hotel & Towers, Mexico City, Mexico

Unwanted immunogenicity of EPO products and related clinical problems (PRCA); the experience in Thailand

Prapassorn Thanaphollert, BS

20 January 2015

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Unwanted immunogenicity of EPO products and related clinical problems (PRCA); the experience in Thailand

Prapassorn Thanaphollert

Thai FDA Adviser, Former Director of Bureau of Drug Control

First Latin American Educational Workshop on Similar Biotherapeutic Products – regulatory approval, pharmacovigilance and risk management

20 January 2015, Mexico City

Outline

- Background information: Thailand experience
- PRCA known immunogenicity – Worldwide
- Attempt from healthcare professionals
- Thai FDA's risk management strategy
- Regulatory pathway enforcement
- Challenges

Background information: Thailand experience

- MAA of EPO products were granted for more than 20 years
- No specific regulatory requirements of EPO and non-existing Biosimilar guideline
- EPO products are widely used in Thailand to treat patients with chronic renal failure (CRF) by SC route to ease self administration at home

Background information: Thailand experience

- Thai FDA received increasing number of PRCA immunogenicity report cases confirmed from administration of EPO via SC route
- Thai FDA implemented administrative order applicable to all MAH of EPO based on recommendation from Subcommittee on ADR to add warning statement of expected PRCA from SC use on the labels (package insert and box)
- Incidences of reported PRCA cases in 2013 app. 50 times more than other countries worldwide

PRCA known immunogenicity – Worldwide

The New England Journal of Medicine

VOLUME 346 FEBRUARY 14, 2002 NUMBER 7

PURE RED-CELL APLASIA AND ANTIERYTHROPOIETIN ANTIBODIES IN PATIENTS TREATED WITH RECOMBINANT ERYTHROPOIETIN

NICOLE CASADEVALL, M.D., JOELLE NATAF, M.D., BÉATRICE VIRON, M.D., AMIR KOLTA, M.D., JEAN-JACQUES KILADJIAN, M.D., PHILIPPE MARTIN-DUPONT, M.D., PATRICK MICHAUD, M.D., THOMAS PAPO, M.D., VALÉRIE UGO, M.D., IRÈNE TEYSSANDIER, B.S., BRUNO VARET, M.D., AND PATRICK MAYEUX, PH.D.

Attempt from healthcare professionals

- Voluntary implementation of Thailand EPO registry in most of medical schools hospitals under research protocol
- Objective: to detect the incidence of PRCA cases and loss of effect in Thailand
- Identification and report of switching brand of EPO products where applicable
- Preliminary report showed similar pattern of PRCA immunogenicity from SC route regardless of origin

Thai FDA's risk management strategy

- Regulatory approaches:

➢ Short term: Seek cooperation from healthcare professionals to prescribe EPO to be administered via IV rather than SC route to avoid/minimize PRCA

➢ Long term: Regulatory enforcement of Ministerial Order No. 942/2556

Regulatory pathway enforcement

- Ministerial Ordinance No.942/2556 related to mandatory requirements of re-evaluation of all MAA granted to EPO alpha and beta to justify quality, safety and efficacy aspects

  - Issued date: 26 Jun 2013
  - Effective date: 17 Jan 2014 MAH shall update CTD on Quality and submit RMP
  - Effective date: 17 November 2014 MAH shall update CTD on Non-Clinical and Clinical

- MAA granted to 17 brands of EPO alpha and 1 EPO beta registered as stand alone (all strengths and presentations).
- MAV:
  - EPO alpha: 11 brands submitted as stand alone and 6 brands as Biosimilar (???)
  - EPO beta: 1 brand as stand alone

Centralized procurement of EPO by NHSO (National Health Security Office)

Total demand (EPO-Alpha)	Vials/Year
Under universal coverage fund	1,740,000

Challenges

- Existing EPO products
  - To review MAV under limited resources (less experts, no fee, short timeline)
  - To ensure quality by lab testing
  - To meet high expectation of safety and efficacy of EPO from healthcare professionals and patients
  - To handle with unmet medical needs

Challenges

- New EPO products
  - To cope with new applications under same limitation

Thank you for your attention!