# Optimising the use of the EURD list – the key to the single assessment

Menno van der Elst
Alternate PRAC Member
Medicines Evaluation Board

Periodic Safety Update Report Information Day
28 October 2016 | London, UK

# Disclaimer

The views and opinions expressed in the following PowerPoint slides are those of the individual presenter and should not be attributed to Drug Information Association, Inc. (“DIA”), its directors, officers, employees, volunteers, members, chapters, councils, Special Interest Area Communities or affiliates, or any organisation with which the presenter is employed or affiliated.

These PowerPoint slides are the intellectual property of the individual presenter and are protected under the copyright laws of the United States of America and other countries. Used by permission. All rights reserved. Drug Information Association, DIA and DIA logo are registered trademarks or trademarks of Drug Information Association Inc. All other trademarks are the property of their respective owners.

# Outline of this presentation - optimising use of the EURD list

- EURD list – the main aspects and principles
- Granularity and Periodicity Advisory Group (GPAG)
- EURD list – unique aspects key to the single assessment
- How is the EURD list used to support the PSUSA procedure?
- Collaboration to optimise the EURD list
- Short term and long term initiatives to optimise utilisation of the EURD list

# EURD list – the main aspects and principles

- General principles:
  - 1 entry = (1) substance ≠ 1 product
  - entry should cover product(s) authorised in more than 1 MS
  - by default no PSUR submissions for products authorised under Articles 10(1), 10a, 14 and 16a of Directive 2001/83/EC as amended
  - risk based approach when defining PSUR cycle plus DLP and/or when requiring PSUR submission for Article 10(1), 10a, 14 and 16a products
  - international harmonisation respected

  - more than 3,400 entries
  - list maintained by EMA
  - Granularity and Periodicity Advisory Group (GPAG) provides advice to PRAC

# Granularity and Periodicity Advisory Group (GPAG)

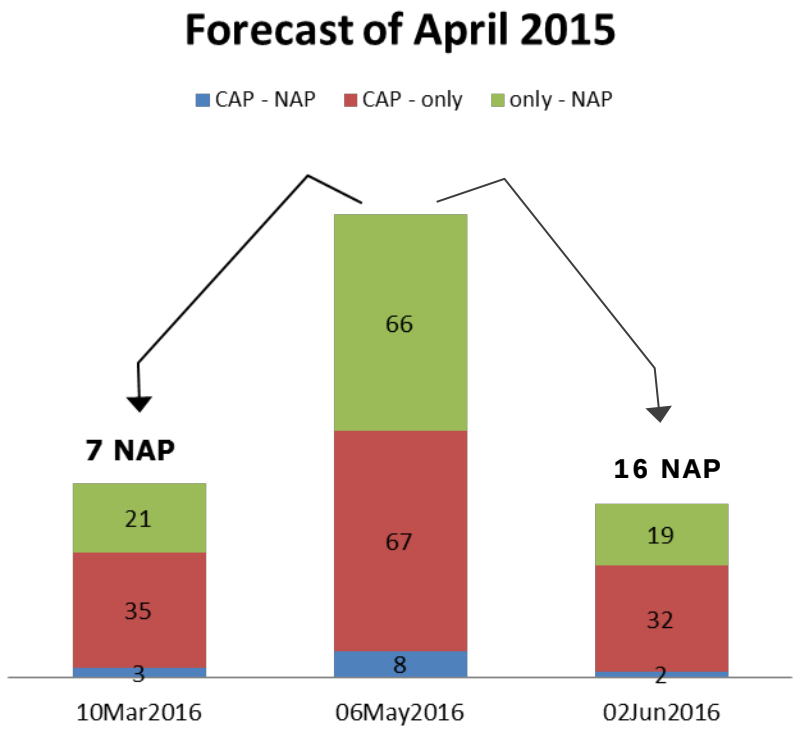
- Group composed of EMA staff, PRAC delegate, CMDh delegate, and NCA representatives. Ad-hoc consultation of other experts in the network
- Monthly meetings (in sync with monthly EURD list updates)
- GPAG  advises PRAC
- Mandate and annual work programme adopted by PRAC:
  - Monthly requests to update the EURD List
  - Estimation of workload related to single assessment procedures and monitoring the capacity of the network
  - Scope of the PSUR single assessment procedure and EURD scientific grouping
  - Develop guidance and criteria to set the periodicity of single assessment procedures

# EURD list – unique aspects key to the single assessment

- Two main variables utilised to optimise the single assessment:
  - Granularity of the EURD list entries – splitting or merging entries
    - Important since PSUSA outcome is applicable to all products in scope – consistent recommendations for similar products
  - Assigning appropriate PSUR cycle
    - Risk proportional approach: balancing public health needs and available capacity in the EU regulatory network
    - (Maturity) of the safety profile and robustness of the B/R balance are leading
    - Available resources allocated were most needed and useful

# How the EURD list is used to support the PSUSA procedure

- Review of workload:
  - Avoiding (very) high peaks in certain months – shifting DLPs when possible
  - Critical review of requests for PSUR submission for Article 10(1), 10a, 14 and 16a products initially made in 2010-2012



# How the EURD list is used to support the PSUSA procedure

- Scope of the PSUR single assessment procedure and EURD scientific grouping
  - Operational aspect: linking entry and products in Article 57 database
  - Scientific grouping: list follows general principle (entry=substance) and amendments are made where appropriate

# Granularity as tool to support single assessment

| | | | | |
|---|---|---|---|---|
| glimepiride / pioglitazone hydrochloride, metformin / pioglitazone, pioglitazone | 13-10-2000 | 1 year | 31-7-2016 | 9-10-2016 |

| | | | | |
|---|---|---|---|---|
| alprostadil (erectile dysfunction) | 23/07/1981 | 5 years | 31-1-2016 | 30-4-2016 |
| alprostadil (indicated in peripheral arterial occlusive diseases) | 28/11/1984 | 5 years | 31-7-2017 | 29-10-2017 |
| alprostadil (patency of the ductus arteriosus) | 23-7-1981 | 3 years | 22-7-2018 | 20-10-2018 |

| | | | | |
|---|---|---|---|---|
| mycophenolate mofetil | 3-5-1995 | 1 year | 2-5-2016 | 11-7-2016 |
| mycophenolic acid (apart from mycophenolate mofetil) | 14-2-1996 | 1 year | 2-5-2016 | 11-7-2016 |

| | | | | |
|---|---|---|---|---|
| moxifloxacin (systemic use) | 31-5-1990 | 3 years | 31-5-2016 | 29-8-2016 |
| moxifloxacin (topical ophthalmic use) | 31/05/1999 | 5 years | 31-5-2016 | 29-8-2016 |

# Periodicity as tool to support single assessment

- Example: revision of PSUR cycle seasonal influenza vaccines
  - 1-Yearly PSURs covering from 16 March to 15 March (instead of 4 / 8 monthly):
  - Submission in May/June -> PRAC recommendation in October at start of influenza vaccination season
  - Period will fully cover the previous southern hemisphere season (March-September) and the northern hemisphere vaccination season (Oct - Feb/March)
  - Any early safety issues arising from the next  southern hemisphere season could be included as late breaking information (Submission date: May/June),
  - Additional data from the southern hemisphere could also be requested within the 30 days commenting phase (by mid September)

# Collaboration to optimise the EURD list

- Via MAH input on substance level, but also on group level

- Example: allergens have been removed due to issues linking entries to products
- Re-introduction of allergens: individual substances to return to EURD list on risk based approach
- Entries have been formulated to cover specifically the 3 MRP products identified
- Ongoing consolidation of the proposals submitted by 2 MAHs

# Long term initiative to optimise utilisation of the EURD list

- Aim is to develop guidance and criteria to set the periodicity of single assessment procedures
  - define general rules on periodicity based on scientific judgement taking into account the B/R profile of substances and other regulatory tools to monitor and review the safety and the benefit-risk profile of a product and/or substance(s).
  - PSUR cycles and DLPs to be defined on a risk-based approach
  - based on criteria provided by GVP VII, including information on risks or benefits, patient populations, potential for misuse, medication error, risk of overdose or dependency, size of the clinical safety database and post marketing exposure to the medicinal product.
  - use of readily available data (e.g. from EudraVigilance) to support decision making for determining PSUR frequencies in the EURD list.

# Long term initiative to optimise utilisation of the EURD list

- Currently taking stock of what information is readily available: signal detection outcomes, referrals, PASS, RMP, EudraVigilance data etc.
- Next step will be to determine what information/variables to include in a model
- Feasibility do build and operate a model
- Testing of model(s) for substances in certain different therapeutic areas
- Final aim is to develop a tool to support decision making on changing PSUR frequencies.

- Optimising the use of the EURD list to support the single assessments
  - General principles remain leading
  - Granularity and periodicity are key variables to optimise the single assessment
  - GPAG to support PRAC with both monthly maintenance and more long term strategic advice
  - Joint effort – both among regulators and with support from industry

# Ask