Introducing the Post-Licensing Department at the Medicines Authority

The PLD Team

- **Director:** Prof John J Borg
- **Paediatric assessor:** Dr Herbert Lenicker
- **Safety Assessor:** Amy Tanti
- **Pharmacists:** Benjamin Micallef
  Francesca Schembri

Trainees

Responsibilities in a nutshell

- Pharmacovigilance
- Advertising

At a management level, PLD co-ordinates

- Approval of clinical trials
- Compassionate use programs
- Scientific Advice

Staff Involved in

- Safety/Efficacy assessments
- Centralised rapporteurship, RMS and National Assessments

Background

❖All medicinal product require a **Marketing Authorisation**

❖Independent assessments of:

- ❖**Quality**
- ❖**Safety**
- ❖**Efficacy**

❖Premarketing efficacy and provisional safety data come from **RCTs**

❖The safety information at the time of first marketing has uncertainties

❖Regulators and marketing authorisation holders MUST maintain vigilance for safety issues that emerge with **widespread real world** use of a medicinal product.

Pharmacovigilance.

Definition of Pharmacovigilance

"The science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine-related problem (WHO 2002)

The **objectives of pharmacovigilance** within the EU are:

• Preventing harm from adverse reactions in humans arising from the use of authorised medicinal products within or outside the terms of marketing authorisation or from occupational exposure; and

• Promoting the safe and effective use of medicinal products, in particular through providing timely information about the safety of medicinal products to patients, healthcare professionals and the public

Legal basis of Pharmacovigilance in Malta

❖**Directive 2001/83/EC**

❖**Directives 2010/84/EU** and **2012/26/EU**

Transposed:

❖ **Medicines Act of 2003**

❖ Subsidiary Legislation to the Medicines Act (**S.L.458.35 as amended**), Pharmacovigilance Regulations.

Also

❖**Commission Implementing Regulation (EU) No 520/2012** on the performance of pharmacovigilance activities

ADR Reporting

Introduced in May 2004

ADR system remain the primary means of data collection for post-authorisation safety surveillance of medicinal products in Malta and world.

But what is an ADR?

Adverse Drug Reaction (ADR)

A response[a] to a medicinal product which is noxious and unintended [DIR 2001/83/EC Art 1(11)]

*a. Response in this context means that a **causal** relationship between a medicinal product and an adverse event is at least a reasonable possibility.*

Adverse reactions may arise from use of the product within or outside[b] the terms of the marketing authorisation or from occupational exposure [DIR 2001/83/EC Art 101(1)]

b. Conditions of use outside the marketing authorisation include off-label use, overdose, misuse, abuse and medication errors.

Serious adverse reaction

An adverse reaction which results in death, is life-threatening[a], requires in-patient hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, or is a congenital anomaly/birth defect [DIR 2001/83/EC Art 1(12)] (2)

(a. Life-threatening in this context refers to a reaction in which the patient was at risk of death at the time of the reaction; it does not refer to a reaction that hypothetically might have caused death if more severe (see ICH-E2D Guideline))

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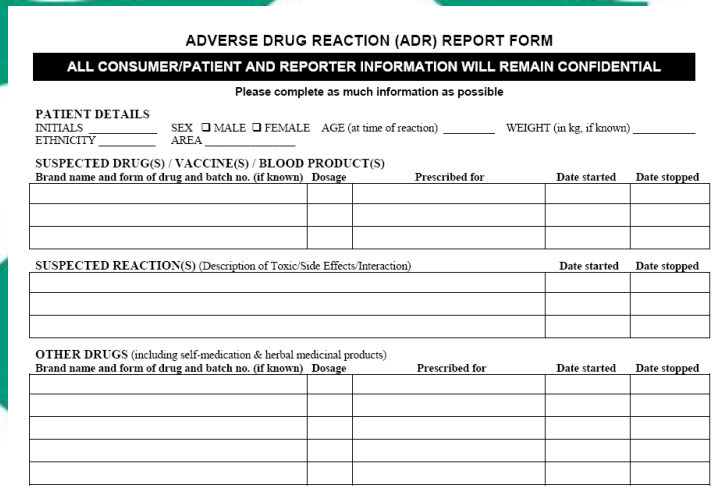
Medication error

Any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in control of the health-care professional, patient or consumer. (National Coordinating Council for Medication Error Reporting and Prevention).

The ADR Form



ADVERSE DRUG REACTION (ADR) REPORT FORM

ALL CONSUMER/PATIENT AND REPORTER INFORMATION WILL REMAIN CONFIDENTIAL

Please complete as much information as possible

PATIENT DETAILS

INITIALS _____ SEX ❑ MALE ❑ FEMALE AGE (at time of reaction) _____ WEIGHT (in kg, if known) _____
ETHNICITY _____ AREA _____

SUSPECTED DRUG(S) / VACCINE(S) / BLOOD PRODUCT(S)

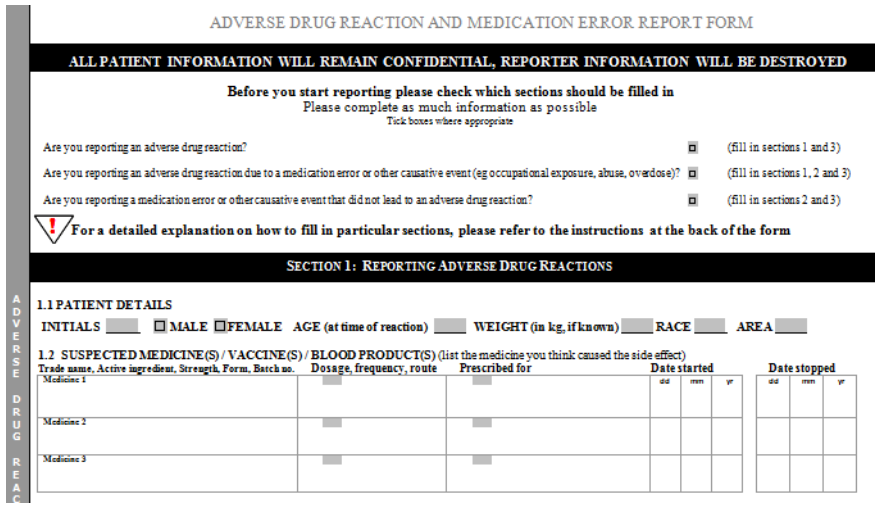
Brand name and form of drug and batch no. (if known)	Dosage	Prescribed for	Date started	Date stopped

SUSPECTED REACTION(S) (Description of Toxic/Side Effects/Interaction)

	Date started	Date stopped

OTHER DRUGS (including self-medication & herbal medicinal products)

Brand name and form of drug and batch no. (if known)	Dosage	Prescribed for	Date started	Date stopped



ADVERSE DRUG REACTION AND MEDICATION ERROR REPORT FORM

ALL PATIENT INFORMATION WILL REMAIN CONFIDENTIAL, REPORTER INFORMATION WILL BE DESTROYED

Before you start reporting please check which sections should be filled in
Please complete as much information as possible
Tick boxes where appropriate

Are you reporting an adverse drug reaction? ❑ (fill in sections 1 and 3)
Are you reporting an adverse drug reaction due to a medication error or other causative event (eg occupational exposure, abuse, overdose)? ❑ (fill in sections 1, 2 and 3)
Are you reporting a medication error or other causative event that did not lead to an adverse drug reaction? ❑ (fill in sections 2 and 3)

For a detailed explanation on how to fill in particular sections, please refer to the instructions at the back of the form

SECTION 1: REPORTING ADVERSE DRUG REACTIONS

ADVERSE DRUG REAC

1.1 PATIENT DETAILS

INITIALS ____ ☐ **MALE** ☐ **FEMALE** **AGE (at time of reaction)** ____ **WEIGHT (in kg, if known)** ____ **RACE** ____ **AREA** ____

1.2 SUSPECTED MEDICINE(S) / VACCINE(S) / BLOOD PRODUCT(S) (list the medicine you think caused the side effect)

Trade name, Active ingredient, Strength, Form, Batch no.	Dosage, frequency, route	Prescribed for	Date started dd	Date started mm	Date started yr	Date stopped dd	Date stopped mm	Date stopped yr
Medicine 1								
Medicine 2								
Medicine 3								

- New ADR form. Redesigned and launched in 2013
- Combines ADR and ME reporting into one form
- Added Information sheet and Decision Tree

How to Report

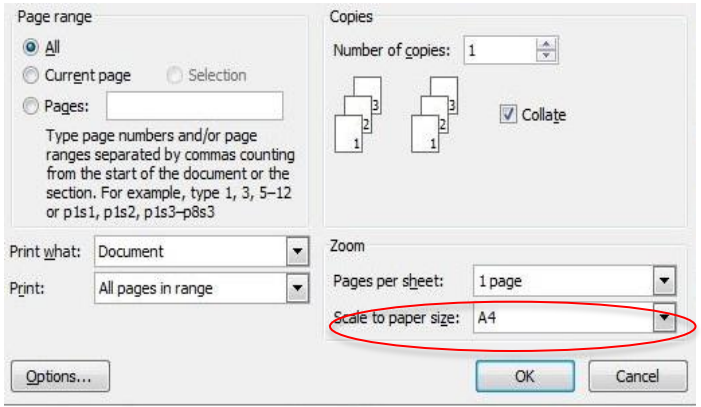
- Print form* and Fill in ink. Link to paper form: **http://www.medicinesauthority.gov.mt/adrportal** - Send it to Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000

Or

- Fill in word and Email to: **postlicensing.medicinesauthority@gov.mt**

Or

- Send to the Marketing Authorisation holder of that product. Details on the MAH may be found on the PIL inside every box



*Print to Scale A4

Signal Detection

Table 1. Calculation of PRRs

	Drug of interest	All other drugs in database
Reaction(s) of interest	a	b
All other reactions	c	d

EudraVigilance (European Union Drug Regulating Authorities Pharmacovigilance)

EU system for monitoring the safety of medicines.

Its components facilitate electronic reporting of suspected adverse reactions related to medicines and the effective analysis of data.

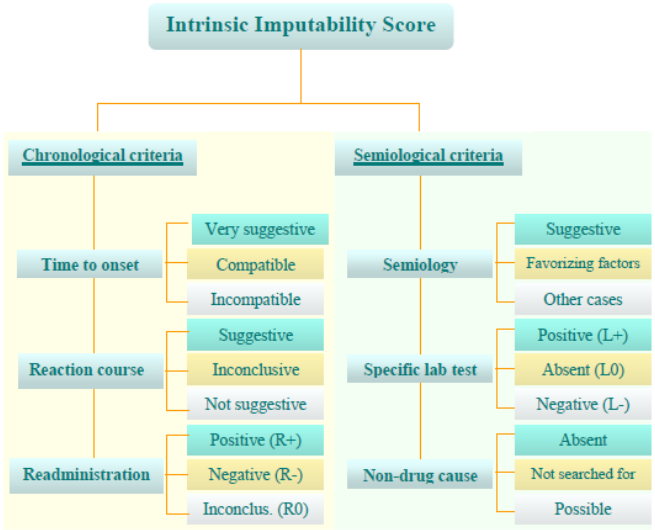
This enables the detection of potential safety issues.

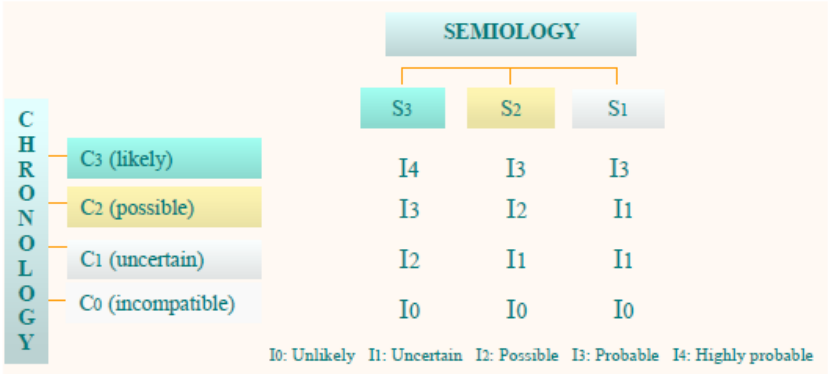
Causality Assessment

French method;

- French regulatory agency since 1977
  - Separates an intrinsic imputability (possible cause between drug and clinical event) from an extrinsic imputability (bibliographical data) using seven criteria (three chronological and four semiological) in two different tables.

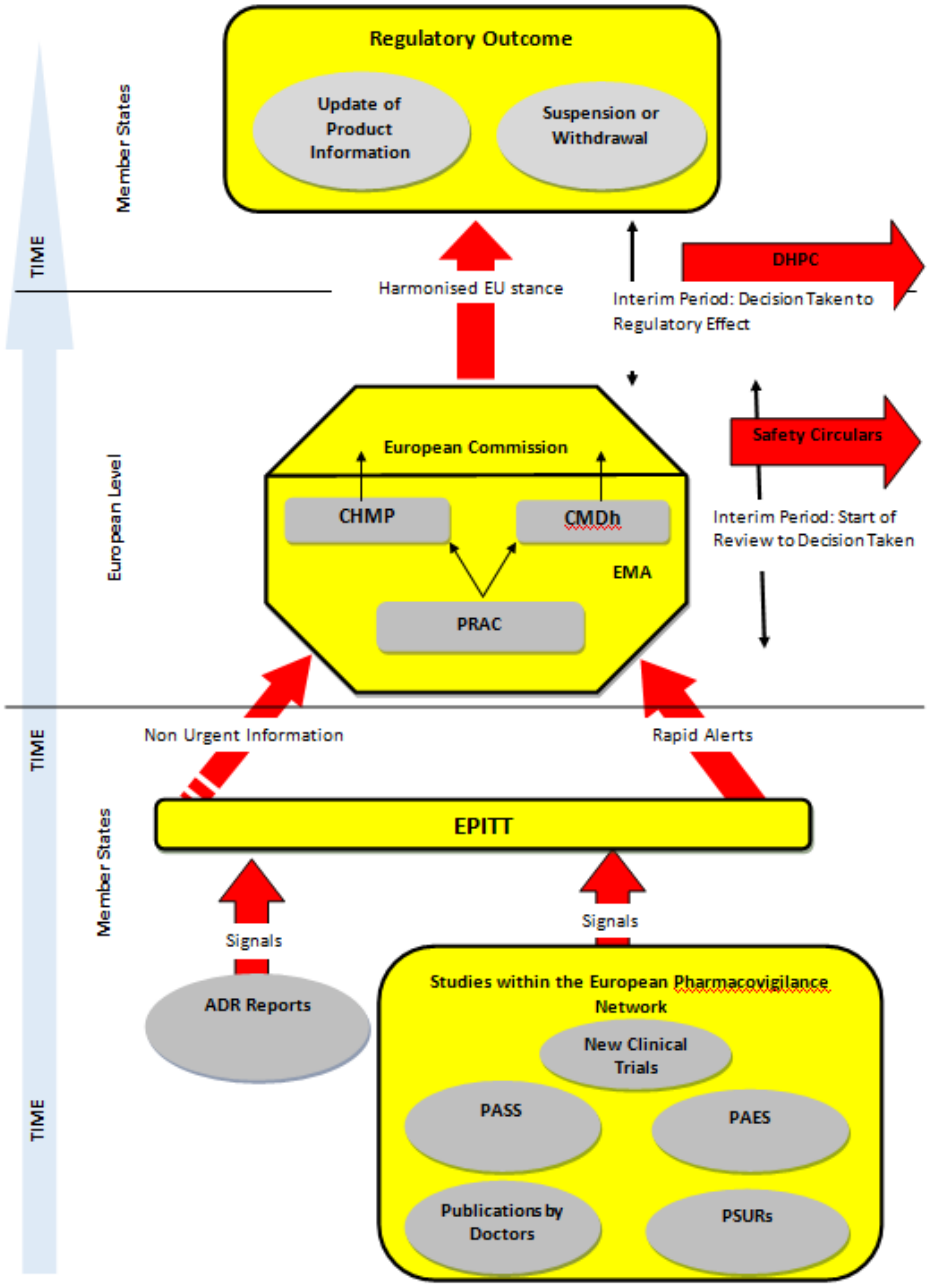
The official French method of causality assessment





Outcomes of ADR reporting – How does it fit in?

- PSURs – Periodically analysing the benefit-risk balance of a drug product based on emerging safety data
- RMPs – A holistic plan to minimise the risks associated medicines
- DHPCs – To disseminate urgent information on risks/safety issues
- Safety Circulars – to disseminate information on ongoing and finalised reviews on medicines
- Safety Recalls – The withdrawal of medicinal products with negative benefit-risk balance
- Pharmacovigilance Inspections – Ensure that MAHs fulfil their pharmacovigilance obligations.



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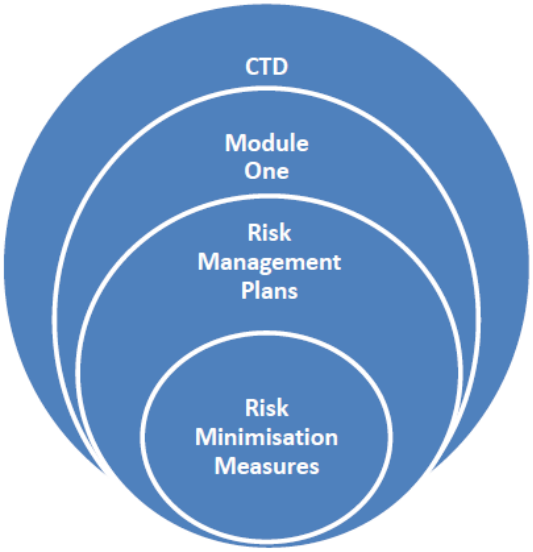
Abbreviations

- **DHPC** – Direct Healthcare Professional Communication
- **CHMP** – Committee for human Medicinal product
- **CMDh** – Coordination Group for Mutual Recognition and Decentralised Procedures (human)
- **PRAC** – Pharmacovigilance risk assessment committee
- **EMA** – European medicines Agency
- **EPITT** - European Pharmacovigilance Issues Tracking Tool
- **PASS** – Post Authorization Safety Study
- **PAES** – Post authorization efficacy Study
- **PSUR**- Periodic Safety update Report

RMP includes: Risk Minimisation Measures

Routine RMM – SPCs and PIL, ADR reporting

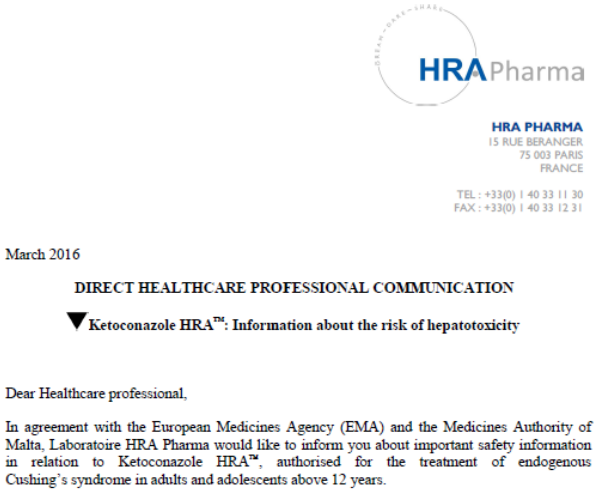
Additional RMM : Educational material,
Patient alert cards
Pregnancy Prevention Programs



A RMM is defined by GVP as '' a public health intervention intended to prevent or reduce the possibility of the occurrence of an adverse reaction associated with the exposure to a medicine or to reduce the severity should it occur''

http://www.medicinesauthority.gov.mt/rmm

Safety Communications



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March 2016

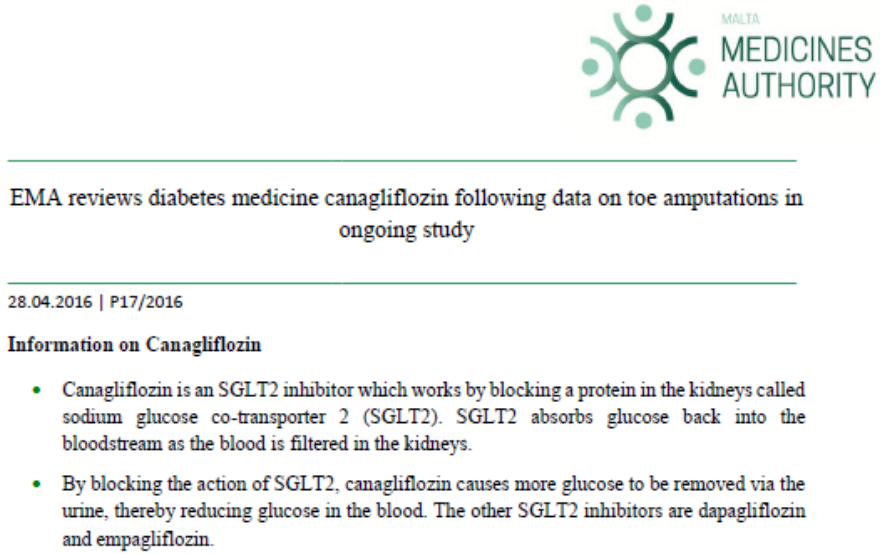
DIRECT HEALTHCARE PROFESSIONAL COMMUNICATION

▼Ketoconazole HRA™: Information about the risk of hepatotoxicity

Dear Healthcare professional,

In agreement with the European Medicines Agency (EMA) and the Medicines Authority of Malta, Laboratoire HRA Pharma would like to inform you about important safety information in relation to Ketoconazole HRA™, authorised for the treatment of endogenous Cushing's syndrome in adults and adolescents above 12 years.

DHPC



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EMA reviews diabetes medicine canagliflozin following data on toe amputations in ongoing study

28.04.2016 | P17/2016

Information on Canagliflozin

- Canagliflozin is an SGLT2 inhibitor which works by blocking a protein in the kidneys called sodium glucose co-transporter 2 (SGLT2). SGLT2 absorbs glucose back into the bloodstream as the blood is filtered in the kidneys.
- By blocking the action of SGLT2, canagliflozin causes more glucose to be removed via the urine, thereby reducing glucose in the blood. The other SGLT2 inhibitors are dapagliflozin and empagliflozin.

Safety Circular

http://www.medicinesauthority.gov.mt/safetycirculars
http://medicinesauthority.gov.mt/dhpc

Safety Recalls

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Procedure started → Under evaluation → PRAC recommendation → CMDh Position → European Commission final decision

CMDh endorses revocation of authorisations for fusafungine sprays used to treat airway infections

Medicines to be withdrawn due to serious allergic reactions and limited evidence of benefit

Safety recall Page:
http://www.medicinesauthority.gov.mt/safetyrecalls?l=1

Advertising

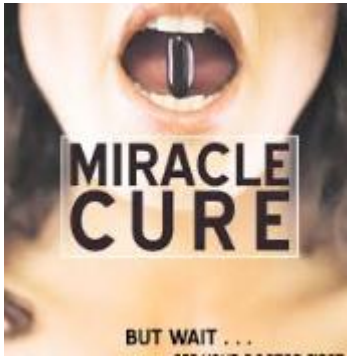
- The legal basis Medicines Act, 2003 and the Medicinal Products (Advertising) Regulations, 2005. (L.N. 380 of 2005)

- The regulations explain the different requirements for advertising to the general public and healthcare professionals.

- The control of medicines advertising in Malta, from 1 May 2004, is based on the system of self-regulation.

- Reactive rather than Pro-Active

http://medicinesauthority.gov.mt/regulationadvertisingofmedicines



Reference and Further reading

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Thank You for Attention