Assignment Assessing an ADR report

Aim
In this exercise students are trained in (i) classification of ADRs, (ii) causality assessment, (iii) communication with healthcare professionals.
This assignments can be used for training PV Key aspect, 3 (Recognizing ADR), 5 (Reporting ADR).

Source
The Netherlands Pharmacovigilance Centre Lareb, WHO Collaborating Centre for Pharmacovigilance in Education and Patient Reporting

Learning outcomes
The student …

- … has knowledge about ADR classification, risk factors, confounding factors
- … is able to assess causality of a potential ADR is a written patient case
- … developed an open mind for adverse outcomes of drug use in pharmacotherapy.

Description
You received a report about an ADR OR you visit your patient that has an ADR. The event has been reported to a pharmacovigilance centre.
A real ADR report of a well-documented description from a patient file should apply to this assignment. As an example, an ADR report has been attached in this document.
The student should assess this ADR report, considering ADR classification, causality and writing a feedback letter.
The feedback letter can be written to the reporter, being a healthcare professional or a patient. This feedback letter should contain a short overview of what is known about this ADR and how strong the causal relationship is in the case.

Example
ADR: enalapril and angioedema

ADR report form:

___ ***A Adverse drug reaction*** _____		
ADR (1)		
.	Description of the ADR	Swelling of eyes and tongue
.	Start date of the ADR	January, 10th, 2017
.	How long did the patient use the drug before the ADR first occured?	3 years
.	What is the outcome of this ADR is the patient?	recovering
Information about the ADR		
.	Has the ADR been treated?	Yes, the drug enalapril was withdrawn
.	Did the patient use the drug causing this ADR before?	Yes
.	Did a similar ADR occur?	No
.	Are there other circumstances that could have caused or aggravated this ADR?	No
.	Did the ADR lead to one of the following situations? (Hospitalisation (prolonged), Disability, Life-threatening situation, Death)	Yes, hospitalisation
.	Extra information	The patient could not remember any other episode of swelling of lips, eyes or tongue before.
___ ***B Drug*** _____		
Drug [1]		
.	Suspect drug	Enalapril 10 mg
.	Startdate drug	January 2014
.	Dose	1 times per day 1 dose
.	Administration route	Oral
.	Indication	Hypertension
.	Has the use of the drug been adjustment after the occurrence of the ADR	Withdrawn
.	Possible interaction with other drugs?	No
.	Does the patient use concomitant medication?	Yes
Concomitant medication [2]		
.	Drug name	Acetylsalicylic acid 80 mg
.	Dose	1 time daily 80 mg
.	Startdate	2014
Concomitant medication		
.	Drug name	Pantoprazole 20 mg
.	Dose	1 time daily 20 mg
.	Startdate	2014
___ ***C PATIËNT*** _____		
.	Gender	Male
.	Birth date / Age	75 years
.	Weight	75 kg
.	Medical history.	Hypertension
___ ***D Reporter*** _____		
.	Profession or specialism	General practitioner
.		

Questions:

- How would you classify this adverse drug reaction? Type A or B? and why?
- Give a description of the pros and cons for the causal relationship between enalapril and angioedema.
- Write a feedback for the reporter, in this case a healthcare professional. In this feedback, mention all items that you take into consideration during the causality assessment.

Example of answer:

Secundary ADR, Type B ADRs: non-allergic hypersensitivity

DoTS: Do - Therapeutic dose (collateral effect), T - Intermediate reaction (60% in first week) also time-independent, S-race (risk increased in African people), age, comorbidity (hereditary angioedema)

Causality assessment

PRO	**CON**
Known ADR (SmPC, literature)	Other causes excluded? Example C1-esterase inhibitor deficiency or allergy.
Reports in databases	Race and comorbidity unknown from report
Positive dechallenge	

Dear sir, madam,

You reported angioedema (swelling of eyes and tongue) caused by enalapril by your patient N (aged 75 years) after three years of use. Fortunately, he recovered completely after withdrawal of enalapril.

The official summary of productcharacteristics mentions angio-edema as a possible adverse drug reaction, which occurs rather often, in 1 to 10 to 100 patients [2-3]. Other frequently used handbooks and information services also mention that angio-edema can occur during any time of treatment with ACE-inhibitors [4].

To the national pharmacovigilance centre, angio-edema has been reported over 200 times with enalapril. Also other angio-edema related symptoms have been reported, like facial swelling (13 reports), oral edema mond (1 report), swelling of eyelids (3 reports), tong edema (8 reports), periorbital edema (5 reports) and oedema in general (6 reports). Also the other ACE-inhibitors are associated with angio-edema [5].

Patient characteristics that are involved in causality assessment of this ADR, are African descent, age > 65 years and medical history of hereditary angioedema, seasonal allergies and drug allergies. These features are supposed to be risk factors. Recovery of the symptoms after drug withdrawal (positive dechallenge) is an important argument for an adverse drug reaction.

The occurence of angioedema is unpredictable. Angioedema develops by an increase of vasodilatation and vasopermeability in (sub)cutaneous and tissues. There are many causes for angioedema, for example C1-esterase inhibitor deficiency, symptom of type 1 IgE mediated allergy, but sometimes is idiopathic without a clear cause. ACE-inhibitor induced angioedema is caused by an increase of bradykinin and substance P causing increased vasopermeability [9-11].

When other relevant information becomes available considering risk factors or other causes of this ADR in your patient, please inform me.

Yours sincerely,

Literature references:

1. Summary of product characteristics via: htpp://www.cbg-meb.nl ; http://www.geneesmiddeleninformatiebank.nl/
2. Farmacotherapeutisch Kompas enalapril via: https://www.farmacotherapeutischkompas.nl/bladeren-volgens-boek/preparaatteksten/e/enalapril
3. KNMP-kennisbank via: https://kennisbank.knmp.nl/article/Informatorium_Medicamentorum-_-S2005.html
4. Micromedex® Healthcare Series, (electronic version). Thomson Micromedex,Greenwood Village, Colorado, USA
5. Lareb Bijwerkingendatabank via: http://databank.lareb.nl/Bijwerkingen/
6. Lareb Bijwerkingendatabank via: http://www.lareb.nl/LarebCorporateWebsite/media/publicaties/BCL_Angio_oedeem_2004.pdf
7. Lareb Bijwerkingendatabank via: http://www.lareb.nl/Publicaties/pws2004_1538.aspx
8. Can J. Caridol (2007). Late-onset angioedema due to an angiotensin-converting enzyme inhibitor. The Canadian Journal Of Cardiology. Volume 23, issue 4 via: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2647891/
9. Lareb Bijwerkingendatabank via http://www.lareb.nl/Home.aspx
10. Sabine A. Fuchs, Ronald H. B. Meyboom, Eugène P. Van Puijenbroek & Henk-Jan Guchelaar (2004). Use of angiotensin receptor antagonists in patients with ACE inhibitor induced angioedema. Pharm World Sci. Volume 26 via: http://www.lareb.nl/Publicaties/pws2004_1538.aspx
11. Robert Matthew Bramante, M.D., and Masha Rand, M.D. (2011). Angioedema. The New England Journal Of Medicine. Volume 365 via: http://www.nejm.org/doi/full/10.1056/NEJMicm1014034

Evaluation form (for teacher)

Student name(s)	Date:	Teacher:
Subject	**Title DRUG and ADR**	
Evaluation on content (based on letter and/or oral presentation) Critical aspects that should be mentioned:		
1. What is known? - Sources (SmPC, PIL, handbooks, literature, PV databses) - Symptoms - Frequency / epidemiology	Essential information can be mentioned here	
2. Patient / event related factors (latency, de/rechallenge, risk factors, cofactors, test results)		
3. Drug related factors - Pharmacology, pathophysiology - Drug interactions		
4. Pros and Cons of causality assessment		
5.If relevant: questions for follow up information		
6. Clinical relevance and Signal or new information?		
Performance		
Oral presentation		
Letter (zorgverlener en patiënt)		
Final rating	☐ **Not on track** ☐ **On track** ☐ **Fast on track**	
Tips		
Tops		
Remarks		