Drug Safety

Safety Communication Tools and Healthcare Professionals' Awareness of Specific Drug Safety Issues in Europe: A Survey Study

Sieta T. de Vries, PhD; Maartje J.M. van der Sar, MSc; Anna Marie Coleman; Yvette Escudero; Alfonso Rodríguez Pascual; Miguel-Ángel Maciá Martínez; Amelia Cupelli; Ilaria Baldelli; Ivana Šipić; Adriana Andrić; Line Michan, PhD; Petra Denig, PhD; Peter G.M. Mol, PhD; on behalf of SCOPE work package 6

Corresponding author:
P.G.M. Mol, PhD
Department of Clinical Pharmacy and Pharmacology, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands
Dutch Medicines Evaluation Board, Utrecht, The Netherlands

✉ p.g.m.mol@umcg.nl

Supplemental Digital Content

This Supplemental Digital Content contains the appendix referred to in the full version of this article, which can be found at http://adisonline.com/drugsafety

Electronic Supplementary Material 1. English version of the survey

Screen 1

Welcome

Safety communications and their effectiveness

Survey of the views of healthcare professionals

In this survey we will ask you about three specific types of safety communications that are used by <name of the national competent authority (NCA)>:

- letters sent to healthcare professionals (Direct Healthcare Professional Communications or DHPCs);
- national regulatory agency communications;
- educational materials.

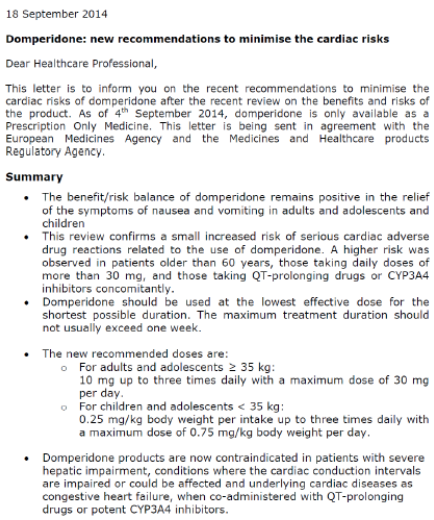
In addition, will we ask for your general preferences on safety communication about medicines and your response to such communication.

Screen 2

Direct Healthcare Professional Communications
(DHPCs, also known as 'dear doctor letters')

DHPCs are distributed by the pharmaceutical company once the content is agreed with <name NCA>. These letters are sent to individual healthcare professionals. The letter indicates that it is sent in agreement with <name NCA>.

Two examples of recent DHPCs:



18 September 2014

Domperidone: new recommendations to minimise the cardiac risks

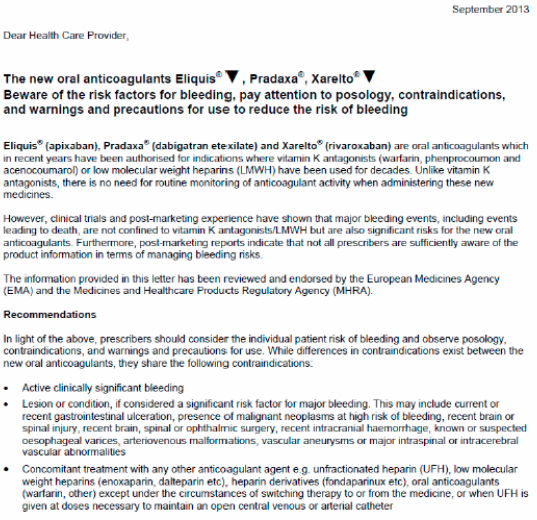
Dear Healthcare Professional,

This letter is to inform you on the recent recommendations to minimise the cardiac risks of domperidone after the recent review on the benefits and risks of the product. As of 4th September 2014, domperidone is only available as a Prescription Only Medicine. This letter is being sent in agreement with the European Medicines Agency and the Medicines and Healthcare products Regulatory Agency.

Summary

- The benefit/risk balance of domperidone remains positive in the relief of the symptoms of nausea and vomiting in adults and adolescents and children
- This review confirms a small increased risk of serious cardiac adverse drug reactions related to the use of domperidone. A higher risk was observed in patients older than 60 years, those taking daily doses of more than 30 mg, and those taking QT-prolonging drugs or CYP3A4 inhibitors concomitantly.
- Domperidone should be used at the lowest effective dose for the shortest possible duration. The maximum treatment duration should not usually exceed one week.
- The new recommended doses are:
  - For adults and adolescents ≥ 35 kg:
    10 mg up to three times daily with a maximum dose of 30 mg per day.
  - For children and adolescents < 35 kg:
    0.25 mg/kg body weight per intake up to three times daily with a maximum dose of 0.75 mg/kg body weight per day.
- Domperidone products are now contraindicated in patients with severe hepatic impairment, conditions where the cardiac conduction intervals are impaired or could be affected and underlying cardiac diseases as congestive heart failure, when co-administered with QT-prolonging drugs or potent CYP3A4 inhibitors.

click here to view a larger version



September 2013

Dear Health Care Provider,

The new oral anticoagulants Eliquis® ▼, Pradaxa®, Xarelto® ▼
Beware of the risk factors for bleeding, pay attention to posology, contraindications, and warnings and precautions for use to reduce the risk of bleeding

Eliquis® (apixaban), Pradaxa® (dabigatran etexilate) and Xarelto® (rivaroxaban) are oral anticoagulants which in recent years have been authorised for indications where vitamin K antagonists (warfarin, phenprocoumon and acenocoumarol) or low molecular weight heparins (LMWH) have been used for decades. Unlike vitamin K antagonists, there is no need for routine monitoring of anticoagulant activity when administering these new medicines.

However, clinical trials and post-marketing experience have shown that major bleeding events, including events leading to death, are not confined to vitamin K antagonists/LMWH but are also significant risks for the new oral anticoagulants. Furthermore, post-marketing reports indicate that not all prescribers are sufficiently aware of the product information in terms of managing bleeding risks.

The information provided in this letter has been reviewed and endorsed by the European Medicines Agency (EMA) and the Medicines and Healthcare Products Regulatory Agency (MHRA).

Recommendations

In light of the above, prescribers should consider the individual patient risk of bleeding and observe posology, contraindications, and warnings and precautions for use. While differences in contraindications exist between the new oral anticoagulants, they share the following contraindications:

- Active clinically significant bleeding
- Lesion or condition, if considered a significant risk factor for major bleeding. This may include current or recent gastrointestinal ulceration, presence of malignant neoplasms at high risk of bleeding, recent brain or spinal injury, recent brain, spinal or ophthalmic surgery, recent intracranial haemorrhage, known or suspected oesophageal varices, arteriovenous malformations, vascular aneurysms or major intraspinal or intracerebral vascular abnormalities
- Concomitant treatment with any other anticoagulant agent e.g. unfractionated heparin (UFH), low molecular weight heparins (enoxaparin, dalteparin etc), heparin derivatives (fondaparinux etc), oral anticoagulants (warfarin, other) except under the circumstances of switching therapy to or from the medicine, or when UFH is given at doses necessary to maintain an open central venous or arterial catheter

click here to view a larger version

1. **Are you familiar with this type of safety information?**
   - Yes
   - No, I have heard of DHPCs, but I have never seen one
   - No, I have never heard of DHPCs

2. **Do you read the DHPCs you receive?**
   Multiple responses possible
   - Yes, if they contain safety information that is important to me
   - Yes, only when the envelope indicates it contains important, non-commercial information
   - Yes, I read all letters from the pharmaceutical industry
   - No, I do not read any letter from the pharmaceutical industry
   - Not applicable

If you have any comments, please let us know
Optional
[……..]

Screen 3

Usefulness of DHPCs

3. **How useful do you find a DHPC in general?**
    - Not useful at all
    - Not useful
    - Neutral
    - Useful
    - Very useful

   Please specify why you think DHPCs are useful or not

   Optional
   [……..]

4. **How often do you take the action that is recommended in this type of communications?**
   Please click and move the slider to represent your position between the two options
   never……..always

   Please specify why you may or may not always take the recommended action
   Optional
   [……..]

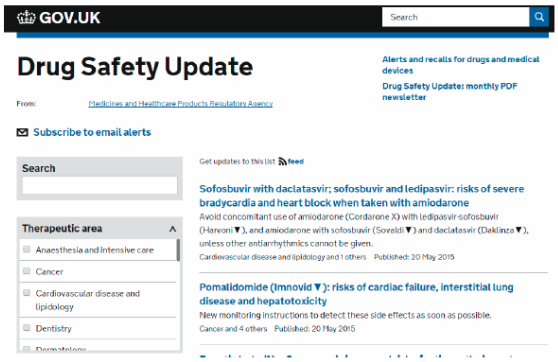
5. **Would it be sufficient for you to only receive an electronic DHPC instead of a hardcopy version?**
    - Yes
    - No
    - Other, please specify…

   If you have any comments, please let us know
   Optional
   [……..]

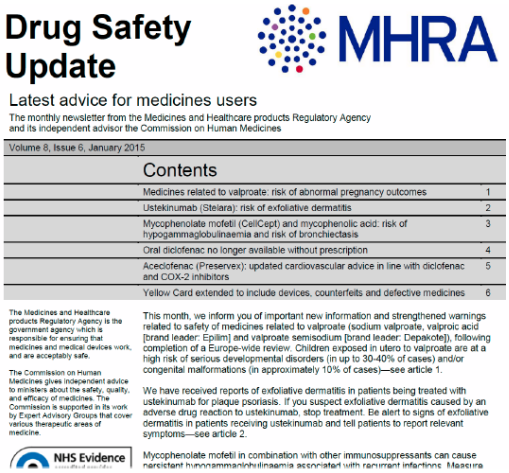
Screen 4

National regulatory agency communications

National regulatory agencies such as <*name NCA*> assess and monitor the efficacy, risks and quality of medicinal products. <*link to NCA website*>
National regulatory agency communications include <*country specific information*>
Two examples of national regulatory agency communication:



Click here to view a larger version.



Click here to view a larger version.

6. **Are you familiar with this method of safety information?**
    - Yes, I have received this type of safety information and I am (somewhat) familiar with its content
    - Yes, I have received this type of safety information, but I have never read it
    - No

If you have any comments, please let us know
Optional
[……..]

Screen 5

Usefulness of national regulatory agency communications

7. **How useful do you find national regulatory agency communications in general?**

    - Not useful at all
    - Not useful
    - Neutral
    - Useful
    - Very useful

    Please specify why you think national regulatory agency communications are useful or not
    Optional
    [……..]

8. **How often do you take the action that is recommended in this type of communication?**
    Please click and move the slider to represent your position between the two options
    never……always

    Please specify why you may or may not always take the recommended action
    Optional
    [……..]

9. **Would it for you be sufficient to only receive an electronic version of national regulatory agency communication instead of a hardcopy version?**

    - Yes
    - No
    - Other, please specify…

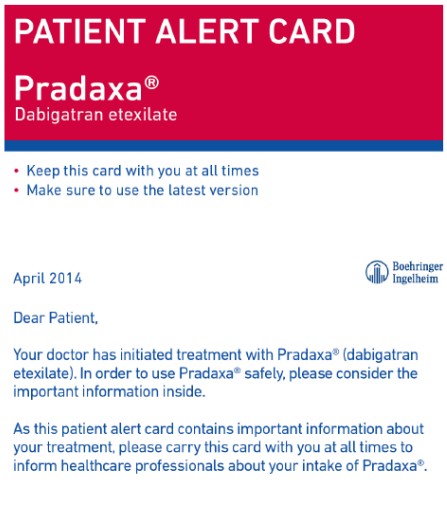
    If you have any comments, please let us know
    Optional
    [……..]

Screen 6

Educational materials

Educational materials include prescriber checklists and booklets for healthcare professionals with information about certain risks. Educational materials may also include cards and/or brochures to give to patients to help explain an adverse drug reaction of a specific medicine. These are distributed by the relevant pharmaceutical companies once the content is agreed with <*name NCA*>.

Two examples of this type of communication:


PATIENT ALERT CARD

Pradaxa®
Dabigatran etexilate

- Keep this card with you at all times
- Make sure to use the latest version

April 2014

Boehringer Ingelheim

Dear Patient,

Your doctor has initiated treatment with Pradaxa® (dabigatran etexilate). In order to use Pradaxa® safely, please consider the important information inside.

As this patient alert card contains important information about your treatment, please carry this card with you at all times to inform healthcare professionals about your intake of Pradaxa®.

Click here to view a larger version.


Important safety information for Tresiba® ▼ (insulin degludec)

Information on the correct use of Tresiba®, a new basal insulin, to minimise the risk of medication errors

- Tresiba® is available in two strengths – 100 units/mL and 200 units/mL – for the treatment of diabetes mellitus in adults. The 200 units/mL strength is higher than that of other existing insulin products available in the UK.
- The information and recommendations below are provided in order to minimise the risk of medication errors when prescribing Tresiba®.
- Patients must be advised to seek medical advice immediately if they administer an incorrect dose of Tresiba®.

Differentiation of the two Tresiba® strengths and the pen devices

Tresiba® FlexTouch® 100 units/mL pen

Tresiba® FlexTouch® 200 units/mL pen

Up to 80 units per injection | 300 total units per pen | 1-unit dose adjustments

Up to 160 units per injection | 600 total units per pen | 2-unit dose adjustments

The Tresiba® packaging and the respective pens have been designed to clearly differentiate between the two strengths.
The Tresiba® 100 units/mL label and packaging are light green while the Tresiba® 200 units/mL label and packaging are dark green with striping.
The Tresiba® 200 units/mL label and packaging also have a red box highlighting the strength.

Tresiba® FlexTouch® 100 units/mL package 5 pens per carton

Tresiba® FlexTouch® 200 units/mL package 3 pens per carton

200 UNITS/ML

The strength of the insulin is indicated with a 200 units/mL label.

Caution: One step equals 2 units - the pen shows the dose

The package clearly indicates that one step equals 2 dose units.

Dose conversion should not be done – the pen shows the dose in units.

When switching between strengths of Tresiba® dose conversion should not be done – the pen shows the dose in units.

Click here to view a larger version.

10. Are you familiar with this type of safety information?

- ○ Yes, I have received this type of safety information and I am (somewhat) familiar with its content
- ○ Yes, I have received this type of safety information, but I have never read it
- ○ No

If you have any comments, please let us know
Optional
[……..]

Screen 7

Usefulness of educational materials

11. **How useful do you find educational materials in general?**

    - Not useful at all
    - Not useful
    - Neutral
    - Useful
    - Very useful

    Please specify why you think educational materials are useful or not
    Optional
    [……..]

12. **If educational material for the patient is available, either for explanation during a consult or to be read at home, how do you value the following delivery methods?**

	Very negative	Negative	Neutral	Positive	Very positive
Hardcopy versions	○	○	○	○	○
Online or web-based tools	○	○	○	○	○

13. **Please tick all the following contents that you think should be included in educational materials for patients:**

    - ○ Warnings about serious adverse drug reactions and how the risk may be minimized
    - ○ Information on how to correctly use/take the product
    - ○ A summary of both the benefits and risks of using the product
    - ○ Other, please specify…
    - ○ None of the above

14. **Have you ever used educational materials as part of a discussion about a medicine with a patient?**
    Multiple responses possible

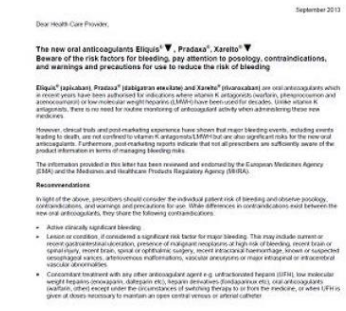
    - ○ Yes
    - ○ No, I do not routinely prescribe medicines for which educational materials are available
    - ○ No, I do not know if educational materials are available for the medicines I prescribe
    - ○ No, I do not find these materials helpful for patients
    - ○ No, I think the Patient Information Leaflet provides already sufficient information
    - ○ No, because …

    If you have any comments, please let us know
    Optional
    [……..]

Screen 8

General preferences and behaviour towards medicines safety information

As a healthcare professional you may receive medicines safety information (e.g. DHPCs, national regulatory agency communications or educational materials) through different channels and from different sources. It is known that various factors may influence whether healthcare professionals take subsequent action in their daily practice. In this section, we would like to ask you about your preferences for channels and sources [who is sending the information] and the factors that may affect your response to the safety communications you receive.



DHPC

National regulatory agency communication

Educational material

15. How do you value the following sources as a sender of safety messages?

	Very negative	Negative	Neutral	Positive	Very positive
<name NCA>	○	○	○	○	○
European Medicines Agency (EMA)	○	○	○	○	○
Professional body (e.g. *<national example>*)	○	○	○	○	○
Pharmaceutical companies	○	○	○	○	○
Colleague	○	○	○	○	○
Public press (e.g. through local newspaper article or news program on television)	○	○	○	○	○
Independent researchers (e.g. through publications in a medical journal)	○	○	○	○	○
Other, please specify…	○	○	○	○	○

16. In general, do you prefer to receive safety information in hardcopy (paper) or electronically?

- ○ Hardcopy
- ○ Electronically
- ○ No preference

17. **Below you can find some channels, which can be both in a hardcopy and electronic format. Independent of the format, how do you value each channel to keep up to date on the safety of medicines?**

	Very negative	Negative	Neutral	Positive	Very positive
Personalised letter	○	○	○	○	○
Medical journal	○	○	○	○	○
Summary of Product Characteristics / Patient information leaflet	○	○	○	○	○
Medicines reference book (e.g. <national example>)	○	○	○	○	○
Newspaper	○	○	○	○	○
National clinical guidelines (e.g. <national example>)	○	○	○	○	○

18. **How do you value the following alternative channels to keep up to date on the safety of medicines?**

	Very negative	Negative	Neutral	Positive	Very positive
E-mail	○	○	○	○	○
Social media (e.g. Twitter)	○	○	○	○	○
Mobile phone text (e.g. SMS)	○	○	○	○	○
Point-of-care alerts (e.g. pop-up notification at the time of prescribing or dispensing)	○	○	○	○	○
Website	○	○	○	○	○
Television or radio	○	○	○	○	○
Mobile app	○	○	○	○	○
In person (e.g. face-to-face meeting, course, medical congress or seminar)	○	○	○	○	○
Phone call	○	○	○	○	○
Other, please specify…	○	○	○	○	○

19. **In general, how often do you prefer to receive safety-related information?**

- ○ An **immediate** update of individual safety issues
- ○ A **weekly** update of all safety issues
- ○ A **monthly** update of all safety issues
- ○ A **quarterly** update of all safety issues

20. **Do you think it is useful when a safety message is repeated after a certain period of time?**

- ○ Yes
- ○ No
- ○ Other, please specify…

21. **In general, how much do you agree with the following statements? I only read the safety information if, ...**

	Strongly disagree	Disagree	Neutral	Agree	Strongly agree
I like the channel through which the information is sent (e.g. e-mail, hardcopy letter)	○	○	○	○	○
I trust the sender of the safety message	○	○	○	○	○
I like the lay-out of the document	○	○	○	○	○

the document is not too lengthy	○	○	○	○	○
I have enough time to read the information	○	○	○	○	○
the safety information is relevant for my daily practice	○	○	○	○	○
I do not receive a new safety message too often	○	○	○	○	○
Other factors? Please specify…	○	○	○	○	○

22. In general, how much do you agree with the following statements about safety information? I only take action in response to a safety warning if, …

	Strongly disagree	Disagree	Neutral	Agree	Strongly agree
the adverse drug reaction is severe or causes irreversible harm	○	○	○	○	○
I trust the sender of the safety message	○	○	○	○	○
I receive sufficient background information on the basis for the safety message	○	○	○	○	○
I agree with the recommendation in the safety information	○	○	○	○	○
my colleagues or multidisciplinary team agree with the safety message	○	○	○	○	○
the message is incorporated in clinical or professional society guidelines	○	○	○	○	○
a patient requests an action in response to safety information she/he has found	○	○	○	○	○
recommendations are clear	○	○	○	○	○
a recommendation can easily be implemented in routine daily practice	○	○	○	○	○
the safety information is relevant for my daily practice	○	○	○	○	○
Other factors? Please specify…	○	○	○	○	○

23. Are you aware of updates to the safety profiles of the following medicines? If yes, how did you hear about them?
Please tick all that apply

	No	Yes, via DHPC	Yes, via website or newsletter	Yes, via educational materials	Yes, via professional body	Yes, via a colleague	Yes, via medical journal	Yes, via lay media (newspaper / television)	Other, please specify below
Combined Hormonal Contraceptives – update on the risk of venous thromboembolism	○	○	○	○	○	○	○	○	○
Diclofenac – new cardiovascular precautions	○	○	○	○	○	○	○	○	○
alproate – further	○	○	○	○	○	○	○	○	○

restrictions for use in women and girls									
Ivabradine – the need to take additional measures to minimize the risk of cardiovascular events and severe bradycardia	○	○	○	○	○	○	○	○	○

If you heard about one of the updates to the safety profiles of the medicines above via a channel that was not mentioned, please specify below
[……..]

If you have any comments, please let us know
Optional
[……..]

Screen 9

General questions

24. What is your gender?

- ○ Male
- ○ Female

25. What is your age?

- ○ <35
- ○ 35 – 45
- ○ 46 – 55
- ○ >55

26. What is your profession?

- ○ General practitioner
- ○ Cardiologist
- ○ Pharmacist
- ○ Other, please specify…

27. What is your primary employment setting?

- ○ Community based - public practice
- ○ Community based - private practice
- ○ Hospital based - public practice
- ○ Hospital/clinic based - private practice
- ○ Other, please specify…

28. Where is your practice located?

- ○ Rural area
- ○ Urban area
- ○ Other… (if applicable)

29. How long do you have a healthcare professional accreditation?

- ○ <5 years
- ○ 5 – 20 years
- ○ >20 years

30. Do you use an electronic system to prescribe or dispense medicines?

- ○ Yes, always
- ○ Yes, but not always
- ○ No

31. How often do you use the following options to keep your medicines knowledge up to date?

	Daily	**Weekly**	**Monthly or less**	**Never**
Training or courses, organised by e.g.: … <text field>	○	○	○	○
A medicines reference book (e.g. …)	○	○	○	○
Summary of Product Characteristics / Patient information leaflet	○	○	○	○

National clinical guidelines (e.g. …)	○	○	○	○
International clinical guidelines (e.g. from the “European Society of Cardiology”)	○	○	○	○
<NCA name> website/newsletter	○	○	○	○
EMA website/newsletter	○	○	○	○
If applicable: medicines advisory committees	○	○	○	○
Medical journals	○	○	○	○
Company representatives	○	○	○	○
A mobile phone app	○	○	○	○
Blogs	○	○	○	○
Other, please specify…	○	○	○	○

Screen 10

Thank you for your participation.

32. **We would be grateful for any additional comments you may have on how safety communications could be improved**
    [……..]

33. **If the results of the survey are published, would you like to receive a copy of the publication?**
    If yes, please also fill in your e-mail address below

    - Yes
    - No

34. **Do you want to participate in the prize draw to win a voucher?**
    If yes, please also fill in your e-mail address below

    - Yes
    - No

35. **Please leave your e-mail address if you answered yes to one of the questions above. The e-mail address will be saved separately from your answers.**
    [……..]