10 April 2012
EMA/204889/2012
Quality Review of Documents Group (QRD)

Quality Review of Documents (QRD) human product information annotated template: revision of the product information

Draft

Draft agreed by Quality Review of Documents Group (QRD)	March 2012
Start of consultation	20 April 2012
End of consultation (deadline for comments)	7 May 2012
Agreed by Quality Review of Documents Group (QRD)	May 2012
Adopted by Pharmacovigilance Risk Assessment Committee (PRAC)	<DD Month YYYY>
Date for coming into effect	<DD Month YYYY>

Comments should be provided using the enclosed **template**. The completed comments form should be sent to **QRD@ema.europa.eu**

Keywords	***Package leaflet, PL, summary of product characteristics, SmPC, QRD, template, labelling, product information***

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

Introduction

The purpose of this revision is to implement the new provisions from the pharmacovigilance legislation in the QRD human product information template.

The main aspects of the new pharmacovigilance legislation to be addressed in the product information are:

- **Additional monitoring**: a black symbol and a standardised explanatory statement have to be included in the summary of product characteristics (SmPC) and package leaflet (PL) of the medicinal products subject to additional monitoring. Also, the sentence 'This product is subject to additional monitoring' should be preceded by the black symbol and should be followed by the explanatory statement.
- **Encouragement of reporting of adverse reactions**: a standardised text to encourage the reporting of adverse reactions has to be included in the summary of product characteristics (SmPC) and package leaflet (PL) of all medicinal products.

This consultation aims to present the proposals (**text in blue**) for the location and wording of the explanatory statement for the additional monitoring and for the wording of the standardised text to encourage the reporting of adverse reactions. Two proposals are also included in this document for the 'black symbol', which have come up during the consultation with Member States and stakeholders.

Specific questions have been included in the **template for comments** regarding:

- The proposals for the black symbol.
- The location of the black symbol and of the explanatory statement for medicinal product subject to additional monitoring.
- The wording of the explanatory statement for medicinal product subject to additional monitoring.
- The location and wording of the standardised text to encourage reporting of adverse reactions.

Comments should be provided using the enclosed **template**. The completed comments form should be sent to QRD@ema.europa.eu.

Legal basis

- Regulation (EU) No 1235/2010 of the European Parliament and of the Council of 15 December 2010 amending, as regards pharmacovigilance of medicinal products for human use, Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, and Regulation (EC) No 1394/2007 on advanced therapy medicinal products.
- Directive 2010/84/EU of the European Parliament and of the Council of 15 December 2010 amending, as regards pharmacovigilance, Directive 2001/83/EC on the Community code relating to medicinal products for human use.

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

[Bracketing convention:
{text}: Information to be filled in
<text>: Text to be selected or deleted as appropriate.]

{Black symbol*} – During the revision of the QRD human product information template to accommodate the new pharmacovigilance legislation, several consultations have taken place with Member States and stakeholders (patients, consumers and healthcare professional organisations).

As part of the consultations, several symbols have been identified by the consulted parties to be used as the 'black symbol' referred to in the pharmacovigilance legislation.

The two preferred options resulting from the consultations are:
- An 'inverted black triangle', similar to the symbol currently used in the United Kingdom and Belgium to identify products under intensive surveillance.
- A 'magnifying glass', as a possible symbol to be developed.

[For medicinal products subject to additional monitoring ONLY:
The black symbol and the statements should only appear preceding section 1]

<{Black symbol*} This medicinal product is subject to additional monitoring to allow any safety information to be identified rapidly. Healthcare professionals are encouraged to report any suspected adverse reactions. See section 4.8.>

1. NAME OF THE MEDICINAL PRODUCT

[For medicinal products subject to additional monitoring ONLY:
The black symbol should only appear preceding the invented name in the section 1]

<{Black symbol}>{(Invented) name strength pharmaceutical form}

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

<2.1 General description> [For advanced therapy product only]

<2.2 Qualitative and quantitative composition> [For advanced therapy product only]

<Excipient(s) with known effect:>

<For the full list of excipients, see section 6.1.>

3. PHARMACEUTICAL FORM

<The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.>
<The score line is not intended for breaking the tablet.>
<The tablet can be divided into equal doses.>

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

<This medicinal product is for diagnostic use only.>

<{X} is indicated in <adults> <neonates> <infants> <children> <adolescents> <aged {x to y}> <years> <months>.>

4.2 Posology and method of administration

Posology

Paediatric population

<The <safety> <and> <efficacy> of {X} in children aged {x to y} <months> <years> {or any other relevant subsets, e.g. weight, pubertal age, gender} <has> <have> not <yet> been established.>
<No data are available.>
<Currently available data are described in section <4.8> <5.1> <5.2> but no recommendation on a posology can be made.>

<{X} should not be used in children aged {x to y} <years> <months> {or any other relevant subsets, e.g. weight, pubertal age, gender} because of <safety> <efficacy> concern(s).>

<There is no relevant use of {X} <in the paediatric population> <in children aged {x to y} <years> <months> {or any other relevant subsets, e.g. weight, pubertal age, gender} <in the indication...>.>

<{X} is contraindicated in children aged {x to y} <years> <months> {or any other relevant subsets, e.g. weight, pubertal age, gender} <in the indication...> (see section 4.3).>

Method of administration

<Precautions to be taken before handling or administering the medicinal product>

<For instructions on <reconstitution> <dilution> of the medicinal product before administration, see section <6.6> <and> <12>.>

4.3 Contraindications

<Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1 <or {name of the residue(s)}>.>

4.4 Special warnings and precautions for use

<Paediatric population>

4.5 Interaction with other medicinal products and other forms of interaction

<No interaction studies have been performed.>

<Paediatric population>

<Interaction studies have only been performed in adults.>

4.6 Fertility, pregnancy and lactation

<Pregnancy>
<Breast-feeding>
<Fertility>

4.7 Effects on ability to drive and use machines

<{Invented name} has <no or negligible influence> <minor influence> <moderate influence> <major influence> on the ability to drive and use machines.>

<Not relevant.>

4.8 Undesirable effects

<Paediatric population>

[For ALL medicinal products:
The new sub-heading should appear at the end of the section 4.8]

Reporting of suspected adverse reactions

Reporting suspected adverse reactions is an important way to continuously monitor the benefit/risk balance of the medicinal product in the real conditions of use. Any suspected adverse reactions should be reported according to {insert information on the relevant 'national reporting system' – *details will be defined at national level*}.

4.9 Overdose

<Paediatric population>

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: {group}, ATC code: {code} <not yet assigned>

<{(Invented) Name} is a biosimilar medicinal product. Detailed information is available on the website of the European Medicines Agency http://www.ema.europa.eu.>

<Mechanism of action>
<Pharmacodynamic effects>
<Clinical efficacy and safety>
<Paediatric population>

<The European Medicines Agency has waived the obligation to submit the results of studies with {(Invented) Name} in all subsets of the paediatric population in {condition as per Paediatric Investigation Plan (PIP) decision, in the granted indication} (see section 4.2 for information on paediatric use).>

<The European Medicines Agency has deferred the obligation to submit the results of studies with {(Invented) Name} in one or more subsets of the paediatric population in {condition, as per Paediatric Investigation Plan (PIP) decision in the granted indication} (see section 4.2 for information on paediatric use).>

<This medicinal product has been authorised under a so-called 'conditional approval' scheme. This means that further evidence on this medicinal product is awaited.
The European Medicines Agency will review new information on this medicinal product at least every year and this SmPC will be updated as necessary.>

<This medicinal product has been authorised under 'exceptional circumstances'. This means that <due to the rarity of the disease> <for scientific reasons> <for ethical reasons> it has not been possible to obtain complete information on this medicinal product.
The European Medicines Agency will review any new information which may become available every year and this SmPC will be updated as necessary.>

5.2 Pharmacokinetic properties

<Absorption>
<Distribution>
<Biotransformation>
<Elimination>
<Linearity/non-linearity>
<Pharmacokinetic/pharmacodynamic relationship(s)>

5.3 Preclinical safety data

<Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction and development.>

<Effects in non-clinical studies were observed only at exposures considered sufficiently in excess of the maximum human exposure indicating little relevance to clinical use.>

<Adverse reactions not observed in clinical studies, but seen in animals at exposure levels similar to clinical exposure levels and with possible relevance to clinical use were as follows:>

<Environmental Risk Assessment (ERA)>

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

<None.>

6.2 Incompatibilities

<Not applicable.>

<In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.>

<This medicinal product must not be mixed with other medicinal products except those mentioned in section <6.6> <and> <12>.>

6.3 Shelf life

<...> <6 months> <...> <1 year> <18 months> <2 years> <30 months> <3 years> <...>

6.4 Special precautions for storage

<For storage conditions after <reconstitution> <dilution> <first opening> of the medicinal product, see section 6.3.>

6.5 Nature and contents of container <and special equipment for use, administration or implantation>

<Not all pack sizes may be marketed.>

6.6 Special precautions for disposal <and other handling>

<Use in the paediatric population>

<No special requirements <for disposal>.>

<Any unused medicinal product or waste material should be disposed of in accordance with local requirements.>

7. MARKETING AUTHORISATION HOLDER

{Name and address}
<{tel}>
<{fax}>
<{e-mail}>

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

<Date of first authorisation: {DD month YYYY}>
<Date of latest renewal: {DD month YYYY}>

10. DATE OF REVISION OF THE TEXT

<{MM/YYYY}>
<{DD/MM/YYYY}>
<{DD month YYYY}>

<11. DOSIMETRY>

<12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS>

<Any unused medicinal product or waste material should be disposed of in accordance with local requirements.>

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

B. PACKAGE LEAFLET

Package leaflet: Information for the <patient> <user>

[For medicinal products subject to additional monitoring ONLY:
The black symbol should only appear preceding the invented name in the title]

<{Black symbol}> {(Invented) name strength pharmaceutical form}
{Active substance(s)}

<{Black symbol} This medicine is subject to additional monitoring to allow any safety information on the medicine to be identified rapidly. You can help by reporting any side effects you may get*. See section 4.>

[* NOTE: Standard statements given in the template must be used whenever they are applicable. If the applicant needs to deviate from these headings/statements to accommodate medicine-specific requirements (e.g. for medicines for children administered by parents, "you may get" could be replaced by "your child may get"), alternative or additional statements will be considered on a case-by-case basis.]

<**Read all of this leaflet carefully before you start <taking> <using> this medicine because it contains important information for you.**
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your <doctor> <,> <or> <pharmacist> <or nurse>.
<- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.>
- If you get any side effects, talk to your <doctor> <,> <or> <pharmacist> <or nurse>. This includes any possible side effects not listed in this leaflet>. See section 4.

<**Read all of this leaflet carefully before you start <taking> <using> this medicine because it contains important information for you.**
Always <take> <use> this medicine exactly as described in this leaflet or as your <doctor> <,> <or> <pharmacist> <or nurse> <has> <have> told you.
- Keep this leaflet. You may need to read it again.
- Ask your pharmacist if you need more information or advice.
- If you get any side effects, talk to your <doctor> <,> <or> <pharmacist> <or nurse>. This includes any possible side effects not listed in this leaflet.
- You must talk to a doctor if you do not feel better or if you feel worse <after {number of} days>.>

What is in this leaflet

1. What X is and what it is used for

<You must talk to a doctor if you do not feel better or if you feel worse <after {number of} days>.>

2. What you need to know before you <take> <use> X

Do not <take> <use> X<:>

- <if you are allergic to {active substance(s)} or any of the other ingredients of this medicine (listed in section 6).>

Warnings and precautions
Talk to your doctor <or> <,> <pharmacist> <or nurse> before <taking> <using> X

Children <and adolescents>

Other medicines and X
<Tell your <doctor> <or> <pharmacist> if you are <taking> <using>, have recently <taken> <used> or might <take> <use> any other medicines.>

X with <food> <and> <,> <drink> <and> <alcohol>

Pregnancy <and> <,> breast-feeding <and fertility>
<If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your <doctor> <or> <pharmacist> for advice before taking this medicine.>

Driving and using machines

<X contains {name the excipient(s)}>

3. How to <take> <use> X

<Always <take> <use> this medicine exactly as your doctor <or pharmacist> has told you. Check with your <doctor> <or> <pharmacist> if you are not sure.>

<The recommended dose is...>

<Always <take> <use> this medicine exactly as described in this leaflet or as your <doctor> <,> <or> <pharmacist> <or nurse> <has> <have> told you. Check with your <doctor> <or> <,> <pharmacist> <or nurse> if you are not sure.>

<The recommended dose is...>

<Use in children <and adolescents>>

<The score line is only there to help you break the tablet if you have difficulty swallowing it whole.>
<The tablet can be divided into equal doses.>
<The score line is not intended for breaking the tablet.>

<If you <take> <use> more X than you should>

<If you forget to <take> <use> X>
<Do not take a double dose to make up for a forgotten <tablet> <dose> <…>.>

<If you stop <taking> <using> X>
<If you have any further questions on the use of this medicine, ask your <doctor> <,> <or> <pharmacist> <or nurse>.>

4. Possible side effects

<Additional side effects in children <and adolescents>>

[For ALL medicinal products:
The new sub-heading should appear at the end of the section 4]

Reporting of side effects

If you get any side effects, talk to your <doctor> <or> <,> <pharmacist> <or nurse>. This includes any possible side effects not listed in this leaflet. You can also report any side effects directly to the national reporting system via the internet at {insert link to the relevant 'national reporting system website' - *details will be defined at national level*}; alternatively you can report via {insert alternative ways of reporting – *details will be defined at national level*}. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store X

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the <label> <carton> <bottle> <…> <after {abbreviation used for expiry date}.> <The expiry date refers to the last day of that month.>

<Do not use this medicine if you notice {description of the visible signs of deterioration}.>

<Do not throw away any medicines via wastewater <or household waste>. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.>

6. Contents of the pack and other information

What X contains

- The active substance(s) is (are)…
- The other ingredient(s) <(excipient(s))> is (are)...

What X looks like and contents of the pack

Marketing Authorisation Holder and Manufacturer

{Name and address}
<{tel}>
<{fax}>
<{e-mail}>

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

België/Belgique/Belgien
{Nom/Naam/Name}
<{Adresse/Adres/Anschrift }
B-0000 {Localité/Stad/Stadt}>
Tél/Tel: + {N° de téléphone/Telefoonnummer/ Telefonnummer}

Luxembourg/Luxemburg
{Nom}
<{Adresse}
L-0000 {Localité/Stadt}>
Tél/Tel: + {N° de téléphone/Telefonnummer}
<{e-mail}>

<{e-mail}>

България
{Име}
<{Адрес}
{Град} {Пощенски код}>
Тел.: + {Телефонен номер}
<{e-mail}>

Česká republika
{Název}
<{Adresa}
CZ {město}>
Tel: +{telefonní číslo}
<{e-mail}>

Danmark
{Navn}
<{Adresse}
DK-0000 {by}>
Tlf: + {Telefonnummer}
<{e-mail}>

Deutschland
{Name}
<{Anschrift}
D-00000 {Stadt}>
Tel: + {Telefonnummer}
<{e-mail}>

Eesti
(Nimi)
<(Aadress)
EE - (Postiindeks) (Linn)>
Tel: +(Telefoninumber)
<{e-mail}>

Ελλάδα
{Όνομα}
<{Διεύθυνση}
GR-000 00 {πόλη}>
Τηλ: + {Αριθμός τηλεφώνου}
<{e-mail}>

España
{Nombre}
<{Dirección}
E-00000 {Ciudad}>
Tel: + {Teléfono}
<{e-mail}>

France
{Nom}
<{Adresse}

Magyarország
{Név}
<{Cím}
H-0000 {Város}>
Tel.: +Telefonszám}
<{e-mail}>

Malta
{Isem}
<{Indirizz}
MT-0000 {Belt/Raħal}>
Tel: + {Numru tat-telefon}
<{e-mail}>

Nederland
{Naam}
<{Adres}
NL-0000 XX {stad}>
Tel: + {Telefoonnummer}
<{e-mail}>

Norge
{Navn}
<{Adresse}
N-0000 {poststed}>
Tlf: + {Telefonnummer}
<{e-mail}>

Österreich
{Name}
<{Anschrift}
A-0000 {Stadt}>
Tel: + {Telefonnummer}
<{e-mail}>

Polska
{Nazwa/ Nazwisko:}
<{Adres:}
PL – 00 000{Miasto:}>
Tel.: + {Numer telefonu:}
<{e-mail}>

Portugal
{Nome}
<{Morada}
P-0000–000 {Cidade}>
Tel: + {Número de telefone}
<{e-mail}>

România
{Nume}
<{Adresă}

F-00000 {Localité}>
Tél: + {Numéro de téléphone}
<{e-mail}>

Ireland
{Name}
<{Address}
IRL - {Town} {Code for Dublin}>
Tel: + {Telephone number}
<{e-mail}>

Ísland
{Nafn}
<{Heimilisfang}
IS-000 {Borg/Bær}>
Sími: + {Símanúmer}
<{Netfang }>

Italia
{Nome}
<{Indirizzo}
I-00000 {Località}>
Tel: + {Numero di telefono}>
<{e-mail}>

Κύπρος
{Όνομα}
<{Διεύθυνση}
CY-000 00 {πόλη}>
Τηλ: + {Αριθμός τηλεφώνου}
<{e-mail}>

Latvija
{Nosaukums}
<{Adrese}
{Pilsēta}, LV{Pasta indekss }>
Tel: + {Telefona numurs}
<{e-mail}>

Lietuva
{pavadinimas}
<{adresas}
LT {pašto indeksas} {miestas}>
Tel: +370{telefono numeris}
<{e-mail}>

{Oraş} {Cod poştal} – RO>
Tel: + {Număr de telefon}
<{e-mail}>

Slovenija
{Ime}
<{Naslov}
SI-0000 {Mesto}>
Tel: + {telefonska številka}
<{e-mail}>

Slovenská republika
{Meno}
<{Adresa}
SK-000 00 {Mesto}>
Tel: + {Telefónne číslo}
<{e-mail}>

Suomi/Finland
{Nimi/Namn}
<{Osoite/Adress}
FIN-00000 {Postitoimipaikka/Stad}>
Puh/Tel: + {Puhelinnumero/Telefonnummer}
<{e-mail}>

Sverige
{Namn}
<{Adress}
S-000 00 {Stad}>
Tel: + {Telefonnummer}
<{e-mail}>

United Kingdom
{Name}
<{Address}
{Town} {Postal code} – UK>
Tel: + {Telephone number}
<{e-mail}>

This leaflet was last revised in <{MM/YYYY}> <{month YYYY}.>

<This medicine has been given 'conditional approval'. This means that there is more evidence to come about this medicine.
The European Medicines Agency will review new information on this medicine at least every year and this leaflet will be updated as necessary.>

<This medicine has been authorised under 'exceptional circumstances'. This means that <because of the rarity of this disease> <for scientific reasons> <for ethical reasons> it has been impossible to get complete information on this medicine.
The European Medicines Agency will review any new information on this medicine every year and this leaflet will be updated as necessary.>

<Other sources of information>

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu. <There are also links to other websites about rare diseases and treatments.>

<This leaflet is available in all EU/EEA languages on the European Medicines Agency website.>

<---------->

<The following information is intended for healthcare professionals only:>