Section Guidance for Part 4 — Summary of Product Characteristics (SmPC) — of a WHO Public Assessment Report (WHOPAR)

The Summary of Product Characteristics (SmPC) is submitted by the applicant when submitting a finished pharmaceutical product to WHO for prequalification. After evaluation by the assessment team it will be included as Part 4 of the WHO Public Assessment Report that will be posted on the website of the WHO Prequalification Team: medicines, should the product attain prequalification.

Guidance regarding Sub-sections 4.6, 4.8 and 6.4 of the SmPC are given below.

Guidance for Sections 4.6 and 6.4 is based on the European Medicines Agency's Guideline on Risk Assessment of Medicinal Products on Human Reproduction and Lactation: from Data to Labelling. Guidance for Section 4.8 is based on MedDRA[1] guidance.

1. SECTION 4.6 (FERTILITY, PREGNANCY AND LACTATION)

Statements for use in *Sub-section 4.6 Fertility, Pregnancy and lactation* of the SmPC are given below.

<text> signifies text to be selected or deleted as appropriate while {text} refers to information to be added.

1.1 WITH RESPECT TO 'PREGNANCY'

[1] < Based on human experience (specify) <{Active substance} causes congenital malformations (specify) when administered during pregnancy.

[or]

harmful pharmacological effects during pregnancy and/or on the foetus/new-born child.>

{Invented name} is contraindicated <during pregnancy><during {trimester} of pregnancy> [this case is a strict contraindication] (see section 4.3).

<Women of childbearing potential have to use effective contraception <during and up to {number} weeks after> treatment.>>

[2] < Based on human experience (specify) {Active substance} <is suggested / suspected to cause congenital malformations (specify) when administered during pregnancy.

A <Studies in animals have shown reproductive toxicity (see section 5.3).>

[or]

B <Animal studies are insufficient with respect to reproductive toxicity (see section 5.3).>
{Invented name} should not be used<during pregnancy><during {trimester} of pregnancy> unless the clinical condition of the woman requires treatment with {active substance}.

[1] http://www.meddra.org/

<Women of childbearing potential have to use effective contraception <during <and up to {number} weeks after)> treatment. >>

[3] < Based on human experience (specify) {Active substance} <is suggested / suspected to cause congenital malformations (specify) when administered during pregnancy.

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).

{Invented name} should not be used<during pregnancy><during {trimester} of pregnancy> unless the clinical condition of the woman requires treatment with {active substance}.

<Women of childbearing potential have to use effective contraception <during <and up to {number} weeks after)> treatment, >>

[4] <There are no or limited amount of data from the use of {Active substance} in pregnant women>

A <Studies in animals have shown reproductive toxicity (see section 5.3).>

[or]

B <Animal studies are insufficient with respect to reproductive toxicity (see section 5.3).>

{Invented name}} is not recommended < during pregnancy > <during {trimester} of pregnancy > and in women of childbearing potential not using contraception >

[5] <There are no or limited amount of data (less than 300 pregnancy outcomes) from the use of {Active substance} in pregnant women>

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).

As a precautionary measure, it is preferable < to avoid the use of {invented name} <during pregnancy > <during {trimester} of pregnancy >.

[6] <A moderate amount of data on pregnant women (between 300-1000 pregnancy outcomes) indicate no malformative or feto/ neonatal toxicity of {Active substance}>.

A <Animal studies have shown reproductive toxicity (see section 5.3).

[or]

B <Animal studies are insufficient with respect to reproductive toxicity (see section 5.3)>.

As a precautionary measure, it is preferable < to avoid the use of {invented name}> <during pregnancy > <during {trimester} of pregnancy >

[7] <A moderate amount of data on pregnant women (between 300-1000 pregnancy outcomes) indicate no malformative or feto/ neonatal toxicity>.

Animal studies do not indicate reproductive toxicity (see section 5.3).

The use of {invented name} may be considered <during pregnancy > <during {trimester} of pregnancy >, if necessary.

[8] <A large amount of data on pregnant women (more than 1000 exposed outcomes) indicate no malformative nor feto/ neonatal toxicity>.

{Invented name} can be used <during pregnancy > <during {trimester} of pregnancy > if clinically needed.

[9] <No effects during pregnancy are anticipated, since systemic exposure to {Active substance} is negligible>. {Invented name} can be used during pregnancy. (E.g. medicinal products for which negligible systemic exposure/negligible pharmacodynamic systemic activity has been demonstrated in clinical situation).

1.2 WITH RESPECT TO 'LACTATION'

1. < {Active substance}/metabolites are excreted in human milk and effects have been shown in breastfed newborns/infants of treated mothers. >

[or]

< {Active substance}/metabolites have been identified in breastfed newborns/infants of a treated mother. <The effect of {Active substance} on newborns/infants is unknown.> *[or]* <There is insufficient information on the effects of {Active substance} in newborns/infants.>

[or]

{Active substance}/metabolites are excreted in human milk to such an extent that effects on the breastfed newborns/infants are likely.

{Invented name}< is contraindicated during breast-feeding (see section 4.3) > *[or]* < should not be used during breast-feeding > *[or]* < Breast-feeding should be discontinued during treatment with {Invented name}> *[or]* < A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from {Invented name} therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.>

2. <It is unknown whether {Active substance}/metabolites are excreted in human milk>

[or]

< There is insufficient information on the excretion of {Active substance}/metabolites in human milk. >

[or]

<There is insufficient information on the excretion of {Active substance}/metabolites in animal milk>

[or]

<Available pharmacodynamic/toxicological data in animals have shown excretion of {Active substance}/metabolites in milk (for details see 5.3)>

[or]

< Physico-chemical data suggest excretion of {Active substance}/metabolites in breast milk>

A risk to the suckling child cannot be excluded.

Invented name} < is contraindicated during breast-feeding (see section 4.3) > [or[< should not be used during breast-feeding > [or] < Breast-feeding should be discontinued during treatment with {Invented name}> [or] < A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from {Invented name} therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

3. < No effects of {Active substance} have been shown in breastfed newborns/infants of treated mothers>

[or]

< No effects on the breastfed newborn/infant are anticipated since the systemic exposure of the breast-feeding woman to {Active substance} is negligible>

[or]

< {Active substance}/metabolites have not been identified in plasma of breastfed newborns/infants of treated mothers.>

[or]
< {Active substance}/metabolites are not excreted in human milk. >

[or]

< {Active substance}/metabolites are excreted in human milk, but at therapeutic doses of {Invented name} no effects on the breastfed newborns/infants are anticipated.>

{Invented name} can be used during breast-feeding.

2. SECTION 4.8 (UNDESIRABLE EFFECTS)

The table below, extracted from MedDRA[2] guidance gives the terminology that should be used when drafting Sub-section 4.8 Undesirable effects.

[MedDRA frequency convention]
<Very common (>1/10)>
<Common (>1/100, <1/10)>
<Uncommon (>1/1,000, <1/100)>
<Rare (>1/10,000, <1/1,000)>
<Very rare (<1/10,000), <including isolated reports>>
[MedDRA system organ class database]
Infections and infestations
Neoplasms benign, malignant and unspecified (including cysts and polyps)
Blood and lymphatic system disorders
Immune system disorders
Endocrine disorders
Metabolism and nutrition disorders
Psychiatric disorders
Nervous system disorders
Eye disorders
Ear and labyrinth disorders

[2] Medical Dictionary for Regulatory Activities. See www.meddra.org

Cardiac disorders
Vascular disorders
Respiratory, thoracic and mediastinal disorders
Gastrointestinal disorders
Hepatobiliary disorders
Skin and subcutaneous tissue disorders
Musculoskeletal and connective tissue disorders
Renal and urinary disorders
Pregnancy, puerperium and perinatal conditions
Reproductive system and breast disorders
Congenital, familial and genetic disorders
General disorders and administration site conditions
Investigations
Injury, poisoning and procedural complications
Surgical and medical procedures

3. SECTION 6.4 (SPECIAL PRECAUTIONS FOR STORAGE) OF THE SUMMARY OF PRODUCT CHARACTERISTICS

The SmPC should include a description of any special precautions to be taken relating to storage conditions as *Sub-section 6.4: Special precautions for storage*. Suggested content for this section is given below.

<text> signifies text to be selected or deleted as appropriate.

<Do not store above <25 ℃> <30 ℃>> or
<Store below <25 ℃> <30 ℃>>

<Store in a refrigerator (2 ℃ – 8 ℃)>

<Store and transport refrigerated (2 ℃ – 8 ℃)>*

<Store in a freezer {temperature range}>

<Store and transport frozen {temperature range}>**

<Do not <refrigerate> <or> <freeze>>

<Store in the original <package>>

<Keep the {container}*** tightly closed>

<Keep the {container}*** in the outer carton>

<This medicinal product does not require any special storage conditions>

<in order to protect from <light> <moisture>>.