19 July 2012
EMA/CHMP/448578/2012
Committee for Medicinal Products for Human Use (CHMP)

Overview of comments on 'Draft guideline on core summary of product characteristics and package leaflet for fludeoxyglucose (^{18}F)' (EMA/CHMP/547466/2012)

Interested parties (organisations or individuals) that commented on the draft document as released for consultation.

Stakeholder no.	Name of organisation or individual
1	Eckert & Ziegler Radiopharma GmbH
2	CBG-MEB, Medicines Evaluation Board, The Netherlands
3	IFAPP = International Federation of Associations of Pharmaceutical Physicians
4	GEHC (GE HealthCare)

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1. General comments

Stakeholder number *(To be completed by the Agency)*	General comment (if any)	Outcome (if applicable) *(To be completed by the Agency)*
3	IFAPP is in agreement with the contents of this guideline	

2. Specific comments on text

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
page 14 – 15 Dosimetry table	1	Comment: the data in the dosimetry table are not in line with ICRP Publication 106, some values have been rounded (e.g. breasts, skin) Proposed change (if any): the data from ICRP Publication 106 should be used	Comment implemented. Alignment with core SmPC and PL.
Lines 249-252 and 297-299	2	Comment: The following generic statement is stated in section 4.2: "*Renal and hepatic impairment* Extensive dose-range and adjustment studies with this medicinal product in normal and special populations have not been performed. The pharmacokinetics of fludeoxyglucose (18F) in renally impaired patients has not been characterised." While in section 4.4 is stated: "Due to the major renal excretion of fludeoxyglucose (18F), in patients with reduced kidney function, careful consideration of the indication is required since an increased radiation exposure is possible in these patients." These two statements do not fully match and a cross-reference in section 4.2 to 4.4 is indicated. In the posology a	The sentence remains as is since it it based on the core SmPC. There was addition of "Activity should be adjusted" for clarity. The crossreference to 4.4 was considered not necessary.

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		statement regarding the involvement of the kidney in excretion of 18F should be made as well. However, the main consequence of renal impairment would be an altered biodistribution, due to the short 18F decay half-life increased radiation exposure seems a smaller problem. Proposed change (if any): A cross-reference in section 4.2 to 4.4 should be included and in the posology a statement regarding the involvement of the kidney in excretion of 18F should be made as well.	
Line 421	2	Comment: Wording regarding fertility should be included conform the current QRD-template.	Comment implemented. Fertility sentence has been added.
Lines 595-810	2	Comment: The proposed PL is not in line with the recently approved core PL for radiopharmaceuticals. Also the currently proposed PL contains quite some wordings which are not written in a patient friendly way.	Comment implemented. Alignment with core SmPC and PL.
Lines 628-632	2	Comment: Some of the wordings (e.g. diagnostic images, medical images) are difficult to understand. Also the indications can be described in better way, e.g like the current PL of Steripet (UK/H/0814/001).	Core SmPC revised taking the comment into consideration
Lines 642-646	2	Comment: Not all warnings and precautions from section 4.4. of the SmPC are listed. Additionally a sentence introductory sentence conform the core PL for radiopharmaceuticals is	The changes were considered relevant to physician and not patient. Not implemented.

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		missing. Proposed change (if any): Lines 642-646 should be changed into: "Warnings and precautions Take special care with X: - if you are a diabetic and your diabetes is currently not equilibrated - if you have an infection or an inflammatory disease - if you are affected by kidney problems - if you recently had surgery - if you had radiotherapy within the last 2-4 months or chemotherapy within the last 6 weeks."	
Line 666	2	Comment: The statement is difficult to understand for patients. Proposed change (if any): Line 666 should be changed into: "agents used to increase the production of blood cells".	Comment implemented.
Lines 670-672	2	Comment: A statement that the patient should drink plenty of water and avoid drinking liquids containing glucose should be included. Also the statement regarding thev blood sugar should be rewritten in a patient friendly way.	Comment implemented with some changes
Lines 680-687	2	Comment: The wording regarding pregnancy and breast-ffeding should be rewritten and made in line with the core PL for radiopharmaceuticals.	Comment implemented. Alignment with core SmPC and PL.

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		Proposed change (if any): Lines 680-687 should be changed into: "If you are pregnant The nuclear medicine doctor will only administer this product during pregnancy if a benefit is expected which would outweigh the risks. If you are breast-feeding Do not breast-feed if you are given X. This is because small amounts of radioactivity may pass into the mother's milk. If you are breast-feeding, your doctor may wait until you have finished breast-feeding before using X. If it is not possible to wait your doctor may ask you to: - stop breast□feeding for 12 hours, and - use formula feed for your child, and - express (remove) breast milk and throw away the milk. Your doctor will let you know when you can start breast-feeding again."	
Lines 692-695	2	Comment: This section should be written according to the core PL for radiopharmaceuticals.	Comment implemented. Alignment with core SmPC and PL.
Lines 703-704	2	Comment: The statement regarding the excipients should be reworded in a more patient friendly way.	Comment implemente but sentence modified to patient friendly wording
Lines 728-729	2	Comment: Already after injection the patient should be	Comment implemented with some changes.

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		completely at rest. This should be reflected in the PL. Proposed change (if any): Line 728 should be changed into: "After injection and during the test, you will…"	
Line 747-749	2	Comment: The recommendations after administration of should not be put between brackets <…> and the time to avoid any close contact with young children and pregnant women should be filled in (12 hours). Proposed change (if any):Lines 747-749 should be changed into: "- avoid any close contact with young children and pregnant women for the 12 hours following the injection. - urinate frequently in order to eliminate the product from your body."	Comment implemented. Alignment with core SmPC and PL.
Section 2.	4	GEHC comment: "per vial" may need to be changed as presentations may vary	Comment implemented
		GEHC suggests the following re-wording: "Fluorine - 18 decays to stable oxygen - 18 with a half-life of 110 minutes by emitting positrons of maximum energy of 634keV, followed by annihilation gamma photons of 511 keV."	Comment not implemented
Section 4.2; Paediatric population	4	GEHC comment: We do not support the recommendation to use the EANM paediatric dosing card included in this section - please refer to" GE Healthcare Position Statement on Radiopharmaceutical Paediatric Posology." We suggest	Comment not implemented as it is not in line with the current Core SmPC.

<table>
<tr><th>Line number(s) of the relevant text

(e.g. Lines 20-23)</th><th>Stakeholder number

(To be completed by the Agency)</th><th>Comment and rationale; proposed changes

(If changes to the wording are suggested, they should be highlighted using 'track changes')</th><th>Outcome

(To be completed by the Agency)</th></tr>
<tr><td></td><td></td><td>deleting text marked as scored out and replacing with the inserted text - which is essentially the original text contained in the previous FDG core SPC (2005).

“…determined from the recommended activity for adults on the basis of body mass, using the following multiplying coefficient:…”
<table>
<tr><td>3 kg = 0.10</td><td>12 kg = 0.32</td><td>22kg = 0.50</td></tr>
<tr><td>4 kg = 0.14</td><td>14 kg = 0.36</td><td>24 kg = 0.53</td></tr>
<tr><td>6 kg = 0.19</td><td>16 kg = 0.40</td><td>26 kg = 0.56</td></tr>
<tr><td>8 kg = 0.23</td><td>18 kg = 0.44</td><td>28 kg = 0.58</td></tr>
<tr><td>10 kg = 0.27</td><td>20 kg = 0.46</td><td>30 kg = 0.60</td></tr>
</table>
<table>
<tr><td>32 kg = 0.62</td><td>42 kg = 0.78</td><td>52-54 kg = 0.90</td></tr>
<tr><td>34 kg = 0.64</td><td>44 kg = 0.80</td><td>56-58 kg = 0.92</td></tr>
<tr><td>36 kg = 0.66</td><td>46 kg = 0.82</td><td>60-62 kg = 0.96</td></tr>
<tr><td>38 kg = 0.68</td><td>48 kg = 0.85</td><td>64-66 kg = 0.98</td></tr>
<tr><td>40 kg = 0.70</td><td>50 kg = 0.88</td><td>68 kg = 0.99</td></tr>
</table></td><td></td></tr>
<tr><td>Section 4.2; method of administration</td><td>4</td><td>GEHC comment: replace 'activimeter' with dose calibrator'</td><td>Comment not implemented, dose calibrator is calibrating by the dose which is in mSv or mGy</td></tr>
</table>

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	4	GEHC comment: "short period" is too general and needs to be quantified to give better guidance. The time will depend on the amount of activity administered.	Comment not implemented since this will depend on the clinical physician
Section 4.4; Individual benefit/risk justification	4	GEHC comment: This should be re-worded to explain the potential for an increased dose exists because it is renally excreted.	Comment has been implemented in the core SmPC
Section 4.4; Patient preparation – Oncology and neurology and infectious diseases	4	GEHC comment: Need to give guidance on how long physical exercise must be avoided before examination.	Comment not implemented as no further details are provided by the company.
	4	GEHC comment: Need to define "less background noise" - less than what?	Comment implemented
Section 4.4; Interpretation of the PET images with 18F		For the paragraph that start with "Sensitivity of coincidence PET…" up to "… imaging modalities (eg. CT, ultrasonography, MRI)" GEHC comment: 1) The highlighted text contains very specific direction which may be interpreted prescriptively and a) will get out of date and b) may exclude other modalities. 2) CDET is an older technology and in our experience rarely used.	Comment not implemented as smaller countries may still use CDET
	4	GEHC comment: Ultrasonography is not tomographic.	Comment implemented. "Ultrasonography" replaced with echotomography"
	4	Include the wording "attenuation-corrected" in the sentence:	Comment implemented.

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		"When a hybrid PET-CT scanner is used with or without administration CT contrast media, some artefacts may occur on the attenuation-corrected PET images."	
Section 4.4; specific warnings	4	GEHC comment: This paragraph is confusing as it implies that according to the time of preparation the content of sodium may differ? Re-word so meaning is clear.	Comment implemented.
Section 4.9; Overdose	4	GEHC comment: The latter sentence in this paragraph is ambiguous as it appears to imply that the extent of the forced diuresis should be dependent on how high or low is the estimated effective dose. We suggest to delete the latter sentence.	Do not agree. Comment not implemented
Section 12; Instructions for preparation of radiopharmaceutical	4	GEHC comment: replace 'activimeter' with dose calibrator'	Comment not implemented see previous comment