HAUTE AUTORITÉ DE SANTÉ

The legally binding text is the original French version

TRANSPARENCY COMMITTEE

OPINION

9 March 2011

IASOflu 2.0 GBq/mL solution for injection
Multidose vial with activity of between 0.37 GBq and 22.0 GBq (CIP code: 573 228 0)

Applicant: IASON GmbH

^{18}F sodium fluoride
ATC code: V09IX06

Date of Marketing Authorisation: 21 July 2008 (National procedure)

List I
Medicinal product reserved for hospital use

Radiopharmaceuticals should be received, used and administered only by authorised persons in designated clinical settings. Their receipt, storage, use, transfer and disposal are subject to the regulation described in article R 1333-24 of the French Public Health Code.

Reason for request: Inclusion on the list of medicines approved for hospital use.

Medical, Economic and Public Health Assessment Division

1 CHARACTERISTICS OF THE MEDICINAL PRODUCT

1.1. Active ingredient

Sodium fluoride-(^{18}F)

1.2. Indication

This medicinal product is for diagnostic use only.

Sodium fluoride-(^{18}F) is indicated for use with positron emission tomography (PET).

IASOflu is indicated for functional imaging where abnormally altered osteogenic activity is the diagnostic target.
The following indications for PET with sodium fluoride-(18F) have been particularly documented:
Detection and localisation of bone metastases in case of proven cancer in adults;
As an aid in the evaluation of back pain of ambiguous origin, when conventional imaging modalities are inconclusive;
For children: as an aid in the detection of the presence of bone lesions relatated to suspected child abuse.

1.3. Dosage

The radioactivity usually recommended for adults is -5 MBq/kg of body mass depending on the PET(/CT) machine in use and acquisition mode, administered by direct intravenous injection.

Only few clinical data are available for patients aged under 18 years concerning the safety and diagnostic efficacy of this product. The use in children and adolescents has to be considered carefully, based upon clinical needs and assessing the risk/benefit ratio in this patient group.
The emission scans are usually started 60 minutes after the injection of sodium fluoride-(^{18}F)."

2 SIMILAR MEDICINAL PRODUCTS

2.1. ATC Classification (2011)

V	Various
V09	Diagnostic radiopharmaceuticals
V09I	Tumour detection
V09IX	Other diagnostic radiopharmaceuticals for tumour detection
V09IX06	Sodium fluoride-(^{18}F)

2.2. Medicines in the same therapeutic category

- CISNAF 100 MBq/mL sodium fluoride-(^{18}F), solution for injection

2.3. Medicines with the same diagnostic aim

Most available radiopharmaceuticals are used with gamma cameras for planar mode single-photon emission computed tomography (SPECT), while IASOFLU is used with positron emission tomography (PET).

Technetium pertechnetate (DPD) (ATC code: V09BA04)

- TECEOS, kit for the preparation of technetium [^{99m}Tc] 3,3-diphosphono-1,2 propanedicarboxylic acid (DPD) injection.
  Indication: after reconstitution with sodium pertechnetate (^{99m}Tc) solution for injection the agent may be used for bone scintigraphy, where it delineates areas of altered osteogenesis (most recent Transparency Committee opinion: actual benefit = substantial, improvement in actual benefit (IAB) = V).

Sodium oxidronate (or sodium hydroxymethylene diphosphonic acid - HMDP) (ATC code: V09BA01)

- OSTEOCIS, powder for solution for injection. Kit for the preparation of technetium oxidronate ^{99m}Tc solution for injection
  Indication: this medicinal product is for diagnostic use only. After reconstitution with sodium pertechnetate (^{99m}Tc) solution for injection, technetium [^{99m}Tc] oxidronate solution for injection is indicated as a skeletal imaging agent to delineate areas of abnormal osteogenesis (actual benefit = substantial, IAB = V).

- TECHNESCAN HDP, powder and kit for preparation of technetium [^{99m}Tc] oxidronate solution for injection.
  Indication: bone scintigraphy to delineate areas of osteogenesis in the process of remodelling.

Sodium medronate (ATC code: V09BA02)

- AMERSCAN MEDRONATE II, kit for the preparation of technetium (^{99m}Tc) medronate solution for injection.
  Indication: after reconstitution with sodium pertechnetate (^{99m}Tc) solution for injection, the agent may be used for bone scintigraphy, where it delineates areas of altered osteogenesis (Actual benefit = substantial, IAB = V).

Fludeoxyglucose (ATC Code: V09IX04)

- FLUDEOXYGLUCOSE [^{18}F]-IBA, solution for injection
- FLUCIS, fludeoxyglucose [^{18}F] (250 MBq/ml) solution for injection (Actual benefit = substantial, IAB = V).
  FLUDEOXYGLUCOSE [^{18}F] CIS BIO INTERNATIONAL, solution for injection (Actual benefit = substantial, IAB = V).
- GLUCOTEP, solution for injection
  Indication: fludeoxyglucose [^{18}F] is indicated in oncology as an imaging examination used for a functional assessment of disease, organs or tissues to look for abnormal glucose metabolism […] (Actual benefit = substantial, IAB=V).

3 ANALYSIS OF AVAILABLE DATA

3.1. Efficacy

The studies included in the dossier are derived from bibliographical data. The same studies were used in the Marketing Authorisation dossier.

3.1.1. Indications in oncology

The use of ^{18}F sodium fluoride in PET to detect oncological lesions has been studied in five trials comparing ^{18}F sodium fluoride (^{18}F Na) with ^{99m}Tc-labelled bisphosphonates. This marker is the best comparator, as the other radiopharmaceuticals, ^{18}F fludeoxyglucose, ^{18}F fluorodopa, ^{18}F fluorocholine do not have the specific indication of detection of bone lesions (see Table 2).

Table 2: Comparison of technical performance between PET with ^{18}F sodium fluoride (^{18}F Na) and bone scintigraphy with ^{99m}Tc-labelled bisphosphonates

Trial reference Year	Aims Design	Treatments compared Dosages Treatment duration Populations in each group (randomised and analysed)	Characteristics of the population included	Primary endpoint (I) and most relevant secondary endpoints (II)	Efficacy results for primary endpoint (and most relevant secondary endpoints)
Schirrmeister[1] 1999 A	Detection of bone metastases of prostate, thyroid (stage III or IV) and lung cancer.	Comparison of performance of ^{18}F Na PET and bone scintigraphy (planar BS)	Cancer: Prostate: N=20 Thyroid: N=19 Lung: N=5	(I) Global sensitivity (Se) and specificity (Sp) of both methods (II) Area under the curve	Se ^{18}F Na PET 15/15=100% BS 13/15=87% Sp ^{18}F Na PET 29/29=100% BS 20/29=69% Area under the curve ^{18}F Na PET 0.99 BS 0.64, p<0.05
Schirrmeister[2] 1999 B	Detection of bone metastases of breast cancer The reference investigation was a panel of diagnostic tests.	Comparison of performance of ^{18}F Na PET and bone scintigraphy (planar BS) with ^{99m}-Tc–methylene diphosphonic acid	Breast cancer: N=34 Mean age = 52 years [37-75]	(I) Sensitivity and specificity of both methods (II) Area under the curve	Se ^{18}F Na PET 17/17=100% BS 11/17=65% Sp ^{18}F Na PET 17/17=100% BS 12/17=70% Area under the curve ^{18}F Na PET 1.00 BS 0.82, p<0.05
Hetzel[3] 2003	Detection of vertebral bone metastases of lung cancer	Comparison of performance of ^{18F} Na PET and bone scintigraphy (planar BS and SPECT)	Lung cancer N=103 72 men, 31 women Mean age = 62 years [38-81]	(I) Sensitivity of the 3 methods (II) Area under the curve	Se ^{18}F Na PET 28/33=85% BS 17/33=52% BS SPECT 26/33=79% Area under the curve ^{18}F Na PET 0.99 BS 0.77 BS SPECT 0.87, p<0.005 PET F Na 10/103=9.7% BS SPECT 8/103=7.8%

[1] Schirrmeister H [1999A], Guhlmann A, Kotzerke J, Santjohanser C, Kuhn T, Kreienberg R, Messer P, Nussle K, Elsner K, Glatting G, Trager H, Neumaier B, Diederichs C, Reske SN. Early detection and accurate description of extent of metastatic bone disease in breast cancer with fluoride ion and positron emission tomography. J Clin Oncol 1999; 17: 2381-89.
[2] Schirrmeister H [1999B], Guhlmann A, Elsner K, Kotzerke J, Glatting G, Rentschler M, Neumaier B, Trager H, Nussle K, Reske SN. Sensitivity in detecting osseous lesions depends on anatomic localization: planar bone scintigraphy versus 18F PET. J Nucl Med 1999; 40: 1623-9.

Even-Sapir[4] 2006	Detection of bone metastases of prostate cancer	Comparison of performance of ^{18}F Na PET and bone scintigraphy (planar BS) and SPECT (technetium medronate)	Prostate cancer: N=44 Mean age: 71.6 years	(I) Sensitivity and specificity of the 3 methods	Se ^{18}F Na PET 23/23=100% BS 13/23=57% BS SPECT 18/23=78% Sp ^{18}F Na PET 21/21=100% BS 12/21=57% BS SPECT 14/21=67%
Beheshti[5] 2008	Detection of bone metastases of prostate cancer	Comparison of performance of ^{18}F Na PET and ^{18}F Fluorocholine PET (FCH)	Prostate cancer: N=38 men 321 sites Prostate cancer confirmed by biopsy. Mean age: 69 years	(I) Sensitivity and specificity of both methods (II) Impact on treatment	Se ^{18}F Na PET 81% FCH PET 74%, p=0.12 NS Sp ^{18}F Na PET 93% FCH PET 99%, p=0.01 No change in treatment between the 2 groups.

[3] Hetzel M, Arslandemir C, Konig HH, Buck AK, Nussle K, Glatting G, Gabelmann A, Hetzel J, Hombach V, Schirrmeister H. F-18 NaF PET for detection of bone metastases in lung cancer: accuracy, cost-effectiveness, and impact on patient management. J Bone Miner Res 2003; 18: 2206-14.

[4] Even-Sapir E, Metser U, Mishani E, Lievshitz G, Lerman H, Leibovitch I. The detection of bone metastases in patients with high-risk prostate cancer: 99mTc-MDP planar bone scintigraphy, single- and multi-field-of-view TEMP, 18F-Fluoride PET, and 18F-Fluoride PET/CT. J Nucl Med 2006; 47: 287-97.

[5] Beheshti M, Vali R, Waldenberger P, Fitz F, Nader M, Loidl W, Broinger G, Stoiber F, Fogelman I, Langsteger W. Detection of bone metastases in patients with prostate cancer by F-18 fluorocholine and F-18 fluoride PET-CT: a comparative study. Eur J Nucl Med Mol Imaging 2008; 35: 1766-74.

Small case series have been described in other indications, particularly in the diagnosis of metastases of thyroid and kidney cancer. In view of the low-level evidence of these studies, they have not been included in this document.

3.1.2. Indications other than cancer

Comparative studies of diagnostic performances of sodium fluoride-(18F) PET(/CT) and conventional imaging include 15 to94 patients. Three studies have been carried out in patients with back pain of ambiguous origin (indication “aid in the evaluation of back pain of ambigous origin, when conventional imaging modalities are not conclusive”), and one retrospective study in detection of abuse-related fractures in children (indication: “aid in the detection of the presence of bone lesions related to suspected child abuse”). Results are given in Table 3.

Table 3: Impact of ^{18}F sodium fluoride (^{18}F Na) on detection of non-cancer lesions

	Indications and number of patients		Imaging	Endpoint	Impact on treatment	Outcome
Drubach 2010[6]	Abused children < 2 years	22	^{18}F Na PET radiographs	Lesion detection rate: 85% 72%	Not stated	Not available
Lim 2007[7]	[Low] back pain in young patients 4-26 years	94	^{18}F Na PET	Detection rate 52/94=55%	Not stated	Not available
Ovadia 2007[8]	[Low] back pain in adolescents (9-19 years)	15	^{18}F Na PET/CT	Detection rate 10/15=67% 0% (conventional imaging)	9/15=60%	10 patients with positive results on PET included 4 cases of spondylolisthesis, 3 fractures, 2 osteoid osteomas, 1 osteitis, 1 sacroiliitis and 2 herniated discs. No patients whose therapy was tailored to PET findings continued to have pain.

[6] Drubach LA, Johnston PR, Newton AW, et al. Skeletal trauma in child abuse: detection with 18F-NaF PET. Radiology. 2010; 255: 173-81.
[7] Lim R, Fahey FH, Drubach LA et al. Early experience with fluorine-18 sodium fluoride bone PET in young patients with back pain. J Pediatr Orthop. 2007; 27: 277-82.
[8] Ovadia D, Metser U, Lievshitz G, et al. Back pain in adolescents: assessment with integrated 18F-fluoride positron-emission tomography-computed tomography. J Pediatr Orthop 2007; 27: 90-93.

Gamie 2009[9]	Low back pain	67 42/67 without surgery 25/67 after spinal surgery	F Na PET/CT conventional imaging	Group A: no surgery Se=37/42=88% Total Se=56/67=84% Group B: Postoperative 19/25=76%	Not available	Not available

[9] Gamie S, El-Maghraby T. The role of PET/CT in evaluation of facet and disc abnormalities in patients with low back pain using (18)F-Fluoride. Nucl Med Rev Cent East Eur. 2008; 11: 17-21.

3.2. Tolerance

The Summary of Product Characteristics states that no serious side effects have been reported to date.
It also states that exposure to ionising radiation can lead to cancer or development of hereditary defects. However, experience has shown that the frequency of such adverse events associated with diagnostic procedures involving nuclear medicine is very low, as a result of the low levels of radioactivity employed.

3.3. Conclusion

In five published studies that included between 34 and 103 patients, the performance of PET/CT after administration of ^{18}F sodium fluoride (^{18}F Na) was superior for the detection and localisation of bone metastases to that of the reference examination, bone scintigraphy using technetium-^{99m}-labelled biphosphonates. The sensitivity of IASOflu was 81-00% (compared with 52-87% for the comparator), and specificity was 93-100% (compared with 57-70% for the comparator). The small number of patients included in the studies is explained by limitations related to carrying them out (limited availability of equipment, problems with carrying out a number of diagnostic examinations using radiation in the same patient, etc.).
However, it is regrettable that these studies did not present results for positive predictive value and negative predictive value, as these indicators provide information about the probability of disease being present when findings are positive and the probability of disease being absent when findings are negative.
Four studies that included between 15 and 94 patients assessed PET in low back pain and in child abuse. It is difficult to draw any conclusions from these studies in view of the small number of patients included, and the fact that sensitivity and specificity of diagnostic performance were not evaluated in two of the four studies.
As ^{18}F sodium fluoride (^{18}F Na) is a diagnostic medicine, it has no direct effect on quality of life or survival.
The tolerance of the method as a whole are related to the ionising radiation and would seem to be uncommon in view of the low levels of activity used.

The use of this product requires radiation protection.

4 TRANSPARENCY COMMITTEE CONCLUSIONS

4.1. Actual benefit

4.1.1. Detection and localisation of bone metastases in adults with confirmed cancer

The findings of the examination are used to establish disease severity.

This proprietary medicinal product is intended for diagnostic purposes.

The efficacy/ adverse effects ratio for this medicinal product is high in this indication.

Alternatives to this product exist.

> Public health benefit: the main indication for positron emission tomography examinations (PET) is to detect metastases and to monitor cancer patients, particularly those with breast, prostate or lung cancer.
>
> Metastatic cancer is a condition which is a major burden. Improvement in screening for breast cancer is one of the priorities included in the French law of 09 August 2004 relating to public health policy.
>
> In view of the data from clinical trials, PET after administration of ^{18}F sodium fluoride has better diagnostic performance than the comparator, bone scintigraphy performed using ^{99m}Tc-labelled bisphosphonates. However, in population terms, no improvement in patient care has been demonstrated.
>
> Consequently, the public health benefit of IASOflu it is expected to be low.

The actual benefit of this proprietary medicinal product is substantial in the indication "detection and localisation of bone metastases in adults with confirmed cancer".

4.1.2. Aid in the evaluation of back pain of ambiguous origin, when conventional imaging modalities are inconclusive

The findings of the examination are used to establish disease severity.

This proprietary medicinal product is intended for diagnostic purposes.

The efficacy/adverse effects ratio for this medicinal product is unknown in this indication.

Alternatives to this product exist.

> Public health benefit: low back pain is defined as pain in the lower part of the spinal column. In 95% of cases, its origin is not clearly defined (no identifiable abnormalities on imaging examinations). Its severity is related to pain that has become chronic (present for more than 180 days), when low back pain leads to incapacity and disability, deterioration in quality of life, and social and professional isolation. In particular, low back pain is the most common reason for stopping work[10]. In a survey carried out 2004, the estimated prevalence of chronic low back pain in France was 7-

[10] GTNDO report [GTNDO = French expert group that defines public health objectives], Paris: Ministry of Health, Family and Disabled People; 2003.

8.5%[11]. The burden of chronic low back pain is therefore substantial. Reducing the prevalence of low back pain in the general population is one of the aims of the 2004 French law on public health.

The available data (series including a total of 176 patients) are inadequate for assessing the impact of IASOFLU in population terms in identifying the cause of chronic low back pain. In addition, there is no way of estimating any improvement in care of patients with low back pain for which the cause has been diagnosed using of IASOFLU.

The proprietary medicinal product IASOFLU does not satisfy an identified public health need.

Consequently, it is not anticipated that there will be any public health benefit from the proprietary medicinal product IASOFLU in this indication.

The actual benefit of this proprietary medicinal product is inadequate in the indication "aid to diagnosis of low back pain of unknown origin, when conventional imaging modalities are inconclusive".

4.1.3. In children: aid to detection of bone lesions in relation to suspected child abuse.

The findings of the examination are used to establish disease severity.

The proprietary medicinal product is intended for diagnostic purposes.

The efficacy/ ratio for this medicinal product is indeterminate in this indication.

Alternatives to this product exist.

Public health benefit: The public health burden caused by intentional trauma in childhood is substantial. Prevention of child abuse is one of the aims of the 2004 French law on public health, renewal of which was proposed by the Haut conseil de la santé publique (HCSP) (the French High Council for Public Health) in 2010. Detecting intentional trauma in children is a public health need.

The available data (one case series including/assessing 22 children) are insufficient for drawing any conclusion on the impact of IASOFLU in population terms of IASOFLU in detecting intentional trauma in children.

Consequently, it is not anticipated that there will be any public health benefit from the proprietary medicinal product IASOFLU in this indication.

The actual benefit of this proprietary medicinal product is inadequate in the indication “aid to detection of bone lesions in relation to suspected child abuse."

4.2. Improvement in actual benefit (IAB):

IASOflu does not provide any improvement in actual benefit (IAB V) compared with CISNAF in its indications.

[11] Leclerc A, Chastang JF, Ozguler A, Ravaud JF. Chronic back problems among persons 30 to 64 years old in France. Spine 2006; 31 (4): 479-84.

4.3. Diagnostic use

The investigations for initial extension of lung, prostate and breast cancer include bone scintigraphy to look for metastases, at least in cancers that are advanced at the time of diagnosis, as these forms of cancer tend to metastasise to bone[7]. During follow-up, the reasons for performing investigations to look for bone metastases are in particular onset of bone pain, or an increased concentration of tumour marker (CEA, CA 15.3, PSA). It is not anticipated that both imaging examinations (scintigraphy and PET with ^{18}F sodium fluoride) will be carried out in succession in the same patient, although in certain cases it is acceptable, after discussion, that PET with ^{18}F sodium fluoride may be carried out to provide more information about a suspicious image found during bone scintigraphy. The discovery of bone metastases changes the disease stage and affects treatment (cancellation of curative surgery and indication for chemotherapy at initial staging, hormone therapy or radiotherapy for a single location when discovered during follow-up, etc).

Positron emission tomography (PET) is a functional imaging method with demonstrated clinical benefit, mainly in oncology[12]. The tracer most frequently used is ^{18}F fluorodeoxyglucose or FDG[13]. In addition, a Guide to the proper use of medical imaging examinations has been produced by the learned societies and professional bodies concerned, with the support of the French nuclear authority (the Directorate General for Nuclear and Radiation Protection (DGSNR)), and by HAS[14]. The Guide addresses the benefit of PET. It is currently being updated by HAS.
PET with FDG is indicated particularly as part of the pretreatment workup for breast cancer, to look for remote metastases in advanced forms and those with a poor prognosis, and during follow-up of breast cancer to check for any recurrence on the wall, in the lymph nodes or as metastases (Grade B recommendation).
For tests for metastatic spread, there is no consensus on the tests required (chest radiograph, abdominal and pelvic ultrasound, bone scintigraphy, etc.). They are therefore prescribed according to the patient's age and general condition, the clinical stage of disease and the normal practice of the teams managing the patient[15].

PET with FDG is also indicated as one of the investigations to look for metastases in lung cancer (Grade B recommendations) and in patients eligible for surgery to determine any local, regional or remote metastases[16].

For tests for metastatic spread of prostate cancer, imaging examinations are only performed if they may affect patient treatment and for localised tumours according to risk of recurrence established by the D'Amico classification[17]:
- in low-risk patients: tests for lymph node or metastatic extension are not indicated.
- in intermediate or high-risk patients: tests may include bone scintigraphy, abdominal and pelvic CT scan or MRI[18] .

[12] NICE METHODS, EVIDENCE & GUIDANCE. The Diagnosis and Treatment of Lung Cancer, February 2005.
[13] *Standards, options et recommandations pour l'utilisation de la tomographie par émission de positons au fludésoxyglucose [18F] (PET-FDG) en cancérologie.* Fédération Nationale des Centres de lutte contre le Cancer; February 2002.
[14] Combined positron emission tomography/computed tomography, HAS; 2005.
[15] Place of Breast MRI in the Pre-Treatment Locoregional Spread Assessment of Breast Cancer. Health technology assessment, HAS March 2010
[16] Long-term condition (ALD) guide no. 30 - Malignant neoplasms of lymphatic or haematopoietic tissue. Lung cancer and malignant pleural mesothelioma HAS-INCA 2009 [in French].

[17] D'Amico A, Altschuler M, Whittington R, Kao G, Malkowicz SB, Wein A. The use of clinical parameters in an interactive statistical package to predict pathological features associated with local failure after radical prostatectomy for prostate cancer.,Clin Perform Qual Health Care. 1993; 1 (4): 219-22.

[18] HAS-INCA Long-term condition (ALD) guide no. 30 - Prostate cancer - September 2008 [in French].

Bone scintigraphy may be performed by planar or tomographic gamma scintigraphy (using ^{99m}Tc-labelled bisphosphonates), or by PET/CT after administration of ^{18}F sodium fluoride. As with scintigraphy, PET now includes "whole-body" acquisition and makes it possible to visualise the whole skeleton in a single examination. So in principle, PET/CT after administration of ^{18}F sodium fluoride may replace bone scintigraphy by gamma scintigraphy, with better image quality.
Finally, the consequences of the current shortage of ^{99m}Tc generators could be avoided as ^{18}F is produced in a medical cyclotron rather than a nuclear reactor.

Place of ^{18}F sodium fluoride in the diagnostic strategy:
In principle, PET after administration of IASOflu may replace bone scintigraphy by gamma scintigraphy, with better image quality and the advantage of requiring a medical cyclotron rather than a nuclear reactor. The waiting time for a test is shorter, with better quantification of radiopharmaceutical binding for detecting bone metastases in prostate, breast and lung cancer. It has the advantage of not using bisphosphonates (^{99m}Tc), which avoids deterioration in image quality in patients taking bisphosphonates and the adverse events which had been reported with bisphosphonates, even at the low doses used in scintigraphy.
In two of the three cancers cited that metastasise to bone (lung and breast), there is also an indication for PET after administration of FDG, which logically should be performed before PET with ^{18}F sodium fluoride as it is also effective in detecting malignant neoplasms situated in the abdominal organs as well as most bone metastases, including intramedullary lesions. The ideal indication for PET with ^{18}F sodium fluoride would be in problem cases, e.g. in suspected sclerotic bone metastases.

4.4. Target population

In theory, PET with ^{18}F can replace bone scintigraphy, which is currently the examination generally used in oncology to look for bone metastases.
According to national health insurance data (the *Echantillon Généraliste des Bénéficiaires* (EGB) database, a representative sample of individuals covered by French National Insurance)[19], 1325 patients had bone scintigraphy in 2010[20] and 682 (51%) of them were classed as qualifying for the ALD 30 regimen ("malignant neoplasm"). The EGB makes it possible to evaluate the frequency of scintigraphy procedures carried out in the private sector, but not the frequency of procedures carried out in the public sector.
According to an InVS/IRSN[21] report, an estimated total of 493 588 bone scintigraphy procedures were carried out in France in 2007 (taking public and private sectors together).
As 51% of bone scintigraphy examinations are carried out in the context of an oncological indication, this represents about 250 000 bone scintigraphy examinations a year.
The theoretical estimated target population for PET with ^{18}F is therefore 250 000 procedures a year.
In practice, PET with ^{18}F will only be appropriate for a limited number of patients because of the availability of PET/CT equipment, the cost, and also because in oncology PET is primarily carried out using FDG (particularly in lung and breast cancer), with PET with ^{18}F being reserved for problem cases (see Diagnostic strategy).

4.5. Transparency Committee recommendations

The transparency Committee recommends inclusion on the list of medicines approved for hospital use and various public services in the indication "detection and localisation of bone metastases in adults with confirmed cancer".

[19] *L'échantillon généraliste de bénéficiaires : représentativité, portée et limites. Points de repère* no. 25. September 2009.
[20] Selected CCAM procedures: PAQL001 to PAQL010
[21] InVS. *Exposition de la population française aux rayonnements ionisants liée aux actes de diagnostic médical en 2007.* http://www.invs.sante.fr

The Committee does not recommend inclusion on the list of medicines approved for use by hospitals and various public services in the indications:
- Aid to diagnosis of low back pain of unknown origin, when conventional imaging modalities are inconclusive;
-In children: aid to diagnosis of bone lesions in relation to suspected child abuse.

The Transparency Committee will reassess the actual benefit of proprietary medicinal products containing ^{18}F sodium fluoride in one year, as part of an updated review of their place in the diagnostic strategy.