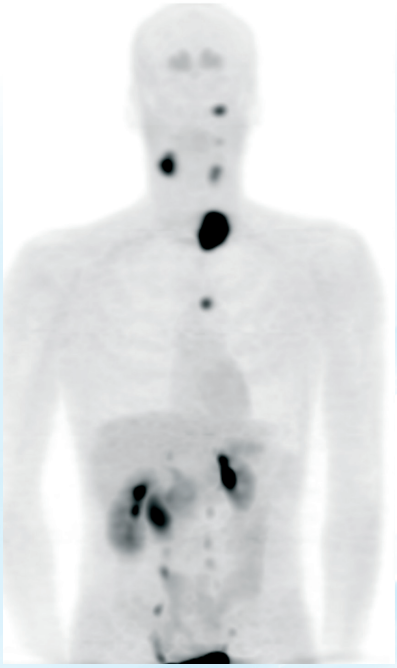
IASOdopa®
6-fluoro-(^{18}F)-L-dihydroxyphenylalanine

Marketing Authorisation countries

Countries	1st Marketing Authorisation	Marketing Authorisation number
France	16.11.2006	34009 578 256 2 1 (15ml) ; 34009 566 897 8 1 (25ml)
Austria	29.11.2007	4-00032
Germany	31.08.2007	69747.00.00
Italy	12.09.2013	038449029 (15 ml) ; 038449017 (25 ml)



IASOdopa® PET/CT scan:
Patient with multiple head and neck paragangliomas

Courtesy of: Dr. Taieb, MD-PhD, Department of Nuclear Medicine, La Timone University Hospital, European Center for Research in Medical Imaging, Aix-Marseille University, Marseille, France

CLINICAL PARTICULARS

This medicinal product is for diagnostic use only.
6-fluoro-(^{18}F)-L-dopa is indicated for use with positron emission tomography (PET) in adults and paediatric population.

Neurology
PET with 6-fluoro-(^{18}F)-L-dopa is indicated for detecting loss of functional dopaminergic neuron terminals in the striatum. It can be used for diagnosis of Parkinson's disease and differentiation between essential tremor and parkinsonian syndromes.

Oncology
Among medical imaging modalities, PET with 6-fluoro-(^{18}F)-L-dopa provides a functional approach of pathologies, organs or tissues where enhanced intracellular transport and decarboxylation of the amino acid dihydroxyphenylalanine is the diagnostic target. The following indications have been particularly documented:

Diagnosis
- Diagnosis and localisation of focal hyperplasia of beta islet cells in the case of hyperinsulinism in infants and children
- Diagnosis and localisation of paragangliomas in patients with a gene mutation of the succinate dehydrogenase D variant
- Localisation of pheochromocytoma

Staging
- Phaeochromocytoma and paraganglioma
- Well differentiated neuroendocrine tumours of midgut

Detection in case of reasonable suspicion of recurrences or residual disease
- Primary brain tumours of all grades of differentiation
- Phaeochromocytoma and paraganglioma
- Medullary thyroid cancer with elevated serum levels of calcitonin
- Well differentiated neuroendocrine tumours of midgut
- Other endocrine digestive tumours when somatostatin receptor scintigraphy is negative

IASON GmbH
Feldkirchner Strasse 4, A-8054 Graz-Seiersberg
Tel. +43-(0)316-28 43 00-0, Fax +43-(0)316-28 43 00-114, e-mail: info@iason.eu, www.iason.eu

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CLINICAL PARTICULARS

4.2. Posology and method of administration

Posology

Adults and elderly population

In oncology, the recommended activity for an adult weighting 70 kg is 2 to 4 MBq/kg (this activity has to be adapted according to the body weight of the patient, the type of camera used PET(/CT), and acquisition mode), administered by direct slow intravenous injection over approximately one minute.

One half of this activity may be administered for neurological indications not requiring whole body images.

Renal / Hepatic impairment

Careful consideration of the activity to be administered is required since an increased radiation exposure is possible in these patients.

Paediatric population

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 activities to be administered to children and adolescents may be calculated according to the recommendations of the European Association of Nuclear Medicine (EANM) paediatric dosage card; the activity administered to children and to adolescents may be calculated by multiplying a baseline activity (for calculation purposes) by the body-mass-dependent coefficients given in the table below.

$A[MBq]_{Administered}$ = Baseline Activity × Coefficient

The Baseline Activity for 2D imaging is 25.9 MBq and for 3D imaging 14.0 MBq (recommended in children).

Weight [kg]	Multiple	Weight [kg]	Multiple	Weight [kg]	Multiple
3	1	**22**	5.29	**42**	9.14
4	1.14	**24**	5.71	**44**	9.57
6	1.71	**26**	6.14	**46**	10.00
8	2.14	**28**	6.43	**48**	10.29
10	2.71	**30**	6.86	**50**	10.71
12	3.14	**32**	7.29	**52-54**	11.29
14	3.57	**34**	7.72	**56-58**	12.00
16	4.00	**36**	8.00	**60-62**	12.71
18	4.43	**38**	8.43	**64-66**	13.43
20	4.86	**40**	8.86	**68**	14.00

Method of administration

For intravenous use : the fluoro-(^{18}F)-L-dopa must be administered by slow intravenous injection, over approximately one minute.

For multidose use.

The activity of 6-fluoro-(^{18}F)-L-dopa has to be measured with activimeter immediately prior to injection.

The injection of 6-fluoro-(^{18}F)-L-dopa must be intravenous in order to avoid irradiation as a result of local extravasation, as well as imaging artefacts.

For instructions on extemporaneous preparation of the medicinal product before administration, see sections 6.6 and 12.

For patient preparation, see section 4.4.

Image acquisition

Neurology

- "dynamic" acquisition of PET images of the brain during 90 to 120 minutes right after injection,
- or one "static" PET acquisition starting 90 minutes after the injection.

Oncology

To detect foci in the liver, pancreas or brain area, early "static" images can be acquired starting 5 minutes after injection, or a "dynamic" acquisition starting right after the injection during 10 minutes.

- Brain tumours: "static" acquisition 10 to 30 minutes after injection.
- Whole-body: images are usually acquired 60 minutes after injection

4.3. Contraindications

- Hypersensitivity to the active substance, to any of the excipients listed in section 6.1 or to any of the components of the pH-adjusted radiopharmaceutical.
- Pregnancy (see section 4.6).

4.4. Special warnings and precautions for use

Potential for hypersensitivity or anaphylactic reactions

If hypersensitivity or anaphylactic reactions occur, the administration of the medicinal product must be discontinued immediately and intravenous treatment initiated, if necessary. To enable immediate action in emergencies, the necessary medicinal products and equipment such as endotracheal tube and ventilator must be immediately available.

Individual benefit/risk justification

For each patient, the radiation exposure must be justifiable by the likely benefit. The activity administered should in every case be as low as reasonably achievable to obtain the required diagnostic information.

Renal / hepatic impairment

Careful consideration of the benefit risk ratio in these patients is required since an increased radiation exposure is possible.

Paediatric population

For information on the use in paediatric population, see section 4.2.

Careful consideration of the indication is required since the effective dose per MBq is higher than in adults (see section 11).

Patient preparation

IASOdopa should be given to patients fasting for a minimum of 4 hours without limiting water intake.

In order to obtain images of best quality and to reduce the radiation exposure of the bladder, patients should be encouraged to drink sufficient amounts and to empty their bladder prior to and after the PET examination.

In neurological indications, it is recommended to suspend any antiparkinsonian treatment at least 12 hours before the PET examination.

The administration of 100 to 200 mg of carbidopa one to one and a half hours before the injection of 6-fluoro-(^{18}F)-L-dopa is recognized for neurological indications but less frequent for oncological indications.

Interpretation of 6-fluoro-(^{18}F)-L-dopa PET images

Neurology

The interpretation of 6-fluoro-(18F)-L-dopa uptake values in the different parts of the brain requires the comparison to age and sex matched controls. Recent publications refer to data base of normal cases and voxel-based Statistical Parametric Mapping (SPM) and automated region of interest (ROI) analysis.

Oncology

False positive results in inflammatory lesions seem to be very rare with 6-fluoro-(^{18}F)-L-dopa PET. Nevertheless, the possibility of an inflammatory lesion should be kept in mind when an unexpected 6-fluoro-(^{18}F)-L-dopa focus is detected. The physiologic biodistribution must be taken into account in the interpretation; in particular uptake in the basal ganglia, diffuse uptake in the pancreas, uptake in the gallbladder leading to subsequent activity in the gut, and uptake in the kidney leading to "hot spots" aspect in the ureters and a high activity in the bladder.

After the procedure

Close contact with infants and pregnant women should be restricted during the initial 12 hours following the injection.

Specific warnings

Depending on the time when you administer the injection prepared extemporaneously after pH adjustment, the content of sodium given to the patient may in some cases be greater than 1 mmol (23 mg). This should be taken into account in patient on low sodium diet.

Precautions with respect to environmental hazard : see section 6.6.

4.5. Interaction with other medicinal products and other forms of interaction

Carbidopa

Prior to 6-fluoro-(^{18}F)-L-dopa administration, use of carbidopa may increase 6-fluoro-(^{18}F)-L-dopa bioavailability to the brain by inhibiting peripheral decarboxylase activity and restricting peripheral 6-fluoro-(^{18}F)-L-dopa metabolism with 3-O-methyl-6-fluoro-(18F)-L-dopa formation.

Haloperidol

Increased intracerebral dopamine turnover caused by haloperidol may result in increased accumulation of 6-fluoro-(18F)-L-dopa.

Monoamine oxidase (MAO) inhibitors

Concurrent use with MAO inhibitors may result in increased accumulation of 6-fluoro-(^{18}F)-L-dopa in the brain.

Reserpine

Reserpine-induced depletion of the contents of intraneuronal vesicles may prevent retention of 6-fluoro-(18F)-L-dopa in the brain.

Paediatric population

Interaction studies have only been performed in adults.

4.6. Fertility, pregnancy and lactation

Women of childbearing potential

When an administration of radiopharmaceuticals to a woman of childbearing potential is intended, it is important to determine whether or not she is pregnant. Any woman who has missed a period should be assumed to be pregnant until proven otherwise. If in doubt about her potential pregnancy (if the woman has missed a period, if the period is very irregular, etc.), alternative techniques not using ionising radiation (if there are any) should be offered to the patient.

Pregnancy

The use of 6-fluoro-(^{18}F)-L-dopa is contraindicated in pregnant women due to preventive radiation protection of the foetus (see section 4.3).

Breastfeeding

Before administering radiopharmaceuticals to a mother who is breastfeeding consideration should be given to the possibility of delaying the administration of radionuclide until the mother has ceased breastfeeding, and to what is the most appropriate choice of radiopharmaceuticals, bearing in mind the secretion of activity in breast milk. If the administration is considered necessary, breastfeeding should be interrupted for 12 hours and the expressed feeds discarded.

Close contact with infants should be restricted during the initial 12 hours following the injection.

Fertility

No studies on fertility have been performed.

4.7. Effects on ability to drive and use machines

Not relevant.

4.8. Undesirable effects

No undesirable effects have been observed to date.

Pain at injection has been reported in rare cases which resolved within minutes without corrective measures.

Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. As the effective dose is 7 mSv when the maximal recommended activity of 280 MBq is administered, these adverse reactions are expected to occur with a low probability.

Paediatric population

Not reported.

Reporting of suspected adverse reactions:

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.

4.9. Overdose

An overdose in the pharmacological sense is unlikely given with the doses used for diagnostic purposes.

In the event of administration of a radiation overdose with 6-fluoro-(^{18}F)-L-dopa the absorbed dose to the patient should be reduced where possible by increasing the elimination of the radionuclide from the body by forced diuresis and frequent bladder voiding. It might be helpful to estimate the effective dose that was applied.

IASON GmbH
Feldkirchner Strasse 4, A-8054 Graz-Seiersberg
Tel. +43-(0)316-28 43 00-0, Fax +43-(0)316-28 43 00-114, e-mail: info@iason.eu, www.iason.eu

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