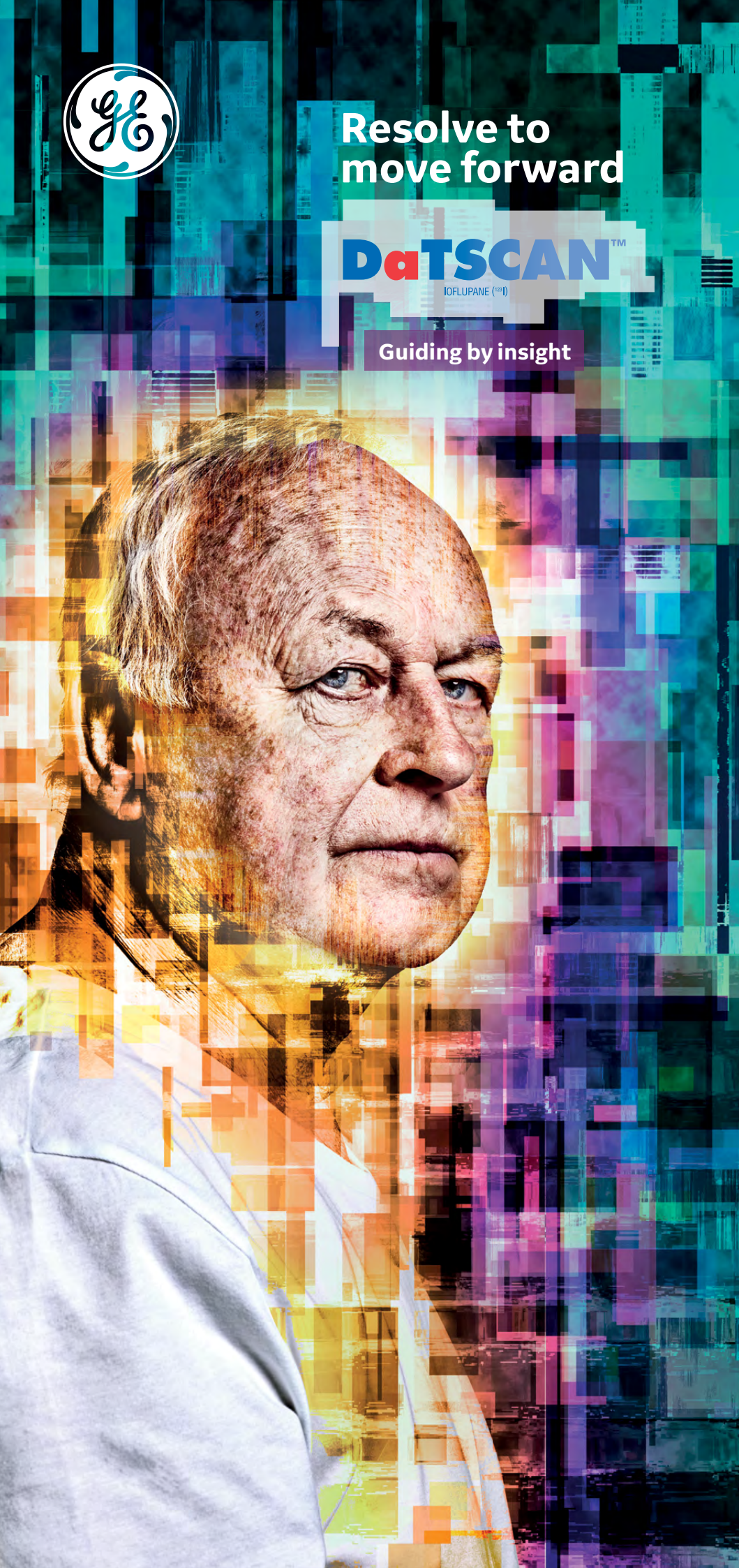
Resolve to move forward

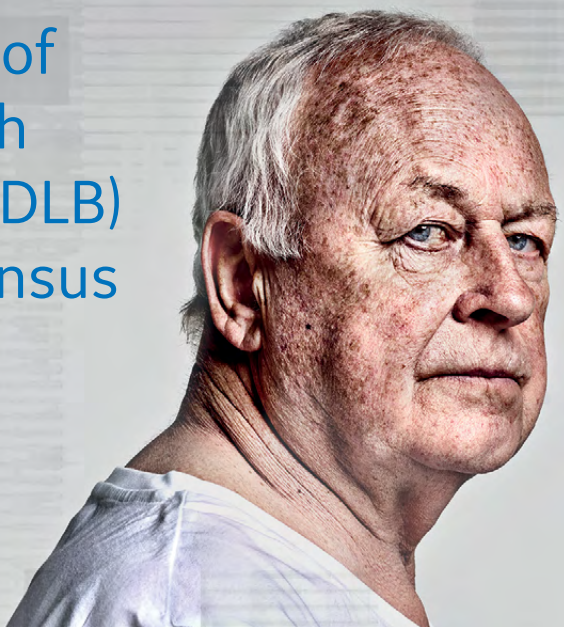
DaTSCAN™

IOFLUPANE (^{123}I)

Guiding by insight



Diagnosis and Management of Dementia with Lewy Bodies (DLB) Fourth Consensus Report[1]



Summary of changes

While maintaining their previous structure, the revised DLB clinical diagnostic criteria improve on earlier versions[2,3] by distinguishing clearly between clinical features and diagnostic biomarkers, with guidance about optimal methods to establish and interpret these.

Clinical signs and symptoms are weighted as core or supportive, and biomarkers as indicative or supportive, based upon their diagnostic specificity and the volume of good quality evidence available.[1]

Abbreviations:
AD: Alzheimer disease
CT: computed tomography
DaT: dopamine transporter
DLB: dementia with Lewy bodies
EEG: electroencephalogram
FDG-PET: fluorodeoxyglucose positron emission tomography
MIBG: metaiodobenzylguanidine
MRI: magnetic resonance imaging
PDD: Parkinson disease dementia
PET: positron emission tomography
PS: Parkinsonian syndromes.
REM: rapid eye movement
SPECT: single-photon emission computed tomography

Diagnosis and management of dementia with Lewy bodies – Fourth consensus report of the DLB Consortium[1]

Revised[1,2] criteria for the clinical diagnosis of probable and possible dementia with Lewy bodies (DLB)

Essential for a diagnosis of DLB is dementia, defined as a progressive cognitive decline of sufficient magnitude to interfere with normal social or occupational functions, or with usual daily activities. Prominent or persistent memory impairment may not necessarily occur in the early stages but is usually evident with progression. Deficits on tests of attention, executive function, and visuoperceptual ability may be especially prominent and occur early.

Core clinical features ***(The first 3 typically occur early and may persist throughout the course.)***

- Fluctuating cognition with pronounced variations in attention and alertness.
- Recurrent visual hallucinations that are typically well formed and detailed.
- REM sleep behavior disorder, which may precede cognitive decline.
- One or more spontaneous cardinal features of parkinsonism: these are bradykinesia (defined as slowness of movement and decrement in amplitude or speed), rest tremor, or rigidity.

Supportive clinical features

Severe sensitivity to antipsychotic agents; postural instability; repeated falls; syncope or other transient episodes of unresponsiveness; severe autonomic dysfunction, e.g., constipation, orthostatic hypotension, urinary incontinence; hypersomnia; hyposmia; hallucinations in other modalities; systematized delusions; apathy, anxiety, and depression.

Indicative biomarkers

Reduced dopamine transporter uptake in basal ganglia demonstrated by SPECT or PET. Abnormal (low uptake) ^{123}iodine-MIBG myocardial scintigraphy. Polysomnographic confirmation of REM sleep without atonia.

Supportive biomarkers

Relative preservation of medial temporal lobe structures on CT/MRI scan. Generalized low uptake on SPECT/PET perfusion/metabolism scan with reduced occipital activity ± the cingulate island sign on FDG-PET imaging. Prominent posterior slow-wave activity on EEG with periodic fluctuations in the pre-alpha/theta range.

Probable DLB can be diagnosed if:

a. Two or more core clinical features of DLB are present, with or without the presence of indicative biomarkers, or
b. Only one core clinical feature is present, but with one or more indicative biomarkers.

Probable DLB should not be diagnosed on the basis of biomarkers alone.

Possible DLB can be diagnosed if:

a. Only one core clinical feature of DLB is present, with no indicative biomarker evidence, or
b. One or more indicative biomarkers is present but there are no core clinical features.

DLB is less likely:

a. In the presence of any other physical illness or brain disorder including cerebrovascular disease, sufficient to account in part or in total for the clinical picture, although these do not exclude a DLB diagnosis and may serve to indicate mixed or multiple pathologies contributing to the clinical presentation, or
b. If parkinsonian features are the only core clinical feature and appear for the first time at a stage of severe dementia.

DLB should be diagnosed when dementia occurs before or concurrently with parkinsonism. The term Parkinson disease dementia (PDD) should be used to describe dementia that occurs in the context of well-established Parkinson disease. In a practice setting the term that is most appropriate to the clinical situation should be used and generic terms such as Lewy body disease are often helpful. In research studies in which distinction needs to be made between DLB and PDD, the existing 1-year rule between the onset of dementia and parkinsonism continues to be recommended.

Help resolve how to move forward with DLB

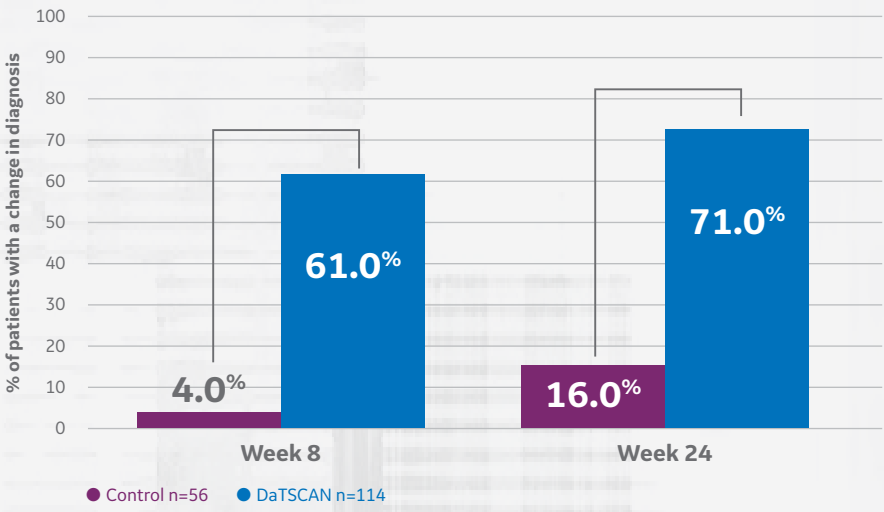
Inform guide clinical management with evidence of DaT status

Imaging often leads to a change in diagnosis and clinical management[4]

DaTSCAN can influence clinical management of patients with DLB by:

- Significantly contributing to a change in diagnostic category[4]
- Helping avoid inappropriate treatment with neuroleptics[5]

DaT imaging often leads to a change in diagnosis[4]



Adapted from Walker *et al.* 2015

The impact of delayed, inaccurate diagnosis in DLB

Delayed, inaccurate diagnosis of DLB places a burden on patients and healthcare systems by:

Resulting in unnecessary visits and tests[7]

Reducing time on potentially beneficial therapy[7]

Giving patients and caregivers less time to prepare[7]

Exposing patients to inappropriate medications and associated side effects, including neuroleptic sensitivity[8]

PRESCRIBING INFORMATION DaTSCAN™ ioflupane (^{123}I) 74 MBq/ml solution for injection
Please refer to full Summary of Product Characteristics (SPC) before prescribing. Further information available on request.
PRESENTATION Single dose vials containing 185 MBq or 370 MBq ioflupane (^{123}I) at reference time.
INDICATIONS Detecting loss of functional dopaminergic neuron terminals in the striatum.
i) in adult patients with clinically uncertain Parkinsonian Syndromes, for example those with early symptoms in order to help differentiate Essential Tremor from Parkinsonian Syndromes related to idiopathic Parkinson's Disease (PD), Multiple System Atrophy (MSA) and Progressive Supranuclear Palsy (PSP). DaTSCAN is unable to discriminate between PD, MSA and PSP.
ii) in adult patients to help differentiate probable dementia with Lewy bodies (DLB) from Alzheimer's disease. DaTSCAN is unable to discriminate between DLB and Parkinson's Disease dementia.
DOSAGE AND METHOD OF ADMINISTRATION Prior to administration appropriate resuscitation equipment should be available. For use in patients referred by physicians experienced in the management of movement disorders/dementia. Clinical efficiency has been demonstrated across the range of 111-185 MBq; do not use outside this range. Appropriate thyroid blocking treatment must be given prior to injection of DaTSCAN. The safety and efficacy of DaTSCAN in children 0 to 18 years has not been established. No data are available in patients with significant renal or hepatic impairment. DaTSCAN should be used without dilution. Slow intravenous injection (15-20 seconds) via an arm vein is recommended. SPECT imaging should take place 3-6 hours after injection of DaTSCAN.
CONTRAINDICATIONS Pregnancy and hypersensitivity to the active substance or any of the excipients.
WARNINGS AND PRECAUTIONS If hypersensitivity reactions occur, the administration of the medicinal product must be discontinued immediately and, if necessary, intravenous treatment initiated. Resuscitative medicinal products and equipment (e.g. endotracheal tube and ventilator) have to be readily available. This radiopharmaceutical may be received, used and administered only by authorised persons in designated clinical settings. Its receipt, storage, use, transfer and disposal are subject to the regulations and the appropriate licences of the local competent official organisations. For each patient, exposure to ionising radiation must be justifiable on the basis of likely benefit. The activity administered must be such that the resulting dose is as low as reasonably achievable bearing in mind the need to obtain the intended diagnostic result. DaTSCAN is not recommended in cases of moderate to severe renal or hepatic impairment. Contains 39.5 g/l (5% volume) ethanol, up to 197mg per dose, harmful for those suffering from alcoholism. To be taken into account in high-risk groups such as patients with liver disease or epilepsy.
INTERACTIONS Consider current medication. Medicines that bind to the dopamine transporter with high affinity may interfere with diagnosis; these include amfetamine, benzatropine, buproprion, cocaine, mazindol, methylphenidate, phentermine and sertraline. Medicines shown during clinical trials not to interfere with DaTSCAN imaging include a mantadine, trihexyphenidyl, budipine, levodopa, metoprolol, primidone, propranolol and selegiline. Dopamine agonists and antagonists acting on the postsynaptic dopamine receptors are not expected to interfere with DaTSCAN imaging and can therefore be continued if desired. In animal studies pergolide does not interfere with DaTSCAN imaging.
PREGNANCY AND LACTATION Contraindicated in pregnancy. Information should be sought about pregnancy from women of child bearing potential. A woman who has missed her period should be assumed to be pregnant. If uncertain, radiation exposure should be the minimum needed for satisfactory imaging. Consider alternative techniques. If administration to a breast feeding woman is necessary, substitute formula feeding for breast feeding for 3 days.
UNDESIRABLE EFFECTS The following undesirable effects are recognised for DaTSCAN: Common side effects include headache. Uncommon side effects include vertigo, increased appetite, formication, dizziness, dysgeusia, nausea and dry mouth. Intense pain or burning sensation on injection has been reported uncommonly following administration into small veins. Hypersensitivity occurs with unknown frequency, as well as erythema, pruritus, rash, urticaria, hyperhidrosis, dyspnea, vomiting, decreased blood pressure and feeling hot. Exposure to ionising radiation is linked with cancer induction and a potential for hereditary defects. Because of the low radiation dose incurred these adverse events are expected to occur with a low probability.
DOSIMETRY Effective dose from 185 MBq is 4.63 mSv.
OVERDOSE Encourage frequent micturition and defecation.
MARKETING AUTHORISATION HOLDER GE Healthcare B.V., De Rondom 8, 5612 AP, Eindhoven, The Netherlands.
CLASSIFICATION FOR SUPPLY Subject to medical prescription.
MARKETING AUTHORISATION NUMBERS EU/1/00/135/001 (2.5ml) and EU/1/00/135/002 (5.0ml).
DATE OF REVISION OF TEXT 16 January 2019
UK PRICE £525.00/185MBq.

Adverse events should be reported.
Reporting forms and information can be found at https://yellowcard.mhra.gov.uk/.
Adverse events should also be reported to GE Healthcare at gpv.drugsafety@ge.com.

References:

1. McKeith IG *et al.* 2017 Diagnosis and management of dementia with Lewy bodies Fourth consensus report of the DLB Consortium. Neurology 2017; 89: 1–13.
2. McKeith IG, Galasko D, Kosaka K *et al.* Consensus guidelines for the clinical and pathologic diagnosis of dementia with Lewy bodies (DLB): report of the Consortium on DLB International Workshop. Neurology 1996; 47: 1113–24.
3. McKeith IG, Dickson DW, Lowe J *et al.* Dementia with Lewy bodies: diagnosis and management: third report of the DLB Consortium. Neurology 2005; 65: 1863–72.
4. Walker Z *et al.* Clinical usefulness of dopamine transporter SPECT imaging with ^{123}I-FP-CIT in patients with possible dementia with Lewy bodies: randomised study.. British J Psychiat 2015; 206(2): 145-52.
5. Aarsland D *et al.* Frequency and case identification of dementia with Lewy bodies using the revised consensus criteria. Dement Geriatr Cogn Disord 2008; 25(3): 195-205.
6. Vossius C *et al.* Am J Geriatr Psychiatry 2014; 22(4): 381-8.
7. Galvin JE *et al.* Alzheimers Dis Assoc Disord 2010; 24(2): 177-81.
8. Walker Z, Cummings JL. Alzheimer's and Dementia 2012; 8: 74-83.

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