HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use TAUKLARIFY safely and effectively. See full prescribing information for TAUKLARIFY.

TAUKLARIFY (florquinitau F 18 injection), for intravenous use
Initial U.S. Approval: 2026

----------INDICATIONS AND USAGE----------
TAUKLARIFY is a radioactive diagnostic drug indicated for positron emission tomography (PET) of the brain in adults with cognitive impairment who are being evaluated for Alzheimer's disease to identify patients with tau neurofibrillary tangle (NFT) pathology. (1)

Limitations of Use
The safety and effectiveness of TAUKLARIFY have not been established for the evaluation of non-Alzheimer's disease tauopathies.

----------DOSAGE AND ADMINISTRATION----------
- Recommended dose is 185 MBq (5 mCi), administered as a bolus intravenous injection. (2.2)
- Initiate imaging approximately 90 minutes after drug administration. (2.3)
- See full prescribing information for additional preparation, administration, imaging, and radiation dosimetry information. (2)

----------DOSAGE FORMS AND STRENGTHS----------
Injection: 37 MBq/mL to 1,480 MBq/mL (1 mCi/mL to 40 mCi/mL) of florquinitau F 18 in up to 10 mL at end of synthesis in a multiple-dose vial. (3)

----------CONTRAINDICATIONS----------
None (4)

----------WARNINGS AND PRECAUTIONS----------
- Risk of Misdiagnosis in Patients Being Evaluated for Alzheimer's Disease: A negative scan does not necessarily exclude the presence of tau NFT pathology, and a positive scan does not necessarily confirm the presence of tau NFT pathology. Consider additional evaluation when clinical uncertainty remains. (5.1)
- Radiation Risk: TAUKLARIFY contributes to a patient's long-term cumulative radiation exposure. Ensure safe drug handling to protect patients and health care providers from unintentional radiation exposure. Advise patients to hydrate before and after administration and to void frequently after administration. (2.1, 5.2)

----------ADVERSE REACTIONS----------
The most commonly reported adverse reactions (incidence ≥ 0.1%) were headache, nausea, injection site reactions, dizziness, and abdominal discomfort. (6.1)

----------DRUG INTERACTIONS----------
CYP1A2 inducers: Avoid use of CYP1A2 inducers, including tobacco smoking, at least 7 days before TAUKLARIFY administration. (7)

----------USE IN SPECIFIC POPULATIONS----------
Lactation: Temporarily discontinue breastfeeding. A lactating woman should pump and discard breast milk for a minimum of 4 hours after TAUKLARIFY administration. (8.2)

To report SUSPECTED ADVERSE REACTIONS, contact Cerveau at 1-800-362-2668 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 8/2026

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

TAUKLARIFY is indicated for positron emission tomography (PET) of the brain in adults with cognitive impairment who are being evaluated for Alzheimer's disease to identify patients with tau neurofibrillary tangle (NFT) pathology.

Limitations of Use

The safety and effectiveness of TAUKLARIFY have not been established for the evaluation of non-Alzheimer's disease tauopathies.

2 DOSAGE AND ADMINISTRATION

2.1 Radiation Safety - Drug Handling

Handle TAUKLARIFY with appropriate safety measures to minimize radiation exposure during administration *[see Warnings and Precautions (5.2)]*. Use waterproof gloves and effective radiation shielding, including syringe shields, when handling and administering TAUKLARIFY.

Radiopharmaceuticals, including TAUKLARIFY, should be used by or under the control of healthcare providers who are qualified by specific training and experience in the safe use and handling of radionuclides, and whose experience and training have been approved by the appropriate governmental agency authorized to license the use of radionuclides.

2.2 Recommended Dosage and Administration Instructions

Recommended Dosage

The recommended amount of radioactivity of TAUKLARIFY is 185 MBq (5 mCi), administered as an intravenous bolus injection in up to 10 mL approximately 90 minutes prior to imaging.

Patient Preparation

Instruct patients to drink water prior to administration of TAUKLARIFY to ensure adequate hydration and to continue drinking and voiding frequently following administration to reduce radiation exposure *[see Warnings and Precautions (5.2)]*.

Administration

- Use aseptic technique and radiation shielding during the preparation and administration of TAUKLARIFY *[see Dosage and Administration (2.1)]*.
- Visually inspect TAUKLARIFY prior to administration. Do not use TAUKLARIFY if it contains particulate matter or if it is discolored. TAUKLARIFY is a clear, colorless to pale yellow solution.
- Calculate the necessary volume to administer based on calibration time and required dose.

- Assay the dose in a suitable dose calibrator prior to administration.

Post-Administration Instructions

- Follow the TAUKLARIFY injection with an intravenous flush of 0.9% sodium chloride injection.
- Dispose of any unused TAUKLARIFY in compliance with applicable regulations.

2.3 Image Acquisition Instructions

- Position the patient supine with the head positioned to center the brain (including the cerebellum) in the PET scanner field of view. Tape or other flexible head restraints may be used to reduce head movement.
- Obtain a 20-minute PET image starting approximately 90 minutes after TAUKLARIFY administration.

2.4 Preparation for Image Interpretation

The goal of the read is to identify and locate areas of florquinitau F 18 signal intensity that are greater than the background signal intensity in the medial temporal lobe (MTL) and neocortical areas.

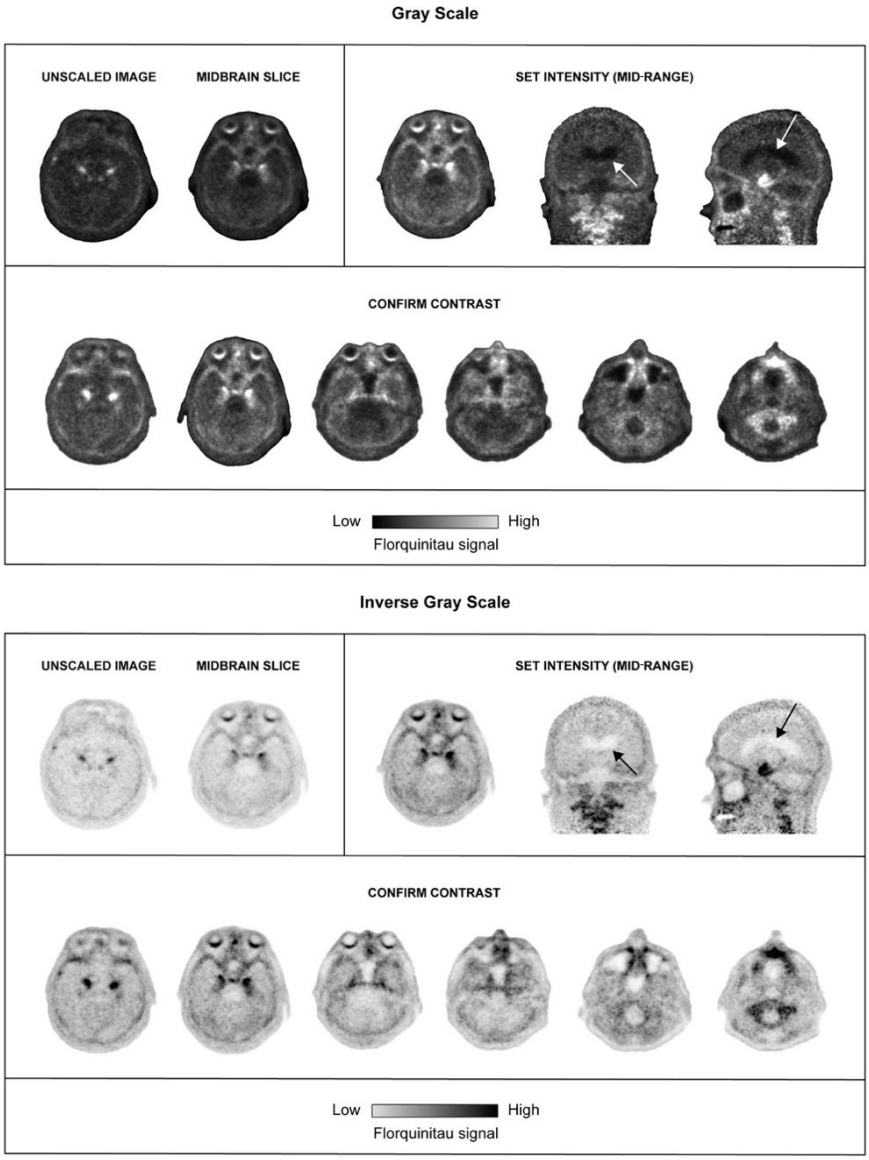
Image Display

- Confirm that the PET image is of sufficient quality for visual assessment.
- Ensure the scan includes the entire brain, including the cerebellum.
- Display images in the axial plane with access as needed to the coronal and sagittal planes.
- Set the primary display to gray scale or inverted gray scale. Software that provides a single color linear representation of the signal progression from low- to high-intensity may also be used.

Adjustment of Signal Intensity and Contrast Gradient

- The appropriate signal intensity and contrast gradient can be set using either gray scale or inverted gray scale. The patient scan can then be assessed in gray scale or inverted gray scale, or both, to provide greater interpretability.
- First, set the signal intensity by identifying a midbrain slice and adjusting the signal to appear mid-range. This process is patient scan-specific as there is no absolute target value, and the signal intensity range may vary from one patient scan to another.
- Confirm the signal intensity setting is appropriate by scrolling through the images. The outline of the ventricles should be distinguishable.
- Once the intensity level has been set, adjust the contrast gradient in order to achieve the greatest dynamic range (separation) between areas of low signal (e.g., inferior cerebellum) and areas of high signal (e.g., retina) (see Figure 1).

Figure 1: Signal Intensity and Contrast Gradient for Gray Scale and Inverse Gray Scale



The white and black arrows in the "SET INTENSITY (MID-RANGE)" images in the gray and inverse gray scale indicate the outline of the ventricles in the coronal view (middle image) and the sagittal view (right image).

2.5 Image Interpretation

Evaluation of Medial Temporal Lobe and Neocortical Uptake

- Interpret TAUKLARIFY images based upon the pattern and density of the signal within the medial temporal lobe (MTL) and neocortical gray matter (not within white matter or in regions outside of the brain). Only the signal intensity in these regions should contribute to scan interpretation.

- Evaluate images sequentially from the inferior aspect of the brain to the superior aspect.

- Compare the uptake in the neocortex with the ventricles to get a sense of background signal intensity.

- Examine the regions of the neocortex that show greater signal intensity than the inferior cerebellar cortex. Signal around the junction between the base of the skull and the meninges should be considered off-target and should not contribute to image interpretation (see Figure 3).

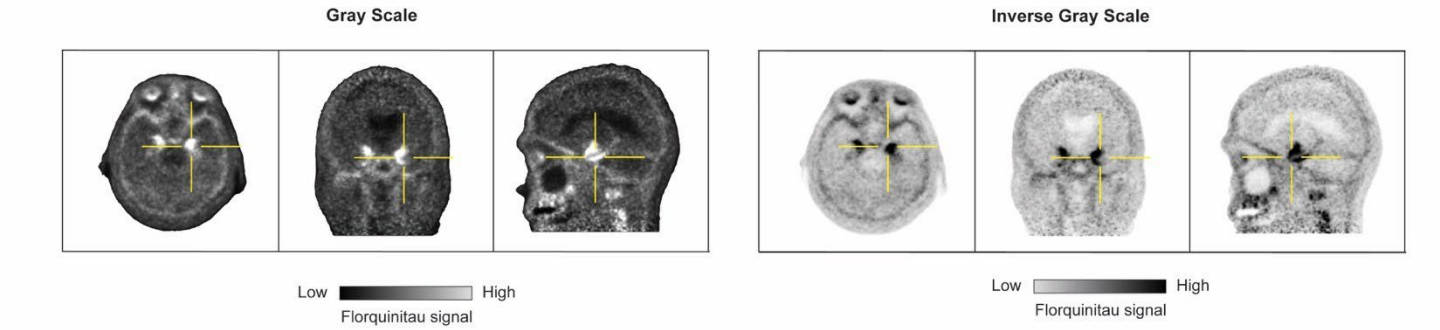
- Assess signal intensity in the MTL (see Figure 2):

    - Start with the entorhinal cortex. A coronal and sagittal view can be supportive for visualizing structures in this region.

    - Uptake in the MTL is meaningful when there is increased signal intensity through multiple contiguous voxels in the entorhinal cortex. Signal intensity restricted to only one or two isolated voxels should not be considered to represent meaningful uptake in the MTL.

    - After examining the entorhinal cortex, assess other structures in the MTL, including the amygdala and hippocampus. The presence of signal within these structures increases the likelihood of meaningful uptake within the MTL.

Figure 2: Involvement of the Medial Temporal Lobe with Signal in the Amygdala and Hippocampus



Factors Affecting Image Interpretation

Some scans may be difficult to interpret due to image noise or motion artifact. Motion-corrupted PET images appear overly smooth or low in resolution. The uptake pattern should not be assessed if it cannot be reasonably related to its underlying anatomy. For cases where there is uncertainty as to the location of cortical signal, use co-registered anatomical imaging to improve localization of signal.

Off-target signal can be seen in the meninges in the form of isolated hotspots or a ring-like appearance. Some cases have meningeal uptake but no cortical uptake, while some cases have both. Other off-target sites include the cerebellum and subcortical structures such as the striatum or

substantia nigra. The signal intensity in these off-target sites does not contribute to the scan interpretation.

Image Interpretation Criteria

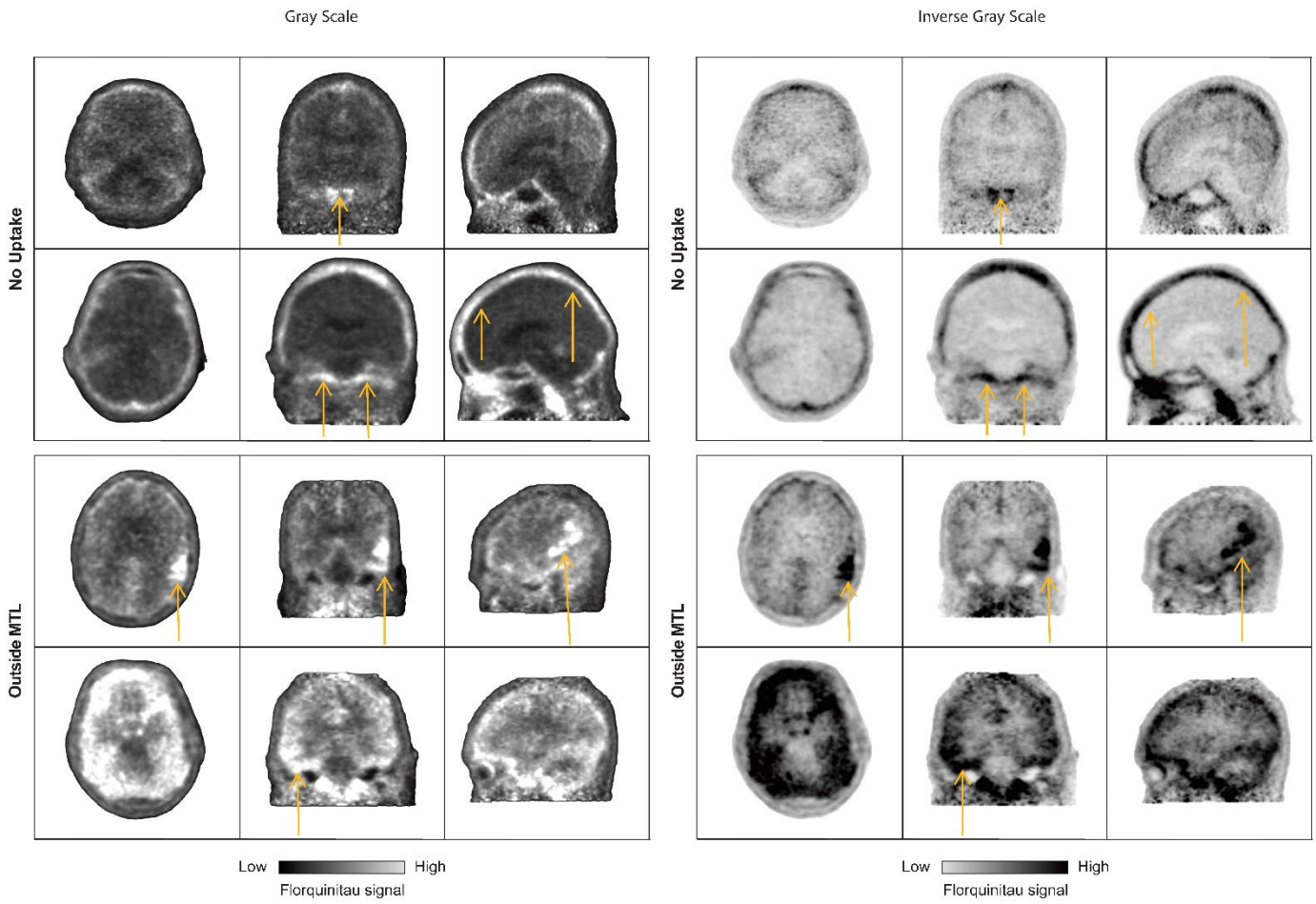
Negative TAUKLARIFY Scan

Scans with no increased signal in the MTL, with or without increased signal in neocortical, subcortical, or off-target regions (e.g., cerebellum, striatum, or midbrain), are considered negative. See Figure 3 for examples of negative TAUKLARIFY scans (the image panels on the left and right show the same scans in gray scale and inverse gray scale).

Positive TAUKLARIFY Scan

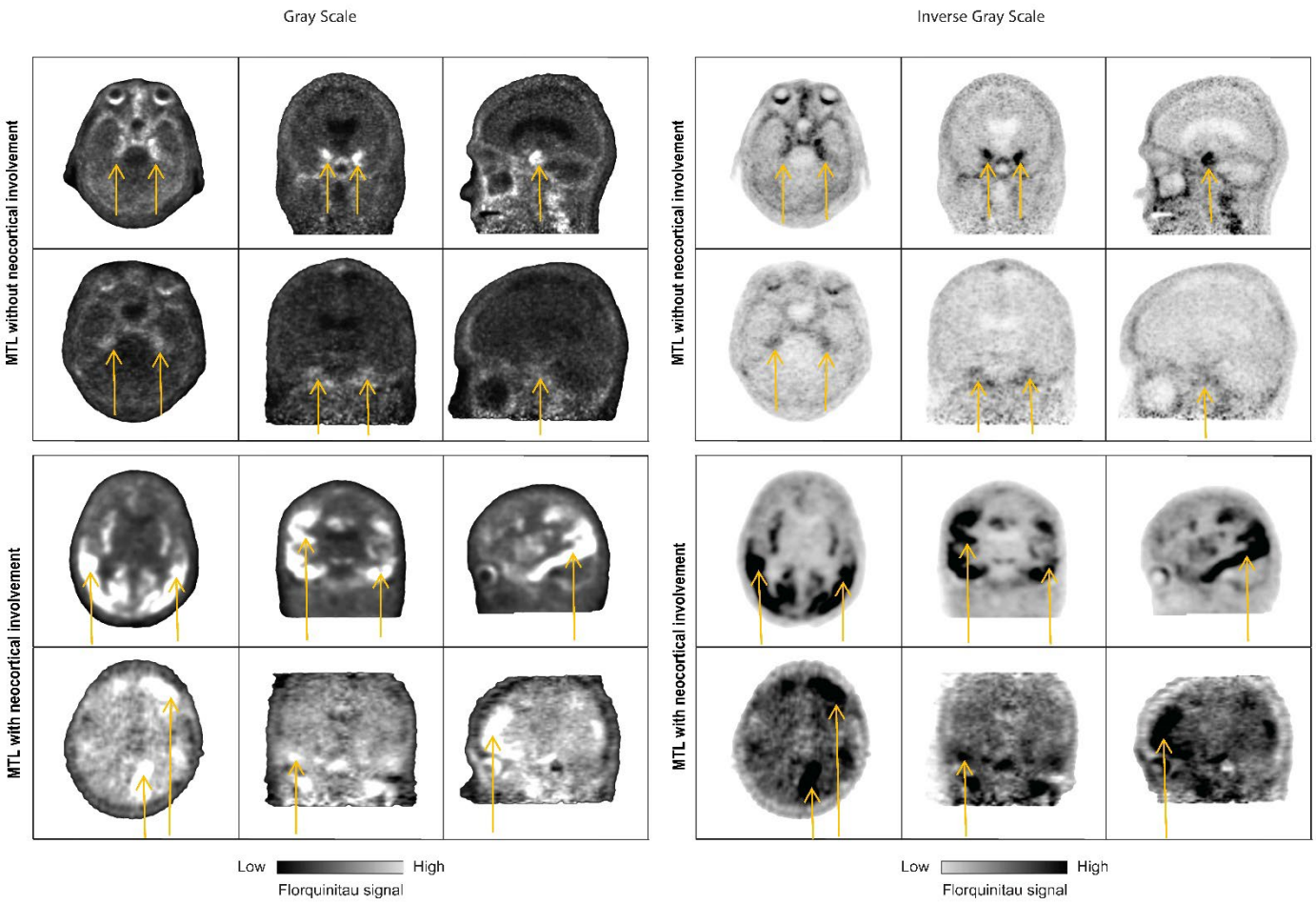
Scans with increased signal in the MTL or with increased signal in at least one neocortical region and the MTL, in either or both hemispheres, are considered positive. See Figure 4 for examples of positive TAUKLARIFY scans (the image panels on the left and right show the same scans in gray scale and inverse gray scale).

Figure 3: Examples of Negative TAUKLARIFY Scans



Images from left to right show transverse, coronal, and sagittal views in both gray and inverse gray scale.
Row 1: Example of a negative case with no uptake and off-target binding around the base of the skull (single arrow in the coronal views).
Row 2: Example of a negative case with no uptake and off-target binding around the base of the skull (two arrows in the coronal views) and in the meninges (two arrows in the sagittal views).
Row 3: Example of a negative case with isolated uptake outside the MTL in the lateral temporoparietal cortex (single arrow in the transverse, coronal, and sagittal views).
Row 4: Example of a negative case with isolated uptake outside the MTL in the lateral temporal lobe (single arrow in the coronal views).

Figure 4: Examples of Positive TAUKLARIFY Scans



Images from left to right show transverse, coronal, and sagittal views in both gray and inverse gray scale.
Row 1: Example of a positive case with uptake in the MTL (two arrows in the transverse and coronal views, single arrow in the sagittal views).
Row 2: Example of a positive case with uptake in the MTL (two arrows in the transverse and coronal views, single arrow in the sagittal views).
Row 3: Example of a positive case with uptake in the MTL and neocortical regions including the temporal cortex (two arrows in the transverse views and right arrow in the coronal views), parietal cortex (left arrow in the coronal views), and occipital cortex (single arrow in the sagittal views).
Row 4: Example of a positive case with uptake in the MTL and neocortical regions including the frontal cortex (right arrow in the transverse views and single arrow in the sagittal views), temporal cortex (single arrow in the coronal views), and occipital cortex (left arrow in the transverse views).

2.6 Radiation Dosimetry

Radiation absorbed dose estimates for adults from intravenous administration of TAUKLARIFY are shown in Table 1. Critical organs include the gallbladder wall, small intestine, upper large intestine wall, and urinary bladder wall. The whole-body effective dose resulting from administration of 185 MBq (5 mCi) of TAUKLARIFY to an adult is estimated to be 5.4 mSv. When PET/computed tomography (CT) is performed, exposure to radiation will increase by an amount dependent on the settings used in the CT acquisition.

Table 1: Estimated Radiation Absorbed Doses in Organs and Tissues in Adults Who Received TAUKLARIFY

Organ/Tissue	**Mean Absorbed Dose Per Unit Administered Activity (microGy/MBq)**
Adrenal Glands	13
Brain	9
Breasts	6
Gallbladder Wall	202
Lower Large Intestine Wall	46
Small Intestine	116
Stomach Wall	17
Upper Large Intestine Wall	128
Heart Wall	16
Kidneys	34
Liver	34
Lungs	20
Muscle	9
Ovaries	28
Pancreas	15
Red Marrow	19
Osteogenic Cells	17
Skin	6
Spleen	18
Testes	3
Thymus	7
Thyroid	6
Urinary Bladder Wall	128
Uterus	26
Total Body	2
Effective Dose (microSv/MBq)	**29**

3 DOSAGE FORMS AND STRENGTHS

Injection: 37 MBq/mL to 1,480 MBq/mL (1 mCi/mL to 40 mCi/mL) of florquinitau F 18 in a maximum volume of 10 mL at end of synthesis (EOS) as a clear, colorless to pale yellow solution in a multiple-dose vial.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Risk of Misdiagnosis in Patients Being Evaluated for Alzheimer's Disease

TAUKLARIFY performance for identifying patients with tau NFT pathology was assessed in subjects who were expected to have predominantly no tau NFT pathology (i.e., cognitively unimpaired and amyloid beta PET-negative) or predominantly clinically significant levels of tau NFT pathology associated with Alzheimer's disease (i.e., cognitively impaired and amyloid beta PET-positive). TAUKLARIFY performance for identifying patients with tau NFT pathology may be lower in patients in earlier stages of the pathological spectrum *[see Clinical Studies (14)]*.

A negative TAUKLARIFY scan does not necessarily exclude the presence of tau NFT pathology, and a positive TAUKLARIFY scan does not necessarily confirm the presence of tau NFT pathology. Consider additional evaluation when clinical uncertainty remains.

5.2 Radiation Risk

TAUKLARIFY contributes to a patient's overall long-term cumulative radiation exposure. Long-term cumulative radiation exposure is associated with an increased risk of cancer. Ensure safe drug handling to protect patients and health care providers from unintentional radiation exposure. Advise patients to hydrate before and after administration and to void frequently after administration *[see Dosage and Administration (2.1, 2.2, 2.6)]*.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

The safety of TAUKLARIFY was evaluated in a total of 1,734 subjects in two clinical trials, Trial A and Trial B.

Trial A enrolled 807 subjects (426 cognitively unimpaired subjects, 258 subjects with mild cognitive impairment, and 123 subjects with mild Alzheimer's disease dementia) who received at least one intravenous dose, ranging from approximately 142 MBq to 202 MBq (3.8 mCi to 5.5 mCi). The recommended dose of TAUKLARIFY is 185 MBq (5 mCi) *[see Dosage and Administration (2.2)]*. The mean age was 74 years (range 51 years to 96 years), and 51% of subjects were female. No other demographic data were available for this trial.

Trial B enrolled 927 subjects (cognitively unimpaired subjects at increased risk for cognitive decline and dementia) who received at least one intravenous dose, ranging from approximately 122 MBq to 352 MBq (3.3 mCi to 9.5 mCi). The recommended dose of TAUKLARIFY is 185 MBq (5 mCi) *[see Dosage and Administration (2.2)]*. The mean age was 68 years (range 60 years to 79 years), and 61% of subjects were female. Of the trial population, 73% were White, 15% African American or

Black, 3% Asian, 3% of other race, and 6% were missing race data; 9% were Hispanic or Latino and 91% not Hispanic or Latino.

Table 2 lists adverse reactions reported in ≥ 0.1% of subjects who received TAUKLARIFY from the clinical trials.

Table 2: Adverse Reactions Reported in ≥ 0.1% of Subjects Who Received TAUKLARIFY in Clinical Trials

Adverse Reaction	**TAUKLARIFY (n=1,734) n (%)**
Headache	13 (0.7%)
Nausea	3 (0.2%)
Injection Site Reactions[#]	2 (0.1%)
Dizziness	2 (0.1%)
Abdominal Discomfort*	2 (0.1%)

[#]Injection Site Reactions includes injection site rash, injection site discomfort, and injection site injury.
*Abdominal Discomfort includes abdominal pain and abdominal discomfort.

Adverse reactions reported in <0.1% of subjects included asthenia, fatigue, peripheral swelling, confusion, and diarrhea.

7 DRUG INTERACTIONS

CYP1A2 Inducers

Avoid use of CYP1A2 inducers, including tobacco smoking, at least 7 days before TAUKLARIFY administration. Use of CYP1A2 inducers can be resumed after completion of imaging.

Florquinitau F 18 is a substrate of the CYP1A2 enzyme *[see Clinical Pharmacology (12.3)]*. Concomitant use of florquinitau F 18 with CYP1A2 inducers, including tobacco smoking, may decrease the florquinitau F 18 parent fraction in plasma and reduce brain regional signal intensity, which may complicate interpretation of imaging results.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no available data on the use of TAUKLARIFY during pregnancy to evaluate for a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Animal reproduction studies have not been conducted with florquinitau F 18 to evaluate its effect on female reproduction and embryo-fetal development.

All radiopharmaceuticals, including TAUKLARIFY, have the potential to cause fetal harm depending on the stage of fetal development and the magnitude of the radiation dose. If considering TAUKLARIFY administration to a pregnant woman, inform the patient about the potential for adverse pregnancy outcomes based on the radiation dose from the drug and the gestational timing of exposure.

TAUKLARIFY contains ethanol (a maximum of 0.789 grams ethanol per dose). The lower limit of safety for ethanol use during pregnancy has not been established. Published studies have demonstrated that ethanol is associated with fetal harm including central nervous system abnormalities, behavioral disorders, and impaired intellectual development. If considering TAUKLARIFY administration to a pregnant woman, inform the patient about the potential for adverse pregnancy outcomes associated with ethanol exposure during pregnancy.

The background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defects, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

8.2 Lactation

Risk Summary

There are no data on the presence of florquinitau F 18 in human or animal milk, its effects on the breastfed infant, or the effects on milk production. To minimize radiation exposure to the breastfed infant from TAUKLARIFY, advise a lactating woman to temporarily discontinue breastfeeding and to pump and discard breast milk for a minimum of 4 hours after administration of TAUKLARIFY.

8.4 Pediatric Use

The safety and effectiveness of TAUKLARIFY in pediatric patients have not been established.

8.5 Geriatric Use

Of the total number of subjects in clinical studies of TAUKLARIFY, 1,393 (80%) were 65 years of age and older, while 501 (29%) were 75 years of age and older. No overall differences in safety or effectiveness of TAUKLARIFY were observed between subjects 65 years of age and older and younger adult subjects.

10 OVERDOSAGE

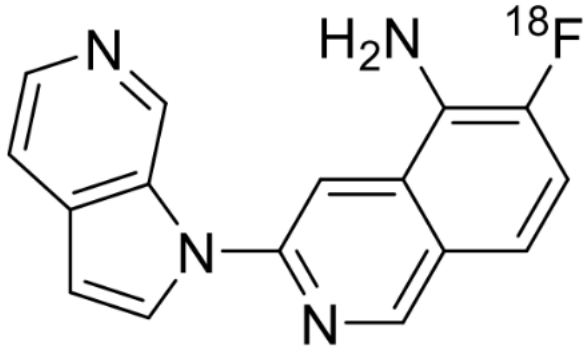
In the event of administration of a radiation overdose with TAUKLARIFY, hydration and frequent urination should be encouraged to minimize radiation exposure to the patient.

11 DESCRIPTION

11.1 Drug Characteristics

TAUKLARIFY (florquinitau F 18 injection) is a radioactive diagnostic drug for intravenous use.

The chemical name of florquinitau F 18 is 6-[^{18}F]Fluoro-3-(1H-pyrrolo[2,3-c]pyridin-1-yl)isoquinolin-5-amine. The molecular weight is 277.3 g/mol, the molecular formula is $C_{16}H_{11}{}^{18}FN_4$, and the structural formula is:



TAUKLARIFY is a sterile, clear, colorless to pale yellow, particulate-free solution.

Each milliliter (mL) contains up to 2 mcg of florquinitau, 37 MBq to 1,480 MBq (1 mCi to 40 mCi) of florquinitau F 18 at EOS, and the following inactive ingredients: 5 mg to 15 mg ascorbic acid, up to 10% (v/v) of ethanol in 0.9% sodium chloride injection, and hydrochloric acid added to adjust pH. The pH of the solution is between 5.0 and 7.0.

The specific activity is at least 250 mCi/micromol at the time of administration.

11.2 Nuclear Physical Characteristics

Fluorine-18 (F 18) decays by positron (β+) emission to stable oxygen-18 and has a half-life of 109.8 minutes. The principal photons useful for diagnostic imaging are the coincident pair of 511 keV gamma photons, resulting from the interaction of the emitted positron with an electron (Table 3).

Table 3: Principal Radiation Produced from Decay of Fluorine-18

Radiation	Energy Level (keV)	Abundance (%)
Positron	249.8	96.7
Gamma	511	193.5

The point source air-kerma coefficient for F 18 is $3.74E^{-17}$ Gy m^2/(Bq s). The first half-value thickness of lead (Pb) for F 18 gamma rays is approximately 0.6 cm. The relative reduction of radiation emitted by F 18 that results from various thicknesses of lead shielding is shown in Table 4. The use of 8 cm of lead will decrease the radiation transmission (i.e., exposure) by a factor of about 10,000.

Table 4: Radiation Attenuation of 511 keV Gamma Rays by Lead Shielding

Lead Shield Thickness (cm)	Coefficient of Attenuation
0.6	0.5
2	0.1
4	0.01
6	0.001
8	0.0001

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Florquinitau F 18 binds to aggregated tau protein. In the brains of patients with Alzheimer's disease, tau aggregates combine to form NFTs, one of two components required for the neuropathological diagnosis of Alzheimer's disease. *In vitro* binding studies using postmortem human brain homogenates containing tau NFTs, the dissociation constant (K_d) for florquinitau was 0.3 nM.

12.2 Pharmacodynamics

Following intravenous injection, florquinitau F 18 crosses the blood-brain barrier and accumulates in brain regions that contain tau NFTs. The signal intensity of florquinitau F 18 increases after time zero and is stabilized by approximately 40 minutes to 60 minutes post-injection.

12.3 Pharmacokinetics

The pharmacokinetics of florquinitau F 18 were evaluated in healthy subjects and patients with Alzheimer's disease following single intravenous doses of 160 MBq and 370 MBq (0.86 and 2 times the recommended dose, respectively). The area under the time concentration curve (AUC) increased in a dose proportional manner over the dosage range. Pharmacokinetic parameters are presented as mean ± standard deviation unless otherwise specified. The maximum plasma radioactivity concentration (C_{max}) was 61.5 ± 19.9 (kBq/mL) and the AUC was 10.5 ± 3.2 (h×kBq/mL) for 160 MBq (0.86 times the recommended dose).

Distribution

Florquinitau F 18 was 84% bound to plasma proteins.

Florquinitau F 18 distributed rapidly throughout the body with peak brain uptake within about 3 minutes after injection.

Elimination

The clearance of florquinitau F 18 is 16.1 ± 4.1 L/h. The terminal half-life is 2.3 ± 0.5 hours.

Metabolism

Florquinitau F 18 is primarily metabolized via CYP1A2-mediated oxidation. The plasma parent florquinitau F 18 fraction was >85% at 2 minutes following administration and declined to 20% at 15 minutes following administration.

Excretion

Based on imaging dosimetry, injected radioactivity from TAUKLARIFY was eliminated by hepatobiliary and renal excretion. After administration of a single dose of TAUKLARIFY, 21.1 ± 7.3% of injected radioactivity was excreted in urine by 2 hours.

Drug Interaction Studies

In Vitro Studies

CYP450 enzymes: Florquinitau is not a substrate of CYP3A4, CYP2C8, CYP2C9, CYP2C19, CYP2D6, or CYP2B6.

Transporter systems: Florquinitau is not a substrate of P-gp, BCRP, OCT2, MATE1, MATE2-K, OAT1, OAT3, OATP1B1, or OATP1B3.

Florquinitau is not an inhibitor of P-gp, BCRP, OCT2, MATE1, MATE2-K, OAT1, OAT3, OATP1B1, or OATP1B3.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Animal studies to assess the carcinogenicity potential of florquinitau F 18 have not been conducted.

Mutagenesis

No adequate studies have been conducted to evaluate the mutagenic potential of florquinitau F 18.

Impairment of Fertility

No animal studies with florquinitau F 18 have been performed to evaluate the potential impairment of fertility in males or females.

14 CLINICAL STUDIES

The effectiveness of TAUKLARIFY for the identification of patients with tau neurofibrillary tangle (NFT) pathology was evaluated in two blinded read studies (Study 1 and Study 2) that analyzed TAUKLARIFY PET images acquired from subjects enrolled in three clinical trials. The clinical trials included subjects with mild Alzheimer's disease dementia (consistent with Stage 4 Alzheimer's disease), subjects with mild cognitive impairment (consistent with Stage 3 Alzheimer's disease), and cognitively unimpaired subjects. All subjects received an amyloid beta PET scan. For the tau PET scan, subjects received an approximate intravenous dose of 185 MBq (5 mCi) of TAUKLARIFY.

For Study 1 and Study 2, TAUKLARIFY scans were interpreted by two distinct groups of five independent readers who underwent training on image interpretation and were blinded to subjects' clinical information and amyloid beta PET results. Each scan was classified using a binary image interpretation method (negative or positive) for tau NFT pathology *[see Dosage and Administration (2.5)]* and compared against a pre-established reference standard (RS) based on a subject's cognitive status and amyloid beta PET result:

- Tau RS negative: Cognitively unimpaired and amyloid beta PET-negative
- Tau RS positive: Cognitively impaired (either mild cognitive impairment due to Alzheimer's disease or mild Alzheimer's disease dementia) and amyloid beta PET-positive

Subjects who did not fit these categories (i.e., cognitively unimpaired with a positive amyloid beta PET, or cognitively impaired with a negative amyloid beta PET) were not included in the read studies because they did not contribute to the reference standard.

In Study 1, images from 279 subjects were analyzed. The mean age was 70 years (range 51 to 80), and 50% of subjects were female. Of the study population, 89% were White, 6% African American or Black, 1% Asian, and 4% of other race; 4% of subjects were Hispanic with ethnicity unknown for the remaining 96%. There were 139 amyloid beta PET-positive subjects (63 with mild cognitive impairment due to Alzheimer's disease and 76 with mild Alzheimer's disease dementia) and 140 amyloid beta PET-negative subjects with no cognitive impairment on clinical evaluation.

In Study 2, images from 338 subjects were analyzed. The mean age was 70 years (range 54 to 80), and 51% of subjects were female. Of the study population, 37% were White, 6% African American or Black, 2% Asian, 1% American Indian or Alaska Native, and 54% of unknown race; 5% of subjects were Hispanic, 45% not Hispanic, and ethnicity was unknown for the remaining 50%. There were 170 amyloid beta PET-positive subjects (94 with mild cognitive impairment due to Alzheimer's disease and 76 with mild Alzheimer's disease dementia) and 168 amyloid beta PET-negative subjects with no cognitive impairment on clinical evaluation.

Results are shown in Table 5.

Table 5: TAUKLARIFY Scan Reader Performance for Tau NFT Pathology

Reader	True Positive	True Negative	False Positive	False Negative	PPA*, % (95% CI)	NPA**, % (95% CI)
Study 1 (n=279)						
1	115	138	2	24	83 (76, 88)	99 (95, 100)
2	123	137	3	16	88 (82, 93)	98 (94, 99)
3	111	139	1	28	80 (72, 86)	99 (96, 100)
4	119	138	2	20	86 (79, 90)	99 (95, 100)
5	123	137	3	16	88 (82, 93)	98 (94, 99)
Study 2 (n=338)						
1	138	157	11	32	81 (75, 86)	93 (89, 96)
2	136	166	2	34	80 (73, 85)	99 (96, 100)
3	140	160	8	30	82 (76, 87)	95 (91, 98)
4	116	167	1	54	68 (61, 75)	99 (97, 100)
5	137	167	1	33	81 (74, 86)	99 (97, 100)

Abbreviation: CI = confidence interval
*PPA (Positive Percent Agreement) represents the percentage of patients with a positive TAUKLARIFY PET result among those who were tau reference standard positive.
**NPA (Negative Percent Agreement) represents the percentage of patients with a negative TAUKLARIFY PET result among those who were tau reference standard negative.

Inter-reader agreement in each study was evaluated and generalized Fleiss' kappa (95% CI) of 0.92 (0.89, 0.96) and 0.86 (0.82, 0.89) were observed in Studies 1 and 2, respectively.

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

TAUKLARIFY (florquinitau F 18 injection) is supplied in a multiple-dose vial (NDC 11994-624-01) containing a clear, colorless to pale yellow solution containing 37 MBq/mL to 1,480 MBq/mL (1 mCi/mL to 40 mCi/mL) of florquinitau F 18 at EOS in a maximum volume of 10 mL.

Storage and Handling

Store TAUKLARIFY upright in the original container with radiation shielding at 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature].

The expiration date and time are provided on the container label. Use TAUKLARIFY within 10 hours

from the time of EOS.

Dispose of unused product in accordance with all federal, state, and local laws and institutional requirements.

This preparation is for use by persons under license by the Nuclear Regulatory Commission or the relevant regulatory authority of an Agreement State.

17 PATIENT COUNSELING INFORMATION

Radiation Risk

Advise patients of the radiation risk of TAUKLARIFY. Instruct patients to drink water to ensure adequate hydration prior to administration of TAUKLARIFY and to continue drinking and voiding frequently following administration to reduce radiation exposure *[see Warnings and Precautions (5.2)]*.

Drug Interactions with CYP1A2 Inducers

Inform patients that certain medications and smoking can affect TAUKLARIFY imaging and should be stopped temporarily at least 7 days before TAUKLARIFY administration. Patients may resume their regular medications and smoking after completion of imaging *[see Drug Interactions (7)]*.

Pregnancy

Inform pregnant women of the potential risks of fetal exposure to radiation from TAUKLARIFY and the potential risks of exposure to ethanol present in TAUKLARIFY *[see Use in Specific Populations (8.1)]*.

Lactation

Advise a lactating woman to temporarily discontinue breastfeeding and to pump and discard breast milk for a minimum of 4 hours after TAUKLARIFY administration to minimize radiation exposure to the breastfed infant *[see Use in Specific Populations (8.2)]*.

Manufactured for Cerveau Technologies, Inc., a Lantheus Company, Bedford, MA 01730 (USA)

516186-0625