SODIUM FLUORIDE F 18- sodium fluoride f-18 injection
BAMF Health Inc.

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use SODIUM FLUORIDE F 18 INJECTION safely and effectively. See full prescribing information for SODIUM FLUORIDE F 18 INJECTION.

SODIUM FLUORIDE F 18 INJECTION

For Intravenous Use

Initial U.S. Approval: 1/2011

INDICATIONS AND USAGE

Sodium Fluoride F 18 Injection is a radioactive diagnostic agent for positron emission tomography (PET) indicated for imaging of bone to define areas of altered osteogenic activity. (1)

DOSAGE AND ADMINISTRATION

• Sodium Fluoride F 18 Injection emits radiation and must be handled with appropriate safety measures. (2.1)
• Administer 300-450 MBq (8-12 mCi) as an intravenous injection in adults. (2.4)
• Administer approximately 2.1 MBq/kg in children with a minimum of 19 MBq (0.5 mCi) and a maximum of 148 MBq (4 mCi) as an intravenous injection. (2.5)
• Imaging can begin 1-2 hours after administration; optimally at one hour post administration. (2.7)
• Encourage patients to void immediately prior to imaging the lumbar spine and bony pelvis. (2.7)

DOSAGE FORMS AND STRENGTHS

Multiple-dose vial containing 370-7,400 MBq/mL (10-200 mCi/mL) of no-carrier-added sodium fluoride F 18 at the end of synthesis (EOS) reference time in aqueous 0.9% sodium chloride solution (3). Sodium Fluoride F 18 Injection, USP is a clear, colorless, sterile, pyrogen-free, and preservative-free solution for intravenous administration.

CONTRAINDICATIONS

None. (4)

WARNINGS AND PRECAUTIONS

• Allergic Reactions: As with any injectable drug product, allergic reactions and anaphylaxis may occur. Emergency resuscitation equipment and personnel should be immediately available. (5.1)
• Cancer Risks: Sodium Fluoride F 18 Injection may increase the risk of cancer. Use the smallest dose necessary for imaging and ensure safe handling to protect the patient and health care worker. (5.2)

ADVERSE REACTIONS

No adverse reactions have been reported for Sodium Fluoride F 18 Injection based on a review of the published literature, publicly available reference sources, and adverse drug reaction reporting systems. (6)
To report SUSPECTED ADVERSE REACTIONS, contact BAMF Health at 1-616-272-5777 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch. (6)

USE IN SPECIFIC POPULATIONS

• Pregnancy: No human or animal data. Any radiopharmaceutical, including Sodium Fluoride F 18 Injection may cause fetal harm. Use only if clearly needed. (8.1)
• Nursing: A decision should be made whether to interrupt nursing after Sodium Fluoride F 18 Injection administration or not to administer Sodium Fluoride F 18 Injection taking into consideration the importance of the drug to the mother. (8.3)
• Pediatrics: Children are more sensitive to radiation and may be at higher risk of cancer from Sodium Fluoride F 18 Injection. (8.4)
See 17 for PATIENT COUNSELING INFORMATION.

Revised: 12/2022

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Sodium Fluoride F 18 Injection is indicated for diagnostic positron emission tomography

(PET) imaging of bone to define areas of altered osteogenic activity.

2 DOSAGE AND ADMINISTRATION

2.1 Radiation Safety - Drug Handling

• Wear waterproof gloves and effective shielding when handling Sodium Fluoride F 18 Injection. Use appropriate safety measures, including shielding, consistent with proper patient management to avoid unnecessary radiation exposure to the patient, occupational workers, clinical personnel, and other persons.

• Radiopharmaceuticals should be used by or under the control of physicians 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.

• Use aseptic technique to maintain sterility during all operations involved in the manipulation and administration of Sodium Fluoride F 18 Injection.

• The dose of Sodium Fluoride F 18 Injection should be minimized consistent with the objectives of the procedure, and the nature of the radiation detection devices employed.

• The final dose for the patient should be calculated using proper decay factors from the time of End of Synthesis (EOS), and measured by a suitable radioactivity calibration system before administration *[see Description (11.2)]* .

2.2 Radiation Safety - Patient Preparation

• To minimize radiation-absorbed dose to the bladder, encourage adequate hydration. Encourage the patient to ingest at least 500 mL of fluid immediately prior and subsequent to the administration of Sodium Fluoride F 18 Injection.

• Encourage the patient to void one-half hour after administration of Sodium Fluoride F 18 Injection and as frequently thereafter as possible for the next 12 hours.

2.3 Drug Preparation and Administration

• Calculate the necessary volume to administer based on calibration time and dose.

• Inspect Sodium Fluoride F 18 Injection visually for particulate matter and discoloration before administration, whenever solution and container permit.

• Do not administer Sodium Fluoride F 18 Injection containing particulate matter or discoloration; dispose of these unacceptable or unused preparations in a safe manner, in compliance with applicable regulations.

• Aseptically withdraw Sodium Fluoride F 18 Injection from its container.

2.4 Recommended Dose for Adults

Administer 300-450 MBq (8-12 mCi) as an intravenous injection.

2.5 Recommended Dose for Pediatric Patients

In reported clinical experience in approximately 100 children, weight based doses (2.1

MBq/kg) ranging from 19 MBq-148 MBq (0.5 mCi-4 mCi) were used.

2.6 Radiation Dosimetry

The age/weight-based estimated absorbed radiation doses (mGy/MBq) from intravenous injection of Sodium Fluoride F 18 Injection are shown in Table 1. These estimates were calculated based on human data and using the data published by the Nuclear Regulatory Commission [1] and the International Commission on Radiological Protection for Sodium Fluoride Injection [2]. The bone, bone marrow, and urinary bladder are considered target and critical organs.

Table 1. Estimated Absorbed Radiation Doses after Intravenous Administration of Sodium Fluoride F 18 Injection, USP

Organ	Estimated Radiation Dose mGy/MBq				
	Adult 70 kg [1]	15 year 56.8 kg [2]	10 year 33.2 kg [2]	5 year 19.8 kg [2]	1 year 9.7 kg [2]
Adrenals	0.0062	0.012	0.018	0.028	0.052
Brain	0.0056	N/A	N/A	N/A	N/A
Bone surfaces	0.060	0.050	0.079	0.13	0.30
Breasts	0.0028	0.0061	0.0097	0.015	0.030
Gallbladder wall	0.0044	N/A	N/A	N/A	N/A
Stomach wall	0.0038	0.008	0.013	0.019	0.036
Small intestine	0.0066	0.012	0.018	0.028	0.052
Upper large intestine wall	0.0058	0.010	0.016	0.026	0.046
Lower large intestine wall	0.012	0.016	0.025	0.037	0.063
Heart wall	0.0039	N/A	N/A	N/A	N/A
Kidneys	0.019	0.025	0.036	0.053	0.097
Liver	0.0040	0.0084	0.013	0.021	0.039
Lungs	0.0041	0.0084	0.013	0.020	0.039
Muscle	0.0060	N/A	N/A	N/A	N/A

Ovaries	0.011	0.016	0.023	0.036	0.063
Pancreas	0.0048	0.0096	0.015	0.023	0.044
Red marrow	0.028	0.053	0.088	0.18	0.38
Skin	0.0040	N/A	N/A	N/A	N/A
Spleen	0.0042	0.0088	0.014	0.021	0.041
Testes	0.0078	0.013	0.021	0.033	0.062
Thymus	0.0035	N/A	N/A	N/A	N/A
Thyroid	0.0044	0.0084	0.013	0.020	0.036
Urinary bladder wall	0.25	0.27	0.4	0.61	1.1
Uterus	0.019	0.023	0.037	0.057	0.099
Other tissue	N/A	0.010	0.015	0.024	0.044
Effective Dose Equivalent mSv/MBq	**0.027**	**0.034**	**0.052**	**0.086**	**0.17**

[1] Data from Nuclear Regulatory Commission Report, *Radiation Dose Estimates for Radiopharmaceuticals*, NUREG/CR-6345, page 10, 1996.
[2] Data from ICRP publication 53, *Radiation Dose to Patients from Radiopharmaceuticals*, Ann ICRP, Volume 18, pages 15 and 74, 1987.

2.7 Imaging Guidelines

• Imaging of Sodium Fluoride F 18 Injection can begin 1-2 hours after administration; optimally at 1 hour post administration.

• Encourage the patient to void immediately prior to imaging the fluoride F 18 radioactivity in the lumbar spine or bony pelvis.

3 DOSAGE FORMS AND STRENGTHS

Multiple-dose vial containing 370-7,400 MBq/mL (10-200 mCi/mL) at EOS reference time of no-carrier-added sodium fluoride F 18 in aqueous 0.9% sodium chloride solution. Sodium Fluoride F 18 Injection, USP is a clear, colorless, sterile, pyrogen-free, and preservative-free solution for intravenous administration.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Allergic Reactions

As with any injectable drug product, allergic reactions and anaphylaxis may occur. Emergency resuscitation equipment and personnel should be immediately available.

5.2 Radiation Risks

Sodium Fluoride F 18 Injection may increase the risk of cancer. Carcinogenic and mutagenic studies with Sodium Fluoride F 18 Injection have not been performed. Use the smallest dose necessary for imaging and ensure safe handling to protect the patient and health care worker *[see Dosage and Administration (2.1)]* .

6 ADVERSE REACTIONS

No adverse reactions have been reported for Sodium Fluoride F 18 Injection based on a review of the published literature, publicly available reference sources, and adverse drug reaction reporting systems. However, the completeness of these sources is not known.

7 DRUG INTERACTIONS

The possibility of interactions of Sodium Fluoride F 18 Injection with other drugs taken by patients undergoing PET imaging has not been studied.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C
Any radiopharmaceutical including Sodium Fluoride F 18 Injection has a potential to cause fetal harm. The likelihood of fetal harm depends on the stage of fetal development, and the radionuclide dose. Animal reproductive and developmental toxicity studies have not been conducted with Sodium Fluoride F 18 Injection. Prior to the administration of Sodium Fluoride F 18 Injection to women of childbearing potential, assess for presence of pregnancy. Sodium Fluoride F 18 Injection should be given to a pregnant woman only if clearly needed.

8.3 Nursing Mothers

It is not known whether Sodium Fluoride F 18 Injection is excreted into human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to interrupt nursing after administration of Sodium Fluoride F 18 Injection or not to administer Sodium Fluoride F 18 Injection, taking into account the importance of the drug to the mother. The body of scientific information related to radioactive decay, drug

tissue distribution, and drug elimination shows that less than 0.01% of the radioactivity administered remains in the body after 24 hours (10 half-lives). To minimize the risks to a nursing infant, interrupt nursing for at least 24 hours.

8.4 Pediatric Use

In reported clinical experience in approximately 100 children, weight based doses (2.1 MBq/kg) ranging from 19 MBq-148 MBq (0.5 mCi-4 mCi) were used. Sodium Fluoride F 18 was shown to localize to areas of bone turnover including rapidly growing epiphyses in developing long bones. Children are more sensitive to radiation and may be at higher risk of cancer from Sodium Fluoride F 18 Injection.

11 DESCRIPTION

11.1 Chemical Characteristics

Sodium Fluoride F 18 Injection is a positron emitting radiopharmaceutical, containing no-carrier-added, radioactive fluoride F 18 that is used for diagnostic purposes in conjunction with PET imaging. It is administered by intravenous injection. The active ingredient, sodium fluoride F 18, has the molecular formula Na[^{18}F] with a molecular weight of 40.99, and has the following chemical structure:

Na $^{+18}$F $^{-}$

Sodium Fluoride F 18 Injection is provided as a ready-to-use, isotonic, sterile, pyrogen-free, preservative-free, clear, and colorless solution. Each mL of the solution contains between 370 MBq to 7,400 MBq (10 mCi to 200 mCi) sodium fluoride F 18, at the EOS reference time, in 0.9% aqueous sodium chloride. The pH of the solution is between 4.5 and 8. The solution is presented in 30 mL multiple-dose glass vials with variable total volume and total radioactivity in each vial.

11.2 Physical Characteristics

Fluorine F 18 decays by positron (β+) emission and has a half-life of 109.7 minutes. Ninety-seven percent of the decay results in emission of a positron with a maximum energy of 633 keV and 3% of the decay results in electron capture with subsequent emission of characteristic X-rays of oxygen. The principal photons useful for diagnostic imaging are the 511 keV gamma photons, resulting from the interaction of the emitted positron with an electron (Table 2). Fluorine F 18 atom decays to stable ^{18}O-oxygen.

Table 2. Principal Emission Data for Fluoride F 18

Radiation/Emission	% per Disintegration	Mean Energy
Positron (β+)	96.73	249.8 keV

Gamma (±)*	193.46	511.0 keV

*Produced by positron annihilation
[3] Kocher, D.C. Radioactive Decay Data Tables DOE/TIC-11026, 69, 1981.

The specific gamma ray constant for fluoride F 18 is 5.7 R/hr/mCi (1.35 x 10^{-6} Gy/hr/kBq) at 1 cm. The half-value layer (HVL) for the 511 keV photons is 4.1 mm lead (Pb). A range of values for the attenuation of radiation results from the interposition of various thickness of Pb. The range of attenuation coefficients for this radionuclide is shown in Table 3. For example, the interposition of an 8.3 mm thickness of Pb with a coefficient of attenuation of 0.25 will decrease the external radiation by 75%.

Table 3. Radiation Attenuation of 511 keV Photons by Lead (Pb) Shielding

Shield Thickness (Pb) mm	Coefficient of Attenuation
0	0.00
4	0.50
8	0.25
13	0.10
26	0.01
39	0.001
52	0.0001

Table 4 lists the fraction of radioactivity remaining at selected time intervals from the calibration time. This information may be used to correct for physical decay of the radionuclide.

Table 4. Physical Decay Chart for Fluoride F 18

Time Since Calibration	Fraction Remaining
0*	1.00
15 minutes	0.909
30 minutes	0.826
60 minutes	0.683
110 minutes	0.500
220 minutes	0.250
440 minutes	0.060
12 hours	0.011
24 hours	0.0001

*Calibration Time

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Fluoride F 18 ion normally accumulates in the skeleton in an even fashion, with greater deposition in the axial skeleton (e.g. vertebrae and pelvis) than in the appendicular skeleton and greater deposition in the bones around joints than in the shafts of long bones.

12.2 Pharmacodynamics

Increased fluoride F 18 ion deposition in bone can occur in areas of increased osteogenic activity during growth, infection, malignancy (primary or metastatic) following trauma, or inflammation of bone.

12.3 Pharmacokinetics

After intravenous administration, fluoride F 18 ion is rapidly cleared from the plasma in a biexponential manner. The first phase has a half-life of 0.4 h, and the second phase has a half-life of 2.6 h. Essentially all the fluoride F 18 that is delivered to bone by the blood is retained in the bone. One hour after administration of fluoride F 18, only about 10% of the injected dose remains in the blood. Fluoride F 18 diffuses through capillaries into bone extracellular fluid space, where it becomes bound by chemisorption at the surface of bone crystals, preferentially at sites of newly mineralizing bone.

Deposition of fluoride F 18 in bone appears to be primarily a function of blood flow to the bone and the efficiency of the bone in extracting the fluoride F 18. Fluoride F 18 does not appear to be bound to serum proteins. In patients with normal renal function, 20% or more of the fluorine ion is cleared from the body in the urine within the first 2 hours after intravenous administration.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Studies to assess reproductive toxicity, mutagenesis, and carcinogenesis potential of Sodium Fluoride F 18 Injection have not been performed.

14 CLINICAL STUDIES

14.1 Metastatic Bone Disease

The doses used in reported studies ranged from 2.7 mCi to 20 mCi (100 MBq to 740 MBq), with an average median dose of 10 mCi (370 MBq) and an average mean dose of 9.2 mCi (340 MBq). In PET imaging of bone metastases with Sodium Fluoride F 18 Injection, focally increased tracer uptake is seen in both osteolytic and osteoblastic bone

lesions. Negative PET imaging results with Sodium Fluoride F 18 Injection do not preclude the diagnosis of bone metastases. Also, as benign bone lesions are also detected by Sodium Fluoride F 18 Injection positive PET imaging results cannot replace biopsy to confirm a diagnosis of cancer.

14.2 Other Bone Disorders

The doses used in reported studies ranged from 2.43 mCi to 15 mCi (90 MBq to 555 MBq), with an average median dose of 8.0 mCi (300 MBq) and an average mean dose of 7.6 mCi (280 MBq).

15 REFERENCES

1. Stabin, M.G., Stubbs, J. B., and Toohey R. E., Radiation Dose Estimates for Radiopharmaceuticals, U.S. Nuclear Regulatory Commission report NUREG/CR-6345, page 10, 1996.
2. Radiation Dose to Patients from Radiopharmaceuticals, ICRP publication 53, Ann ICRP, 18, pages 15 and 74, 1987.
3. Kocher, D. C., “Radioactive Decay Data Tables: A Handbook of decay data for application to radiation dosimetry and radiological assessments” DOE/TIC-11026, page 69, 1981.

16 HOW SUPPLIED/STORAGE AND HANDLING

Sodium Fluoride F 18 Injection, USP is supplied in a multiple-dose Type 1 glass vial with elastomeric stopper and aluminum crimp seal containing between 370 and 7,400 MBq/mL (10-200 mCi/mL) of no-carrier-added sodium fluoride F 18, at the EOS reference time, in aqueous 0.9% sodium chloride solution. The total volume and total radioactivity per vial are variable. Each vial is enclosed in a shielded container of appropriate thickness. The product is available in a 30 mL vial configuration with a variable fill volume. The NDC number is: 81759-002-30.

Storage
Store at 25°C (77°F) in a shielded container; excursions permitted to 15-30°C (59-86°F). Use the solution within 12 hours of the EOS reference time.

Handling
Receipt, transfer, handling, possession, or use of this product is subject to the radioactive material regulations and licensing requirements of the U.S. Nuclear Regulatory Commission, Agreement States or Licensing States as appropriate.

17 PATIENT COUNSELING INFORMATION

17.1 Pre-study Hydration

Encourage patients to drink at least 500 mL of water prior to drug administration.

17.2 Post-study Voiding

To help protect themselves and others in their environment, patients should take the following precautions for 12 hours after injection: whenever possible, use a toilet and flush several times after each use; wash hands thoroughly after each voiding or fecal elimination. If blood, urine or feces soil clothing, wash the clothing separately.

Manufactured & Distributed by:

BAMF Health Inc.

Grand Rapids, MI 49503

Revised: 12/2022

PRINCIPAL DISPLAY PANEL

SODIUM FLUORIDE F 18 INJECTION, USP
(10 – 200 mCi/mL @ End of Synthesis (EOS))
Diagnostic – For intravenous use only
Sterile, Non-pyrogenic

Batch #: _____

EOS Date: _____ EOS Time: _____

Activity @ EOS: _____ mCi

Concentration: _____ mCi/mL

Volume: _____mL

Exp. Date: _____Exp. Time: _____

NDC #: 81759-002-30
CAUTION: RADIOACTIVE MATERIAL
Rx ONLY – 30 mL Multiple-Dose Vial
^{18}F Half-Life = 109.7 min

Calculate correct dosage from date and time of calibration
Expiration: Use within 12 hours of EOS
Each mL contains 0.37 GBq to 7.4 GBq (10 to 200 mCi) of no-carrier added sodium [^{18}F]fluoride in aqueous 0.9% sodium chloride solution at EOS.
Do not use if cloudy or contains particulate matter.
Store at 25°C (77°F); excursion permitted to 15-30°C (59-86°C) [see USP controlled room temperature]). Store upright in a shielded container. Aseptically withdraw and handle doses.

Manufactured by: BAMF Health, Inc. Grand Rapids, MI 49503, USA

SODIUM FLUORIDE F 18 INJECTION, USP
(10 – 200 mCi/mL @ End of Synthesis (EOS))
Diagnostic – For intravenous use only
Sterile, Non-pyrogenic

Batch #: _____

EOS Date: _____ EOS Time: _____

Activity @ EOS: _____ mCi

Concentration: _____ mCi/mL

Volume: _____mL

Exp. Date: _____Exp. Time: _____

NDC #: 81759-002-30
CAUTION: RADIOACTIVE MATERIAL
Rx ONLY – 30 mL Multiple-Dose Vial
^{18}F Half-Life = 109.7 min
Calculate correct dosage from date and time of calibration
Expiration: Use within 12 hours of EOS

Each mL contains 0.37 GBq to 7.4 GBq (10 to 200 mCi) of no-carrier added sodium [18F]fluoride in aqueous 0.9% sodium chloride solution at EOS.

Do not use if cloudy or contains particulate matter.

Store at 25°C (77°F); excursion permitted to 15-30°C (59-86°C) [see USP controlled room temperature]). Store upright in a shielded container. Aseptically withdraw and handle doses.

BAMF Health

Manufactured by: BAMF Health, Inc. Grand Rapids, MI 49503, USA

SODIUM FLUORIDE F 18
sodium fluoride f-18 injection

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:81759-002
Route of Administration	INTRAVENOUS		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
SODIUM FLUORIDE F-18 (UNII: 9L75099X6R) (FLUORIDE ION F-18 - UNII:4M4WE5N2GE)	FLUORIDE ION F-18	200 mCi in 1 mL

Inactive Ingredients	
Ingredient Name	**Strength**
SODIUM CHLORIDE (UNII: 451W47IQ8X)	9 mg in 1 mL

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:81759-002-30	1 in 1 CONTAINER	12/06/2022	
1		10 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA204328	12/06/2022	

Labeler - BAMF Health Inc. (117208762)

Registrant - BAMF Health Inc. (117208762)

Establishment

Name	Address	ID/FEI	Business Operations
BAMF Health		118390069	positron emission tomography drug production(81759-002)

Revised: 12/2023 BAMF Health Inc.