TNC-2C

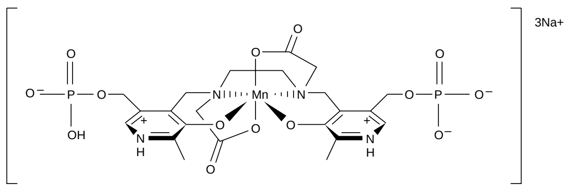
TESLASCAN® 50 μmol/mL
(mangafodipir trisodium) Injection

R_X ONLY

DESCRIPTION

TESLASCAN® (mangafodipir trisodium) Injection is an intravenous contrast agent for magnetic resonance imaging.

TESLASCAN Injection is formulated with mangafodipir trisodium, a solution of trisodium trihydrogen (*OC*-6-13)-[[*N,N'*-1,2-ethanediylbis[*N*-[[3-hydroxy-2-methyl-5-[(phosphonooxy)methyl]-4-pyridinyl]methyl]glycinato]] (8-)] manganate (6-). Mangafodipir trisodium ($C_{22}H_{27}MnN_4Na_3O_{14}P_2$) has a molecular weight of 757.33 (anhydrous) and the manganese content of the molecule is 7.25%. Its structural formula is illustrated below:



TESLASCAN Injection is a sterile, clear yellow solution. Each milliliter of TESLASCAN Injection contains 37.9 mg (or 50 μmol/mL) mangafodipir trisodium; ascorbic acid, 2.0 mg; sodium chloride, 2.0 mg; fodipir, 0.25 mg; and Water for Injection. The pH is adjusted to 8.8 ± 0.4 with hydrochloric acid and/or sodium hydroxide. The osmolality is 298 mOsmol/kg water. TESLASCAN Injection does not contain a preservative.

Pertinent physicochemical data are provided below:

PHYSICOCHEMICAL DATA

	@ 37°C
Viscosity (cP)	0.8
Density (g/mL)	1.02
Specific Gravity	1.03
Osmolality (mOsmol/kg water)	298

CLINICAL PHARMACOLOGY

GENERAL

TESLASCAN Injection (mangafodipir trisodium) is a complex formed between a chelating agent (fodipir) and a paramagnetic metal ion, manganese. Mangafodipir shortens the spin lattice (longitudinal) relaxation time (T_1) of targeted tissues during MRI, leading to an increase in signal intensity (brightness) of the tissues.

PHARMACOKINETICS

Mangafodipir has two components: fodipir and a manganese (II) ion. Each has different pharmacokinetics, metabolism, and modes of elimination. After intravenous administration of TESLASCAN, the pharmacokinetics of each component were investigated.

Fodipir: When TESLASCAN is labeled with the ^{14}C-label residing in the fodipir, after a single intravenous dose of 5 μmol/kg of ^{14}C-TESLASCAN in 6 healthy volunteer men, the mean ± SD area under the radioactivity plasma concentration curve (AUC) is 22.7 ± 3.2 μg*h/mL.

Manganese (II) ion: Generally, the total body store of manganese in adults is 20 mg. Most of this is from dietary intake (2-5 mg/day). TESLASCAN Injection contains 2.75 mg/mL of chelated manganese. In a 70 kg adult, 5 μmol/kg of TESLASCAN Injection contains 19.2 mg of chelated manganese. Therefore, a single injection of TESLASCAN will approximately double the total body store of manganese before excretion occurs. In a study of 31 healthy volunteers (16 men and 15 women), after a single intravenous dose of 5 μmol/kg TESLASCAN, areas under the manganese serum concentration versus time curves (AUC) were 15.8 ± 5.8 μM*h (mean ± SD) and 16.0 ± 2.9 μM*h (mean ± SD), respectively. (See Elimination section for details on excretion.)

DISTRIBUTION

Mangafodipir itself does not bind to plasma proteins *in vitro*; however, manganese (II) and manganese (III) are known to bind to plasma proteins *in vitro.*

In pregnant rats who received ^{54}Mn, radioactivity was detected in the placenta and in the fetus. (See Pregnancy section.)

METABOLISM

After intravenous injection, mangafodipir trisodium is metabolized by the removal of two phosphate groups and the exchange of the manganese ion for an endogenous zinc ion. This produces two major metabolites, manganese dipyridoxyl ethylenediamine diacetic acid (MnPLED) and zinc dipyridoxyl ethylenediamine diacetic acid (ZnPLED).

In plasma, the mangafodipir trisodium is not detected after 2 hours. The MnPLED concentration peaks within ten minutes and is not detected after 1 hour. The ZnPLED metabolite reaches maximum concentration 20 minutes after injection and then decreases slowly. By 24 hours the two major metabolites (MnPLED and ZnPLED) represent 12% and 57% of the administered dose, respectively.

ELIMINATION

Fodipir: When TESLASCAN is labeled with the ^{14}C in the fodipir, after intravenous administration of 5 μmol/kg ^{14}C-mangafodipir trisodium to 6 healthy volunteer men, approximately 92% of the radioactivity administered is eliminated in the urine over 24 hours. Negligible amounts (0.3%) are recovered in feces over 168 hours. The total plasma clearance of radioactivity was 11.6 ± 2.1 L/h (0.15 ± 0.02 L/h/kg mean ± SD). The apparent terminal half-life (mean ± SD) of elimination of radioactivity from plasma is 2.09 ± 0.47 hours.

Manganese (II) ion: After intravenous administration of TESLASCAN, the initially high serum manganese concentrations drop rapidly and approach detection limits (or baseline levels) within a few hours. Approximately 15% of the dose administered of the manganese (II) ion of mangafodipir is eliminated in the urine within the first 24 hours after injection and an additional 59% is excreted in the feces over the following 5 days. The remainder is eliminated in urine and feces gradually.

The dialyzability of TESLASCAN Injection and its metabolites has not been studied.

SPECIAL POPULATIONS

Hepatic Insufficiency: A single intravenous dose of 5 μmol/kg of TESLASCAN was administered to 31 subjects with normal hepatic function (16 men and 15 women) and 10 subjects with impaired hepatic function (5 men and 5 women). In the patients with impaired hepatic function (5 men and 5 women), after a single intravenous dose of 5 μmol/kg TESLASCAN, for manganese, AUCs were 23.3 ± 4.3 μM*h (mean ± SD) and 24.6 ± 4.0 μM*h (mean ± SD), respectively. (See Pharmacokinetics of Manganese Ion for comparative values in healthy volunteers.)

Manganese (II) ion serum levels at 1 hour after injection were 10% or less of maximal values.

Manganese (II) ion half-life: In both healthy subjects and subjects with hepatic impairment, the immediate distribution half-life (determined over the interval from 5 minutes to 2 hours after injection) was 24.4 ± 7.7 min (mean ± SD). However, the terminal half-lives were longer, $t_{1/2}$ = 10.1 ± 20.3 hrs and $t_{1/2}$ = 26.7 ± 19.0 hrs, respectively, for healthy and hepatically impaired subjects.

GENDER

Statistically significant differences were not detected in the elimination half-lives between men and women who were either healthy or had hepatic impairments, nor were there differences in the overall urinary or fecal recovery of manganese (II) ion in men and women who were either healthy or had hepatic impairments. (See Table 1 for details.)

TABLE 1

SIMILARITY IN ELIMINATION PROFILES OF NORMAL AND HEPATICALLY IMPAIRED MEN AND WOMEN (mean ± SD)

Population	Elimination $t_{1/2}$		Urine or Fecal Recovery*	
	Men	Women	Men	Women
Healthy Volunteers	13.9 ± 27.4	5.8 ± 4.0	73.9 ± 22.8	73.4 ± 22.9
Hepatically Impaired	30.6 ± 16.6	22.9 ± 22.3	77.8 ± 14.7	66.6 ± 9.8

* Collected over 0 - 5 days

AGE

Pharmacokinetic differences due to age in adults or in pediatric patients after intravenous TESLASCAN were not studied.

RACE

Pharmacokinetic differences due to race after intravenous TESLASCAN were not studied.

DRUG-DRUG INTERACTIONS

Drug interactions were not studied.

DIETARY EFFECTS

Pharmacokinetic studies with intravenous TESLASCAN were performed with nonfasted volunteers or patients.

PHARMACODYNAMICS

Mangafodipir enhances T_1 signal intensity. In a study of 12 healthy volunteer men, mangafodipir began to increase the signal intensity of liver tissue within 1-3 minutes, and steady-state enhancement was reached in about 5-10 minutes. Liver enhancement after TESLASCAN Injection administration is detectable in patients up to 24 hours after injection. After mangafodipir trisodium administration, liver lesions may present in a number of different patterns of contrast enhancement. (See Clinical Trials section.)

CLINICAL TRIALS

TESLASCAN Injection was studied in four multicenter, randomized, blinded, controlled clinical trials in a total of 546 adults who underwent hepatic MRI for evaluation of known or suspected focal liver disease.

In two of these studies, 404 adults (244 men, 160 women; 79% Caucasian, 10% Black, 6% Asian, 5% other races; mean age 58; range, 19-86 yr) received TESLASCAN 5 μmol/kg. Of these, 369 patients had images that were evaluated for efficacy.

All patients were imaged in three ways: 1) by contrast-enhanced computed tomography (CECT), 2) by unenhanced magnetic resonance imaging (MRI) and 3) by TESLASCAN Injection MRI. TESLASCAN Injection MRIs were obtained 15 minutes after injection (median, 20 minutes; range, 2-134 minutes). The sets of images were evaluated blindly as CECT alone, unenhanced MR images alone, TESLASCAN-enhanced MR images alone, and paired comparisons of the unenhanced and TESLASCAN-enhanced MRIs. Each liver lesion identified was rated for the presence of a specific cellular process (hepatocellular, nonhepatocellular, malignant, nonmalignant, or uncertain disease); a specific diagnosis (focal nodular hyperplasia, regenerative nodule, fatty infiltration, hepatoma/hepatocellular carcinoma, metastasis, cyst, adenoma, hemangioma or unknown); and the lesion's pattern of enhancement (homogeneous, inhomogeneous, central, peripheral thin rim, peripheral thick rim, peripheral linear foci, peripheral nodular, or no enhancement). Histopathology was obtained for some lesions. An overall final diagnosis was based on clinical, histopathologic, and all imaging information except the TESLASCAN MRI. The analysis is based on the extent of agreement between the diagnosis from the TESLASCAN MRI versus the histopathologic diagnosis for each lesion, the correct number of lesions detected, and the diagnosis of each lesion or disease state. The results are reported as complete agreement (with all lesions and diagnoses) or essential agreement (with diagnoses but not necessarily all lesions).

Based upon these two studies, TESLASCAN Injection enhanced MRI contrast on the T_1-weighted pulse sequences. Table 2 shows the proportions of patients for whom the imaging diagnosis had complete or essential agreement with the final diagnosis. In both studies TESLASCAN MRI alone and the paired reading of TESLASCAN MRI each had a statistically significant higher extent of agreement with the final diagnosis than did unenhanced MRI.

TABLE 2

OVERALL PERCENT OF TOTAL OR ESSENTIAL AGREEMENT OF IMAGE RESULTS[1] WITH THE FINAL CLINICAL DIAGNOSIS[2] IN 2 STUDIES

STUDY		TESLASCAN MRI vs. UNENHANCED MRI	PAIRED TESLASCAN MRI vs. UNENHANCED MRI
Study A	N Patients	187 [3]	187
	% Agreement	71 vs. 63	74 vs. 63
	P value	(*P*<.020)	(*P*<.001)
Study B	N Patients	182 [4]	182
	% Agreement	57 vs. 50	59 vs. 50
	P value	*P* = 0.04	(*P*< 0.01)

[1] Obtained with CECT, unenhanced MRI, TESLASCAN MRI, and the paired read of unenhanced and TESLASCAN images.

[2] Using all available clinical information except the TESLASCAN MRI. Histopathology was the basis of the final diagnosis in 105 (25%) of the patients.

[3] 15 (7%) of the 202 patients in study A were not evaluable (7 withdrew, 8 did not have full data sets).

[4] 20 (10%) of the 202 patients in study B were not evaluable (12 withdrew, 8 did not have full data sets).

TABLE 3

COMPARISON OF PROPORTION OF CORRECTLY CHARACTERIZED LESIONS WITH HISTOPATHOLOGIC CONFIRMATION (N = 105 LESIONS)

	Detected by Imaging		Not Detected by Imaging
	Correctly Characterized	Not Correctly Characterized	
Paired TESLASCAN MRI*	49 (47%)	34 (32%)	22 (21%)
Unenhanced MRI	28 (27%)	48 (46%)	29 (28%)
CECT	34 (32%)	35 (33%)	36 (34%)

* Of the 105 histopathologically confirmed lesions, 83 (79%) lesions were detected by paired TESLASCAN MRI. Of the lesions detected by the respective image sets, 59% (49/83) were correctly characterized by the paired TESLASCAN MRI, 37% (28/76) by unenhanced MRI, and 49% (34/69) by CECT (statistically significant).

In the above two studies, 105 individual lesions had histopathologic confirmation. Of these confirmed lesions, the proportion of correctly detected and correctly characterized lesions is shown in Table 3.

In two other studies of patients who received 5 μmol/kg of TESLASCAN, the efficacy of TESLASCAN Injection during delayed imaging was evaluated. In these two studies, 142 adult patients were given TESLASCAN (84 men, 58 women; 77% Caucasian, 15% Black, 4% Asian, 4% other races; mean age 58; range, 24-83 years). TESLASCAN-enhanced images for 140 patients were blindly evaluated for efficacy. TESLASCAN MRI imaging was performed at 15 minutes, 4 hours, and 24 hours after injection. The contrast enhancement results were comparable to those in the above studies and were similar at all time points.

In all four studies, each individual lesion's pattern of enhancement was coded as homogeneous, inhomogeneous, central, peripheral thin rim, peripheral thick rim, peripheral linear foci, peripheral nodular, or no enhancement. For the majority of histopathologically confirmed lesions, the pattern of TESLASCAN enhancement correlated with the hepatocellular disorders (having homogeneous, inhomogeneous, or central enhancement) or with the nonhepatocellular disorders (having peripheral or no enhancement). In the 121 patients who had malignant disease, 58 (47.9%) did not enhance, 20 (16.5%) were inhomogeneous, 15 (12.4%) had a thin peripheral rim, 12 (9.9%) had a thick peripheral rim, 12 (9.9%) were homogeneous and 4 (3.3%) had a variety of other patterns. For the 24 patients with nonmalignant disease, 13 (54%) did not enhance, 8 (33.3%) had homogeneous patterns, and 3 (12%) had a variety of other patterns. Table 4 shows the patterns of enhancement that are seen in patients with histologically confirmed hepatocellular or nonhepatocellular disease.

Malignancy cannot be distinguished by the pattern of enhancement, or by the presence or absence of enhancement.

TABLE 4

PATTERN OF TESLASCAN CONTRAST ENHANCEMENT SEEN IN 147 PATIENTS WITH HISTOPATHOLOGICALLY CONFIRMED HEPATOCELLULAR & NONHEPATOCELLULAR LESIONS [1,2] FOR 4 STUDIES[3].

Pattern	Hepatocellular disorders N = 68 patients	Nonhepatocellular disorders N = 79 patients
Homogeneous	17 (25%)	3 (4%)
Inhomogeneous	22 (32%)	1 (1%)
No enhancement	16 (24%)	56 (71%)
Other Patterns[4]	13 (19%)	19 (24%)

[1] Reproducible patterns useful in distinguishing malignant and benign disease were not detected.

[2] Reproducible patterns useful in distinguishing specific hepatocellular and nonhepatocellular diseases were not detected.

[3] Overall, 147/546 (27%) of the patients had completely evaluable data sets and histopathology.

[4] Peripheral pattern subtypes of thick, thin, linear or nodular were inconsistent; central patterns were reported in 2 patients only.

INDICATIONS AND USAGE

TESLASCAN Injection is indicated for intravenous administration as an adjunct to MRI in patients to enhance the T_1-weighted images used in the detection, localization, characterization, and evaluation of lesions of the liver.

CONTRAINDICATIONS

TESLASCAN Injection is contraindicated in patients with known allergic or hypersensitivity reactions to manganese, fodipir or any of the inert ingredients.

WARNINGS

Patients with a history of drug reactions to contrast media, other allergies, or immune system disorders should be observed for several hours after drug administration.

A fully equipped emergency cart, or equivalent supplies and equipment, and personnel competent in recognizing and treating anaphylactic reactions should be available.

Caution should be exercised before administering TESLASCAN to patients who have or cannot tolerate nausea or vomiting. The possibility of complications from nausea and vomiting should be considered when administering TESLASCAN Injection to patients who cannot tolerate vomiting, who have reflux esophagitis (especially if it is increased in a supine position) or who cannot roll over to prevent aspiration. Of the 652 total patients in clinical studies, 17 vomited after TESLASCAN, 10 for less than 8 minutes, 5 for more than 2 hours, and 2 for an unrecorded time. Sixty-seven patients had nausea, 41 patients had nausea of 10 minutes or less, and 16 had nausea of 20 minutes or more. Ten patients had nausea of unknown duration.

PRECAUTIONS

GENERAL: THE DECISION TO USE CONTRAST ENHANCEMENT SHOULD INCLUDE A CONSIDERATION OF THE RISK OF THE DRUG, THE RISK OF THE PROCEDURE, THE EXPECTED BENEFIT OF THE IMAGE AND THE PATIENT'S UNDERLYING DISORDER. THE DECISION TO USE TESLASCAN INJECTION SHOULD BE BASED UPON CAREFUL EVALUATION OF CLINICAL DATA, OTHER RADIOLOGIC DATA AND THE RESULTS OF UNENHANCED MRI.

TESLASCAN Injection is cleared from the body partially by glomerular filtration and partially by hepatobiliary excretion (see CLINICAL PHARMACOLOGY section). Dose adjustments in renal or hepatic impairment have not been studied. Caution should be exercised in patients with impaired renal or impaired hepatobiliary function.

Diagnostic procedures involving the use of contrast agents should be conducted under supervision of a physician with the prerequisite training and a thorough knowledge of the procedure to be performed. Appropriate facilities should be available for coping with any complication of the procedure, as well as for emergency treatment of severe reactions to the contrast agent itself.

Although more lesions are generally visualized on contrast-enhanced images than on unenhanced images, lesions seen on unenhanced images may not all be seen on contrast-enhanced images. Possible causes include changes in imaging parameters, patient motion, misregistration, and effects of the contrast agent.

Repeat Procedures: The safety of repeated doses has not been studied. If the physician determines that imaging needs to be repeated, repeat images could be obtained up to 24 hours after the original injection without reinjection.

INFORMATION FOR PATIENTS

Patients receiving TESLASCAN should be instructed before injection to:

1. Inform their physician or health care provider if they are pregnant or nursing. (See Precautions - Pregnancy Category C section.)
2. Inform their physician or health care provider if they have a history of renal or hepatic disease or seizure.
3. Inform their physician or health care provider if they have a history of allergic reaction, immune system disorder, or reaction to other radiocontrast drugs.
4. Inform their physician or health care provider if they have abdominal pain, nausea, or vomiting.

Patients should be informed that:

1. TESLASCAN Injection has been prescribed for liver enhancement during MRI.
2. TESLASCAN Injection may cause nausea and vomiting.

DRUG INTERACTIONS

Drug interactions with other contrast agents and other drugs were not studied.

LABORATORY TEST INTERACTIONS

Transmetalation of manganese may occur. The extent to which this might affect laboratory assays of ferritin, iron, bilirubin, and zinc is not known.

CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY

Long-term animal studies have not been performed to evaluate the carcinogenic potential of TESLASCAN Injection. The results of the following genotoxicity assays were negative: bacterial reverse mutation assay, CHO/HGPRT forward mutation assay, CHO chromosome aberration assay, and the *in vivo* mouse micronucleus assay.

TESLASCAN was positive in an *in vitro* mouse BALB/c-3T3 assay, but negative when the test was repeated; the assays were performed with the same final concentrations of TESLASCAN in the culture medium. The contrast agent did not affect male or female rat reproductive performance when administered at daily doses up to 100 µmol/kg (3.33 times the clinical dose based on body surface area, 20 times based on body weight).

PREGNANCY CATEGORY C

TESLASCAN may cause harm to the fetus when administered to a pregnant woman. Manganese causes embryo toxicity and fetal toxicity in various animal species. In rats, TESLASCAN was teratogenic (increased incidence of skeletal malformations) and fetotoxic (decreased fetal body weight) after 12 consecutive daily injections with 10, 20 and 40 µmol/kg (days 6 through 17 of gestation). These doses did not produce toxicity in the dams. Adverse effects were not observed in fetal rats at doses of 5 µmol/kg/day (each daily dose was 0.16 of the single imaging dose based on body surface area and the same as the imaging dose based on body weight). In another developmental study of rats injected with TESLASCAN for 3 consecutive days, in 20-60% of the litters at the lowest daily dose tested (20 µmol/kg, each daily dose was 0.64 times the single imaging dose based on surface area; 4 times based on body weight) had skeletal abnormalities observed at each of the four 3-day intervals studied. In rabbits, TESLASCAN was embryotoxic and fetotoxic (increased post-implantation losses and resorptions, and decreased number of viable fetuses) following 13 consecutive daily doses of 40 and 60 µmol/kg on days 6 through 18 of gestation; these doses did not produce toxicity in the does. Adverse effects were not observed in fetal rabbits at doses of 20 µmol/kg (each daily dose was 1.33 times the single imaging dose based on body surface area, 4 times based on body weight).

Animal studies have shown that ^{54}Mn manganese crosses the placenta and locates in the fetus. At least 24 hours after injection, radioactivity is detected in liver and bones of the fetus. It has been reported that manganese enters nerve terminals, accumulates in nervous tissue and could be associated with neurotoxicity in fetuses.

Adequate and well controlled studies were not conducted in pregnant women. If TESLASCAN is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be told of the potential hazard to the fetus.

NURSING MOTHERS

The rate and extent to which manganese or mangafodipir is excreted in human milk after TESLASCAN Injection has not been studied. In the literature, there are reports that manganese is excreted in human milk. Also, in comparison to adults, neonates have higher intestinal absorption and bioavailability of manganese. The relationship between the bioavailability of manganese from human milk and subsequent toxicity in developing infants is not known. Because of the potential risk to nursing infants from manganese exposure, consideration should be given to temporarily discontinuing nursing to allow clearance of mangafodipir and manganese. (See CLINICAL PHARMACOLOGY - Elimination section.)

PEDIATRIC USE

Safety and effectiveness of TESLASCAN Injection in adolescents are expected to be the same as in adults.

Safety, effectiveness or pharmacokinetics of TESLASCAN Injection in pediatric patients below the age of 12 years have not been established.

ADVERSE REACTIONS

In clinical trials, a total of 637 subjects (57 healthy volunteers and 580 patients) with known or suspected liver lesions received the contrast agent at a dose of 5 µmol/kg. Of these subjects, there were 387 men and 250 women with a mean age of 56 years (19 to 86). There were 497 (78%) Caucasian, 72 (11%) Black, 32 (5%) Oriental, and 36 (6%) in other racial groups.

Of these 637 subjects, 481 (76%) reported at least one adverse event. In clinical trials, there were 4 deaths and 2 serious events. The serious events included prolonged vomiting in one patient. The deaths occurred in patients with advanced multisystem disease (hepatocellular carcinoma, esophageal variceal bleeding, sepsis, and pneumonia) and were attributed to the underlying disorders.

The most commonly noted adverse experiences were injection site discomfort 430 (67%), headache - 32 (5%), and any gastrointestinal event - 79 (12%). (See Table 5 for details.)

TABLE 5 ADVERSE EVENTS REPORTED IN ≥0.5% OF PATIENTS WHO RECEIVED TESLASCAN IN CLINICAL TRIALS	
Patients Exposed to TESLASCAN	637
Patients with Any Adverse Event	481 (76%)
Patients with Any Injection Site Discomfort	430 (67%)
Gastrointestinal	79 (12%)
Nausea	67 (11%)
Vomiting	17 (3%)
Abdominal Pain	14 (2%)
Body as a Whole	25 (4%)
Headache	32 (5%)
Chest Pain	4 (0.6%)
Central & Peripheral Nervous System	48 (8%)
Dizziness	9 (1%)
Skin & Appendages	12 (2%)
Pruritus	7 (1%)

As with other contrast media, patients receiving TESLASCAN reported injection-associated discomfort. Overall 430 (67%) of the patients receiving TESLASCAN reported mild to moderate injection-associated discomfort. Of these, the discomfort was described as heat 266 (42%), flushing 234 (36%), pressure 26 (4%), pain 19 (3%), and cold 9 (1%).

The following selected adverse events occurred in <0.5% of the subjects. The majority (93%) of these adverse events were of mild to moderate intensity: chest pain, dizziness, hot flushes, hypersensitivity, hypertension, palpitation, pruritus, rash, taste perversion, urticaria.

In another 798 subjects who received the contrast agent in foreign clinical trials, similar types and rates of adverse events were reported.

OVERDOSAGE

Clinical consequences of overdosage with TESLASCAN Injection have not been reported. Treatment of an overdose is directed toward the support of all vital functions, and prompt institution of symptomatic therapy. The minimum lethal dose of mangafodipir trisodium when administered intravenously to mice as a bolus was >2000 μmol/kg (400 times the recommended human dose of 5 μmol/kg based on body weight and 17 times based on body surface area).

The dialyzability of TESLASCAN Injection and its metabolites has not been studied. Mangafodipir itself does not undergo protein binding *in vitro*; however, manganese (II) and manganese (III) are known to bind to plasma proteins *in vitro*.

DOSAGE AND ADMINISTRATION

TESLASCAN Injection should be administered as a peripheral intravenous injection at a dose of 5 μmol/kg (0.1 mL/kg) over approximately one minute. The maximum dose should not exceed 15 mL. (See the Dosage Chart.)

TESLASCAN Injection should be drawn into the syringe and administered using sterile technique. If nondisposable equipment is used, scrupulous care should be taken to prevent residual contamination with traces of cleansing agents. Unused portions of the drug must be discarded.

Imaging can begin within minutes after TESLASCAN Injection. If it is determined that imaging needs to be repeated, repeat images could be obtained up to 24 hours after the original injection without reinjection. The safety of repeat doses has not been studied. (See Pharmacodynamics and Clinical Trials.)

DOSAGE CHART

BODY WEIGHT kg	lb	VOLUME (mL)
40	88	4
50	110	5
60	132	6
70	154	7
80	176	8
90	198	9
100	220	10
110	242	11
120	264	12
150	330	15

Dose should not exceed 15 mL.

Other drugs should not be physically mixed with contrast agents because of the potential for chemical incompatibility. If the injection is made through tubing, the injection should be followed by a 5 mL flush with 0.9% sodium chloride.

Parenteral products should be inspected visually for particulate matter and discoloration prior to administration. Do not use if the solution is other than clear yellow or if particulate matter is present.

HOW SUPPLIED

10 mL vial, box of 5, NDC 0407-0695-10

STORAGE

Store in the original, unopened container between 15˚C and 30˚C (59˚F to 86˚F). **Protect from freezing**. Do not use product if it has been frozen. Freezing may compromise the package integrity.

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