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The latest Japanese text is available on PMDA website.

Revised: April 2023 (3rd version of new form)

Standard Commodity Classification Number of Japan
877219

Storage: Room temperature

Shelf Life: 3 years

Therapeutic Category: Non-ionic contrast medium

Regulatory Classification : Prescription-only drug[Note)]

Note) Use only as directed by a physician.

Iomeron 300 injection			
	20mL	50mL	100mL
Approval Number	22100AMX00721000	22100AMX00722000	22100AMX00723000
Date of Initial Marketing in Japan	May 1994		

Iomeprol solution for injection

Iomeron® 300 injection 20mL
Iomeron® 300 injection 50mL
Iomeron® 300 injection 100mL
Iomeron® 350 injection 20mL
Iomeron® 350 injection 50mL
Iomeron® 350 injection 100mL
Iomeron® 400 injection 50mL
Iomeron® 400 injection 100mL

Iomeron 350 injection			
	20mL	50mL	100mL
Approval Number	22100AMX00696000	22100AMX00694000	22100AMX00695000
Date of Initial Marketing in Japan	May 1994		

Iomeron 400 injection		
	50mL	100mL
Approval Number	22100AMX00698000	22100AMX00699000
Date of Initial Marketing in Japan	May 1994	

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1. WARNINGS

1.1 Serious adverse reactions such as shock may occur. [see 8.1-8.5, 9.1.8, 9.1.9, 11.1.1-11.1.3]

1.2 Do not use this drug for cisternography or myelography because its intracerebral and intrathecal administration may cause serious adverse reactions. [see 14.2.1]

2. CONTRAINDICATIONS (This drug is contraindicated to the following patients.)

2.1 Patients with a history of hypersensitivity to iodine or iodinated contrast media [see 8.1]

2.2 Patients with serious thyroid disease [Administration of this drug can cause higher blood concentration of iodine in the thyroid gland, affecting thyroid gland function, which can lead to aggravation of symptoms.] [see 9.1.14]

3. COMPOSITION AND PRODUCT DESCRIPTION

3.1 Composition

Each syringe contains the following ingredients:

Brand name		Iomeron 300 injection			Iomeron 350 injection			Iomeron 400 injection	
Iodine concentration (mg/mL)		300			350			400	
Content (mL)		20	50	100	20	50	100	50	100
Active ingredient	Iomeprol (g) (iodine (g))	12.25 (6)	30.62 (15)	61.24 (30)	14.29 (7)	35.72 (17.5)	71.44 (35)	40.82 (20)	81.65 (40)

Brand name		Iomeron 300 injection			Iomeron 350 injection			Iomeron 400 injection	
Excipients	Trometamol (mg)	20	50	100	20	50	100	50	100
	Hydrochloric acid	Adequate dose							

3.2 Product Description

Brand name	Iomeron 300 injection	Iomeron 350 injection	Iomeron 400 injection
Description	Colorless and clear solution		
pH	6.5 - 7.5		
Osmotic pressure ratio (ratio relative to isotonic sodium chloride solution)	Approximately 2	Approximately 2	Approximately 3
Viscosity (37°C, mPa・s)	4.3	7.0	13.6

4. INDICATIONS

<Iomeron 300 injection>

Cerebral angiography, Thoracic angiography, Abdominal angiography, Peripheral angiography, Intravenous digital subtraction angiography, Intraarterial digital subtraction angiography, Computed tomography (CT) enhancement, Intravenous urography.

<Iomeron 350 injection>

Angiocardiography, Thoracic angiography, Abdominal angiography, Peripheral angiography, Intravenous digital subtraction angiography, Intraarterial digital subtraction angiography, Computed tomography (CT) enhancement, Intravenous urography.

<Iomeron 400 injection>

Angiocardiography, Thoracic angiography, Abdominal angiography, Intravenous urography.

6. DOSAGE AND ADMINISTRATION

The usual adult dosage is indicated below. The dosage may be determined by the patient's age, body weight, symptoms and indication. In the case of multiple administration, a total dosage of 250 mL should not be exceeded.

Indication		Iomeron 300 injection	Iomeron 350 injection	Iomeron 350 injection
Cerebral angiography		5 - 15mL	—	—
Angiocardiography	Imaging of heart chambers	—	20 - 50mL	20 - 40mL
	Imaging of coronary arteries	—	3 - 10mL	3 - 8mL
Thoracic angiography		5 - 50mL	5 - 50mL	5 - 50mL
Abdominal angiography		5 - 60mL	5 - 60mL	5 - 60mL
Peripheral angiography		10 - 80mL	10 - 80mL	—
Intravenous digital subtraction angiography		10 - 50mL	10 - 50mL	—
Intraarterial digital subtraction angiography		3 - 40mL	3 - 40mL	—
CT enhancement		40 - 100mL	40 - 100mL	—
		When administering, intravenous drip infusion, etc. should be used as appropriate.	When administering, intravenous drip infusion, etc. should be used as appropriate. For dynamic CT enhancement in the hepatic region, 1.8	

		mL/kg can be intravenously administered by body weight (up to 135 mL)	
Intravenous urography	40 - 100mL	30 - 100mL	50mL
	When administering, intravenous drip infusion, etc. should be used as appropriate.		When administering, intravenous injection should be used as appropriate.

7. PRECAUTIONS CONCERNING DOSAGE AND ADMINISTRATION

For dynamic CT enhancement in the hepatic region with Iomeron 350, refer to this table for the dosage by body weight.

Body Weight (kg)	Dosage (mL)
<56	40 - 100
Not to exceed 1.8 mL/kg for 56 - 75 kg	
60	108 (1.8 mL/kg body weight)
65	117 (1.8 mL/kg body weight)
70	126 (1.8 mL/kg body weight)
75	135 (1.8 mL/kg body weight)
75<	135

8. IMPORTANT PRECAUTIONS

8.1 Patients should be carefully interviewed to take measures against shock, etc. [see 1.1, 2.1, 9.1.8, 9.1.9, 11.1.1-11.1.3]

8.2 Hypersensitivity reaction to this drug may occur independently of the dosage or the route of administration. Serious adverse reactions due to this drug such as shock are not necessarily hypersensitivity to iodine, and those reactions are not predictable. For administering this drug, make sure that appropriate emergency measures should be immediately available. [see 1.1, 11.1.1-11.1.3]

8.3 This drug should be administered carefully, monitoring the patient's condition from the start of administration, with special attention for the occurrence of hypersensitivity reaction. In case of any abnormality observed, administration should be discontinued immediately, and appropriate measures should be taken. [see 1.1, 11.1.1-11.1.3]

8.4 During and after the administration of this drug, the patient's condition should be monitored carefully since serious delayed adverse reactions, etc. (including shock) may occur. [see 1.1, 11.1.1-11.1.3].

8.5 When administrating this drug to outpatients, it is necessary to explain delayed adverse reactions may occur from one hour to several days after the administration, and to instruct to contact the attending physician immediately if any symptoms such as queasiness, chest pain, back pain, pyrexia, skin eruptions and itching, occur. [see 1.1, 11.1.1-11.1.3]

8.6 Ensure adequate hydration since iodinated contrast media may impair renal functions. [see 9.1.5, 9.1.13, 9.1.15, 9.2.1, 9.2.2, 9.8, 11.1.11, 14.1.2 and 14.3]

9. PRECAUTIONS CONCERNING PATIENTS WITH SPECIFIC BACKGROUNDS

9.1 Patients with Complication or History of Diseases, etc.

9.1.1 Patients with an extremely poor general condition

Do not administer this drug unless it is deemed unavoidable for diagnosis.

9.1.2 Patients with bronchial asthma

Do not administer this drug unless it is deemed unavoidable for diagnosis. Higher incidence of adverse reactions has been reported in patients with bronchial asthma.

9.1.3 Patients with serious cardiac disorders

Do not administer this drug unless it is deemed unavoidable for diagnosis. This drug can cause deterioration of hemodynamics, which can lead to impairment of cardiac function.

9.1.4 Patients with macroglobulinemia

Do not administer this drug unless it is deemed unavoidable for diagnosis. There have been reports of other iodinated contrast media in which gel formation of the blood occurred and patients deceased.

9.1.5 Patients with multiple myeloma

Do not administer this drug unless it is deemed unavoidable for diagnosis. There have been reports of other iodinated contrast media in which renal tubule obstruction occurred due to binding to urinary protein. [see 8.6 and 11.1.11]

9.1.6 Patients with tetany

Do not administer this drug unless it is deemed unavoidable for diagnosis. Blood calcium decreased may occur, leading to aggravation of the symptom.

9.1.7 Patients known or suspected of having pheochromocytoma

Do not administer this drug unless it is deemed unavoidable for diagnosis. If examination is necessary for unavoidable reason, this drug should be administered cautiously with the intravenous access secured. Appropriate measures should be readily available to treat attacks of blood pressure increased, tachycardia, arrhythmia or other symptoms. An example of such measures is to prepare a sufficient amount of alpha-blocker such as phentolamine mesilate or beta-blocker such as propranolol hydrochloride.

9.1.8 Patients whose a personal, parents or siblings have allergic predisposition, such as bronchial asthma, rash or urticaria, etc.

[See 1.1, 8.1, 11.1.1-11.1.3]

9.1.9 Patients with a history of drug hypersensitivity

[See 1.1, 8.1, 11.1.1-11.1.3]

9.1.10 Patients with dehydration

Dehydration may be aggravated.

9.1.11 Patients with hypertension

Hemodynamics may be aggravated.

9.1.12 Patients with arteriosclerosis

Hemodynamics may be aggravated.

9.1.13 Patients with diabetes mellitus

Renal functions may be impaired. [see 8.6 and 11.1.11]

9.1.14 Patients with thyroid disease (except patients with serious thyroid disease)

Administration of this drug can cause higher blood concentration of iodine in the thyroid gland, affecting thyroid gland function, which can lead to aggravation of symptoms. [see 2.2]

9.1.15 Patients with acute pancreatitis

Provide sufficient intravenous fluids before and after the administration of this drug in accordance with guidelines, etc. Symptoms may be aggravated. [see 8.6, 14.1.2 and 14.3]

9.1.16 Patients with myasthenia gravis

Occurrence of cardiopulmonary arrest, etc. has been reported. Symptoms may be aggravated.

9.1.17 Patients with central nervous system disorders

Cerebrovascular disorder or convulsions, etc. may occur.

9.2 Patients with Renal Impairment

9.2.1 Patients with serious renal impairment

Do not administer this drug unless it is deemed unavoidable for diagnosis. Since contrast media are excreted mainly through the kidneys, the excretion may be delayed and renal function may be aggravated. [see 8.6, 9.8, 11.1.11 and 16.6.1]

9.2.2 Patients with impaired renal function

Renal function may be aggravated. [see 8.6, 9.8, 11.1.11 and 16.6.1]

9.3 Patients with Hepatic Impairment

9.3.1 Patients with serious hepatic impairment

Do not administer this drug unless it is deemed unavoidable for diagnosis. Symptoms may be aggravated. [see 11.1.7]

9.3.2 Patients with impaired hepatic function

Hepatic functions may be aggravated. [see 11.1.7]

9.5 Pregnant Women

Administration of this drug to women who are or may be pregnant should be limited to the case in which the diagnostic benefit is considered to surpass the risk. Administration of this drug is followed by X-ray radiation.

9.6 Breast-feeding Women

Diagnostic benefit using this drug and the benefit of breast milk nutrients should be weighed for consideration of continuing or discontinuing breastfeeding. Excretion of this drug into breast milk has been reported in animal studies (rats, intravenous administration).

9.7 Pediatric Use

No clinical study has been conducted in pediatric patents.

9.8 Geriatric Use

This drug should be administered to the elderly patients with careful monitoring. This drug is excreted mainly through the kidneys. Since renal function of the elderly tends to be decreased, this drug blood concentration may remain high. [see 8.6, 9.2.1 and 9.2.2]

10. INTERACTIONS

10.2 Precautions for Co-administration (This drug should be administered with caution when co-administered with the following.)

Drugs	Clinical symptoms / Measures	Mechanism / Risk factors
Biguanide class antidiabetic agents Metformin hydrochloride Buformin hydrochloride, etc.	Lactic acidosis has been reported due to coadministration with iodinated contrast media and biguanide class antidiabetic agents. When administering this drug, appropriate measures such as temporarily discontinuing biguanide class antidiabetic agents should be taken.	The decrease in renal excretion of biguanide class antidiabetic agents is considered to lead to the increase of its blood concentration.

11. ADVERSE REACTIONS

Following adverse reactions may occur. Monitor patients' condition carefully and take appropriate measures such as discontinuing the administration upon onset of any abnormality.

11. 1 Clinically Significant Adverse Reactions

<General>

11. 1. 1 Shock

Syncope, loss of consciousness, dyspnoea, respiratory arrest, cardiac arrest, etc. may occur, as symptoms of shock (including delayed reaction) (frequency unknown). Patients should be monitored carefully since even mild hypersensitivity symptom can lead to serious symptoms. [see 1.1, 8.1-8.5, 9.1.8 and 9.1.9]

11. 1.2 Anaphylaxis

Anaphylaxis (including delayed reaction) (frequency unknown) such as dyspnoea or pharyngeal/laryngeal edema may occur. [see 1.1, 8.1-8.5, 9.1.8, 9.1.9 and 11.1.3]

11.1.3 Acute coronary syndrome accompanying allergic reaction (frequency unknown) [see 1.1, 8.1-8.5, 9.1.8, 9.1.9, 11.1.2 and 11.1.6]

11.1.4 Pulmonary edema (frequency unknown)

11.1.5 Acute respiratory distress syndrome (frequency unknown)

11.1.6 Ventricular fibrillation and coronary arteriospasm (frequency unknown for both) [see 11.1.3]

11.1.7 Hepatic impairment and jaundice (frequency unknown for both)

Hepatic impairment such as increased AST, ALT and γ-GTP or jaundice may occur. [see 9.3.1 and 9.3.2]

11.1.8 Cerebrovascular disorders

Transient or permanent cerebral circulatory failure (cerebral ischemia) (frequency unknown) may occur.

11.1.9 Seizure (frequency unknown)

11.1.10 Consciousness disturbed and syncope

Since consciousness disturbed (frequency unknown) or syncope (frequency unknown) without shock may occur, patients should be monitored carefully for the level of consciousness, etc. even after completion of the examination.

11.1.11 Renal failure

Acute kidney injury (0.04%) may occur. [see 8.6, 9.1.5, 9.1.13, 9.2.1 and 9.2.2]

11.1.12 Platelets decreased (frequency unknown)

11.1.13 Skin disorder

Oculomucocutaneous syndrome (Stevens-Johnson syndrome) (frequency unknown), and acute generalized exanthematous pustulosis (frequency unknown) may occur. Patients should be carefully monitored and appropriate measures should be taken immediately if pyrexia, erythema, small pustules, itchy sensation, ocular hyperaemia, stomatitis, or other symptoms are observed.

<Cerebral angiography>

11.1.14 Paralysis (frequency unknown)

<Cerebral angiography, Thoracic angiography, Angiocardiography>

11.1.15 Contrast-induced encephalopathy (frequency unknown)

Disturbed consciousness, paralysis, aphasia, cortical blindness, or other central nervous system symptoms may occur as a result of extracerebrovascular leakage of this drug. Minimum effective dosages should be administered and appropriate measures should be taken if any abnormalities are observed.

11.2 Other Adverse Reactions

	≥ 0.1%　< 1.5%	< 0.1%	Frequency unknown
Hypersensitivity	Rash, Itching, Urticaria		Redness, Wheals
Psychoneurotic disorders	Headache, Dizziness	Tremor, Photophobia, Aphasia	Light headedness, Sleepiness (Somnolence), Anxiety (Unrest), Weakness, Amnesia, Language disorder, Visual impairment such as transient blindness
Gastrointestinal disorders	Nausea, Vomiting	Thirst, Diarrhea	Abdominal pain, Anorexia, Saliva increased, Oral discomfort, Stomatitis
Cardiovascular disorders	Blood pressure decreased, Blood pressure increased	ST depressed, Bradycardia, Extrasystoles, Palpitations	Tachycardia, Arrhythmia, Cardiac failure, Facial pallor, Cyanosis
Respiratory disorders	Sneezing	Dyspnoea, Rhinitis, Cough	Wheezing, Hoarseness, Pharyngolaryngeal discomfort
Endocrine disorders			Hypothyroidism
Others	Facial hot flushes, Blood potassium increased, Chest pain, Malaise, Chills, Taste abnormality/Dysosmia	Back pain, Pyrexia, Feeling hot, Heavy sweating	BUN increased, Serum creatinine increased, Anuria, Edema, Numbness, Vascular pain, Hiccups, Conjunctivitis, Lacrimation, Eye abnormalities

12. INFLUENCE ON LABORATORY TESTS

In case a diagnosis using radioactive iodine tests such as thyroid function tests are required, they should be conducted prior to the administration of this drug. Radioactive iodine test should not be performed for at least one month after the administration of this drug.

14. PRECAUTIONS CONCERNING USE

14.1 Precautions Prior to Administration of the Drug

<General>

14.1.1 Warm this drug to body temperature before administration.

14.1.2 Do not restrict fluid intake prior to administration of this drug. [see 8.6 and 9.1.15]

<Intravenous urography>

14.1.3 Intestinal gas should be eliminated prior to the examination, and the patients should be fasted until the examination completes.

14.2 Precautions Concerning Administration of the Drug

14.2.1 Do not use this drug for cisternography or myelography. [see 1.2]

14.2.2 Rate of administration of Iomeron 350 is up to 5.0 mL/second for the dynamic CT enhancement in the hepatic region.

14.2.3 Vascular pain may occur after intravenous administration of this drug.

14.2.4 Since non-ionic contrast media have less anti-coagulant activity *in vitro* than ionic media, intravascular catheters should be flushed frequently in the angiography with this drug. This drug should not be allowed to remain in contact with blood for long time in a syringe or catheter in administration.

14.2.5 Since mixing this drug with antihistamines or corticosteroids can cause incompatibility, they should be administered separately if used in combination.

14.2.6 In case extravasation of contrast media occur, patient may develop redness, swelling, blister, or vascular pain, etc. Extreme caution during administration is necessary to avoid extravasation.

14.3 Precautions Concerning Post-Administration of the Drug

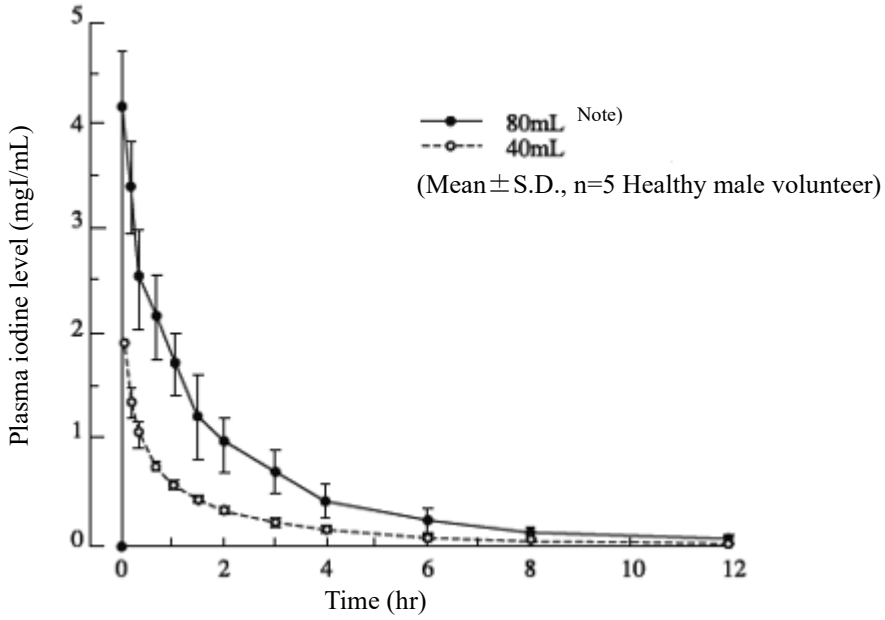
After the administration of this drug, ensure adequate hydration to allow prompt excretion of the contrast medium. [see 8.6 and 9.1.15]

16. PHARMACOKINETICS

16.1 Blood Level

A single dose of 40 mL or 80 mL[Note)] of Iomeprol 400 mgI/mL was administered intravenously to 10 healthy male volunteer at a rate of 10 mL/min, plasma iodine level changed almost in proportion to the dosage, and showed a biphasic elimination after completion of administration. The elimination half-lives in plasma, t1/2α (distribution phase) and t1/2β (excretion phase) were 22.3 minutes and 1.95 hours, respectively. The volume of distribution (Vc) was 0.11 L/kg, and the total clearance was 99.0 mL/min. [1)]

Note) The maximum single dose of Iomeprol 400 mgI/mL approved is 60 mL.



Mean plasma iodine level - time curve after administration of 40 mL and 80 mL[Note)] of Iomeprol 400 mgI/mL

Pharmacokinetic parameters after single intravenous administration of Iomeprol 400 mgI/mL

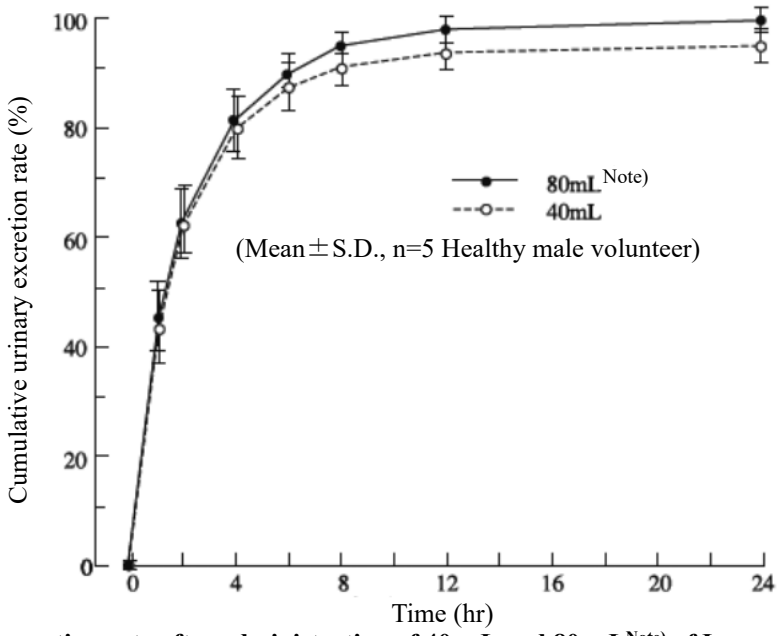
t1/2α (min)	t1/2β (hr)	Vc (L/kg)	Vd (L/kg)	CL (mL/min)
22.33±6.79	1.95±0.15	0.11±0.02	0.24±0.05	99.03±21.22

(Mean±S.D., n=10 Healthy male volunteer)

16.5 Excretion

A single dose of 40 mL or 80 mL[Note)] of Iomeprol 400 mgI/mL was administered intravenously to 10 healthy male volunteer at a rate of 10 mL/min, 80.0% of the dosage was excreted as unchanged Iomeprol in urine in 4 hours, and 97.5% in 24 hours of administration.[1)]

Note) The maximum single dose of Iomeprol 400 mgI/mL approved is 60 mL.



Cumulative urinary excretion rate after administration of 40 mL and 80 mL[Note)] of Iomeprol 400 mgI/mL

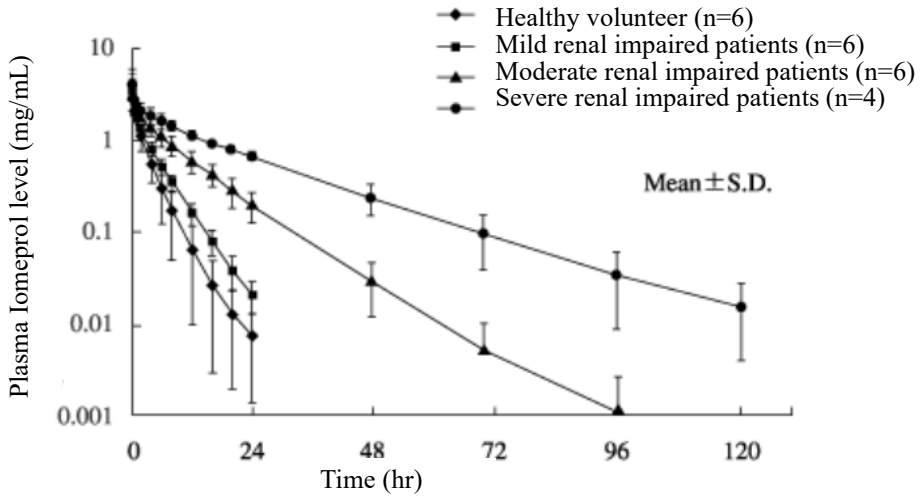
16.6 Patients with Specific Backgrounds

16.6.1 Patients with renal impairment

A single dose of 50 mL of Iomeprol 400 mgI/mL was administered intravenously to 6 healthy volunteer with normal renal function (GFR[Note)]>100mL/min/1.73m^2), 6 patients with mild renal impairment (GFR[Note)] 51-75 mL/min/1.73m^2), 6 patients with moderate renal impairment (GFR[Note)] 26-50 mL/min/1.73m^2), and 4 patients with severe renal impairment (GFR[Note)]<25 mL/min/1.73m^2), and plasma and urinary Iomeprol levels were determined.

Plasma Iomeprol level and pharmacokinetic parameters after the administration of Iomeprol are as follows. In patients with renal impairment, the elimination half-life (t1/2β) is prolonged and the renal clearance and glomerular filtration rate decreased in proportion to severity of renal impairment, compared with healthy volunteer. The urinary excretion rate up to 120 hours of Iomeprol administration decreases in proportion to severity of renal impairment in the same manner; decrease to 68.3% in patients with severe renal impairment, compared with 93.5% in healthy volunteer. The urinary excretion rate of patients with mild renal impairment and those with moderate impairment is 90.4% and 85.1% respectively, and the decrease was not as significant as the one for patients with severe renal impairment[2)] (data of non-Japanese). [see 9.2.1 and 9.2.2]

Note) Inulin clearance measurement



Plasma Iomeprol level-time curve after single dose of intravenous administration of 50 mL of Iomeprol 400 mgI/mL (data of non-Japanese)

Pharmacokinetic parameters of Iomeprol in healthy volunteer and patients with renal impairment (data of non-Japanese)

Pharmacokinetic parameter	Healthy volunteer (n=6)	Severity of renal impairment		
		Mild (n=6)	Moderate (n=6)	Severe (n=4)
t1/2β (hr)	2.34±0.44	3.67±0.46	6.9±1.6	15.1±4.3
$AUC_{0-\infty}$ (hr)	7.7±2.6	10.3±1.2	22.1±4.5	46.4±3.1
Vd (L)	8.3±1.7	8.7±0.9	8.2±2.5	10.7±3.3
CL_T (mL/min)	95±25	66.8±8.2	31.8±6.5	14.7±0.9
CL_R (mL/min)	88.3±30[Note1)]	60.5±8.1	27.3±7.5	10.1±1.8
GFR[note2)] (mL/min)	120±30	72±9.8	38.3±6.8	20.0±3.16
Urinary excretion rate $_{0\text{-}120hr}$ (%)	93.5±5.5[Note1)]	90.4±4.6	85.1±9.0	68.3±10.6

Note1) n＝5　　Note2) Inulin clearance measurement

17. CLINICAL STUDIES

17.1 Clinical Studies for Efficacy and Safety

< Urography/ angiography and CT >

17.1.1 Domestic phase III clinical study

In comparative study and general clinical studies conducted using the vial formulation, the effective rate of the contrast effect in the 1,925 patients for whom contrast effect was assessed was 98.2% (1,891 patients).

Out of 2,147 subjects of comparative study and general clinical studies (combined Iomeron 300/350/400 injections [vial products] and Iomeron 300/350 syringes), adverse reactions were reported regarding 120 patients (5.59%) , and the major adverse reactions were nausea in 31 patients (1.44%) and rash in 24 patients (1.12%).

Among adverse reactions occurred, delayed adverse reactions occurred after one hour or later of administration were as follows[3), 4), 5)].

Number of patients assessed	Within 1 hour after administration	Within 3 hours after administration	Within 6 hours after administration	Within 12 hours after administration	Within 24 hours after administration	From 24 hours after administration	Total number of events
2,147	114 (70.4)	20 (12.3)	8 (4.9)	4 (2.5)	7 (4.3)	9 (5.6)	162 (100.0)

(　): %

* Abnormality in laboratory test values was excluded since onset time of them were not investigated.

<Dynamic CT enhancement in the hepatic region>

17.1.2 Domestic phase II/III comparative study (Iomeron 350 injections and Iomeron 350 syringes) [6)]

In 173 patients with hepatic mass lesion, the contrast enhanced efficacy on mass lesions of dose groups of 100 mL, 1.5 mL/kg and 1.8 mL/kg body weight were evaluated to be "Excellent " or "Good" (hereafter, "Good" or better), except for one patient in the 100 mL dose group, and the rate of "Good" or better was high, ranging from 98.3% to 100.0%. The rate of patients evaluated "Excellent" was 63.8% in the 100 mL dose group, 57.9% in the 1.5 mL/kg group, and 84.5% in the 1.8 mL/kg group.

As a result of comparing the contrast enhanced efficacy of mass lesions in 100mL dose group and the 1.8mL/kg group, 1.8mL/kg group was demonstrated significantly higher efficacy than the 100mL group. In a paired comparative of 1.5 mL/kg group and 1.8 mL/kg group, 1.8 mL/kg group was significantly better than the 1.5 mL/kg group.

Among adverse reactions occurred, delayed adverse reactions occurred in one hour of administration or later were as follows.

Number of patients assessed	Within 1 hour after administration	Within 3 hours after administration	Within 6 hours after administration	Within 12 hours after administration	Within 24 hours after administration	From 24 hours after administration	Total number of events
173	6 (33.3)	0	1 (5.6)	0	0	11 (61.1)	18 (100.0)

* Excluding feeling hot and vascular pain ( ): %

Adverse reactions which occurred after one hour or later of administration were pruritus (1), rash (1), malaise (1), discomfort (1), blood pressure increased (1), bronchitis (1), epistaxis (1), white blood cell decreased (2), white blood cell increased (1), blood bilirubin increased (1) and ALT increased (1). None of them were serious.

18. PHARMACOLOGY

18.1 Mechanism of contrast enhancement

Three Iodine atoms (atomic number 53, atomic weight 127) coordinated to the benzene ring, which is the basic framework of contrast media, have high absorption of X-rays. With contrast media containing iodine atoms, X-ray photography shows contrast difference between the blood vessels containing contrast media and other organs, and can create images of intended blood vessels or urinary tract, etc.

19. PHYSICOCHEMICAL PROPERTIES

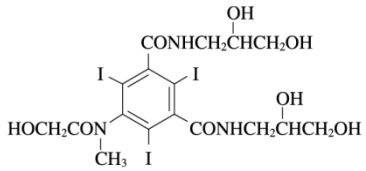
Nonproprietary name : Iomeprol

Chemical name : diastereomeric mixture of N, N'-bis(2, 3-dihydroxypropyl)-5-[(hydroxyacetyl) methylamino]-2, 4, 6-triiodo-1, 3-benzenedicarboxamide

Molecular formula : $C_{17}H_{22}I_3N_3O_8$

Molecular weight :777.09

Structural formula:



Physicochemical description:

Iomeprol is a white crystalline powder, and it is odorless. It is highly water-soluble, soluble in methanol, slightly soluble in ethanol (99.5), and practically insoluble in chloroform and in diethylether.

A solution of Iomeprol (1 in 10) shows no optical rotation.

Partition coefficient : 2.972×10^{-3} (water: 1-octanol)

20. PRECAUTIONS FOR HANDLING

Protect from light after opening package box.

22. PACKAGING

<Iomeron 300 injection 20 mL>
Boxes of 5 vials
<Iomeron 300 injection 50 mL>
Boxes of 5 vials
<Iomeron 300 injection 100 mL>
Boxes of 5 vials
<Iomeron 350 injection 20 mL>
Boxes of 5 vials
<Iomeron 350 injection 50 mL>
Boxes of 5 vials
<Iomeron 350 injection 100 mL>
Boxes of 5 vials
<Iomeron 400 injection 50 mL>
Boxes of 5 vials
<Iomeron 400 injection 100 mL>
Boxes of 5 vials

23. REFERENCES

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24. REFERENCE REQUEST AND CONTACT INFORMATION

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