



Summary of Investigation Results

Iodinated contrast media

July 20, 2020

Non-proprietary name

See Attachment

Branded name (Marketing authorization holder)

See Attachment

Indications

See Attachment

Summary of revisions

e., f., h., j. to m., o. to r.

“Contrast-induced encephalopathy” should be added to the Clinically Significant Adverse Reactions section regarding indications of cerebral angiography, angio cardiography, angiocardiology, angiocardiology (including pulmonary artery angiography), aortography, thoracic aortography, or angiocardiology of pediatrics (including pulmonary artery angiography).

Investigation results and background of the revision

Cases of contrast-induced encephalopathy have been reported in patients treated with iodinated contrast media in Japan. MHLW/PMDA in consultation with expert advisors concluded that revision of the package insert was necessary.

Of note, the drugs were administered for the indication of cerebral angiography or angio cardiography in all the reported cases involving contrast-induced encephalopathy for which a causal relationship between the drug and event was reasonably possible. Since it was considered that contrast-induced encephalopathy occurs when the drug is administered for, besides cerebral angiography and angio cardiography, angiocardiology (including

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pulmonary artery angiography), aortography, thoracic aortography, or angiocardiology of pediatrics (including pulmonary artery angiography), all of which contrast the arteries on the central side from the cerebral arteries, MHLW/PMDA decided in consultation with expert advisors that the scope of the revision should include drugs with indications of cerebral angiography, angio cardiography, angiocardiology, angiocardiology (including pulmonary artery angiography), aortography, thoracic aortography, or angiocardiology of pediatrics (including pulmonary artery angiography).

Number of cases and patient mortalities reported in Japan during the previous 3 fiscal years

Cases involving contrast-induced encephalopathy

a.-b. Sodium amidotrizoate and meglumin amidotrizoate

No cases have been reported to date.

c.-d. Iotrolan

No cases have been reported to date.

e.-f. Iopamidol

A total of 11 cases have been reported to date (including 5 cases for which a causal relationship between the drug and event was reasonably possible).

No patient mortalities have been reported to date.

g. Meglumine iotroxate

No cases have been reported to date.

h.- j. Iohexol

No cases have been reported to date.

k. Iodixanol

No cases have been reported to date.

l.-m. Ioversol

No cases have been reported to date.

n. Ethyl ester of iodinated poppy-seed oil fatty acid

No cases have been reported to date.

o.-p. Iopromide

No cases have been reported to date.

q.-r. Iomeprol

No cases have been reported to date.



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The expert advisors present at the Expert Discussion regarding the current investigation were nominated based on their conflict of interest declarations concerning the relevant products, pursuant to the “Rules for Convening Expert Discussions, etc., by the Pharmaceuticals and Medical Devices Agency” (PMDA Administrative Rule No. 20-8, dated December 25, 2008).

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Attachment

	Non-proprietary name	Brand name	Marketing authorization holder	Indications
a	Sodium amidotrizoate and Meglumine	Urografin Inj. 60%	Bayer Yakuhin, Ltd	Retrograde urography, endoscopic retrograde cholangiopancreatography, percutaneous transhepatic cholangiography, arthrography
		Urografin Inj. 76%		Sialography
b	amidotrizoate	Gastrografin Oral·Enema		Contrastography of the gastrointestinal tract Contrastography of gastrointestinal tract in the following conditions Suspected stenosis Acute haemorrhage Risk of perforation (gastrointestinal ulcer, diverticulum) Any other acute symptoms that require surgery Post operation of gastric and intestinal resection (risk of perforation, risk of anastomotic leakage) Contrastography of foreign bodies and ulcer before endoscopy Gastrointestinal fistulography Contrastography of upper GI in computer-assisted tomography

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c	lotrolan	Isovist Inj. 240		Myelography, ventriculography, cisternography, myelography in computer-assisted tomography Arthrography
d		Isovist Inj. 300		Hysterosalpingography Arthrography
e	lopamidol	lopamiron Inj. 150, and the others	Bayer Yakuhin, Ltd, and the others	Arteriography by digital X-ray method, computer-assisted tomography, intravenous urography, retrograde urography
		lopamiron Inj. 300, and the others		Cerebral angiography, aortography, selective angiography, extremities angiography, venography by digital X-ray method, arteriography by digital X-ray method, computer-assisted tomography, intravenous urography, retrograde urography
		lopamiron Inj. 370, and the others		Angiocardiography (including pulmonary arteriography), aortography, selective angiography, extremities angiography, venography by digital X-ray method, arteriography by digital X-ray method, computer-assisted tomography, intravenous urography
f		lopamiron Inj. Syringe 300, and the		Cerebral angiography, aortography, selective angiography, extremities angiography, venography by digital X-ray method, arteriography by digital X-

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		others		ray method, computer-assisted tomography, intravenous urography, retrograde urography
		Iopamiron Inj. Syringe 370, and the others		Angiocardiology (including pulmonary arteriography), aortography, selective angiography, extremities angiography, venography by digital X-ray method, arteriography by digital X-ray method, computer-assisted tomography, intravenous urography
g	Meglumine iotroxate	Biliscopin DIC 50	Bayer Yakuin, Ltd	Cholecystography/cholangiography
h	Iohexol (for urinary tract, blood vessel)	Omnipaque 140 Injection 50 mL, 220 mL, and the others	GE Healthcare Pharma Ltd, and the others	Arteriography by digital X-ray method, computer-assisted tomography
		Omnipaque 240 Injection 20 mL, 50 mL, 100 mL, and the others		Extremities angiography, computer-assisted tomography, intravenous urography

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		Omnipaque 300 Injection 20 mL, 50 mL, 100 mL, 150 mL, and the others		Cerebral angiography, selective angiography, extremities angiography, arteriography by digital X-ray method, venography by digital X-ray method, computer-assisted tomography, intravenous urography
		Omnipaque 350 Injection 20 mL, 50 mL, 100 mL, and the others		Angiocardiography (including pulmonary arteriography), aortography, selective angiography, extremities angiography, venography by digital X-ray method, computer-assisted tomography, intravenous urography, angiocardiology of pediatrics (including pulmonary arteriography)
i	Iohexol (for cistern, spinal cord)	Omnipaque 180 Injection 10 mL, and the others		Cisternography by computer-assisted tomography, myelography by computer-assisted tomography, lumbar myelography
		Omnipaque 240 Injection		Cisternography by computer-assisted tomography, myelography by computer-assisted tomography Cervical myelography, thoracic myelography, lumbar myelography

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		10 mL, and the others		
		Omnipaque 300 Injection 10 mL, and the others		Myelography by computer-assisted tomography Cervical myelography
j	Iohexol (for urinary tract, blood vessel, CT)	Omnipaque 240 Injection Syringe 100 mL, and the others		Extremities angiography, computer-assisted tomography, intravenous urography

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		Omnipaque 300 Injection Syringe 50 mL, 80 mL, 100 mL, 110 mL, 125 mL, 150 mL, and the others		Cerebral angiography, selective angiography, extremities angiography, arteriography by digital X-ray method, venography by digital X-ray method, computer-assisted tomography, intravenous urography
		Omnipaque 350 Injection Syringe 45 mL, 70 mL, 100 mL, and the others		Angiocardiography (including pulmonary arteriography), aortography, selective angiography, extremities angiography, venography by digital X-ray method, computer-assisted tomography, intravenous urography, angiocardiology of pediatrics (including pulmonary arteriography)
k	Iodixanol		GE Healthcare Pharma Ltd	Cerebral angiography, extremities angiography,

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		Visipaque 270 Injection 20 mL, 50 mL, 100 mL		retrograde urography, endoscopic retrograde cholangiopancreatography
		Visipaque 320 Injection 50 mL, 100 mL		Extremities angiography
I	loversol	Optiray 240 Injection Syringe 100 mL	Guerbet Japan K.K.	Computer-assisted tomography
		Optiray 320 Injection Syringe 75 mL, 100 mL		Cerebral angiography, aortography, selective angiography, extremities angiography, arteriography by digital X-ray method, venography by digital X- ray method, computer-assisted tomography, intravenous urography
		Optiray 350 Injection		Angiocardiology, aortography, selective angiography, abdominal computer-assisted tomography

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		Syringe 100 mL		
		Optiray 350 Injection Syringe 135 mL		Abdominal computer-assisted tomography
m		Optiray 320 Injection 20 mL, 50 mL, 100 mL		Cerebral angiography, aortography, selective angiography, extremities angiography, arteriography by digital X-ray method, venography by digital X-ray method, computer-assisted tomography, intravenous urography
		Optiray 350 Injection 20 mL, 50 mL, 100 mL		Angiocardiography, aortography, selective angiography, abdominal computer-assisted tomography
n	Ethyl ester of iodinated poppy seed oil fatty acid	Lipiodol 480 Inj. 10 mL		Lymphangiography, hysterosalpingography, preparation of drugs or medical devices

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o	Iopromide	Proscope 300 Syringe 50 mL, 80 mL, 100 mL, and the others	Alfresa Pharma Corporation, and the others	Cerebral angiography, thoracic angiography, abdominal angiography, extremities angiography, venography by digital X-ray method, arteriography by digital X-ray method, computer-assisted tomography, intravenous urography
		Proscope 370 Syringe 50 mL, 80 mL, 100 mL, and the others		Angiocardiography, thoracic angiography, abdominal angiography, extremities angiography, venography by digital X-ray method, arteriography by digital X-ray method, computer-assisted tomography, intravenous urography
p		Proscope 300 Injection 20 mL, 50 mL, 100 mL, and the others		Cerebral angiography, thoracic angiography, abdominal angiography, extremities angiography, venography by digital X-ray method, arteriography by digital X-ray method, computer-assisted tomography, intravenous urography

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		Proscope 370 Injection 20 mL, 50 mL, 100 mL, and the others		Angiocardiography, thoracic angiography, abdominal angiography, extremities angiography, venography by digital X-ray method, arteriography by digital X-ray method, computer-assisted tomography, intravenous urography
q	lomeprol	lomeron 300 Injection 20 mL, 50 mL, 100 mL	Bracco-Eisai Co.,Ltd.	Cerebral angiography, thoracic angiography, abdominal angiography, extremities angiography, venography by digital X-ray method, arteriography by digital X-ray method, computer-assisted tomography, and intravenous urography
		lomeron 350 Injection 20 mL, 50 mL, 100 mL		Angio cardiography, thoracic angiography, abdominal angiography, extremities angiography, venography by digital X-ray method, arteriography by digital X-ray method, computer-assisted tomography, intravenous urography
		lomeron 400 Injection 50 mL, 100 mL		Angio cardiography, thoracic angiography, abdominal angiography, intravenous urography

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r	lomeron 300 Injection Syringe 50 mL, 75 mL, 100 mL	Computer-assisted tomography, intravenous urography, cerebral angiography, thoracic angiography, abdominal angiography, extremities angiography, venography by digital X-ray method, arteriography by digital X-ray method
	lomeron 350 Injection Syringe 50 mL, 75 mL, 100 mL, 135 mL	Computer-assisted tomography, intravenous urography, angio cardiography, thoracic angiography, abdominal angiography, extremities angiography, venography by digital X-ray method, arteriography by digital X-ray method

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