**GE HEALTHCARE**

**VISIPAQUE™**

## 1 NAME OF THE MEDICINAL PRODUCT

**VISIPAQUE 270 mg I/ml, 320 mg I/ml**

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

| Active ingredient | Strength | Content pr. ml. |
|---|---|---|
| Iodixanol (INN)<br>Iodixanol (INN) | 270 mg I/ml<br>320 mg I/ml | 550 mg equiv. 270 mg I<br>652 mg equiv. 320 mg I |

Iodixanol is a non-ionic, dimeric, hexaiodinated, water-soluble X-ray contrast medium.
Pure aqueous solutions of iodixanol in all clinical relevant concentrations have a lower osmolality than whole blood and the corresponding strengths of the non-ionic monomeric contrast media. VISIPAQUE is made isotonic with normal body fluids by addition of electrolytes. The osmolality and viscosity values of VISIPAQUE are as follows:

| Concentration | Osmolality * mOsm/kg $H_2O$ | Viscosity (mPa•s) | |
|---|---|---|---|
| | 37°C | 20°C | 37°C |
| 270 mg I/ml<br>320 mg I/ml | 290<br>290 | 11.3<br>25.4 | 5.8<br>11.4 |

* Method: Vapour - pressure osmometry.

For a full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Solution for injection.
VISIPAQUE is supplied ready to use as clear, colourless to pale yellow aqueous solutions.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

X-ray contrast medium for use in adults for cardioangiography, peripheral arteriography (conventional and i.a.DSA), abdominal angiography (i.a.DSA), urography, venography and CT-enhancement. Pediatric use: cardioangiography, urography and CT-enhancement. Myelography - Lumbar, thoracic and cervical myelography.

## 4.2 Posology and method of administration

The dosage may vary depending on the type of examination, the age, weight, cardiac output and general condition of the patient and the technique used. Usually approximately the same iodine concentration and volume is used as with other iodinated X-ray contrast media in current use, but adequate diagnostic information has also been obtained in some studies with iodixanol injection with somewhat lower iodine concentration. Adequate hydration should be assured before and after administration as for other contrast media. The product is for intravenous, intra-arterial and intrathecal use.

The following dosages may serve as a guide. The doses given for intra-arterial use are for single injections that may be repeated.

| Indication/Investigation | Concentration | Volume |
|---|---|---|
| **Intra-arterial use**<br>**Arteriographies** | | |
| Adults | | |
| aortography | 270/320 mg I/ml | 40-60 ml per inj. |
| peripheral | 270/320 mg I/ml | 30-60 ml per inj. |
| peripheral i.a.DSA | 150 mg I/ml | 30-60 ml per inj. |
| selective visceral i.a.DSA | 270 mg I/ml | 10-40 ml per inj. |
| **Cardioangiography** | | |
| Adults | | |
| Left ventricle and aortic root inj., | 320 mg I/ml | 30-60 ml per inj. |
| Selective coronary arteriography | 320 mg I/ml | 4-8 ml per inj. |
| Children | 270/320 mg I/ml | Depending on age, weight and pathology (recommended max total dose 10 ml/kg). |
| **Intravenous use**<br>**Urography** | | |
| Adults | 270/320 mg I/ml | 40-80 ml[(2)] |
| Children < 7 kg | 270/320 mg I/ml | 2-4 ml/kg |
| Children > 7 kg | 270/320 mg I/ml | 2-3 ml/kg<br>All doses depending on age, weight and pathology (max. 50 ml). |
| **Venography** | | |
| Adults | 270 mg I/ml | 50-150 ml/leg |
| **CT-enhancement** | | |
| Adults | | |
| CT of the head | 270/320 mg I/ml | 50-150 ml |

| | | |
|---|---|---|
| CT of the body | 270/320 mg I/ml | 75-150 ml |
| Children, CT of the head and body | 270/320 mg I/ml | 2-3 ml/kg up to 50 ml (in a few cases up to 150 ml may be given) |
| **Intrathecal use (adults only)** | | |
| **Lumbar and thoracic myelography** (lumbar injection) | 270 mg I/ml or 320 mg I/ml | 10-12 ml(3) 10 ml(3) |
| **Cervical myelography** (cervical or lumbar injection) | 270 mg I/ml or 320 mg I/ml | 10-12 ml(3) 10 ml(3) |

(2) In high-dose urography higher doses can be used.
(3) To minimize possible adverse reactions a total dose of 3.2 g iodine should not be exceeded.

**Elderly:** As for other adults.

## 4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1. Manifest thyrotoxicosis.

## 4.4 Special warnings and precautions for use.

Special precautions for use of non-ionic contrast media in general:

Hypersensitivity:
A positive history of **allergy**, **asthma**, or untoward **reactions** to iodinated contrast media indicates a need for special caution. Premedication with corticosteroids or histamine $H_1$ and $H_2$ antagonists might be considered in these cases.

The risk of serious reactions in connection with use of VISIPAQUE is regarded as remote. However, iodinated contrast media may provoke, **anaphylactoid** reactions or other manifestations of **hypersensitivity**. A course of action should therefore be planned in advance, with necessary drugs and equipment available for immediate treatment, should a serious reaction occur. It is advisable always to use an indwelling cannula or catheter for quick intravenous access throughout the entire X-ray procedure.

The possibility of hypersensitivity including serious, life-threatening, fatal anaphylactic/ anaphylactoid reactions should always be considered. The majority of serious undesirable occur within the first 30 minutes. Late onset (that is 1 hour or more after application) hypersensitivity reactions can occur.

Patients should be observed for at least 30 minutes after administration of VISIPAQUE.
Patients using beta blockers may present with atypical symptoms of hypersensitivity which

may be misinterpreted as a vagal reaction.

Coagulopathy:

Non-ionic, iodinated contrast media inhibit blood coagulation in vitro less than ionic contrast media. Clotting has been reported when blood remains in contact with syringes containing contrast media including non-ionic media. The use of plastic syringes in place of glass syringes has been reported to decrease but not eliminate the likelihood of in vitro clotting

Serious, rarely fatal, thromboembolic events causing myocardial infarction and stroke have been reported during angio-cardiographic procedures with both ionic and non-ionic contrast media. Numerous factors, including length of procedure, catheter and syringe material, underlying disease state, and concomitant medications, may contribute to the development of thromboembolic events. For these reasons, meticulous angiographic techniques are recommended, including close attention to guide wire and catheter manipulation, use of manifold systems and/or three-way stopcocks, frequent catheter flushing with heparinized saline solutions, and minimizing the length of the procedure so as to minimize the risk of procedure-related thrombosis and embolism.

Advanced life support facilities should be readily available.

Care should be taken in patients with homocystinuria. (Risk for thromboembolism).

Hydration

Adequate **hydration** should be assured before and after contrast media administration. This applies especially to patients with multiple myeloma, diabetes mellitus, renal dysfunction, as well as to infants, small children and elderly patients. Young **infants** (age < 1 year) and especially **neonates** are susceptible to electrolyte disturbance and haemodynamic alterations.

Cardio-circulatory reactions

Care should also be taken in patients with **serious cardiac disease** and **pulmonary hypertension** as they may develop haemodynamic changes or arrhythmias. Rarely severe life-threatening reactions and fatalities of cardiovascular origin such as cardiac-, cardio-respiratory arrest and myocardial infarction have occurred.

CNS disturbances

Patients with **acute cerebral pathology**, tumours or a history of **epilepsy** are predisposed for seizures and merit particular care. Also **alcoholics** and **drug addicts** have an increased risk for seizures and neurological reactions.

In regard to intravascular application care should be taken in patients with acute stroke or acute intracranial bleeding, in patients with altered blood brain barrier, cerebral edema or acute demyelinisation.

Renal reactions

Major risk factor for contrast medium-induced nephropathy is underlying renal dysfunction. Diabetes mellitus and the volume of iodinated contrast medium administered are contributing factors in the presence of renal dysfunction. Additional concerns are dehydration, advanced arteriosclerosis, poor renal perfusion and the presence of other factors that may be nephrotoxic, such as certain medications or major surgery.

To prevent acute renal failure following contrast media administration, special care should be exercised in patients with pre-existing **renal impairment** and **diabetes mellitus** as they are at risk. Patients with **paraproteinemias** (myelomatosis and Waldenström's macroglobulinemia) are also at risk.

Preventive measures include:
- Identification of high risk patients
- Ensuring adequate hydration. If necessary by maintaining an i.v. infusion from before the procedure until the contrast medium has been cleared by the kidneys.
- Avoiding additional strain on the kidneys in the form of nephrotoxic drugs, oral cholecystographic agents, arterial clamping, renal arterial angioplasty, or major surgery, until the contrast medium has been cleared.
- Dose reducing to a minimum.
- Postponing a repeat contrast medium examination until renal function returns to pre-examination levels.

Iodinated contrast agents can be used by patients on haemodialysis as the agents are removed by the dialysis process.

Diabetic patients receiving metformin:
There is a risk of the development of lactic acidosis when iodinated contrast agents are administered to diabetic patients treated with metformin, particularly in those with impaired renal function. To prevent lactic acidosis, the serum creatinine level should be measured in diabetic patients treated with **metformin** prior to intravascular administration of iodinated contrast media. Normal serum creatinine (<130µmol/litre)/normal renal function: Administration of metformin should be stopped at the time of administration of contrast medium and not resumed for 48 hours unless renal function/serum creatinine remains in the normal range. Abnormal serum creatinine (>130µmol/litre)/impaired renal function: Metformin should be stopped and the contrast medium examination delayed for 48 hours. Metformin should only be restarted if renal function is not diminished (if serum creatinine is not increased) compared to pre-contrast values.

Emergency cases: In emergency cases where renal function is impaired or unknown, the physician should evaluate the risk / benefit of the contrast medium examination, and the following precautions should be implemented: Metformin should be stopped. The patient should be fully hydrated prior to contrast medium administration and for 24 hours afterwards. Renal function (e.g. serum creatinine), serum lactic acid and blood pH should be monitored. A pH<

7.25 or a lactic acid level of >5 mmol/litre are indicative of lactic acidosis. The patient should be observed for symptoms of lactic acidosis. These include vomiting, somnolence, nausea, epigastric pain, anorexia, hyperpnoea, lethargy, diarrhoea and thirst.

Impaired renal and hepatic function

Particular care is required in patients with severe disturbance of both renal and hepatic function as they may have significantly delayed contrast medium clearance. Patients on **haemodialysis** may receive contrast media for radiological procedures. Correlation of the time of contrast media injection with the haemodialysis session is unnecessary

Myasthenia gravis

The administration of iodinated contrast media may aggravate the symptoms of **myasthenia gravis**.

Phaeochromocytoma

In patients with **phaeochromocytoma** undergoing interventional procedures, alpha blockers should be given as prophylaxis to avoid a hypertensive crisis.

Disturbances in thyroid function

Patients at risk of thyrotoxicosis should be carefully evaluated before any use of iodinated contrast medium.
Special care should be exercised in patients with **hyperthyroidism**.
Patients with multinodular **goitre** may be at risk of developing hyperthyroidism following injection of iodinated contrast media.

Paediatric population

One should also be aware of the possibility of inducing transient hypothyroidism in premature infants receiving contrast media.

Thyroid function should be checked in neonates during the first week of life, following administration of iodinated contrast agents to the mother during pregnancy.
Repeat testing of thyroid function is recommended at 2 to 6 weeks of age, particularly in low birth weight newborn or premature newborn.
See also section 4.6.

Extravasation

It is likely that VISIPAQUE due to its isotonicity gives rise to less local pain and extravascular oedema than hyperosmolar contrast media. In case of extravasation, elevating and cooling the affected site is recommended as routine measures. Surgical decompression may be necessary in cases of compartment syndrome.

Observation-time:
After contrast medium administration the patient should be observed for at least 30 minutes, since the majority of serious side effects occur within this time. However, experience shows that hypersensitivity reactions may appear up to several hours or days post injection. The patient should remain in the hospital environment (but not necessarily the radiology department) for one hour after the last injection, and should return to the radiology department if any symptoms develop.

Intrathecal use:
Following **myelography** the patient should rest with the head and thorax elevated by 20° for one hour. Thereafter he/she may ambulate carefully but bending down must be avoided. The head and thorax should be kept elevated for the first 6 hours if remaining in bed. Patients suspected of having a low seizure threshold should be observed during this period. Outpatients should not be completely alone for the first 24 hours.

## 4.5 Interaction with other medicinal products and other forms of interaction

All iodinated contrast media may interfere with tests on thyroid function, *thus* the iodine binding capacity of the thyroid may be reduced for up to *several* weeks.

High concentrations of contrast media in serum and urine *can* interfere with **laboratory tests** *for* bilirubin, proteins or inorganic substances (e.g. iron, copper, calcium and phosphate). These substances should therefore not be assayed on the day of examination.

Use of iodinated contrast media may result in a transient impairment of renal function and this may precipitate lactic acidosis in diabetics who are taking **metformin** (see section 4.4).

Patients treated with **interleukin-2** less than two weeks prior to an iodinated contrast medium injection have an increased risk for delayed reactions (flu-like symptoms or skin reactions).

There is some evidence that use of beta blockers is a risk factor for anaphylactoid reactions to X-ray contrast media (severe hypotension has been seen with X-ray contrast media on beta blocker therapy).

## 4.6 Fertility, Pregnancy and lactation

Pregnancy:
The safety of VISIPAQUE for use in human pregnancy has not been established. An evaluation of experimental animal studies does not indicate direct or indirect harmful effects with respect to reproduction, development of the embryo or fetus, the course of gestation and peri- and postnatal development.

Since, wherever possible, radiation exposure should be avoided during pregnancy, the benefits of any X-ray examination, with or without contrast media, should be carefully weighed against the possible risk. The product should not be used in pregnancy unless benefit outweighs risk and it is considered essential by the physician.

Thyroid function should be checked in neonates during the first week of life, following administration of iodinated contrast agents to the mother during pregnancy.

Repeat testing of thyroid function is recommended at 2 to 6 weeks of age, particularly in low birth weight newborn or premature newborn.

Breast-feeding:
Contrast media are poorly excreted in human breast milk
and minimal amounts are absorbed by the intestine. Breast feeding may be continued normally when iodinated contrast media are
given to the mother.

## 4.7 Effects on ability to drive and use machines

No studies on the ability to drive or use machines have been performed. However, it is not advisable to drive a car or use machines for one hour after the last injection or during the first 24 hours following **intrathecal examination** (see section 4.4).

## 4.8 Undesirable effects

Below are listed possible side effects in relation with radiographic procedures which include the use of VISIPAQUE.

Undesirable effects associated with Visipaque are usually mild to moderate and transient in nature. Serious reactions as well as fatalities are only seen on very rare occasions, these may include acute-on-chronic renal failure, acute renal failure, anaphylactic or anaphylactoid shock, hypersensitivity reaction followed by cardiac reactions (Kounis' syndrome), cardiac or cardio-respiratory arrest and myocardial infarction. Cardiac reaction may be promoted by the underlying disease or the procedure.

**Hypersensitivity reactions** may present as respiratory or cutaneous symptoms like dyspnoea, rash, erythema, urticaria, pruritus, skin reactions angioneurotic oedema, hypotension, fever, laryngeal oedema, bronchospasm or pulmonary oedema.

In patients with autoimmune diseases cases of vasculitis and SJS-like syndrome were observed.

They may appear either immediately after the injection or up to a few days later.
Hypersensitivity reactions may occur irrespectively of the dose and mode of administration and mild symptoms may represent the first signs of a serious anaphylactoid reaction/shock.

Administration of the contrast medium must be discontinued immediately and, if necessary, specific therapy instituted via the vascular access. Patients using **beta blockers** may present with atypical symptoms of hypersensitivity which may be misinterpreted as a vagal reaction.
A minor transient increase in serum creatinine is common after iodinated contrast media, but is usually of no clinical relevance.

The frequencies of undesirable effects are defined as follows*:*
Very common (≥1/10), common ((≥1/100 to < 1/10), uncommon(((≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000) and not known (cannot be estimated from the available data).

The listed frequencies are based on internal clinical documentation and published studies, comprising more than 48,000 patients.

**Intravascular administration:**

Blood and lymphatic system disorders
Not known: Thrombocytopenia

Immune system disorders:
Uncommon: Hypersensitivity
Not known: Anaphylactoid reaction, anaphylactoid shock;

Psychiatric disorders:
Very rare: Agitation, anxiety
Not known: Confusional state

Nervous system disorders:
Uncommon: Headache
Rare: Dizziness
Very rare: Cerebrovascular accident, sensory abnormalities including taste disturbance, amnesia, paraesthesia, syncope.
Not known: Coma, motor dysfunction, disturbance in consciousness, convulsion, transient contrast induced encephalopathy (including hallucination), tremor.

Eye disorders:
Very rare: Transient cortical blindness, visual impairment

Cardiac disorders:
Rare: Arrhythmia (including bradycardia, tachycardia), myocardial infarction
Very rare: Cardiac arrest
Not known: Cardiac failure, Ventricular hypokinesia, myocardial ischaemia, cardiorespiratory arrest, conduction abnormalities, coronary artery thrombosis, angina pectoris, spasm of coronary arteries..

Vascular disorders:
Uncommon: Flushing
Rare: Hypotension
Very rare: Hypertension, ischaemia
Not known: Arterial spasm, thrombosis, thrombophlebitis, shock.

Respiratory, thoracic and mediastinal disorders:
Rare: Cough
Very rare: Dyspnoea
Not known: Pulmonary oedema, respiratory arrest, respiratory failure.

Gastrointestinal disorders:
Uncommon: Nausea, vomiting
Very rare: Abdominal pain/discomfort
Not known: Acute pancreatitis, pancreatitis aggravated, salivary gland enlargement

Skin and subcutaneous system disorders
Uncommon: Rash, pruritus, urticaria
Very rare: angioedema, erythema
Not known: Bullous dermatitis, Stevens-Johnson syndrome, erythema multiforme, toxic epidermal necrolysis, acute generalised exanthematous pustulosis, drug rash with eosinophilia and systemic symptoms, drug eruption, dermatitis allergic, skin exfoliation

Musculoskeletal and connective tissue disorders:
Very rare: Back pain, muscle spasm
Not known: Arthralgia

Renal and urinary disorders:
Very rare: Impairment of renal function including acute renal failure

General disorders and administration site conditions:
Uncommon: Feeling hot, chest pain.
Rare: Pain, discomfort, shivering (chills), pyrexia, administration site reactions including extravasation
Very rare: Feeling cold, asthenic conditions (e.g. malaise, fatigue)

Injury, poisoning and procedural complications:
Not known: Iodism

**Intrathecal administration*:***

Undesirable effects following intrathecal use may be delayed and present some hours or even days after the procedure. The frequency is similar to lumbar puncture alone.
**Meningeal irritation** giving photophobia and meningism and frank chemical meningitis have been observed with other non-ionic contrast media. The possibility of an infective meningitis should also be considered.

Immune system disorders:
Not known: Hypersensitivity, including anaphylactic/ anaphylactoid reactions

Nervous system disorders:
Uncommon: Headache (may be severe and lasting)
Not known: Dizziness, transient contrast induced encephalopathy (including amnesia, hallucinations, confusion)

Gastrointestinal disorders:
Uncommon: Vomiting
Not known: Nausea

Musculoskeletal and connective tissue disorders:
Not known: Muscle spasm

General disorders and administration site conditions:
Not known: Shivering, pain at injection site

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.
Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form https://sideeffects.health.gov.il/
and emailed to the Registration Holder's Patient Safety Unit at: drugsafety@neopharmgroup.com

### 4.9 Overdose

Overdosage is unlikely in patients with a normal renal function. *The duration of the procedure is important for the renal tolerability of high doses of contrast media ($t_{½}$ ~ 2 hours).* In the event of accidental overdosing, the water and electrolyte losses must be compensated by infusion. Renal function should be monitored for at least the next 3 days. If needed, haemodialysis may be used to remove iodixanol from the patient's system. *There is no specific antidote, treatment of overdose is symptomatic.*

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: X-ray contrast medium, iodinated
ATC code: V08A B09

The organically bound iodine absorbs radiation in the blood vessels/tissues when it is injected.

For most of the haemodynamic, clinical-chemical and coagulation parameters examined following intravenous injection of iodixanol in healthy volunteers, no significant deviation from preinjection values has been found. The few changes observed in the laboratory parameters were minor and considered to be of no clinical importance.

VISIPAQUE induces only minor effects on renal function in patients. In 64 diabetic patients with serum creatinine levels of 115 – 308 µmol/L, VISIPAQUE use resulted in 3% of patients experiencing a rise in creatinine of ≥ 44.2 µmol/L and 0% of the patients with a rise of ≥ 88.4 µmol/L. The release of enzymes (alkaline phosphatase and N-acetyl-β-glucosaminidase) from the proximal tubular cells is less than after injections of non-ionic monomeric contrast media and the same trend is seen compared to ionic dimeric contrast media. VISIPAQUE is also well tolerated by the kidney.

## 5.2 Pharmacokinetic properties

Iodixanol is rapidly distributed in the body with a mean distribution half-life of approximately 21 minutes. The apparent volume of distribution is of the same magnitude as the extracellular fluid (0.26 l/kg b.w.), indicating that iodixanol is distributed in the extra-cellular volume only.

No metabolites have been detected. The protein binding is less than 2%.
The mean elimination half-life is approximately 2 hours in normal adults. In infants the elimination of iodixanol is prolonged (t½ approx. 4 hours in newborns). Iodixanol is excreted mainly through the kidneys by glomerular filtration. Approximately 80% of the administered dose is recovered unmetabolized in the urine within 4 hours and 97% within 24 hours after intravenous injection in healthy volunteers. Only about 1.2% of the injected dose is excreted in faeces within 72 hours. The maximum urinary concentration appears within approximately 1 hour after injection.

No dose dependent kinetics has been observed in the recommended dose range.

After intrathecal administration the half-life of iodixanol is prolonged reflecting the rate of elimination from the central nervous system compartment into systemic circulation. The apparent elimination half-life varies, but with a mean value around 12 hours.

## 5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, and toxicity to reproduction.

# 6 PHARMACEUTICAL PARTICULARS

## 6.1 List of excipients

The following excipients are included: Trometamol, sodium chloride, sodium calcium edetate calcium chloride dihydrate, , hydrochloric acid (pH adjustment) and water for injections.
The pH of the product is 6.8 - 7.6.

## 6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products. A separate syringe should be used.

## 6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.

## 6.4 Special precautions for storage

VISIPAQUE should be stored at or below 30°C, protected from light.

## 6.5 Nature and content of container

Glass vials and bottles:
The product is filled in injection vials (20 ml) and infusion bottles (50, 100 and 200 ml). Both containers are made of colourless highly resistant borosilicate glass (Ph.Eur. Type I), closed with halobutyl rubber stoppers (Ph.Eur. Type I), and sealed with complete tear off aluminium caps with coloured plastic “flip-off” tops (polypropylene lid).

Polypropylene bottles:
The product is filled in polypropylene bottles. The bottles of 50,100, 200 and 500 ml are closed with halobutyl rubber stoppers (Ph.Eur. Type I), supplied with a plastic (polypropylene) screw cap which is provided with a tamper proof ring.

The product is supplied as:

**Glass vials/bottles:**

| | |
|---|---|
| 270 mg I/ml: | 10 vials of 20 ml |
| | 10 bottles of 50 ml |
| | 10 bottles of 100 ml |
| | 6 bottles of 200 ml |
| 320 mg I/ml: | 10 vials of 20 ml |
| | 10 bottles of 50 ml |
| | 10 bottles of 100 ml |
| | 6 bottles of 200 ml |

**Polypropylene bottles:**

| | |
|---|---|
| 270 mg I/ml | 10 x 50 ml |
| | 10 x 100 ml |
| | 10 x 200 ml |
| | 6 x 500 ml |
| 320 mg I/ml | 10 x 50 ml |
| | 10 x 100 ml |
| | 10 x 200 ml |
| | 6 x 500 ml |

Not all pack sizes may be marketed.

### 6.6 Special precautions for disposal

Like all parenteral products, VISIPAQUE should be inspected visually for particulate matter, discolouration and the integrity of the container prior to use.

VISIPAQUE may be warmed to body temperature (37°C) before administration. Any unused product or waste material should be disposed of in accordance with local requirements.

Glass vials/bottles and polypropylene bottles up to 200 ml
The product should be drawn into the syringe immediately before use. For single use only, any unused portions must be discarded.

Polypropylene bottles of 500 ml

- The 500 ml contrast medium bottles should only be used in connection with auto injectors/pumps approved for this volume.
- A single piercing procedure should be used.
- Remove the plastic screw cap by tearing off the pull ring.
- After cleaning the stopper with a pad soaked in sporicidal solution followed by a pad soaked in alcohol, puncture the stopper with the needle.
- The line running from the auto injector/pump to the patient must be exchanged after each patient. Any unused portions of the contrast medium remaining in the bottle and all connecting tubes must be discarded after 24 hours.

Instructions from the manufacturer of the auto injector/pump must be followed.

## 7 MANUFACTURER

GE Healthcare AS
Nycoveien 1, P.O. Box 4220 Nydalen, NO-0401 OSLO
NORWAY

## 8 REGISTRATION HOLDER

ELDAN ELECTRONIC INSTRUMENT CO.LTD.
6 Hashiloach Street, P.O.Box 7641, Petach Tiqva 4917001
ISRAEL

## 9 REGI|STRATION NUMBER

VISIPAQUE 270: 100-28-28404
VISIPAQUE 320: 100-29-28405

Revised in July 2022 according to MOHs guidelines.