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GE Healthcare

OMNIPAQUE™

IOHEXOL

NAME OF THE MEDICINAL PRODUCT

OMNIPAQUE injection 140 mg I/ml, 180 mg I/ml, 200 mg I/ml, 240 mg I/ml, 300 mg I/ml, 350 mg I/ml

QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient	Strength	Content per. ml.
Iohexol (INN)	140 mg I/ml	302 mg equiv. 140 mg I
Iohexol (INN)	180 mg I/ml	388 mg equiv. 180 mg I
Iohexol (INN)	200 mg I/ml	431 mg equiv. 200 mg I
Iohexol (INN)	240 mg I/ml	518 mg equiv. 240 mg I
Iohexol (INN)	300 mg I/ml	647 mg equiv. 300 mg I
Iohexol (INN)	350 mg I/ml	755 mg equiv. 350 mg I

Iohexol is a non-ionic, monomeric, triiodinated, water-soluble X-ray contrast medium. Omnipaque in the concentration of 140 mg I/ml is isotonic with blood and tissue fluid.

The osmolality and viscosity values of Omnipaque are as follows:

Concentration	Osmolality ** Osm/kg H_2O	Viscosity (mPa·s)	
	37°C	20°C	37°C
140 mg I/ml	0.29	2.3	1.5
180 mg I/ml	0.36	3.2	2.0
200 mg I/ml	0.41	3.8	2.4
240 mg I/ml	0.51	5.6	3.3
300 mg I/ml	0.64	11.6	6.1
350 mg I/ml	0.78	23.3	10.6

** Method: Vapour - pressure osmometry.

PHARMACEUTICAL FORM

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

CLINICAL PARTICULARS

INDICATIONS

X-ray contrast medium for use in adults and children for cardioangiography, arteriography, urography, phlebography and CT-enhancement. Lumbar, thoracic, cervical myelography and computed tomography of the basal cisterns, following subarachnoid injection. Arthrography, endoscopic retrograde pancreatography, (ERP), endoscopic retrograde cholangiopancreatography (ERCP), herniography, hysterosalpingography, sialography and studies of the gastrointestinal tract.

POSOLOGY AND METHOD OF ADMINISTRATION

The dosage vary depending on the type of examination, age, weight, cardiac output and general condition of the patient and the technique used. Usually the same iodine concentration and volume is used as with other iodinated X-ray contrast media in current use.
Adequate hydration should be assured before and after administration as for other contrast media.
For intravenous, intra-arterial and intrathecal use, and use in body cavities.
The following dosages may serve as a guide.

Guidelines for Intravenous use

Indication	Concentration	Volume	Comments
Urography			
adults:	300 mg I/ml or 350 mg I/ml	40 - 80 ml 40 - 80 ml	80 ml may be exceeded in selected cases
children < 7 kg	240 mg I/ml or 300 mg I/ml	4 ml/kg 3 ml/kg	
children > 7 kg	240 mg I/ml or 300 mg I/ml	3 ml/kg 2 ml/kg (max 40 ml)	
Phlebography (leg)	200 mg I/ml or 240 mg I/ml or 300 mg I/ml	20 - 100 ml/leg	
Digital subtraction angiography	300 mg I/ml or 350 mg I/ml	20 - 60 ml/inj. 20 - 60 ml/inj.	
CT-enhancement adults:	140 mg I/ml or 200 mg I/ml or 240 mg I/ml or 300 mg I/ml or 350 mg I/ml	100 - 400 ml 100 - 300 ml 100 - 250 ml 100 - 200 ml 100 - 150 ml	Total amount of iodine usually 30 - 60 g
Children:	240 mg I/ml or 300 mg I/ml	2-3 ml/kgbw up to 40 ml 1-3 ml/kgbw up to 40 ml	In a few cases up to 100 ml may be given

Guidelines for Intra-arterial use

Indication	Concentration	Volume	Comments
Arteriographies			
arch aortography selective cerebral aortography femoral	300 mg I/ml 300 mg I/ml 350 mg I/ml 300 mg I/ml or 350 mg I/ml	30 - 40 ml/inj 5 - 10 ml/inj 40 - 60 ml/inj 30 - 50 ml/inj	Volume pr. injection depends on the site of injection
various	300 mg I/ml	depending on type of examination	
Cardioangiography			
adults: left ventricle and aortic root inj.	350 mg I/ml	30 - 60 ml/inj.	
selective coronary arteriography children:	350 mg I/ml 300 mg I/ml or 350 mg I/ml	4 - 8 ml/inj. depending on age, weight and pathology (max 8 ml/kg)	
Digital subtraction angiography	140 mg I/ml or 200 mg I/ml or 240 mg I/ml or 300 mg I/ml	1 - 15 ml/inj. 1 - 15 ml/inj. 1 - 15 ml/inj. 1 - 15 ml/inj.	depending on site of inj. occasionally large volumes - up to 30 ml - may be used

Guidelines for Intrathecal use

Indication	Concentration	Volume	Comments
Lumbar and thoracic myelography (lumbar injection)	180 mg I/ml or 200 mg I/ml or 240 mg I/ml	10 - 15 ml 10 - 15 ml 8 - 12 ml	
Cervical myelography (lumbar injection)	240 mg I/ml or 300 mg I/ml	10 - 12 ml 7 - 10 ml	
Cervical myelography (lateral cervical injection) CT cisternography (lumbar injection)	240 mg I/ml or 300 mg I/ml 180 mg I/ml or 200 mg I/ml or 240 mg I/ml	6 - 10 ml 6 - 8 ml 5 - 15 ml 5 - 15 ml 4 - 12 ml	
Paediatric myelography			
<2 years	180 mg I/ml	2 - 6 ml	
2-6 years	180 mg I/ml	4 - 8 ml	
>6 years	180 mg I/ml	6 - 12 ml	

To minimize possible adverse reactions a total dose of 3 g iodine should not be exceeded.

Guidelines for Body cavities

Indication	Concentration	Volume	Comments
Arthrography	200 mg I/ml or 240 mg I/ml or 300 mg I/ml or 350 mg I/ml	5 - 20 ml 5 - 20 ml 5 - 15 ml 5 - 10 ml	
ERP/ERCP	240 mg I/ml	20 - 50 ml	
Herniography	240 mg I/ml	50 ml	The dosage varies with the size of the hernia
Hysterosal-pingography	240 mg I/ml or 300 mg I/ml	15 - 50 ml 15 - 25 ml	
Sialography	240 mg I/ml or 300 mg I/ml	0.5 - 2 ml 0.5 - 2 ml	
Gastrointestinal studies			
Oral use			
Adults:	180 mg I/ml or 200 mg I/ml or 350 mg I/ml	individual individual individual	
Children: - esophagus	300 mg I/ml or 350 mg I/ml	2-4 ml/kgbw 2-4 ml/kgbw	Max. dose 50 ml Max. dose 50 ml
- ventricle/follow trough	140 mg I/ml	4-5 ml/kgbw	
Prematures:	350 mg I/ml	2-4 ml/kgbw	
Rectal use - children:	140 mg I/ml or dilute with tapwater to 100-150 mg I/ml	5-10 ml/kgbw 5-10 ml/kgbw	Example: Dilute Omnipaque 240, 300 or 350 with tap-water 1:1 or 1:2
CT- enhancement			
Oral use			
- adults:	Dilute with tapwater to ~6mgI/ml	800 -2000 ml of the diluted solution over a period of time	Example: Dilute Omnipaque 300 or 350 with tap-water 1:50
- children:	Dilute with tapwater to ~6mgI/ml	15-20 ml/kgbw of the diluted solution	
Rectal use - children:	Dilute with tapwater to ~6mgI/ml	individual	

CONTRA INDICATIONS

Manifest thyrotoxicosis. History of serious reaction to Omnipaque.

SPECIAL WARNINGS AND SPECIAL PRECAUTIONS FOR USE.

Special precautions for use of non-ionic monomeric contrast media in general:
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 Omnipaque is regarded as minor. 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.
Non-ionic contrast media have less effect on the coagulation system *in vitro*, compared to ionic contrast media. When performing vascular catheterization procedures one should pay meticulous attention to the angiographic technique and flush the catheter frequently (e.g.: with heparinized saline) so as to minimize the risk of *procedure-related* thrombosis and embolism.
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. Care should also be taken in patients with **serious cardiac disease** and **pulmonary hypertension** as they may develop haemodynamic changes or arrhythmias. 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. A few patients have experienced a temporary **hearing loss** or even deafness after myelography, which is believed to be due to a drop in spinal fluid pressure by the lumbar puncture per se.
To prevent acute renal failure following contrast media administration, special care should be exercised in patients with preexisting **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.
- Postponing a repeat contrast medium examination until renal function returns to pre-examination levels.

A potential risk of transient hepatic dysfunction exists. 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 provided dialysis is performed immediately afterwards.
The administration of iodinated contrast media may aggravate the symptoms of **myasthenia gravis**. In patients with **phaeochromocytoma** undergoing interventional procedures, alpha blockers should be given as prophylaxis to avoid a hypertensive crisis. Special care should be exercised in patients with **hyperthyroidism**. Patients with multinodular **goiter** may be at risk of developing hyperthyroidism following injection of iodinated contrast media. One should also be aware of the possibility of inducing transient hypothyroidism in premature infants receiving contrast media.
Extravasation of contrast media may on rare occasions give rise to local pain, and oedema, which usually recedes without sequela. However, inflammation and even tissue necrosis have been seen. 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 occurs within this time. However, delayed reactions may occur.
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.

INTERACTIONS WITH OTHER MEDICAMENTS AND OTHER FORMS OF INTERACTION

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 **biguanides** (metformine). As a precaution, biguanides should be stopped 48 hours prior to the contrast medium examination and reinstated only after renal function has stabilized.
Patients treated with **interleukin-2** less than two weeks previously have been associated with an increased risk for delayed reactions (flu-like symptoms or skin reactions).
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.

PREGNANCY AND LACTATION

The safety of Omnipaque 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 whenever possible, radiation exposure should be avoided during pregnancy, the benefits of an X-ray examination, with or without contrast media, should be carefully weighed against the possible risk. Omnipaque should not be used in pregnancy unless the benefit outweighs risk and it is considered essential by the physician.
Contrast media are poorly excreted in human breast milk and minimal amounts are absorbed by the intestine. Harm to the nursing infant is therefore unlikely.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

It is not advisable to drive a car or use machines during the first 24 hours following **intrathecal examination**.

UNDESIRABLE EFFECTS

General (applies to all uses of iodinated contrast media):
Below are listed possible general side effects in relation with radiographic procedures which include the use of non-ionic monomeric contrast media. For side effects specific to mode of administration, please refer to these specific sections.
Undesirable effects associated with the use of iodinated contrast media are usually mild to moderate and transient in nature, and less frequent with non-ionic than with ionic contrast media. Serious reactions as well as fatalities are only seen on very rare occasions.
The most frequent adverse event is a **mild, general sensation** such as a feeling of warmth or a transient metallic taste. Abdominal discomfort/pain is very rare (incidence <1:1000) and **gastrointestinal reactions** like nausea or vomiting are rare (incidence <1:100, but >1:1000).
Hypersensitivity reactions are rare and usually present as mild respiratory or cutaneous symptoms like dyspnoe, rash, erythema, urticaria, pruritus and angioedema. They may appear either immediately after the injection or up to a few days later. Severe manifestations such as laryngeal oedema, bronchospasm or pulmonary oedema are very rare. Severe and even toxic skin reactions have been reported.
Anaphylactoid reactions may occur irrespectively of the dose and mode of administration and mild symptoms of hypersensitivity may represent the first signs of a serious reaction. 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 anaphylaxis which may be misinterpreted as a vagal reaction.
Vagal reactions giving hypotension and bradycardia are seen on very rare occasions.
Headache of **fever** may occur. Episodes of **hypertension** may also occur. **Pyrexia** with rigors are seen on rare occasions.
Iodism or "iodide mumps" is a very rare complication of iodinated contrast media resulting in swelling and tenderness of the salivary glands for up to approximately 10 days after the examination.
Intravascular use (Intraarterial and Intravenous use):
Please first read the section labelled "General". Below, only undesireable events with frequency during intravascular use of non-ionic monomeric contrast media are described.
The nature of the undesirable effects specifically seen during intraarterial use depend on the site of injection and dose given. Selective arteriographies and other procedures in which the contrast medium reaches a particular organ in high concentrations may be accompanied by complications in that particular organ.
Distal **pain or heat sensation** in peripheral angiography is common (incidence >1:10).
A transient increase in S-creatinine is common after iodinated contrast media, but usually of no clinical relevance. Renal failure is very rare. However, renal failure may occur in high risk patients and among such patients fatalities have been reported.
Arterial spasm may follow injection into coronary, cerebral or renal arteries and result in transient ischaemia.
Neurological reactions are very rare. They may include seizures or transient motor or sensory disturbances. On very rare occasions the contrast medium may cross the blood-brain barrier resulting in uptake of contrast medium in the cerebral cortex being visible on CT-scanning until the day following examination, sometimes associated with transient confusion or cortical blindness.
Serious cardiac complications are very rare, including arrhythmias, depression or signs of ischaemia.
Post phlebographic thrombophlebitis or thrombosis is very rare. A very few cases of **arthralgia** has been reported.
Intrathecal use:
Please first read the section labelled "General". Below, only undesireable events with frequency during intrathecal use of non-ionic monomer contrast media are described.
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.
Headache, nausea, vomiting or dizziness are common and may largely be attributed to pressure loss in the subarachnoid space resulting from leakage at the puncture site. Some of these patients may experience a severe headache lasting for several days. Excessive removal of cerebrospinal fluid should be avoided in order to minimize pressure loss.
Mild local **pain, paraesthesia** and **radicular pain** occasionally (incidence <1:10, but >1:100) occur at the site of injection.
Cramping and pain in the lower limbs are seen on very rare occasions.
Meningeal irritation giving photophobia and meningism happens occasionally. Frank chemical meningitis appear on very rare occasions. The possibility of an infective meningitis should also be considered.
On very rare occasions, manifestations of **transient cerebral dysfunction** are seen. These include seizures, transient confusion or transient motor or sensory dysfunction. Changes in the EEG may be noted in a few of these patients.
Use in Body Cavities:
Please first read the section labelled "General". Below, only undesireable events with frequency during use of non-ionic monomeric contrast media in body cavities are described.
Systemic hypersensitivity reactions are rare.
Endoscopic Retrograde Choleangio Pancreatography (ERCP): Some elevation of amylase levels is common. Post ERCP renal opacification is seen on rare occasions and is associated with an increased risk of post ERCP **pancreatitis.** Rare cases of necrotizing pancreatitis have also been described.
Oral use: Gastrointestinal upset occasionally occur.
Hysterosalpingography (HSG): Transient **pain** in the lower abdomen is common.
Arthrography: Post procedural **pain** is common. Frank arthritis is rare. The possibility of infective arthritis should be considered in such cases.
Herniography: Mild postprocedural pain is common.

OVERDOSE
Preclinical data indicate a high safety margin for Omnipaque and no fixed upper dose level has been established for routine intravascular use. Symptomatic overdosing is unlikely in patients with normal renal function unless the patient has received an excess of 2000 mg I/kg body-weight over a limited period of time. The duration of the procedure is important for the renal tolerability of high doses of contrast media ($t_{1/2}$ ~ 2 hours). Accidental overdosing is most likely following complex angiographic procedures in children, particularly when multiple injections of contrast medium with high-concentration are given.
In cases of overdose, any resulting water- or electrolyte imbalance must be corrected. Renal function should be monitored for the next 3 days. If needed, haemodialysis may be used for clearance of excessive contrast medium. There is no specific antidote.

PHARMACOLOGICAL PROPERTIES
PHARMACODYNAMIC PROPERTIES
For most of the haemodynamic, clinical-chemical and coagulation parameters examined following intravenous injection of iohexol 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.

PHARMACOKINETIC PROPERTIES
Close to 100 per cent of the intravenously injected iohexol is excreted unchanged through the kidneys within 24 hours in patients with normal renal function. The maximum urinary concentration of iohexol appears within approximately 1 hour after injection. The elimination half-life is approximately 2 hours in patients with normal renal function.
No metabolites have been detected.
The protein binding of Omnipaque is so low (less than 2 %), that it has no clinical relevance and can therefore be neglected.

PRECLINICAL SAFETY DATA
Iohexol has a very low acute intravenous toxicity in mice and rats. Animal studies have shown that iohexol has a very low protein binding, and is well tolerated by the kidneys. The cardiovascular and neurotoxicity are low. The histamine release ability and the anticoagulant activity have been shown to be less than for ionic contrast media.

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

INCOMPATIBILITIES
Although no incompatibility has been found, Omnipaque should not be directly mixed with other drugs. A separate syringe should be used.

SHELF LIFE
See expiry date printed on the label.

STORAGE CONDITIONS
Omnipaque should be stored according to instructions on the label. The product in glass vials and bottles may be stored at 37 °C for up to 1 month prior to use.
The product in 40, 50, 75, 100, 150, 175, 200 and 500 ml polypropylene bottles may be stored at 37 °C for up to 1 month prior to use.
10, 15 and 20 ml polypropylene bottles may be stored at 37 °C for up to 1 week prior to use.

NATURE AND CONTENT OF CONTAINER
Glass vials and bottles:
The product is filled in injection vials (10, 15, 20 ml) and infusion bottles (40, 50, 75, 100, 200 and 500 ml). Both containers are made of colourless highly resistant borosilicate glass (Ph. Eur. Type I), closed with chlorobutyl rubber stoppers (Ph. Eur. Type I), and sealed with combined "flip off seal/tear off seal - flat plast disc".

Polypropylene bottles:
The product is filled in polypropylene bottles. The bottles of 10, 15, 20 and 40 ml are rigid stand-up bottles with a twist-off top. The bottles of 40, 50, 75, 100, 150, 175, 200 and 500 ml are closed with chlorobutyl rubber stoppers (Ph. Eur. Type I), and supplied with a plastic screw cap, which is provided with a tamper proof ring.

PRESENTATIONS

Glass vials/bottles	
140 mg I/ml	10 bottles of 50 ml 6 bottles of 200 ml
180 mg I/ml	10 vials of 10 ml 10 vials of 15 ml 10 bottles of 50 ml
240 mg I/ml	10 vials of 10 ml 6 vials of 20 ml 25 vials of 20 ml 10 bottles of 50 ml 6 bottles of 200 ml 6 bottles of 500 ml
300 mg I/ml	10 vials of 10 ml 10 vials of 20 ml 25 vials of 20 ml 10 bottles of 50 ml 10 bottles of 100 ml 6 bottles of 150 ml 6 bottles of 500 ml
350 mg I/ml	10 vials of 20 ml 25 vials of 20 ml 10 bottles of 50 ml 10 bottles of 100 ml 6 bottles of 150 ml 10 bottles of 200 ml 6 bottles of 500 ml
Polypropylene bottles	
140 mg I/ml	10 bottles of 50 ml 10 bottles of 100 ml 10 bottles of 200 ml
180 mg I/ml	10 bottles of 10 ml 10 bottles of 15 ml 10 bottles of 50 ml
240 mg I/ml	10 bottles of 10 ml 10 bottles of 20 ml 10 bottles of 50 ml 10 bottles of 100 ml 10 bottles of 200 ml 6 bottles of 500 ml
300 mg I/ml	10 bottles of 10 ml 10 bottles of 20 ml 10 bottles of 40 ml 10 bottles of 50 ml 10 bottles of 75 ml 10 bottles of 100 ml 10 bottles of 150 ml 10 bottles of 175 ml 10 bottles of 200 ml 6 bottles of 500 ml
350 mg I/ml	10 bottles of 20 ml 10 bottles of 40 ml 10 bottles of 50 ml 10 bottles of 75 ml 10 bottles of 100 ml 10 bottles of 150 ml 10 bottles of 175 ml 10 bottles of 200 ml 6 bottles of 500 ml

Please note:
In certain countries some of the indications may not be approved by the health authorities, and some of the concentrations and package sizes may not be available.

INSTRUCTIONS FOR USE/HANDLING
Like all parenteral products, Omnipaque should be inspected visually for particulate contamination, discolouration and the integrity of the container prior to use.
The product should be drawn into the syringe immediately before use. Vials are intended for single use only, any unused portions must be discarded.
Omnipaque may be warmed to body temperature (37°C) before administration.
Additional instruction for autoinjector/pump:
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.
The line running from this 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 at the end of the day. When convenient, smaller bottles can also be used. Instructions from the manufacter of the auto injector/pump must be followed.

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Warning
To be sold by retail on prescription of a Registered Medical Practitioner only.

Manufactured in China by:
GE Healthcare (Shanghai) Co., Ltd.
No. 1, Niudun Road
China (Shanghai) Pilot Free Trade Zone,
Shanghai-201203
China