SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Optiray 350 mg I/ml, solution for injection or infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml solution contains 741 mg ioversol equivalent to 350 mg iodine.

Osmolality: 780 mosmol/kg
Viscosity: 14.3 mPa · s (at 25°C)
Viscosity: 9 mPa · s (at 37°C)
Contains Iodine per ml: 350 mg

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Solution for injection or infusion. Clear, colourless to faint yellow solution.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

This medicinal product is for diagnostic use only.
Optiray 350 is a non-ionic X-ray contrast medium that is indicated in adults for angiography throughout the cardiovascular system including coronary, peripheral, visceral and renal angiography, aortography and left ventriculography. Optiray 350 is also indicated in adults for use in computed tomography of the head and body, intravenous urography, venography and intravenous and intraarterial digital subtraction angiography (IA-DSA and IV-DSA).

4.2. Posology and method of administration

Adults: Recommended dosage schedule

Procedure	Dosage	Maximum Total Dose
Peripheral angiography	10-90 ml	250 ml
Venography	50-100 ml	250 ml
Left ventriculography	30-50 ml	250 ml
Coronary arteriography	1-10 ml	250 ml
Visceral angiography	12-60 ml	250 ml
Aortography	10-80 ml	250 ml
Renal angiography	6-15 ml	250 ml
Urography	50-75 ml	150 ml
Head CT	50-150 ml	150 ml
Body CT	25-150 ml	150 ml
IA-DSA	5-80 ml	250 ml
IV-DSA	30-50 ml	250 ml

Elderly: Dosage as for adults. Where poor demonstration is to be expected, the dosage can be increased to the maximum.

Paediatric population
The safety and efficacy of Optiray 350 in children have not been established. The medicinal product should therefore not be used in children aged up to 18 years, until further data becomes available. For cerebral, peripheral and visceral angiography and for intravenous urography Optiray 300 may be used in children.

It is recommended that intravascularly administered iodinated contrast agents are warmed up to body temperature prior to injection. As with all radiopaque contrast agents, the lowest dose necessary to obtain adequate visualisation should be used.

Appropriate resuscitation equipment should be available.

4.3. Contraindications

Hypersensitivity to iodine-containing contrast media, the active substance, or to any of the excipients listed in section 6.1. Manifest hyperthyroidism.

4.4. Special warnings and precautions for use

General comments
Serious or fatal reactions have been associated with the administration of iodinated X-ray contrast media. It is of utmost importance to be completely prepared to treat any contrast medium reaction.

Diagnostic procedures should be performed under the direction of personnel skilled and experienced in the particular procedure to be performed. A fully equipped emergency cart, or equivalent supplies and equipment, and personnel competent in recognising and treating adverse reactions of all types should always be available. Since severe delayed reactions have been known to occur, the patient should be observed and emergency facilities and competent personnel should be available for at least 30 to 60 minutes after administration.

Hypersensitivity
The patient should also be informed that allergic reactions may develop up to several days post administration; in such case, a physician should be consulted immediately.
The occurrence of severe idiosyncratic reactions has prompted the use of several pre-testing methods. However, pre-testing cannot be relied upon to predict severe reactions and may itself be hazardous to the patient. It is suggested that a thorough medical history with emphasis on allergy and hypersensitivity, prior to the injection of any contrast medium, may be more accurate than pre-testing in predicting potential adverse reactions.
A positive history of allergies does not arbitrarily contraindicate the use of a contrast agent when a diagnostic procedure is thought essential, but caution should be exercised (see section 4.3).
Appropriate resuscitation measures should be immediately available.
Pre-medication with antihistamines and corticosteroids to avoid or minimise allergic reactions should be considered. Reports indicate that such pre-treatment does not prevent serious life-threatening reactions, but may reduce both their incidence and severity.

Intolerance to ioversol
Ioversol may cause anaphylaxis or other manifestations of pseudo-allergic intolerance reactions, e.g. nausea, vomiting, dyspnoea, erythema, urticaria and hypotension. A higher incidence of such reactions has been observed in patients with a history of previous intolerance reactions to other contrast media, or any history of asthma, allergy or hypersensitivity. In such patients, the benefit should clearly outweigh the risks (see section 4.3).

Severe cutaneous adverse reactions (SCAR)
SCAR may develop from 1 hour to several weeks after intravascular contrast agent administration. These reactions include Stevens-Johnson syndrome and toxic epidermal necrolysis (SJS/TEN), acute generalized exanthematous pustulosis (AGEP), and drug reaction with eosinophilia and systemic symptoms (DRESS). Reaction severity may increase and time to onset may decrease with repeat

administration of a contrast agent; prophylactic medications may not prevent or mitigate severe cutaneous adverse reactions. Avoid administering ioversol to patients with a history of a severe cutaneous adverse reaction to ioversol.

Coagulation disorders
The anticoagulant effect of non-ionic X-ray contrast media has been shown, in vitro, to be less than that of conventional ionic agents at comparable concentrations. Similar results were found in some in vivo studies. For this reason, meticulous angiographic techniques are recommended, e.g. frequent flushing of standard angiographic catheters and avoiding prolonged contact of blood with the contrast agent in syringes and catheters.

Thyroid disorders
Reports of thyroid storm following the intravascular use of iodinated radiopaque agents in patients with hyperthyroidism or with an autonomously functioning thyroid nodule suggest that the additional risk be evaluated in such patients before use of any contrast medium (see section 4.3).

Cardiovascular diseases
In angiographic procedures, the possibility of dislodging plaque or damaging or perforating the vessel wall should be considered during catheter manipulation and contrast medium injection. Test injections to ensure proper catheter placement are recommended.
Angiography should be avoided whenever possible in patients with homocystinuria due to an increased risk of thrombosis and embolism.
Patients with congestive heart failure should be observed for several hours following the procedure to detect delayed haemodynamic disturbances, which may be associated with a transitory increase in the circulating osmotic load.

Thromboembolic disorders
In patients with advanced atherosclerosis, serious hypertension, cardiac decompensation, senility, preceding cerebral thrombosis or embolism, special caution should be exercised. Cardiovascular reactions as bradycardia, rising or falling of blood pressure may occur more often.

Central nervous system disorders
Serious neurologic events have been observed following direct injection into cerebral arteries or vessels supplying the spinal cord or in angiocardiography, due to inadvertent filling of the carotids. A cause-effect relationship to the contrast medium has not been established, since the patient's pre-existing condition and procedural techniques are causative factors in themselves.

Encephalopathy has been reported with the use of ioversol (see section 4.8). Contrast-induced encephalopathy may manifest with symptoms and signs of neurological dysfunction such as headache, visual disturbance, cortical blindness, confusion, seizures, loss of coordination, hemiparesis, aphasia, unconsciousness, coma, and cerebral oedema. Symptoms usually occur within minutes to hours after administration of ioversol and generally resolve within days.
Factors which increase blood-brain barrier permeability facilitate the passage of the contrast medium into cerebral tissue, which can lead to central nervous system reactions, e.g. encephalopathy.
If contrast encephalopathy is suspected, appropriate medical management should be initiated, and administration of ioversol must not be repeated.

Renal insufficiency
Combinations with nephrotoxic medicines should be avoided. If this cannot be avoided, laboratory monitoring of renal function must be intensified. Caution must be exercised in patients with severely impaired renal function, combined renal and hepatic disease, diabetes mellitus, homozygous sickle cell disease, multiple myeloma or other paraproteinaemia, anuria, particularly when large doses are administered. Serious renal effects, including acute renal failure, may occur in these patients.
Although neither the contrast agent nor dehydration has been proved separately to be the cause of renal failure, it has been speculated that the combination of both may be causative. The risk in patients

with impaired renal function is not a contraindication to the procedure. However, special precautions, including maintenance of normal hydration and close monitoring, are required.
An effective hydration prior to the administration of ioversol is essential and may decrease the risk of renal injury. Preparatory dehydration is dangerous and may contribute to acute renal failure.

Phaeochromocytoma
Administration of ioversol to patients known or suspected of having phaeochromocytoma should be performed with caution. If, in the opinion of the physician, the possible benefits of such procedures outweigh the considered risks, the procedure may be performed; however, the amount of ioversol injected should be kept to an absolute minimum. Premedication with α- and ß-blockers is advisable when the contrast medium is administered intravascularly due to the risk of a hypertensive crisis. The blood pressure should be assessed throughout the procedure, and measures for treatment of a hypertensive crisis should be available.

Homozygous sickle cell diseaseIn patients with homozygous sickle cell disease, hyperosmolar agents such as ioversol may affect sickling of erythrocytes. Hence, there is a need for careful consideration before the intra-arterial administration of such agents to patients with homozygous sickle cell disease.

Extravasation
Ioversol should be injected with caution to avoid perivascular application. This is especially important in patients with severe arterial or venous disease. However, significant extravasation of ioversol may occur especially during the use of power injectors. Generally, it is tolerated without substantial tissue injury applying conservative treatment. However, serious tissue damage (e.g. ulceration) has been reported in isolated cases requiring surgical treatment.s

Anaesthetised patient
General anaesthesia may be indicated in the performance of some procedures in selected patients; however, a higher incidence of adverse reactions has been reported in these patients, and may be attributable to the inability of the patient to identify untoward symptoms or to the hypotensive effect of anaesthesia.

Venography
In patients with suspected phlebitis, serious ischemia, local infections or a complete occlusion of the venous system, special caution should be exercised.

Peripheral angiography
There should be pulsation in the artery, into which the X-ray contrast medium will be injected. In patients with thromboangiitis obliterans or ascending infections in combination with serious ischemia the angiography should be performed, if at all, with special caution.

Coronary arteriography and left ventriculography
In these procedures cardiac decompensation, serious arrhythmias, ischemia, and myocardial infarction may occur.

Paediatric population
Hypothyroidism or transient thyroid suppression may be observed after exposure to iodinated contrast media.

This adverse reaction should also be observed in newborns whose mothers have received an iodinated contrast medium during pregnancy (see section 4.6).

The incidence of hypothyroidism in patients younger than 3 years of age exposed to iodinated contrast media ranges between 1% and 15% depending on the age of the subjects and the dose of the iodinated contrast agent.

Younger age, very low birth weight, prematurity, and the presence of other conditions, such as, admission to neonatal or pediatric intensive care units, and cardiac conditions are associated with an increased risk.

Pediatric patients with cardiac conditions may be at the greatest risk given that they often require high doses of contrast during invasive cardiac procedures, such as catheterization, and computed tomography (CT).
Special attention should be paid to pediatric patients below 3 years of age because an incident underactive thyroid during early life may be harmful for motor, hearing, and cognitive development and may require transient thyroxin (T4) replacement therapy.

Thyroid function should be evaluated in all pediatric patients younger than 3 years of age within 3 weeks following exposure to iodinated contrast media, especially in premature infants and neonates. If hypothyroidism is detected, thyroid function should be monitored as appropriate even when replacement treatment is given.

Interference with laboratory tests

Ioversol may reduce the capacity of the uptake of iodine by the thyroid gland. For this reason, the results of PBI (protein-bound iodine) and radioactive iodine uptake studies, which depend on iodine estimation, will not accurately reflect thyroid function for up to 16 days following administration of iodinated X-ray contrast media. However, thyroid function tests not depending on iodine estimations, e.g. T3 resin uptake and total or free thyroxine (T4) assays are not affected.

4.5. Interactions with other medicinal products and other forms of interaction

The following interactions have been reported after the administration of other iodinated contrast media. They are generally accepted as being attributable to this class of contrast media.

No interaction studies have been performed.

Metformin
Acute renal failure has been associated with lactic acidosis in patients receiving metformin at the time of an X-ray examination involving parenteral administration of iodinated contrast media. Therefore, in diabetic patients taking metformin, the examination should be performed and intake of metformin stopped before the examination. The use of metformin should not be resumed for 48 hours, and should only be restarted if renal function/serum creatinine remains within the normal range or has returned to baseline.

Interleukin
The literature reports that patients who had been treated with Interleukin may develop a higher rate of adverse reactions as described in section 4.8. The reason has not yet been clarified. According to the literature an increased or delayed occurrence of these reactions within a period of 2 weeks was observed after administration of Interleukin.

Diuretics
In case of diuretic-induced dehydration, patients are at increased risk of acute renal failure when using iodinated contrast media. Close monitoring is required to ensure adequate hydration before administration of ioversol. The lowest necessary dose of ioversol consistent with a diagnostic result should be used.
Vasopressors
The arterial injection of an X-ray contrast medium should never be made following the administration of vasopressors, since they strongly potentiate neurologic effects.

Oral cholecystographic agents
Renal toxicity has been reported in single patients with liver dysfunction, who were given oral cholecystographic agents followed by intravascular contrast agents. Administration of any intravascular X-ray contrast agent should therefore be postponed in patients who have recently received a cholecystographic contrast agent.

4.6. Fertility, pregnancy and lactation

Pregnancy
Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development.
There are, however, no adequate and well controlled studies in pregnant women.
It is not known whether ioversol crosses the placental barrier or reaches foetal tissues. However, many injectable contrast agents cross the placental barrier in humans and appear to enter foetal tissue passively.
Because animal teratology studies are not always predictive of human response, caution should be exercised when prescribing to pregnant women. Since any X-ray investigation during pregnancy may involve a potential risk, the risk/benefit ratio should be carefully weighed. If a better and safer alternative is available, an X-ray investigation involving X-ray contrast media should be avoided.

Ioversol contains iodine which may induce foetal dysthyroidism if the examination takes place after more than 14 weeks of amenorrhoea.

Thyroid function of neonates should be closely monitored during the first week of life if iodinated contrast was administered to the mother during pregnancy. It is recommended that thyroid function be monitored again at 2 weeks of age.

Breast-feeding
It is not known whether Ioversol is excreted in human breast milk. However, many injectable contrast agents are excreted unchanged in breast milk to an amount of approximately 1 % of the given dose. Although it has not been established that adverse events occur to nursing infants, caution should be exercised when intravascular X-ray contrast media are administered to nursing women because of potential adverse events, and consideration should be given to discontinuing nursing for one day.

Fertility
Animal studies did not indicate direct or indirect harmful effects with respect to fertility in humans. There are, however, no adequate and well controlled clinical studies on fertility.

4.7. Effects on ability to drive and use machines

There is no known effect on the ability to drive and operate machines. However, because of the risk of early reactions driving or operating machinery is not advisable for 1 hour following the time of injection.

4.8. Undesirable effects

Frequencies for adverse drug reactions are defined as follows:
Very common (≥1/10)
Common (≥1/100 to <1/10)
Uncommon (≥1/1000 to <1/100)
Rare (≥1/10,000 to <1/1000)
Very rare (<1/10,000)
Not known (cannot be estimated from the available data)

a. Summary of the safety profile

Adverse reactions following the use of Optiray formulations are generally independent of the dose administered. Usually, they are mild to moderate, of short duration and resolve spontaneously (without treatment). However, even mild adverse reactions may be the first indication of a serious, generalized reaction that can occur rarely after iodinated contrast media. Such serious reactions may be life-threatening and fatal, and usually affect the cardiovascular system. Most adverse drug reactions to

Optiray formulations occur within minutes after administration, however contrast related hypersensitivity reactions may occur with a delay of some hours up to several days.

b. Tabulated summary of adverse reactions

From clinical studies, mild discomfort, including sensation of heat or cold, pain during the injection, and/or transient taste perversion, was noted in 10% to 50% of patients. In a large post-marketing study, other side effects occurred in a total of 1.1% of the patients; the most frequent were nausea (0.4%), skin reactions such as urticaria or erythema (0.3%), and vomiting (0.1%). All other events occurred in less than 0.1% of the patients.

The following adverse reactions have been collected after Optiray administration from clinical trials and post-market experience, including post-market surveys.

Infections and infestations	
Rare	rhinitis
Immune system disorders:	
Very rare	anaphylactoid (hypersensitivity) reaction
Not known	anaphylactic shock
Endocrine disorders:	
Not known	hypothyroidism*
Psychiatric disorders:	
Very rare	confusional state; agitation; anxiety
Nervous system disorders:	
Uncommon	dizziness; dysgeusia; headache; paraesthesia
Rare	syncope; tremor;
Very rare	Loss of consciousness; paralysis; speech disorders; somnolence; stupor; aphasia; dysphasia; hypoaesthesia
Not known	seizure; contrast-induced encephalopathy; amnesia; dyskinesia
Eye disorders:	
Rare	vision blurred; eye swelling; periorbital oedema
Very rare	conjunctivitis allergic (including eye irritation, ocular hyperaemia, lacrimation increased, conjunctival oedema)
Not known	blindness transient
Ear and labyrinth disorders:	
Rare	vertigo
Very rare	tinnitus
Cardiac disorders:	
Rare	tachycardia
Very rare	heart block; arrhythmia; angina pectoris; bradycardia; atrial fibrillation; electrocardiogram abnormal
Not known	cardiac arrest; ventricular fibrillation; arteriospasm coronary ; extrasystoles; palpitations
Vascular disorders:	
Uncommon	blood pressure increased
Rare	hypotension; flushing
Very rare	cerebrovascular disorder; phlebitis; hypertension; vasodilation
Not known	shock; thrombosis; vasospasm, cyanosis, pallor

Respiratory, thoracic and mediastinal disorders:

Uncommon	sneezing
Rare	Laryngeal oedema; laryngospasm, dyspnoea; laryngeal obstruction (incl. throat tightness, stridor); nasal congestion; cough; throat irritation
Very rare	pulmonary oedema; pharyngitis; hypoxia
Not known	respiratory arrest; asthma; bronchospasm; dysphonia

Gastrointestinal disorders:

Common	nausea
Uncommon	vomiting
Rare	dry mouth
Very rare	sialoadenitis; abdominal pain; tongue oedema; dysphagia; salivary hypersecretion
Not known	diarrhoea

Skin and subcutaneous tissue disorders:

Uncommon	Urticaria, erythema, pruritus
Rare	rash
Very rare	angioedema; hyperhidrosis (incl. cold sweat)
Not known	Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS syndrome); Acute Generalized Exanthematous Pustulosis (AGEP); Erythema Multiforme (EM), Stevens Johnson Syndrome (SJS) / Toxic Epidermal Necrolysis (TEN)

Musculoskeletal, connective tissue and bone disorders:

Very rare	muscle spasms

Renal and urinary disorders:

Rare	micturition urgency
Very rare	acute kidney injury; abnormal renal function; incontinence; haematuria; creatinine renal clearance decreased; blood urea increased
Not known	anuria; dysuria

Congenital, familial and genetic disorders:

Not known	congenital hypothyroidism

General disorders and administration site conditions:

Very common	feeling hot
Common	pain
Rare	face oedema; pharyngeal oedema, feeling cold, tremor, chills
Very rare	Chest pain; injection site reactions (incl. pain, erythema, and haemorrhage up to necrosis especially after extravasation); malaise; asthenia; fatigue; feeling abnormal; oedema; sluggishness
Not known	pyrexia

c. Description of selected adverse reactions

Adverse reactions may be classified as follows:

a. Hypersensitivity or anaphylactoid reactions are mostly mild to moderate with symptoms like rash, pruritus, urticaria and rhinitis.
   However, serious reactions may occur. Serious anaphylactic reactions generally affect the cardiovascular and respiratory system. These may be life-threatening and include anaphylactic shock, cardiac and respiratory arrest, laryngospasm, angioedema (such as laryngeal oedema), laryngeal obstruction (incl. throat tightness, stridor), or pulmonary oedema. Fatal cases were reported.
   Patients with a history of allergic reactions are at increased risk of developing a hypersensitivity reaction. Other type 1 (immediate) reactions include symptoms like nausea and vomiting, skin rashes, dyspnoea, eye swelling, periorbital oedema, conjunctivitis allergic, rhinitis, sneezing, nasal congestion, cough, throat irritation, paraesthesia or hypotension.
b. Vasovagal reactions e.g. dizziness or syncope which may be caused either by the contrast medium, or by the procedure.
c. Cardiologic side effects during cardiac catheterisation e.g. angina pectoris, ECG changes, cardiac arrhythmias, conductivity disorders, as well as coronary spasm and thrombosis. Such reactions are very rare and may be caused by the contrast medium or by the procedure.
d. Nephrotoxic reactions in patients with pre-existing renal damage or renal vasopathy, e.g. decrease in renal function with creatinine elevation. These adverse effects are transient in the majority of cases. In single cases, acute renal failure has been observed.
e. Neurotoxic reactions after intra-arterial injection of the contrast medium e.g. visual disorders, disorientation, paralysis, convulsions, or fits. These symptoms are generally transient and abate spontaneously within several hours or days. Patients with pre-existing damage of the blood-brain barrier are at increased risk of developing neurotoxic reactions.
f. Local reactions at the injection site may occur in very rare cases and include rashes, swelling, inflammation and oedema. Such reactions occur probably in most cases due to extravasation of the contrast agent. Extended paravasation may necessitate surgical treatment.
g. Extravasation can cause serious tissue reactions including blistering and skin exfoliation, the extent of which is dependent on the amount and strength of the contrast solution in the tissues.

d. Paediatric population

Frequency, type and severity of adverse reactions in children are expected to be the same as in adults. * Thyroid dysfunction was observed in pediatric patients 0 to 3 years of age following the administration of iodinated radiopaque agents.

e. 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. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9. Overdose

As with all iodinated X-ray contrast media, overdoses of Optiray are potentially fatal and may affect the respiratory and cardiovascular system. Treatment should be symptomatic. Dialysis can be used to remove Optiray from the blood.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Watersoluble, nephrotropic, low osmolar X-ray contrast media
ATC code: V08AB07

Optiray 350 is a non-ionic X-ray contrast medium. Intravascular injection of Optiray opacifies those vessels in the path of the flow of the contrast medium, permitting radiographic visualisation of the internal structures until significant haemodilution occurs.

5.2. Pharmacokinetic properties

The pharmacokinetic profile of Optiray, together with its hydrophilic properties and a very low level of binding to serum and plasma proteins, indicate that Optiray is distributed within the extracellular fluid space and eliminated quickly through the kidneys by glomerular filtration. The mean (± se) half-lives after doses of 50 ml and 150 ml were 113 ± 8.4 and 104 ± 15 minutes respectively. Elimination via the faeces is negligible. No significant metabolism, deiodination, or biotransformation of Optiray has been observed.

5.3. Preclinical safety data

There were no findings in the preclinical testing of Optiray which could be of relevance for the prescriber in recognising the safety of this product used for the authorised indications, and which are not already included in other sections of the SPC.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Trometamol, trometamol hydrochloride,
sodium hydroxide and/or hydrochloric acid (for pH: 6.0 to 7.4),
sodium calcium edetate,
water for injections.

6.2. Incompatibilities

No other medicinal product should be mixed with Optiray.

6.3. Shelf life

3 years.
After use, discard the remaining solution.

6.4. Special precautions for storage

Keep the container in the outer carton in order to protect from light. Protect from X-rays. Do not store above 30°C. Optiray can be stored for one month at 37°C in a contrast medium warmer with circulating air. Discard the solution in case of discolouration or particulate matter.

6.5. Nature and contents of container

Optiray 350 is packaged in uncoloured bottles composed of type I glass (Ph. Eur.). Bottles are fitted with either 20 mm or 32 mm bromobutyl rubber closures and aluminium cap seals.
30 ml (box of 1 and 10)
50 ml (box of 1, 10 and 25)
100, 200 ml (box of 1, 10 and 12)

Optiray 350 is also supplied in prefilled hand-held syringes and power injector syringes made of polypropylene. Syringe tip cap and piston are made of natural rubber.

Prefilled hand-held syringes:
30 ml (box of 1 and 10)

50 ml (box of 1, 10 and 20)

Power injector syringes:
50, 75, 100, 125 ml (box of 1, 10 and 20)
50, 75, 100, 125 mL with administration set for Optivantage Injector : polyvinyl chloride based plastic extension line and polyurethane based catheter (box of 1).

Not all pack sizes and box sizes may be marketed.

6.6. Instruction for use, handling and disposal

Hand-held syringes and power injector syringes:
The medicinal product and fluid pathway are sterile; the outside of the syringe is not sterile.
Instructions for assembly and inspection are stated on leaflet.

7. MARKETING AUTHORISATION HOLDER

<[To be completed nationally]>

8. MARKETING AUTHORISATION NUMBER

<[To be completed nationally]>

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: {DD month YYYY}
Date of latest renewal: {DD month YYYY}

<[To be completed nationally]>

10. DATE OF REVISION OF THE TEXT

09/2022

<[To be completed nationally]>