SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

BİEMEXOL 350 mg I/ml Solution for Injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active Substance:
Iohexol 755 mg/ml equivalent to 350 mg/ml iodine

Iohexol is a non-ionic, monomeric, triiodinated, water-soluble X-ray conrast medium.
The osmolality and viscosity values of BİEMEXOL 350 mg I/ml are as follows:

Concentration	Osmolality* Osm/kg H_2O 37^oC	Viscosity(mPa.s)	
		20^oC	37^oC
350 mgI/ml	0.78	23.3	10.6

* Method: Vapour - pressure osmometry.

Excipients: This medicinal product contains 0.012mg sodium per ml

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
BİEMEXOL is a clear, colourless to pale yellow, sterile aqueous solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic use only.
X-ray contrast medium for use in adults and children for angiography, 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.

4.2 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 use in body cavities.

Guidelines for Intravenous Use

Indication	**Concentration**	**Volume**	**Comments**
Urography Adults:	300 mgI/ml or 350 mgI/ml	40-80 ml 40-80 ml	80 ml may be exceeded in selected cases
Children <7 kg:	240 mgI/ml or 300 mgI/ml	4 ml/kg 3 ml/kg	
Children >7 kg:	240 mgI/ml or 300 mgI/ml	3 ml/kg 2 ml/kg	maks 40 ml
Phlebography (leg)	240 mgI/ml or 300 mgI/ml	20-100 ml/leg	
Digital Subtraction Angiography	300 mgI/ml or 350 mgI/ml	20-60 ml/inj. 20-60 ml/inj.	
CT-enhancement Adults:	140 mgI/ml 240 mgI/ml or 300 mgI/ml or 350 mgI/ml	100-400 ml 100-250 ml 100- 200 ml 100-150 ml	Total amount of iodine usually 30-60 g.
Children:	240 mgI/ml or 300 mgI/ml	2-3 ml/kg b.w (up to 40 ml) 1-3 ml/kg b.w (up to 40 ml)	In few cases up to 100 ml may be given

b.w. . Body weight

Guidelines for Intra-arterial use

Indication	**Concentration**	**Volume**	**Comments**
Arteriographies Arch aortography	300 mgI/ml	30-40 ml/inj.	Volume per injection depends on the site of injection
Selective cerebral	300 mgI/ml	5-10 ml/inj.	
Aortography	350 mgI/ml	40-60 ml/inj.	
Femoral	300 mgI/ml or 350 mgI/ml	30-50 ml/inj.	
Various	300 mgI/ml	Depending on type of examination	

Indication	Concentration	Volume	Comments
Cardioangiography Adults: Left ventricle and aortic root injection	350 mgI/ml	30-60 ml/inj.	
Selective coronary arteriography	350 mgI/ml	4-8 ml/inj.	
Children:	300 mgI/ml or 350 mgI/ml	Depending on age, weight and pathology	max 8 ml/kg
Digital Subtraction Angiography	140 mgI/ml or 240 mgI/ml or 300 mgI/ml	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 Body cavities

Indication	Concentration	Volume	Comments
Arthrography	240 mgI/ml or 300 mgI/ml or 350 mgI/ml	5-20 ml 5-15 ml 5-10 ml	
ERP/ERCP	240 mgI/ml	20-50 ml	
Herniography	240 mgI/ml	50 ml	The dosage varies with the size of the hernia.
Hysterosalpingography	240 mgI/ml or 300 mgI/ml	15-50 ml 15-25 ml	
Sialography	240 mgI/ml or 300 mgI/ml	0.5 –2 ml 0.5 –2 ml	

Gastrointestinal studies			
Oral use			
Adults:	180 mgI/ml or 350 mgI/ml	Individual Individual	
Children: - Oesophagus	300 mgI/ml or 350 mgI/ml	2-4 ml/kg b.w.. 2-4 ml/kg b.w.	Max. dose 50 ml Max. dose 50 ml
- Ventricle/follow through	140 mgI/ml	4-5 ml/kg b.w.	
Prematures:	350 mgI/ml	2-4 ml/kg b.w.	

Rectal use Children:	140 mgI/ml or dilute with tap water to 100-150 mgI/ml.	5-10 ml/kg b.w.	Example: Dilute BİEMEXOL 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 BİEMEXOL 300 or 350 with tap-water 1:50
Children:	Dilute with tapwater to ~6mgI/ml	15-20 ml/kg b.w. of the diluted solution	
Rectal use Children:	Dilute with tapwater to ~6mgI/ml		

b.w. body weight

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients
- Significant thyrotoxicosis
- Myelography in important local or systemic infections possible with bacteriamia
- Because of high dosage and technical defects, repetition of myelographic investigation in short time
- Administration of BİEMEXOL with intratecheal corticosteroids

4.4 Special warnings and precautions for use

Intratecheal usage of iodine contrast substances wrongly in spite of there is no intratecheal usage can cause serious advers events. These effects are like dying, convulsions, cerebral bleeding, coma, paralysis, aracnoiditis, acute renal insufficiency, cardiac arrest, seizures, rabdomyolysis, hypertermia and oedema in brain. BİEMEXOL 350 do not administer by intratechally. Be careful for non-administration of this product by intratecheally.

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 patients at risk for intolerance.

The risk of serious reactions in connection with use of BİEMEXOL is regarded as minor. However, iodinated contrast media may provoke serious, life-threatening, fatal anaphylactic/anaphylactoid reactions or other manifestations of hypersensitivity like pollenosis, food allergy. 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 to use an indwelling cannula or catheter for quick intravenous access throughout the entire X-ray procedure.

In case of seeing excess quantity of serebrospinal liquid with blood, risks and benefits of myelography procedure must evaluate for preventing risks to patient.

Patients using β-blockers may present with atypical symptoms of anaphylaxis which may be misinterpreted as vagal reaction.

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 patients

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. Care should taken in patients with multiple sclerosis. 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.

After myelography older patients are under more risk. Because of this, necessity of procedure should be evaluated carefully and care should be taken for dosage, concentration and technique and hidratation situation of patient.

Care should be taken against intrathecal administration with accidentally high dosage or as form of concentrate bolus injection. Furthermore, preventive precautions must be taken for not-increasing of intrathecal levels rapidly (exp; preventing active moving of patients). Direct intrasisternal or ventricular administration of standard radiography (not computarized tomography) should be avoided.

Use of iodinated contrast media may cause contrast induced nephropathy, impairment of renal function or acute renal failure. To prevent these conditions 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 paraproteinaemias (myelomatosis and Waldenström’s macroglobulinaemia plasmocytoma) 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.

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, particular in those with impaired renal function.

To reduce the risk of lactic acidosis, serum creatinine level should be measured in diabetic patients treated with metformin prior to intravascular administration of iodinated contrast medium and the following precautions undertaken in the following circumstances:

Normal serum creatinine (<130 µmol/litre)/normal renal function: Administration of metformin should be stopped at the time of administration of contrast medium and should not be resumed for 48 hours and only be restarted if renal function/serum creatinine remains in the normal range.

Abnormal serum creatinine (>130 µ mol/litre)/impaired renal function: Metformin should be stopped and the contrast medium examination delayed for 48 hours. Metformin should only be restarted 48 hours later 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. It is particularly important that the patient is 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 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 medium for radiological procedures. There is no any correlation between injection time of contrast substance and hemodialysis cycle. Because, there is no evident that hemodialysis prevents neuropathy caused by contrast substance in patients with renal dysfunction.

The administration of iodinated contrast medium 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 medium.

Extravasation of contrast medium may on rare occasions give rise to local pain, and oedema, which usually recedes without sequelae. 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.

Repetition of procedure: According to evaluation of doctor, if repetition of process is necesarry, care should be taken for time needed to clear medicine from body between first applied procedure and second procedure.

Observation time
Patients must be kept under close observation for 30 minutes following the last injection as the majority of severe reactions occur at this time. Furtermore, delayed reactions may occur.

Intratecheal administration
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.

Paediatric population:
Transient hypothyroidism has been reported in premature infants, neonates and in other children after administration of iodinated contrast medium. Premature infants are particularly sensitive to the effect of iodine. It is advisable to monitor thyroid function. Thyroid function should be checked in neonates during the first week of life, following administration of iodinated contrast agents to the mother during pregnancy.

Especially in infants and small children, adequate hydration should be assured before and after contrast media administration. Nephrotoxic medication should be suspended. The age dependent reduced glomerular filtration rate in infants can also result in delayed excretion of contrast agents.

Young infants (age < 1 year) and especially neonates are susceptible to electrolyte disturbance and haemodynamic alterations.

BİEMEXOL contains less than 1 mmol sodium in each dosage (23 mg). So it can be accepted as that “this product does not contain sodium”.

4.5 Interaction with other medicinal products 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 metformin (see section 4.4).

Patients treated with interleukin-2 and interferons 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.

It is not advisable using low threshold drugs with BİEMEXOL, especially phenothiazine derivatives (including antihistaminic or medicines for preventing nausea). MAO inhibitors, tricyclic antidepressants, central nervous system stimulant, psychcoactive drugs must not be used with BİEMEXOL. This type of drugs must be stopped minimum 48 hours before myelography and must not be used after procedure at least for 24 hours. Anticonvulsants should be considered for prophylaxis in patients taking these drugs and having non-elective procedure.

4.6 Fertility, pregnancy and lactation

General advice
Pregnancy category: B

Women with child-bearing potential/ birth control (contraception)

Women childbearing potential should be careful.

Pregnancy:
The safety of BİEMEXOL for use in human pregnancy has not been established.
Since whenever possible, radiation exposure should be avoided during pregnancy, the benefits of an X-ray examination, with or without contrast medium, should be carefully weighed against the possible risk. BİEMEXOL should not be used in pregnancy unless the benefit outweighs risk and it is considered essential by the physician.

Breast-feeding:
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. Breast feeding may be continued normally when iodinated contrast media are given to the mother. The amount of iohexol in breast milk excreted in 24 hours after injection was 0.5% of the weight adjusted dose in a trial. The amount of iohexol ingested by the baby in the first 24 hours after injection corresponds to only 0.2% of the paediatric dose.

Reproduction ability/Fertility

There is no enough data for human.

4.7 Effects on ability to drive and use machines

No studies on the ability to drive or use machines have been performed. There is no known effect on the ability to drive or operate machines. However, because of the risk of reactions, it is not advisable to drive a car or use machines for one hour after the last injection or for 24 hours following intrathecal examination (see section 4.4).
Individual judgement must be performed if there are persistent post-myelographic symptoms.

4.8 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.

Hypersensitivity reactions may occur irrespective 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.

A transient increase in S-creatinine is common after iodinated contrast media, contrast induced nephropathy may occur.

"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.

The listed frequencies are based on internal clinical documentation and published large scale studies, comprising more than 90,000 patients.

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)

Immune system disorders

Rare:	Hypersensitivity (including dyspnoea, rash, erythema, urticaria, pruritus, skin reaction, vasculitis, angioneurotic oedema, laryngeal oedema, laryngospasm, bronchospasm or non-cardiogenic pulmonary oedema). They may appear either immediately after the injection or up to a few days later.
Not known:	Anaphylactic/anaphylactoid reaction, anaphylactic/anaphylactoid shock

Nervous system disorders

Rare:	Headache
Very rare:	Dysgeusia (transient metallic taste)
Not known:	Syncope vasovagal

Cardiac disorders

Rare:	Bradycardia

Vascular disorders

Very rare:	Hypertension, hypotension

Gastrointestinal disorders

Uncommon:	Nausea
Rare:	Vomiting

Very rare:	Diarrhoea, abdominal pain/discomfort
Not known:	Salivary gland enlargement

General disorders and administration site conditions

Common:	Feeling hot
Rare:	Pyrexia
Very rare:	Shivering (chills)

Injury, poisoning and procedural complications

Not known:	Iodism

Intravascular use (Intra-arterial and Intravenous use)

Please first read the section labelled "General". Below, only undesirable events with frequency during intravascular use of non-ionic monomeric contrast media are described.

The nature of the undesirable effects specifically seen during intra-arterial use depends 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.

Immun system disorders

Not-known:	Severe pustular or exfoliative or bullous skin lessions

Endocrine disorders

Not known:	Thyrotoxicosis, transient hypothyroidism

Psychiatric disorders

Not known:	Confusion

Nervous system disorders

Rare:	Dizziness,
Very rare:	Seizures, disturbance in consciousness, encephalopathy, stupor, sensory abnormalities (including hypoaesthesia), paraesthesia, tremor
Not known:	Transient motor dysfunction (including speech disorder, aphasia, and dysarthria), transient memory loss, disorientation, coma, retrograde amnesia

Eye disorders

Not known:	Transient cortical blindness

Ear and labyrinth disorders

Not known:	Transient hearing loss

Cardiac disorders

Rare:	Arrhythmia (including bradycardia, tachycardia).
Very rare:	myocardial infarction
Not known:	Severe cardiac complications (including cardiac arrest, cardio-respiratory arrest), spasm of coronary arteries, chest pain

Vascular disorders

Very rare:	Flushing
Not known:	Shock, arterial spasm, thrombophlebitis and venous thrombosis

Respiratory, thoracic and mediastinal disorders

Rare:	Cough,
Very rare:	Dyspnoea, non-cardionogenic pulmonary oedema
Not known:	Severe respiratory symptoms and signs, bronchospasm, laryngospasm, asthma attack

Gastrointestinal disorders

Rare:	Diarrhoea
Not known:	Aggravation of pancreatitis, acute pancreatitis

Skin and subcutaneous tissue disorders

Not known: Bullous dermatitis, Stevens-Johnson syndrome, toxic epidermal necrolysis, drug rash with eosinophilia and systemic symptoms, psoriasis flare-up.

Musculoskeletal and connective tissue disorders

Not known: Arthralgia

Renal and urinary disorders

Rare: Impairment of renal function including acute renal failure

General disorders and administration site conditions

Common:	Feeling hot
Uncommon:	Pain and discomfort
Rare:	Asthenic conditions (including malaise, fatigue).
Not known:	Administration site reactions, including extravasation, back pain

Intrathecal use

Please first read the section labelled "General". Below, only undesirable 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 may largely be attributed to pressure loss in the sub-arachnoid space resulting from leakage at the puncture site. Excessive removal of cerebrospinal fluid should be avoided in order to minimize pressure loss.

Psychiatric disorders
Not known: Confusion

Nervous system disorders

Very common: Headache (may be severe and prolonged)

Uncommon: Aseptic meningitis (including chemical meningitis)

Rare: Seizures, dizziness

Not known: Electroencephalogram abnormal, meningism, transient contrast-induced encephalopathy including transient memory loss, coma, stupor and retrograde amnesia, motor dysfunction (including speech disorder, aphasia, dysarthria), paraesthesia, hypoesthesia and sensory disturbance

Eye disorders
Not known: Transient cortical blindness, photophobia

Ear and labyrinth disorders
Not known: Transient hearing loss
Gastrointestinal disorders
Common: Nausea, vomiting

Musculoskeletal and connective tissue disorders
Rare: Neck pain, back pain
Not known: Muscle spasm

General disorders and administration site conditions

Rare: Pain in extremity

Not known: Administration site conditions

Use in Body Cavities

Please first read the section labelled "General". Below, only undesirable events with frequency during use of non-ionic monomeric contrast media in body cavities are described.

<u>Endoscopic Retrograde Cholangiopancreatography (ERCP)</u>
Gastrointestinal disorders
Common: Pancreatitis, blood amylase increased

<u>Oral use:</u>
Gastrointestinal disorders
Very common: Diarrhoea
Common: Nausea, vomiting

Uncommon: Abdominal pain

Hysterosalpingography (HSG)
Gastrointestinal disorders
Very common: Lower abdominal pain

Arthrography
Musculoskeletal and connective tissue disorders
Not known: Arthritis

General disorders and administration site conditions
Very common: Pain

Herniography:
General disorders and administration site conditions
Not known: Post procedural pain

Description of selected adverse reactions

Thrombo-embolic complications have been reported in connection with contrast-enhanced angiography of coronary, cerebral, renal and peripheral arteries. The contrast agent may have contributed to the complications (see section 4.4).

Cardiac complications including acute myocardial infarction have been reported during or after contrast-enhanced coronary angiography. Elderly patients or patients with severe coronary artery disease, unstable angina pectoris and left ventricular dysfunction had a higher risk (see section 4.4).

In very rare occasions the contrast medium may cross the blood-brain barrier resulting in uptake of contrast medium in the cerebral cortex that may cause neurological reactions. They may include convulsions, transient motor or sensory disturbances, transient confusion, transient memory loss and encephalopathy (see section 4.4).

Anaphylactoid reaction and anaphylactoid shock may lead to profound hypotension and related symptoms and signs like hypoxic encephalopathy, renal and hepatic failure (see section 4.4).
In several cases, extravasation of contrast media has caused local pain and oedema, which usually receded without sequelae. Inflammation, tissue necrosis and compartment syndrome have occurred (see section 4.4).

Paediatric patients:

Transient hypothyroidism has been reported in premature infants, neonates and in other children after administration of iodinated contrast media. Premature infants are particularly sensitive to the effect of iodine. Transient hypothyroidism in a premature breast fed infant has been reported. The nursing mother was repeatedly exposed to BİEMEXOL (see section 4.4).

Especially in infants and small children, adequate hydration should be assured before and after contrast media administration. Nephrotoxic medication should be suspended. The age

dependent reduced glomerular filtration rate in infants can also result in delayed excretion of contrast agents.

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 Health care representatives must inform any suspicious adverse event to Turkish Pharmacovigilance Association (TÜFAM). (www.titck.gov.tr; e-mail: tufam@titck.gov.tr; phone: 0 800 314 00 08, fax: 0 312 218 35 99).

4.9 Overdose
Preclinical data indicate a high safety margin for BİEMEXOL 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 (t½ ~ 2 hours). Accidental overdosing is most likely following complex angiographic procedures in children, particularly when multiple injections of high-concentration contrast media 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.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: X-Ray Contrast Media, iodinated
ATC code: V08A B02

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.

5.2 Pharmacokinetic properties

Absorbtion:
It is administered by intravenously.

Distribution:
Protein binding ratio of BİEMEXOL is very low (less than 2%) and clinically there is no importance. It can disregard.

Biotransformation:
It does not changed in body. Any metabolites are not found.

Elimination:
In patients with normal renal functions, nearly 100% of intravenous injected iohexole is eliminated by renally as un-changed within 24 hours. In patients with normal renal functions, elimination half life is approximately 2 hours.

5.3 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.
In evaluation of experimental animal studies, directly and non-directly harmful effects on reproduction, embrio or fetus development, pregnancy period, development before and after pregnancy are not shown.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Trometamol
Sodium calcium edetate
Hydrochloric acid (pH adjustment)
Sodium Hyroxide (pH adjustment)
Water for injections

~~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

24 months
The product should be used immediately after opening. Any unused portion must be discarded.

6.4 Special precautions for storage

Store below 25ºC.
Keep container in the outer carton. Protect from secondary x-rays.

6.5 Nature and contents of container

50 and 100 ml, colorless, type 1, glass vial, bromobuthyle closure, blue tear off cap.

6.6 Special precautions for disposal and other handling of the product

Vials are intended for single use only, any unused portions must be discarded.

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

As the product does not contain a preservative, it should be drawn into the syringe immediately before use.

Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Biem Pharmaceuticals.
Anıttepe Mah. Turgut Reis Cad. No: 21
Tandoğan/Çankaya - Ankara
Tel: 0312 230 29 29
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8 MARKETING AUTHORISATION NUMBER

2015/936

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 09.12.2015
Date of last renewal:

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15.04.2016