SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Nolotil 0.4g/ml solution for injection/infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ampoule of 5 ml contains:
Metamizole magnesium 2 g

1 ml of solution for injection/infusion contains 400 mg of magnesium metamizole.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection/infusion.

Clear solution with a slightly yellowish colour.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Acute moderate or intense post-surgery or post-traumatic pain, colicky-type or from tumoral origin. High fever that does not respond to other therapeutic measures including first choice antipyretics.

Parenteral administration is only indicated in acute intense pain if enteral administration is not considered appropriate.

4.2. Posology and method of administration

Posology:

Dosage is determined by the intensity of the pain or fever and individual sensitivity of response to Nolotil. It is essential to choose the lowest dose that controls pain and fever.

In children and adolescents up to 14 years old, 8–16 mg metamizole per kg body weight can be given as a single dose. In the case of fever, a dose of 10 mg metamizole per kilogram body weight is generally enough for children. Adults and adolescents from 15 years of age (>53 kg) can be administered up to 1,000 mg as a single dose.

In dependence on the daily maximum dose a single dose can be taken up to 4 times daily at intervals of 6–8 hours.

A clear effect can be expected 30 minutes after parenteral administration.

The following table shows the recommended single doses and the maximum daily doses according to weight or age:

Body weight		Single dose		Daily maximum dose	
kg	age	ml	mg	ml	mg
5-8	3-11 months	0.1-0.3	40-120	0.4-1.2	160-480
9-15	1-3 years	0.2-0.6	80-240	0.8-2.4	320-960
16-23	4-6 years	0.3-0.9	120-360	1.2-3.6	480-1,440
24-30	7-9 years	0.5-1.2	200-480	2.0-4.8	800-1,920
31-45	10-12 years	0.6-1.8	240-720	2.4-7.2	960-2,880
46-53	13-14 years	0.9-2.1	360-840	3.6-8.4	1,440-3,360
>53	≥15 years	1.0-2.5*	400-1,000*	4.0-10.0*	1,600-4,000*

* If necessary, the single dose can be increased to 6.2 ml (corresponding to 2,480 mg metamizole) and the daily dose to 12.5 ml (corresponding to 5,000 mg metamizole).

In the indication of oncological pain, in adult and adolescent patients from 15 years of age (> 53 kg), half ampoule can be administered in an orally single dose up to 4 times daily, at intervals of 6 to 8 hours, corresponding to a maximum daily dose of 4,000 mg. The oral use of the ampoule for the treatment of oncological pain should not exceed 7 days.

Appropriate equipment for treatment of the rare cases of shock must be present when administered parenterally.

The commonest cause of critical drop in blood pressure and shock is an unduly rapid rate of injection. Intravenous injection must be given very slowly to minimize the risk of a hypotension reaction. Blood pressure, heart rate and breathing must be monitored. In view of the assumption that the non-allergic drop in blood pressure is dose-dependent, parenteral single dose administration of doses higher than 1 g of metamizole should be particularly carefully considered.

This medicine is for short-term use.

Special populations

Elderly population, debilitated patients, and patients with reduced creatinine clearance
The dose should be reduced in elderly people, in debilitated patients and in those with reduced creatinine clearance, as elimination of the metabolic products of metamizole may be prolonged.

Hepatic and renal impairment
As the elimination rate is reduced when renal or hepatic function is impaired, multiple high doses should be avoided. No dose reduction is needed when used for only a short time. To date, there has been insufficient experience with long-term use of metamizole in patients with severe hepatic and renal impairment.

Method of administration

For intravenous (intravenous injection or infusion), intramuscular and oral administration.

This medicine should only be injected by deep intramuscular or intravenous route. Inadvertent intraarterial use may cause necrosis of the distal vascular area. The solution should be warmed up to body temperature prior to injection.

The solution for injection/infusion can be mixed and/or diluted with glucose solution 50 mg/ml (5%), saline solution 9mg/ml (0.9%), or Ringer's lactate solution. As mixtures of this type only remain stable for a short time, however, they must be administered immediately.

4.3. Contraindications

Nolotil is contraindicated in:
- Agranulocytosis in the medical history induced by metamizole, other pyrazolones or pyrazolidines
- Impaired bone marrow function or diseases of the hematopoietic system
- patients who have shown prior hypersensitivity reactions or haematological reactions to medicinal products containing metamizole, other pyrazolones or pyrazolidines (isopropylaminophenazone, propyphenazone, phenazone or phenylbutazone), as well as patients with hypersensitivity to any of the excipients (see section 6.1)
- patients with known analgesic-induced asthma syndrome or known analgesic intolerance of the urticarial-angioedema type, i.e. patients who develop bronchospasm or other anaphylactoid reactions in response to salicylates, paracetamol or other non-narcotic analgesics such as diclofenac, ibuprofen, indomethacin or naproxen
- patients with acute intermittent hepatic porphyria (risk of triggering a porphyria attack).
- patients with genetic glucose-6-phosphate-dehydrogenase deficiency (risk of haemolysis).
- patients with impaired bone marrow function (e.g., during or after treatment with cytostatic agents) or diseases of the hematopoietic system
- third trimester of pregnancy (see section 4.6)
- patients with existing arterial hypotension and unstable circulatory state
- intraarterial injection (see sections 4.4 and 4.2)
- patients who have shown a serious skin reaction in previous exposures

4.4 Special warnings and special precautions for use

Patients should be specially warned that Nolotil is a prescription medicine.

Severe hematologic reactions (such as agranulocytosis or pancytopenia)

Agranulocytosis

Treatment with metamizole can cause agranulocytosis, which may be fatal (see section 4.8). It may occur even after metamizole has previously been used without complications.

Metamizole-induced agranulocytosis is an idiosyncratic adverse reaction. It is not dose-dependent, and may occur at any time during treatment, even shortly after treatment discontinuation.

Patients must be instructed to discontinue their treatment and seek immediate medical attention in case any symptoms suggestive of agranulocytosis appear (e.g. fever, chills, sore throat and painful mucosal changes, especially in the mouth, nose and throat or in the genital or anal region).

If metamizole is taken for fever, some symptoms of emerging agranulocytosis may go unnoticed. Similarly, symptoms may also be masked in patients receiving antibiotic therapy.

If signs and symptoms suggestive of agranulocytosis occur, a complete blood cell count (including differential blood count) should be performed immediately, and treatment must be stopped while waiting for the results. If confirmed, treatment must not be reintroduced (see section 4.3).

In the event of clinical signs or symptoms of agranulocytosis or reduction of red blood cells, leucocytes or platelets on lab tests, Nolotil administration must be discontinued immediately and the blood count (including differential blood count) must be monitored until it has returned to normal (see section 4.8). Discontinuation of treatment must not be delayed until the results

of the lab tests are available. All patients should be advised to discontinue the treatment and immediately consult a physician if during treatment with Nolotil signs and symptoms occur which are suggestive of blood dyscrasia (e.g. general malaise, infection, persistent fever, sore throat, painful changes in the mucosa of the mouth or the nose, bruising, bleeding, pallor or unexpected deterioration of the general condition).

Patients who show immunological reactions to Nolotil such as agranulocytosis, are also at high risk of responding similarly to other pyrazolones and pyrazolidines.

Anaphylactic/anaphylactoid reactions and anaphylactic shock
Nolotil may cause anaphylactic reactions and anaphylactic shock that can be life-threatening for the patient (see section 4.8). When choosing the administration route, it should be borne in mind that parenteral administration of Nolotil presents a higher risk of anaphylactic or anaphylactoid reactions.

The risk of potentially severe anaphylactoid reactions to Nolotil is higher for patients with:

- analgesic-induced asthma syndrome or analgesic intolerance of the urticarial-angioedema type (see section 4.3),
- bronchial asthma, in the presence of rhinosinusitis and nasal polyps,
- chronic urticaria,
- intolerance to colouring agents (e.g., tartrazine) and/or preservatives (e.g., benzoates),
- alcohol intolerance. These patients react to even minute amounts of alcoholic drinks with symptoms such as sneezing, watering eyes and severe facial flushing. Alcohol intolerance of this kind may be an indication of yet undiagnosed analgesic-induced asthma syndrome (see section 4.3).

Therefore, caution is required when using Nolotil in patients with asthma or atopy.

Prior to administration of Nolotil, the patient must be questioned appropriately about the presence of any of the characteristics or mentioned in the contraindications section. In patients at high risk of anaphylactoid reactions, who do not show any situation that contraindicates the use of Nolotil, it should be assessed whether treatment is appropriate. In case it is administered, the patient must be very closely monitored by the doctor and the availability of emergency standby must be guaranteed.

Patients who show anaphylactic or other immunological reaction to Nolotil, are also at high risk of responding similarly to other pyrazolones, pyrazolidines and other non-narcotic analgesics.

Severe hypotensive reactions
Metamizole can cause hypotension reactions (see section 4.8). These reactions may be dose-dependent and are more likely with parenteral rather than enteral administration. The risk of such reactions is also increased in the case of:
- too rapid intravenous injection (see section 4.2.)
- patients with, for example, pre-existing arterial hypotension, hypovolemia or dehydration, unstable circulation or incipient circulatory failure (e.g. in patients with acute myocardial infarction or polytrauma)
- patients with a high fever.

As a result, diagnosis must be carefully established, and close monitoring is needed in case of administration in these patients. Preventive measures (e.g., stabilization of the circulation) may be necessary in order to reduce the risk of hypotension. Use of Nolotil requires close monitoring of the haemodynamic parameters when used in patients for whom a fall in blood pressure must be avoided at all costs, such as in the case of severe coronary artery disease or relevant stenosis of the vessels supplying the brain.

Severe skin reactions

Severe cutaneous adverse reactions (SCARs), including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) and drug reaction with eosinophilia and systemic symptoms (DRESS), which can be life-threatening or fatal, have been reported with metamizole treatment.

Patients should be advised of the signs and symptoms and monitored closely for skin reactions.

If signs and symptoms suggestive of these reactions appear, metamizole should be withdrawn immediately, and must not be re-initiated at any time (see section 4.3).

Gastrointestinal bleeding
Gastrointestinal bleeding cases have been reported in patients treated with metamizole. Many patients had concomitantly received other treatment (e.g., NSAIDs) associated with gastrointestinal bleeding, or used an overdose of metamizole.

Drug-induced liver injury
Cases of acute hepatitis of predominantly hepatocellular pattern have been reported in patients treated with metamizole with an onset of few days to few months following treatment initiation. Signs and symptoms include elevated serum hepatic enzymes with or without jaundice, frequently in context of other drug hypersensitivity reactions (e.g. skin rash, blood dyscrasias, fever, eosinophilia) or accompanied by features of autoimmune hepatitis. Most patients recovered on discontinuation of metamizole treatment nevertheless, in isolated cases, progression to acute liver failure requiring liver transplantation was reported.

The mechanism of metamizole-induced liver injury is not clearly elucidated, but data indicate an immune-allergic mechanism.

Patients should be instructed to contact their physician in case symptoms suggestive of liver injury occur. In such patients metamizole should be discontinued and liver function should be assessed.

Metamizole should not be re-introduced in patients with an episode of hepatic injury during treatment with metamizole for which no other cause of liver injury has been determined.

Risk associated with incorrect route of administration
Attention should be paid to proper injection technique. Inadvertent intra-arterial use may cause necrosis potentially leading to amputation in the distal vascular area.

Risk in specific populations
In elderly patients or patients with impaired renal or hepatic function, Nolotil should only be used after consideration of the benefit-risk ratio and appropriate precautions must be taken (see section 4.2).

4.5 Interactions with other medicinal products and other forms of interaction

Methotrexate and other antineoplastic
Concomitant administration of metamizole with methotrexate or other antineoplastic may increase blood toxicity of antineoplastic particularly in elderly patients. Therefore, this combination should be avoided.

Chlorpromazine
Concomitant use of metamizole and chlorpromazine can cause severe hypothermia.

Acetylsalicylic acid
Metamizole can reduce the antiplatelet effect of acetylsalicylic acid if administered concomitantly. Therefore, Nolotil should be used with caution in patients taking low doses of acetylsalicylic acid as a cardioprotective agent.

Pharmacokinetic induction of metabolising enzymes
Metamizole may induce metabolising enzymes including CYP2B6 and CYP3A4.

Co-administration of metamizole with bupropion, efavirenz, methadone, valproate, cyclosporine, tacrolimus or sertraline, may cause a reduction in plasma concentrations of these drugs with a potential decrease in clinical efficacy. Therefore, caution is advised when metamizole is administered concurrently; clinical response or drug levels should be monitored as appropriate.

Alcohol
Metamizole in combination with alcohol may potentiate each other's effect.

Additional interactions with pyrazolones
Pyrazolones may also cause interactions with oral anticoagulants, captopril, lithium and triamterene. The efficacy of antihypertensives and diuretics may be affected by pyrazolones. It is not known to what extent metamizole causes these interactions.

4.6 Fertility, pregnancy and breast-feeding

Pregnancy
There are only limited data available on the use of metamizole in pregnant women.
Based on published data from pregnant women exposed to metamizole during the first trimester (n=568) no evidence for teratogenic or embryotoxic effects was identified. In selected cases single doses of metamizole during the first and second trimester might be acceptable when no other treatment options exist. However, in general the use of metamizole during the first and second trimester is not recommended. Use during the third trimester is associated with fetotoxicity (renal impairment and ductus arteriosus constriction) and thus the use of metamizole is contraindicated during the third trimester of pregnancy (see section 4.3). In case of inadvertent use of metamizole during the third trimester amniotic fluid and the ductus arteriosus should be controlled by ultrasound and echocardiography.

Metamizole crosses the placental barrier.

In animals metamizole induced reproductive toxicity but no teratogenicity (see Section 5.3).

Breast-feeding
The breakdown products of metamizole pass into breast milk in considerable amounts and a risk to the breastfed infant cannot be excluded. Therefore the repeated use of metamizole during breastfeeding must be avoided. In case of a single administration of metamizole mothers are advised to collect and discard the breastmilk for 48 hours after the dose.

Fertility
No clinical studies on the effect on human fertility have been conducted for metamizole.
Studies in animals performed with metamizole have shown no adverse effects on fertility (see section 5.3).

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. If taken in the recommended dose, this product is not expected to affect concentration or reactions. However, as a precaution, patients should be advised that at least if higher doses are taken, the possibility of impaired reactions should be borne in mind; patients should avoid using machines, driving or conducting hazardous activities. This applies in combination with alcohol.

4.8. Undesirable effects

Adverse reactions have been ranked under headings of frequency using the following MedDRA convention: Very common (≥ 1/10); common (≥ 1/100 and < 1/10); uncommon (≥ 1/1.000 and < 1/100); rare (≥ 1/10.000 and < 1/1.000), very rare (< 1/10.000), frequency not known (cannot be estimated from the available data).

Blood and lymphatic system disorders

Rare	leukopenia
very rare	agranulocytosis (including fatal cases), thrombocytopenia
frequency not known	sepsis, aplastic anaemia, pancytopenia (including fatal cases)

These are presumably immunological reactions. They can occur even if metamizole was administered on previous occasions without complications.

Agranulocytosis is manifested in the form of pyrexia, chills, oropharyngeal pain, dysphagia, stomatitis, rhinitis, pharyngitis, genital tract inflammation, and anal inflammation. These signs or symptoms may be minimal in patients on antibiotics. There is little or no lymphadenopathy or splenomegaly. The sedimentation rate is markedly increased, and granulocytes are considerably reduced or absent altogether. Haemoglobin, red blood cell count and platelet counts may be abnormal.

It is necessary to advise the patient to immediately discontinue the treatment with Nolotil and to consult the doctor if any of agranulocytosis or aplastic anaemia symptom or sign appears.

Immune system disorders, skin and subcutaneous tissue disorders

uncommon	drug eruption, fixed drug eruption, skin reaction
rare	anaphylactic reaction, anaphylactoid reaction (especially after parenteral administration), asthma in patients with analgesic asthma syndrome, rash maculo-papular
very rare	toxic epidermal necrolysis, Stevens-Johnson syndrome
frequency not known	anaphylactic shock including fatal cases, hypersensitivity, drug reaction with eosinophilia and systemic symptoms (DRESS)

Milder reactions (e.g., skin and mucosal reactions such as pruritus, burning sensation, erythema, swelling, as well as dyspnoea and gastrointestinal disorders) may lead on to more severe reactions (e.g., generalised urticaria, severe angioedema including the laryngeal region, severe bronchospasm, arrhythmia, decreased blood pressure with sometimes initially increased blood pressure). Nolotil must therefore be discontinued immediately if skin reactions occur. In case of severe skin reactions, a physician should immediately be consulted.

Severe cutaneous adverse reactions, including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) and drug reaction with eosinophilia and systemic symptoms (DRESS) have been reported in association with metamizole treatment (see section 4.4).

Appropriate treatment should be started as soon as signs/symptoms of anaphylaxis appear.

Anaphylactic reactions can develop during or immediately after injection but can also develop some hours later. Reactions generally occur, however, within the first hour of administration.

Cardiac disorders

frequency not known	Kounis syndrome

Vascular disorders

common	hypotension
uncommon	injection site pain
very rare	shock, phlebitis

frequency not known	injection site reaction

Hypotension reactions may occur during or after treatment with Nolotil and may not go hand in hand with other signs of anaphylactoid and/or anaphylactic reactions. These reactions can lead to shock.

A rapid intravenous injection increases the risk of hypotension reactions. After a too rapid injection, there may be a dose-dependent and critical drop in blood pressure with no other signs of drug intolerance.

Gastrointestinal disorders

frequency not known	gastrointestinal haemorrhage

Renal and urinary disorders

Very rare	acute renal failure, proteinuria, oliguria, anuria, renal impairment, interstitial nephritis
frequency not known	chromaturia

The elimination of the rubazonic acid, a harmless metabolite of the metamizole, may cause reddish discolouration of the urine, which disappears on discontinuation of treatment.

Hepatobiliary disorders

Frequency not known	drug-induced liver injury including acute hepatitis, jaundice, increased liver enzymes (see section 4.4.)

Notification of suspected undesirable effects
It is important to report suspected undesirable effects of the medication after its authorization. This allows a continuous monitoring of the benefit / risk ratio of the medicine. Healthcare professionals are invited to report suspected undesirable effects through the Spanish Pharmacovigilance System for Medicinal Products for Human Use: https://www.notificaram.es

4.9 Overdose

Symptoms
Following acute overdose, nausea, vomiting, abdominal pain, impaired renal function/acute renal failure (e.g. manifest as interstitial nephritis) and, in rarer cases, central nervous symptoms (dizziness, somnolence, coma, seizures) and a drop in blood pressure or even shock and tachycardia have been observed.

After very high doses, elimination of the metabolite rubazonic acid can cause reddish discolouration of the urine.

Therapy:
There is no known specific antidote for metamizole. If metamizole was administered only recently, absorption-reducing measures (e.g. activated charcoal) can be administered to limit absorption by the body. The major metabolite (4-methyl-amino-antipyrine) can be eliminated by means of haemodialysis, hemofiltration, hemoperfusion or plasma filtration.

Treatment of intoxication and prevention of severe complications may require general and specific intensive medical monitoring and treatment.

Acute measures in the event of severe drug intolerance (shock):

At the first symptoms (e.g. skin reactions such as urticaria or erythema, restlessness, headache, profuse sweating, nausea), stop the administration immediately and leave the cannula in the vein or set up another venous access. In addition to other conventional emergency measures such as

positioning the patient on his side, maintaining the airways opened or administering oxygen, the following pharmacological emergency measures may be necessary:

- Immediate administration of epinephrine (adrenaline) intravenously.
  Dilute 1 ml of a solution of adrenaline 1:1000 in 10 ml or use either a 1:10000 solution of adrenaline. Slowly inject 1 ml (equivalent to 0.1 mg adrenaline) of any of the above-mentioned solutions whilst monitoring pulse rate and blood pressure (paying special attention to heart rhythm alterations). The adrenaline dose may be repeated.
- Then administer intravenously fluids e.g. plasma expanders (colloids) or Ringer's lactate solution.
- Additionally, glucocorticoids intravenously,
  for example, 250 - 1000 mg of methylprednisolone. The glucocorticoid dose may be repeated.

The dosages recommended above concerning emergency drug measures refer to normal-weight adults and must be adjusted for body weight if being given to children. Depending on the clinical symptoms, additional therapeutic measures such as artificial respiration and antihistamines should be considered. If cardiac arrest occurs, standard resuscitation measures should be instituted.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other analgesics and antipyretics. Pyrazolones. ATC Code: N02BB

Metamizole, the active ingredient of Nolotil 0.4 g/ml solution for injection/infusion, is a non-narcotic pyrazolone analgesic with analgesic, antipyretic and spasmolytic effects. The mechanism of action is incompletely understood. Data suggest that metamizole and its main metabolite (4-methylamino-antipyrine) may have a combined central and peripheral mode of action. At supra-therapeutic doses an antiphlogistic effect can be achieved which may result from an inhibition of prostaglandin synthesis.

5.2. Pharmacokinetic properties

Absorption
Following oral administration, metamizole is rapidly hydrolysed in the gastric juice to the major metabolite, methylaminoantipyrine (MAA), that is readily absorbed. After oral intake, metamizole is almost completely absorbed. There is no relevant effect of concomitant intake of food on the pharmacokinetics of metamizole.

Distribution
The plasma protein binding of 4-MAA is 58%. The further metabolites of metamizole are bound to the following extent: 4-amino-antipyrine (48%), 4-formylaminoantipyrine (18%) and 4-acetylaminoantipyrine (14%). Metamizole can pass the placental barrier. The metabolites are excreted into breast milk of nursing mothers.

Metabolism or Biotransformation
The main metabolite of metamizole, 4-MAA, is further metabolised in the liver by oxidation and by demethylation which is followed by acetylation. The major metabolites of metamizole are 4-methylaminoantipyrine (4-MAA), 4-amino-antipyrine (4-AA), 4-formylaminoantipyrine (4-FAA) and 4-acetylaminoantipyrine (4-AcAA). Examination of the four main metabolites of metamizole shows that the antipyretic, analgesic and anti-inflammatory effect of metamizole can be attributed to the metabolites 4-MAA and 4-AA.

Elimination

In healthy volunteers, after oral and i.v. administration, more than 90% of the dose is excreted in the urine within 7 days. The elimination half-life of radiolabelled metamizole is about 10 hours.
For 4-MAA, the elimination half-life after a single oral dose is 2.7 hours, for the other main metabolites the elimination half-life is 3.7 to 11.2 hours. Children eliminate the metabolites more rapidly than adults.
In elderly healthy volunteers the elimination half-life of 4-MAA was significantly longer and the clearance significantly lower than in young subjects.
In patients with hepatic insufficiency, elimination half-lives of 4-MAA and 4-FAA rose to about 3-fold. In renally impaired patients, elimination of some metabolites (4-AcAA, 4-FAA) is reduced. High doses are therefore to be avoided in hepatically and renally impaired individuals.

Pharmacokinetics/pharmacodynamical data
All metabolites of metamizole show non-linear pharmacokinetics. A clinical relevance of the phenomenon is not known. During a short-term treatment, accumulation of metabolites is of minor importance.

5.3 Preclinical safety data

Single- and repeat-dose toxicity studies have been conducted in rodents and nonrodents. The acute oral toxicity is low with LD_{50} values between 3,127 – 4,351 mg/kg for mice and rats. There was a good gastric tolerance and erosions only occurred in rats receiving 1,000 mg/kg. Gastrointestinal toxicity may also arise in patients at overdosing After intravenous administration the LD_{50} values were 2,389 mg/kg in both species.

The effects of subcutaneous or intravenous administration of metamizole at daily doses of 50, 150 or 450 mg/kg for 4 weeks were studied in rats and dogs and there was no morphological evidence of organic damage.

Chronic oral toxicity testing was carried out in rats and dogs in a dose range of 100 - 900 mg/kg/day and no morphological changes were observed.

In an oral fertility study in rats no influence on the fertility of the F1- and F2-generation was observed.

In teratogenicity studies there were no malformations observed.

There was no evidence of genotoxicity *in-vivo* and *in-vitro*. Carcinogenicity studies including transplacental carcinogenicity did not show tumorigenic potential.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Water for injectable preparations

6.2. Incompatibilities

This medicinal product should not be mixed with intravenous solutions of large volume pH correcting or for parenteral nutrition (amino acids, lipids).

Due to the possibility of incompatibilities, the solution for injection/infusion mixed with other medicinal products should not be injected or infused with the same syringe (see possible combinations with solutions for infusion in section 4.2)

6.3. Shelf life

3 years

6.4. Special precautions for storage

No special precautions for storage

6.5. Nature and contents of the container

Pack containing 5 or 100 amber glass ampoules of 5 ml for solution for injection/infusion.

6.6. Special precautions for disposal and other handling

(See section 4.2)

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

7. MARKETING AUTHORISATION HOLDER

Boehringer Ingelheim España, S.A.
Prat de la Riba, 50
08174 Sant Cugat del Vallès (Barcelona)
España

8. MARKETING AUTHORISATION NUMBER

42.304

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION:

Date of first authorisation: January 1966
Date of renewal of the authorisation: April 2009

10. DATE OF REVISION OF THE TEXT

November 2024