11 mm Text-free space

Front

7.5 mm Text-free space

Novalgin®

Metamizol Sodium 500mg/ml

SANOFI

Composition

Each ml of injection solution contains 500 mg metamizol sodium $1H_2O$, as active ingredient.

Properties

Novalgin has analgesic effects. As Novalgin can be injected intravenously, it is possible to obtain extremely potent analgesia in a variety of conditions and thus to control pain which would otherwise respond only to products containing opiates. Even in high doses, Novalgin, unlike opiates, cause neither addiction, nor respiratory depression. It does not interfere with intestinal peristalsis, labour contractions of the expulsion of calculi.

Indications

Novalgin injection solution must be used only when oral or rectal administration is inappropriate in the following indications:

- Severe pain, acute or chronic, e.g. in association with headache, toothache or tumours and after injuries or operations.
- Severe pain associated with smooth muscle spasms, acute or, chronic, e.g. muscular spasm or colic affecting the gastrointestinal tract, the biliary passages, kidneys or lower urinary tract.

Novalgin is not to be used in trivial complaints.

Contraindications

Novalgin must not be administrated to patients with:

- Allergy to metamizole or to other pyrazolones (e.g. phenazone, propyphenazone) or to pyrazolidines (e.g. phenylbutazone, oxyphenbutazone) including, for example, previously experienced agranulocytosis to one of these substances.
- Impaired bone marrow function (e.g. following cytostatic treatment) or diseases of the haematopoietic system.
- Patients known to develop bronchospasm or other anaphylactoid reactions (e.g. urticaria, rhinitis, angioedema) to analgesics such as: salicylates, paracetamol, diclofenac, ibuprofen, indometacin, naproxen.
- Allergy to any of the excipients of Novalgin
- Acute intermittent hepatic porphyria (risk of induction of porphyria attacks)
- Congenital glucose 6 phosphate dehydrogenase deficiency (risk of haemolysis).
- Infants under 3 months of age or 5 kg body weight.
- In infants between 3 and 11 months of age, NOVALGIN must not be injected by the intravenous route
- Novalgin must not be given parenterally in patients with hypotension or unstable hemodynamic.
- Pregnancy (see Section "Pregnancy")
- Lactation (see section "Lactation")

Precautions

- **Anaphylactic/anaphylactoid reactions**

When choosing the route of administration, it must be taken into consideration that parenteral administration is associated with a higher risk of anaphylactic/ anaphylactoid reactions.

In particular, the following patients are at special risk for possibly severe anaphylactoid reactions to metamizole (See Section " Contraindications"):

- Patients with bronchial asthma, particularly those with concomitant rhinosinusitis polyposa.
- Patients with chronic urticaria.
- Patients with alcohol intolerance, i.e. patients reacting to even minor quantities of certain alcoholic beverages with symptoms such as sneezing, lacrimation and pronounced redness of the face. Alcohol intolerance may be indicative of a previously undiagnosed analgesic asthma syndrome.
- Patients with intolerance to dyes (e.g. tartrazine) or to preservatives (e.g. benzoates).

Before Novalgin is administered, the patient must be questioned specifically. In patients found to be at special risk for anaphylactoid reactions, Novalgin must only be used after carefully weighing the possible risks against the expected benefit. If Novalgin is to be administered in such circumstances, close medical supervision is required and the facilities for immediate emergency treatment must be available.

- **Isolated hypotensive reactions**

Administration of metamizole may cause isolated hypotensive reactions (see also under "Adverse reactions"). These reactions are possibly dose-dependent and are more likely to occur following parenteral administration. In order to avoid severe hypotensive reactions of this kind:

- the intravenous injection should be given slowly.
- reverse hemodynamic in patients with pre-existing hypotension, with volume depletion or dehydration, or with circulatory instability or with incipient circulatory failure,
- care should be taken in patients with high fever.

In such patients, the indication for metamizole must be established with particular care and, if Novalgin is to be administered in such circumstances, close medical supervision is required. Preventive measures (hemodynamic stabilization) may be necessary to reduce the risk of a hypotensive reaction. Concerning patients with hypotension or unstable circulation, see under Section "Contra-indications".

Metamizole must only be used under close haemodynamic monitoring in patients in whom lowering of blood pressure must be avoided, such as in patients with severe coronary heart disease or stenoses of blood vessels supplying the brain.

In patients with renal or hepatic impairement, it is recommended that high metamizole doses be avoided, since its rate of elimination is reduced in these patients.

The intravenous injection must be given very slowly (not exceeding 1 ml per minute) to ensure that the injection can be halted at the first sign of an anaphylactic/anaphylactoid reaction (see under "Adverse reactions") and to minimize the risk of isolated hypotensive reactions.

WARNINGS :

Agranulocytosis induced by metamizole is an accident of immuno-allergic origin lasting for at least one week. These reactions are very rare, may be severe and life threatening, and could be fatal. They are not dose dependant and may occur at any time during treatment.
All patients should be advised to stop medication and consult their physician immediately if any of the following signs or symptoms possibly related to neutropenia occur: fever, chills, sore throat, ulcerations in oral cavity. In the event of neutropenia (< 1,500 neutrophils/mm3) treatment should be immediately discontinued and complete blood count should be urgently controlled and monitored until they return to normal values.

Anaphylactic shock: These reactions occur principally in sensitive patients. Therefore, metamizole should be prescribed with caution in asthmatic or atopic patients (See Section "Contraindications").

Adverse reactions

- Anaphylactic/anaphylactoid reactions

In rare instances, metamizole may cause anaphylactic/anaphylactoid reactions, which in very rare cases may be severe and life-threatening. They may occur even after Novalgin has previously been used on many occasions without complications.

Such reactions may develop during injection of metamizole or hours later; however, the usual pattern is for them to occur within the first hour after administration.

Typically, milder anaphylactic/anaphylactoid reactions manifest themselves in cutaneous and mucosal symptoms (such as itching, burning, reddening, urticaria, swellings), dyspnoea and less frequently - gastrointestinal complaints.

Milder reactions may progress to severe forms with generalized urticaria, severe angiooedema (even involving the larynx), severe bronchospasm, cardiac arrhythmias, drop in blood pressure (sometimes preceded by a rise in blood pressure), and circulatory shock.

In analgesic intolerant patients asthma syndrome, these reactions typically appear in the form of asthma attacks.

- Other cutaneous and mucosal reactions

Aside from the cutaneous and mucosal manifestations of anaphylactic/ anaphylactoid reactions mentioned above, fixed drug eruptions may occur occasionally, rash may occur rarely, as may Stevens-Johnson syndrome or Lyell's syndrome in isolated cases.

SA//A-1123

210 mm

25 mm

10 mm

150 mm

• Haematological reactions

Rarely, leucopenia and, in very rare cases, agranulocytosis or thrombopenia may develop. These reactions are regarded to be immunological in nature. They may occur even after Novalgin has previously been used on many occasions without complications. Agranulocytosis may be life-threatening, and could be fatal.

Typical signs of agranulocytosis include inflammatory mucosal lesions (e.g. oropharyngeal, anorectal, genital), sore throat, fever (even unexpectedly persistent or recurring fever). However, in patients receiving antibiotic therapy typical signs of agranulocytosis may be minimal. Erythrocyte sedimentation rate is greatly increased, whereas enlargement of lymph nodes is typically slight or absent.

Typical signs of thrombopenia include an increased tendency to bleeding and petechiae on the skin and mucous membranes.

• Isolated hypotensive reactions

Occasionally, isolated transitory hypotensive reasctions (possibly pharmacologically mediated and not accompanied by other signs of an anaphylactic/anaphylactoid reaction) may occur during or after administration; in rare cases, this reaction takes the form of a critical drop in blood pressure. Rapid intravenous injection may increase the risk for such a hypotensive reaction.

• Other reactions

In very rare instances, especially in patients with a history of renal disease, acute worsening of renal function (acute renal failure), in some cases with oliguria, anuria or proteinuria may occur. Acute interstitial nephritis may occur in isolated cases.

Pain and local reactions may occur at the injection site. These may sometimes include phlebitis.

A red coloration has been sometimes observed in the urine, which may be due to a metabolite present at low concentration: rubazonic acid.

PREGNANCY

Metamizole crosses the placenta. There is no evidence that the drug is harmful to the fetus: metamizole did not show teratogenic effects in rats and rabbits, and fetotoxicity was observed only at high dose levels that were maternally toxic. There is, however, insufficient clinical data on the use of Novalgin during pregnancy.
Therefore, it is recommended that Novalgin is not used during the first three months of pregnancy, and that it is used in the following three months only after careful weighing of potential benefit and risk by a physician.

Novalgin must, however, not be used during the last three months of pregnancy. This is because, although metamizole is only a weak inhibitor of prostaglandin synthesis, the possibility of premature ductus arteriosus closure and perinatal complications due to impairment of both maternal and neonatal platelet aggregability cannot be ruled out.

LACTATION

Metamizole metabolites are excreted into the breast milk. Breast-feeding must be avoided during and for 48 hours after administration of Novalgin.

DRIVING A VEHICLE OR PERFORMING OTHER HAZARDOUS TASKS

For the recommended dosage range, no adverse effect on the ability to concentrate and react is known.

However, at least for higher doses, it should be taken into account that the ability to concentrate and react might be impaired, constituting a risk in situations where these abilities are of special importance (e.g. operating a car or machinery), especially when alcohol has been consumed.

INTERACTIONS

Precaution for use

Metamizole may cause a reduction in serum cyclosporine concentration must, therefore, be monitored when metamizole is administered concomitantly.

Dosage

Unless otherwise prescribed, the following dosages are recommended:

Adults and adolescents aged 15 years or overs:

As a single dose, 2 - 5 ml (i.v. or i.m.); as a daily dose up to 10 ml of injection solution.

OVERDOSE:

• Signs and Symptoms:

Reactions such as nausea, vomiting, abdominal pain, impairment of renal function/acute renal failure (e.g. due to interstitial nephritis) and, more rarely, central nervous symptoms (dizziness, somnolence, coma, convulsions) and drop in blood pressure (sometimes progressing to shock) as well as cardiac arrhythmias (tachycardia) have been reported following acute overdose. After very high doses, the excretion of a harmless metabolite (rubazonic acid) may cause red discoloration of the urine.

• Management:

No specific antidote for metamizole is known. If ingestion has only just taken place, attempts may be made to limit further systemic absorption of the active ingredients through measures for primary detoxification (e.g. gastric lavage) or those designed to reduce absorption (e.g. activated charcoal). The main metabolite (4 N-methylaminoantipyrine) can be eliminated by haemodialysis, haemofiltration, haemoperfusion or plasma filtration.

Mode of administration

The requirements for the treatment of shock should be met.

The solution should be warmed to body temperature prior to injection.

The commonest cause of a critical drop in blood pressure and shock is an unduly rapid rate of injection. Therefore, intravenous injections must be given slowly (not more than 1 ml per minute) with the patient lying down. The blood pressure, heart rate, and respiration must be monitored.

In view of the suspicion that the non-allergic drop in blood pressure is dose-dependent, the indication for the administration of doses higher than 1 g should be particularly carefully considered.

Special notes

Because of the possibility of incompatibilities, Novalgin must not be mixed with other drugs in the syringe.

An occasional red coloration of the urine is harmless. It is due to the excretion of rubazonic acid, an innocuous metabolite.

Expiry date

Do not use later than the date of expiry.
Keep medicines out of the reach of children.

Storage:
Store at room temperature (25°-30°C)

Presentation
Injection solution (50%):
5 ampoules of 2 ml
Reg. No.:

Also available: oblong tablets, drops and syrup.

Emergency measures to be taken in the event of anaphylactic shock

Generally, the following emergency procedure is recommended:

At the first signs (sweating, nausea, cyanosis) interrupt the injection immediately, but leave the venous cannula in place or perform venous cannulation. In addition to the usual emergency measures ensure that the patient remains lying, with the legs raised and airways patent.

Emergency drug therapy
Immediately epinephrine (adrenaline) i.v.: Dilute 1 ml of commercially available epinephrine solution 1:1000 to 10 ml. In the first instance, slowly inject 1 ml of this dilution (equivalent to 0.1 mg epinephrine) while monitoring pulse and blood pressure (watch for disturbances of cardiac rhythm). Repeat as required.

Then glucocorticoids i.v., e.g., 250-1000 mg methylprednisolone.
Repeat as required.

Subsequently volume substitution i.v., e.g., plasma expanders, human albumin, balanced electrolyte solution.

Other therapeutic measures: Artificial respiration, oxygen inhalation, antihistamines.

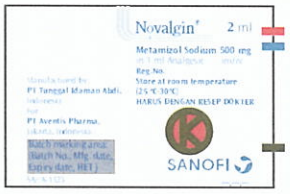
HARUS DENGAN RESEP DOKTER
ON MEDICAL PRESCRIPTION ONLY

Manufactured by:
PT Tunggal Idaman Abdi, Indonesia
for
PT. Aventis Pharma,
Jakarta - Indonesia

SAP / ID. number : PACKING INSERT NOVALGIN INJECTION/XXXXXX
Version number : 1A
Country : Indonesia
Date : 11.12.2013
Dimensions : 150 x 210 mm
Logo version : sanofi-aventis
Version SCV A2 - 03.04.2007
(replaces Version SCV A1 - 28.09.2005)
Film code : SA//A-1123
Min. point size of text: 6.5 pt
Type of texts : OCEAN SANS PRO SAN FAMILY
Colour : PMS Pantone Reflex Blue CVC
Pharmacode : XXXXX
Material : HVS 60 g/m²
Prepared by : Bambang Iswahyudi

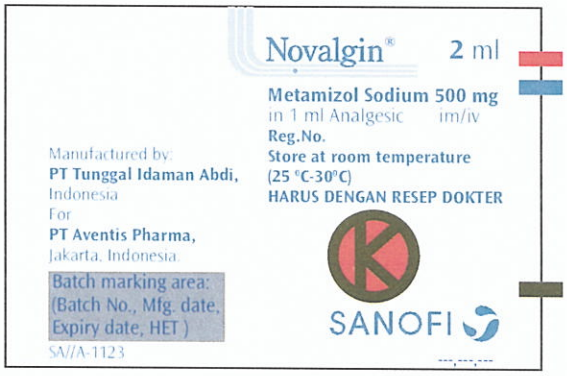
SAP / ID. number : FOLDING BOX NOVALGIN INJECTION /XXXXXX
Version number : 1A
Country : Indonesia
Date : 28.08.2013
Dimensions : 78 x 72 x 23 mm
Logo version : sanofi-aventis
Version A2 - 03.04.2007
(replaces Version A1 - 27.09.2005)
Film code : SA//A-1123
Colours
: Pantone Reflex Blue CVC
: Pantone 186 CVC
: Pantone Black CVC
: Pantone 376 CVC
: Pantone 5415 CVC
: Pantone 3435 CVC
: Pantone 485 CVC
Material : Ivory Coated 300g/m²
Prepared by : Bambang Iswahyudi

Note : Batch marking (batch no, Mfg date, Exp. Date & HET) will not appear on the film. It will be printed using inkjet printer



Note : Batch marking (batch no, Mfg date, Exp. Date & HET) will not appear on artwork. It will be printed in supplier

Scale Up 200 %



SAP / ID. number : STICKER LABEL Novalgin Injection/XXXXXX
Version number : 1A
Country : Indonesia
Date : 12.12.2013
Dimensions : 37 x 25 mm
Logo version : sanofi-aventis
Version SCV A2 - 03.04.2007
(replaces Version SCV A1 - 28.09.2005)
Film code : SA//A-1123
Min. point size of text : 7 Pt
Colours : PMS Pantone 5415 CVC
: PMS Pantone Black
: PMS Pantone 186 CVC
Material : Chromecoated paper 85g/m² self adhesive
Prepared by : Bambang Iswahyudi

PEMERIKSAAN ARTWORK			
Distribusi	**Items to be check**	**Komentar**	**Paraf/Tanggal**
Purchasing	Type & Quality of material used	Ok/Not Ok Ok setelah koreksi	
Product Manager	Artwork lay-out (correctness of teks, lay-out, type & Quality of material used)	Ok/Not Ok Ok setelah koreksi	
Registration	Correctness of text, registration number & storage condition	Ok/Not Ok Ok setelah koreksi	
Packaging	Dimension, lay out, die cut, folded and position for batch marking area	Ok/Not Ok Ok setelah koreksi	
Quality Control	Code bars, colours, storage condition & film code	Ok/Not Ok Ok setelah koreksi	
IQC	Artwork design based on PMS guide & film code	Ok/Not Ok Ok setelah koreksi	
Plant Logistic	Material code & implementation	Ok/Not Ok Ok setelah koreksi	