Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Dicynene 250mg/2 ml Solution for Injection.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient is etamsylate 125mg/ml of injection solution.
(250mg per 2 ml ampoule).

Excipients: Each 2ml ampoule also contains 0.8mg of sodium metabisulphite (E223)

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Solution for injection (injection).
A clear, colourless, aqueous solution for injection (pH 6.2 to 6.8).

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Dicynene injection is indicated in neonates.

Dicynene injection is used clinically for the prophylaxis and treatment of periventricular haemorrhage (bleeding into the brain immediately adjacent to cerebralventricles) in low birth weight infants (< 1.5 Kg).

4.2 Posology and method of administration

Neonates only :

The normal dosage is 12.5mg/kg body weight given by intravenous or intramuscular route within an hour of birth and every six hours for the first 4 days of life.

Clinical studies have not been performed in patients presenting hepatic or renal impairment. Consequently, caution is required when administering Dicynene injection to these patients.

4.3 Contraindications

Use in patients with a known hypersensitivity to etamsylate or to any of the excipients.
Acute porphyria
Bronchial asthma, confirmed hypersensitivity to sulphites.

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4.4 Special warnings and precautions for use

Dicynene injection is intended for neonatal use only.

If the infant develops a fever then treatment should be discontinued.

Due to the risk of a fall in blood pressure during parenteral administration, caution is required in patients presenting unstable pressure or hypotension (see section 4.8 “undesirable effects”).
Dicynene injection solution contains sodium metabisulphite as antioxidant, which may cause allergic reactions, nausea

and diarrhoea in susceptible patients.
The allergic reactions may go as far as anaphylactic shock and cause life threatening
asthma attacks. The prevalence in the population is not known but is probably low. However, hypersensitivity to sulphites is observed more frequently in patient with asthma than in those without asthma (see section 4.3 "Contraindications"). If a hypersensitivity reaction occurs, the administration of Dicynene injection solution must be stopped immediately.

4.5 Interaction with other medicinal products and other forms of interaction

Dicynene injection is incompatible with solutions of sodium bicarbonate and compound sodium lactate.

When Dicynene injection is mixed with saline it should be used immediately.

Thiamine (vitamin B1) is inactivated by the sulphite contained in Dicynene injection.
If a dextran infusion is required, Dicynene must be injected first.

4.6 Fertility, pregnancy and lactation

Clinical use is not relevant for this indication.
There are no clinical data available concerning use in pregnant women.
Animal experiments have not revealed any direct or indirect toxicity affecting pregnancy, embryonic development, foetal development and/or post-natal development.
Caution is required if used during pregnancy.
In the absence of data concerning passage into breast milk, breast-feeding is inadvisable during treatment. Alternatively, the treatment should be stopped if breast-feeding is continued.

4.7 Effects on ability to drive and use machines

Not applicable in this population.

In adults, DICYNENE injection has no effect upon driving capacity and managing of machines.

4.8 Undesirable effects

In infants no major side-effects have been reported.

In adults, the following side effects were described. These side effects are classified according to the MedDRA convention by system organ class and by frequency 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), not known (cannot be estimated from the available data)

Gastrointestinal disorders
Common: nausea, diarrhoea, abdominal discomfort.

Skin and subcutaneous tissue disorders
Common: rash.

General disorders and administration site conditions
Common: asthenia
Very rare: fever.

Nervous system disorders
Common: headache.

Vascular disorders
Very rare: thromboembolism, hypotension.

Blood and lymphatic system disorders
Very rare: agranulocytosis, neutropenia, thrombocytopenia

Musculoskeletal and connective tissue disorders
Rare: arthralgia

Immune system disorders
Very rare: hypersensitivity

These reactions are generally reversible when stopping treatment course.
In case of skin reactions or fever, the treatment must be stopped and the treating physician informed as this may constitute hypersensitivity reactions.

4.9 Overdose

There is no experience of overdosage with Dicynene.
In the event of any overdose, start symptomatic treatment.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code: B02B X01
Other systemic haemostatics.

Dicynene is a non-hormonal agent which reduces capillary exudation and blood loss. Dicynene does not affect the normal coagulation mechanism since administration is without effect on prothrombin times, fibrinolysis, platelet count or function.

Dicynene is thought to act by increasing capillary vascular wall resistance and platelet adhesiveness; in the presence of a vascular lesion, it inhibits the biosynthesis and action of those prostaglandins which cause platelet disaggregation, vasodilation and increased capillary permeability. Dicynene does not have a vasoconstricting action.

5.2 Pharmacokinetic properties

Following intravenous administration maximum blood levels of etamsylate are achieved in 2-3 minutes, while after intramuscular injection, maximum blood levels of etamsylate are achieved after about one hour. Etamsylate is excreted unchanged, largely by the urinary route.

5.3 Preclinical safety data

No further information is available.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium metabisulphite (E223)
Sodium hydrogen carbonate (for pH adjustment)
Water for injections

6.2 Incompatibilities

Dicynene injection is incompatible with solutions of sodium bicarbonate and compound sodium lactate.

6.3 Shelf life

Unopened: 3 years
Once opened: from a microbiological point of view the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are responsibility of the user and would normally not be longer than 24 hours at 2 to 8 ^{o}C, unless dilution has taken place in controlled and validated aseptic conditions

6.4 Special precautions for storage

Store below 25°C. Keep the ampoule in the outer carton.

6.5 Nature and contents of container

2 ml clear, Type I glass ampoules containing a colourless, sterile, aqueous solution.
Outer cartons containing 10 X 2 ml ampoules.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

Discard if solution is coloured.
For single use only, any remaining solution should be discarded.

7 MARKETING AUTHORISATION HOLDER

OM PHARMA S.A.
R. da Industria 2
Quinta Grande
2610-088 Amadora
Lisboa
Portugal

8 MARKETING AUTHORISATION NUMBER

PA 1108/1/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of last renewal: 1st April 2008

10 DATE OF REVISION OF THE TEXT

October 2012