Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Indocollyre 0.1%, eye drops

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

When reconstituted each 5ml contains 5mg of Indometacin, as a 0.1% w/v solution.

For excipients, see 6.1

3 PHARMACEUTICAL FORM

Eye drops, powder and solvent for solution. The appearance of the powder in the vial is white to cream-coloured. The solvent solution appears as a clear, colourless and viscous solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

- Prevention of per-operative miosis during cataract surgery.
- Prevention of inflammatory manifestations related to surgical operations for cataract and to anterior segment of the eye.

4.2 Posology and method of adminstration

Adults

- Prevention of per-operative miosis during cataract surgery, 1 drop every 30 minutes within 2 hours preceding the operation.
- Prevention of inflammatory manifestations related to cataract and to anterior segment of the eye surgery.
- 1 drop 4 to 6 times a day before operation, 1 drop every 30 minutes within 2 hours preceding the operation, and 1 drop 4 times per day for one month.
- To administer treatment, gently pull down the lower lid of the eye and apply one drop of solution while looking upwards.

Children
Safety and efficacy of use in children has not been established.

4.3 Contraindications

This product is contra-indicated in the following situations:

- from the 6th month of pregnancy onwards (see: Pregnancy and Breast-feeding),
- allergy to indomethacin or to drugs with similar activity e.g. other non-steroidal anti-inflammatory drugs or aspirin, allergy to the preservative (thiomersal),
- previous asthma attacks caused by aspirin or other non-steroidal anti-inflammatory drugs.

In general, this product should not be taken:

– in combination with other NSAIDs including high doses of salicylates, oral anticoagulants, injectable heparin, lithium, high doses of methotrexate, ticlopidine, diflunisal (see section: Drug interactions and other forms of interaction),
– during the first 5 months of pregnancy (see: Pregnancy and Breast-feeding),
– during breast-feeding (see: Pregnancy and Breast-feeding).

4.4 Special warnings and special precautions for use

Warning

- Children: no specific studies have been conducted in children.

Precautions of use

- If hypersensitivity is noted, stop the treatment.
- Prescribe appropriate treatment in cases presenting a risk of eye infection.
- A NSAID may retard corneal healing.
- A NSAID may increase bleeding of ocular tissues during surgery, notably in patients with a known tendency to bleed or those receiving other treatments liable to prolong bleeding.
- It is inadvisable to wear contact lenses during treatment with INDOCOLLYRE 0.1% (5 mg/5 ml).
- If at the same time the patient is receiving treatment with another eye-drop preparation containing a different active substance, administer the two solutions at least 15 minutes apart.
- Do not touch the eye with the tip of the bottle.

4.5 Interaction with other medicinal products and other forms of interaction

To avoid diluting the active ingredients, instill products at least 15 minutes apart. If necessary, indometacin administered by ocular route can be combined with eye-drops containing corticosteroids.

Although only small amounts of NSAID pass into the systemic bloodstream after ocular instillation, drugs interactions are nevertheless possible. It is therefore advisable to take account of the interactions observed with NSAIDS administered by general route.

Inadvisable combinations:

- **other NSAIDS, including high doses of salicylates:** increased risk of inducing GI tract ulcers and bleeding through synergy.

- **oral anticoagulants, parenteral heparin:** increased risk of bleeding through inhibition of platelet function and damage to gastro-duodenal mucosa by NSAIDs.
  If such a combination is unavoidable, close clinical and laboratory monitoring is required.

- **lithium** (described with other NSAIDs): lithium blood levels may increase to toxic levels; this effect is due to decreased lithium excretion by the kidney.
  If necessary, monitor lithium blood levels closely and adjust the lithium dosage during combined treatment then after the NSAID is withdrawn.

- **high doses of methotrexate, i.e. 15 mg/week or more:** methotrexate haematological toxicity increases as its renal clearance is decreased by anti-inflammatory drugs.

- **diflunisal:** fatal GI tract bleeding with increased plasma levels of indomethacin (competition for glucuronide conjugating enzymes).

- **ticlopidine:** increased risk of GI tract ulcers and bleeding because of synergy. If such a combination is

unavoidable, close clinical and laboratory monitoring is required, including bleeding time.

Combinations requiring precautions

- **diuretics:** risk of acute renal insufficiency in dehydrated patients caused by decreased glomerular filtration secondary to reduced synthesis of renal prostaglandins.
  Hydrate the patient and monitor kidney function at the start of the treatment.

- **low doses of methotrexate, less than 15 mg/week:** methotrexate haematological toxicity increases as its renal clearance is decreased by anti-inflammatory drugs.
  Weekly haemogram control over the first few weeks of the combination. Increased monitoring if even slight changes occur in kidney function and in elderly patients.

- **pentoxifylline:** increased risk of bleeding.
  Reinforce clinical monitoring and control bleeding time more frequently.

- **zidovudine:** increased risk of red cell toxicity by action on reticulocytes resulting in severe anaemia 8 days after starting the NSAID.
  Control blood count and reticulocytes 8 to 15 days after starting treatment with the NSAID.

Combinations to take into account:

- **antihypertensives such as beta-blockers, ACE inhibitors, diuretics** (by extrapolation from indometacin): reduced antihypertensive effect because the NSAID inhibits the vasodilating prostaglandins;

- **intra-uterine device:** controversial risk of reduced efficacy;

- **thrombolytics:** increased risk of bleeding;

- **desmopressin:** potentiation of anti-diuretic activity.

4.6 Pregnancy and lactation

Pregnancy
No particular malformations have been reported in humans. However, supplementary epidemiological studies are required to confirm that there is no risk.

During the 3rd trimester of pregnancy all inhibitors of prostaglandin synthesis may expose:
- the foetus:
- to cardiopulmonary toxicity (pulmonary hypertension with premature closure of the arterial canal);
- to renal malfunction which may reach renal insufficiency with oligohydramnios.
- the mother and the child at the end of pregnancy to increased bleeding time.

As a precautionary measure, all NSAIDs should therefore be avoided during the first 5 months of pregnancy and are then contra-indicated from the 6th month onwards.

Breast-feeding
As NSAIDs pass into the mother's milk, it is inadvisable to administer these products to women who are breast-feeding.

4.7 Effects on ability to drive and use machines

These eye drops may cause transient blurred vision after instillation. It is recommended not to drive or use machinery until vision has cleared.

4.8 Undesirable effects

Occasional effects:

- a slight, transient burning or stinging sensation and/or vision disorders may occur after instillation

Rare effects:

- hypersensitivity reaction with pruritus and redness
- possible photosensitivity
- punctate keratitis

4.9 Overdose

No available data.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

NON-STEROIDAL ANTI-INFLAMMATORY DRUG for topical use.
(S: sense organs)

Indometacin is an inhibitor of prostaglandin synthetase and is one of the indol group of products.

5.2 Pharmacokinetic properties

No data available.

5.3 Preclinical safety data

No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Boric acid
Dextran
Disodium edetate
Methyl-parahydroxybenzoate
Macrogol 400
Purified water
Sodium borate

6.2 Incompatibilities

None known.

6.3 Shelf Life

Unopened: 18 months
Following reconstitution: 15 days

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

Lyophilisate: a glass vial, with an elastomer stopper, sealed with a PVC film.
Solvent: 5 ml, low-density polyethylene bottle with a polypropylene screw cap.
Reconstituted eye drops: A glass vial fitted with a polyvinylchloride dropper.

6.6 Instructions for use and handling

Container A: Is the vial containing the lyophilisate.
Container B: Is the polyethylene bottle containing the solvent used to reconstitute the lyophilisate.
Carefully remove the seal from the container A. Unscrew the cap from container B and by gently squeezing container B empty all of the contents into container A. Carefully remove the dropper from its packaging and push firmly onto the vial. Mix the product thoroughly before use.

When reconstituted the product appears as a clear solution.

7 MARKETING AUTHORISATION HOLDER

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