SUMMARY OF PRODUCT CHARACTERISTICS

1  NAME

INOCOLLYRE 0.1%  Eye drops
(Indomethacin 0.1%)

2.  LIST OF EXCIPIENTS
See section 6.1

3.  PHARMACEUTICAL FORM
Eye drops. Bottles containing 5 ml.

4.  CLINICAL DATA

4.1  Therapeutic indications

- Inhibition of myosis during surgery.
- Prevention of inflammation subsequent to cataract surgery or surgery of the anterior chamber of the eye.
- Treatment of ocular pain following photorefractive keratectomy for the first few days after surgery.

4.2  Dosage and route of administration

Topical route.
BY OCULAR INSTILLATION.

Dosage in adults

- inhibition of myosis during surgery:
  4 drops the day before surgery and 4 drops in the 3 hours preceding surgery.

- prevention of inflammation subsequent to cataract surgery or surgery of the anterior chamber of the eye:
  1 drop 4 to 6 times daily until complete disappearance of symptoms, starting the treatment 24 hours before surgery.

- treatment of ocular pain following photorefractive keratectomy:
  1 drop 4 times daily for the first few days after surgery.

To administer the treatment, gently pull down the lower lid of the eye and apply one drop of solution while looking upwards.
4.3 Contra-indications

This product is contra-indicated in the following situations:
- from the 6th month of pregnancy onwards (see: Pregnancy and Breast-feeding),
- documented allergy to diclofenac or to drugs with similar activity e.g. other non-steroidal anti-inflammatory drugs (NSAIDs) or aspirin,
- previous asthma attacks caused by aspirin or other NSAIDs,
- active peptic ulcer,
- severe hepatocellular failure,
- severe renal insufficiency.

In general, this medication should not be taken in combination with: (See Drug interactions)
- oral anticoagulants,
- others NSAIDs (including high doses of salicylates, i.e. from 3 g/day in adults),
- heparin,
- lithium,
- high doses of methotrexate,
- ticlopidine.

4.4 Warnings and special precautions

Warnings:

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 the bleeding of ocular tissues during surgery, notably in patients with a known tendency to bleed or in those receiving other treatments liable to prolong bleeding.
- It is inadvisable to wear contact lenses during treatment with INDOCOLLYRE 0.1%.
- 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 Drug interactions and other forms of interaction

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

*Although only small amounts of indomethacin pass into the systemic bloodstream after ocular instillation, drug interactions are nevertheless possible. It is therefore advisable to take account of the interactions observed with NSAIDs administered by general route.*
INADVISABLE COMBINATIONS

++ Oral anticoagulants
Increased risk of the oral anticoagulant causing bleeding (platelet function inhibited and gastro-duodenal mucosa damaged by NSAIDs).
If such a combination is unavoidable, close clinical and laboratory supervision is required.

++ Other NSAIDs
(including salicylates at more than 3 g/day in adults)
Increased risk of inducing GI tract ulcers and bleeding (synergism).

++ Diflunisal
Fatal GI tract bleeding with increased plasma concentrations of indomethacin (competition for glucuronide conjugating enzymes).

++ Heparins
Increased risk of bleeding (inhibition of platelet function and damage to the gastro-duodenal mucosa by NSAIDs).
If such a combination is unavoidable, close clinical supervision (and laboratory monitoring for unfractionated heparins) is required.

++ Lithium
Described for diclofenac, ketoprofen, indomethacin, phenylbutazone, piroxicam
Lithium blood levels may increase to toxic levels (reduced lithium excretion by the kidneys).
If such a combination is unavoidable, monitor lithium blood levels closely and adjust the dosage during combined treatment then after the non-steroidal anti-inflammatory drug is withdrawn.

++ Methotrexate used at doses of 15 mg/week or more
Methotrexate haematological toxicity increases as its renal clearance is decreased by anti-inflammatory drugs.

++ Ticlopidine
Increased risk of bleeding (synergism of anti-platelet activities).
If such a combination is unavoidable, close clinical and laboratory supervision is required, including bleeding time.

COMBINATIONS REQUIRING PRECAUTIONS

++ Diuretics, angiotensin-converting enzyme (ACE) inhibitors
Acute renal insufficiency in dehydrated patients (decreased glomerular filtration by NSAID inhibition of vasolating prostaglandins).
In addition, reduced antihypertensive effect.
Hydrate the patient and monitor kidney function at the start of the treatment.

++ Methotrexate used at doses of less than 15 mg/week
Methotrexate haematological toxicity increases as its renal clearance is decreased by anti-inflammatory drugs.
Weekly blood cell count over the first few weeks of combined treatment.
Closer supervision in cases showing even slight modifications in renal function, and in the elderly.
+- **Pentoxifylline**  
Increased risk of bleeding.  
Reinforce clinical monitoring and control bleeding time more frequently.

+- **Gastrointestinal topical** salts, oxides and hydroxides of magnesium, aluminium and calcium).  
Decreased gastrointestinal absorption of indomethacin.  
Any antacids should be well spaced from the indomethacin (more than 2 hours if possible).

+- **Zidovudine**  
Increased risk of red cell toxicity (effect on reticulocytes) with 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**

+- **Beta-blockers**  
*By extrapolation from indomethacin*  
Reduced antihypertensive effect (NSAIDs inhibit vasodilating prostaglandins).

+- **Ciclosporin**  
Risk of exacerbated nephrotoxicity, particularly in the elderly.

+- **Desmopressin**  
Potentiation of anti-diuretic activity.

+- **Intra-uterine device**  
Risk of reducing IUD efficacy (though this is controversial).

+- **Thrombolytics**  
Increased risk of bleeding.

### 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 possible risk.

In 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 possible increased bleeding time.

In consequence, indomethacin should only be given if absolutely necessary over the first 5 months of pregnancy.  
Indomethacin is contra-indicated from the 6th month of pregnancy onwards.
Lactation

In view of the fact that NSAIDs pass into mother’s milk, their administration in women who are breast-feeding should be avoided as a precautionary measure.

4.7 Effects on ability to drive and use machines

Possible vision disorders after instillation.

4.8 Undesirable effects

Occasional effects:

A slight transient burning or stinging, and/or vision disorders may occur after instillation.

Rare effects:

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

4.9 Overdose

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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

Indomethacin is an inhibitor of prostaglandin synthetase and belongs to the indol group of products.

5.2 Pharmacokinetic properties

5.3 Preclinical safety data

Not applicable.

6. PHARMACEUTICAL DATA

6.1 List of excipients

Thiomersal, arginine, hydroxypropyl-beta-cyclodextrin, concentrated hydrochloric acid, purified water.
6.2. Incompatibilities

6.3 Special storage precautions

Store below 25°C.
Use within 15 days of opening.

6.4 Presentation
Bottles of 5 ml.

7. REGISTRATION NUMBER 134 33 30058 00

8 MANUFACTURER
Laboratoire Chauvin
France.

9. IMPORTER
Salomon, Levin & Elstein Ltd.,
P.O.Box 3696, Petach-Tikva.