ANNEX I

LIST OF THE NAMES, PHARMACEUTICAL FORMS, STRENGTHS OF THE MEDICINAL PRODUCTS, ROUTE OF ADMINISTRATION, MARKETING AUTHORISATION HOLDERS IN THE MEMBER STATES

Member State	Marketing Authorisation Holder	Product name	Strength	Pharmaceutical form	Route of administration
Austria	Takeda Pharma Ges.m.b.H. Seidengasse 33-35 1070 Vienna, Austria	AGOPTON	15 mg	Capsule	Oral use
		AGOPTON	30 mg	Capsule	Oral use
		AGOPTON Rapid	15 mg	Oro-dispersible tablet	Oral use
		AGOPTON Rapid	30 mg	Oro-dispersible tablet	Oral use
Belgium	Sanofi-Synthelabo SA NV Dobbelenberg, 5, Avenue de la Metrologie 1130 Brussels, Belgium	DAKAR	15mg	Capsule	Oral use
		DAKAR	30 mg	Capsule	Oral use
		NIBITOR	30 mg	Capsule	Oral use
Denmark	Wyeth AB BOX 1822, 171 24 Solna, Sweden	LANZO	15 mg	Capsule	Oral use
		LANZO	30 mg	Capsule	Oral use
Finland	Wyeth AB BOX 1822, 171 24 Solna, Sweden	LANZO	30 mg	Capsule	Oral use
		LANZO	15 mg	Oro-dispersible tablet	Oral use
		LANZO	30 mg	Oro-dispersible tablet	Oral use
France	Laboratoires TAKEDA SA 15, quai de Dion Bouton 92816 Puteaux cedex, France	OGAST	15 mg	Capsule	Oral use
		OGAST	30 mg	Capsule	Oral use
	sanofi-aventis 46 quai de la Papee 75601 Paris Cedex 12, France	LANZOR	15 mg	Capsule	Oral use
		LANZOR	30 mg	Capsule	Oral use
Germany	Takeda Pharma GmbH Viktoriaallee 3-5 52066 Aachen, Germany	AGOPTON	15 mg	Capsule	Oral use
		AGOPTON	30 mg	Capsule	Oral use
		LANZOR	15 mg	Capsule	Oral use
		LANZOR	30 mg	Capsule	Oral use

Greece	Vianex S.A.	LAPRAZOL	15 mg	Capsule	Oral use
		LAPRAZOL	30 mg	Capsule	Oral use
		LAPRAZOL FasTab	15 mg	Oro-dispersible tablet	Oral use
		LAPRAZOL FasTab	30 mg	Oro-dispersible tablet	Oral use
Hungary	Gedeon Richter H-1103 Budapest, Gyomroi ut 19-21 Hungary	LANSONE	30 mg	Capsule	Oral use
Ireland	John Wyeth & Brother Limited Trading as Wyeth Pharmaceuticals Huntercombe Lane South Taplow, Maidenhead Berkshire SL6 0PH UK	ZOTON	15 mg	Capsule	Oral use
		ZOTON	30 mg	Capsule	Oral use
		ZOTON FasTab	15 mg	Oro-dispersible tablet	Oral use
		ZOTON FasTab	30 mg	Oro-dispersible tablet	Oral use
	Cyanamid of Great Briain Ltd. Fareham Road, GOSPORT Hampshire PO13 0AS, UK	ZOTON	30mg	Gastro-resistant granules for oral suspension	Oral use
Italy	Takeda Italia Farmaceutici S.p.A. Via Elio Vittorini 129 00144 Roma, Italy	LANSOX	15 mg	Capsule	Oral use
		LANSOX	30 mg	Capsule	Oral use
		LANGAST	15 mg	Capsule	Oral use
		LANGAST	30 mg	Capsule	Oral use
		LANSOX	15 mg	Oro-dispersible tablet	Oral use
		LANSOX	30 mg	Oro-dispersible tablet	Oral use
		LANGAST	15 mg	Oro-dispersible tablet	Oral use
		LANGAST	30 mg	Oro-dispersible tablet	Oral use
	Sigma-Tau S.p.A. Via Pontina km. 30,400 00040 Pomezia, Roma, Italy	LIMPIDEX	15 mg	Capsule	Oral use
		LIMPIDEX	30 mg	Capsule	Oral use
		LIMPIDEX	15 mg	Oro-dispersible tablet	Oral use

		LIMPIDEX	30 mg	Oro-dispersible tablet	Oral use
	Wyeth Lederle S.p.A. Via Nettunense 90 04011 Aprilia (LT), Italy	ZOTON	15 mg	Capsule	Oral use
		ZOTON	30 mg	Capsule	Oral use
		ZOTON	15 mg	Oro-dispersible tablet	Oral use
		ZOTON	30 mg	Oro-dispersible tablet	Oral use
Luxembourg	Sanofi-Synthelabo SA NV Dobbelenberg, 5, Avenue de la Metrologie 1130 Brussels, Belgium	DAKAR	15 mg	Capsule	Oral use
		DAKAR	30 mg	Capsule	Oral use
Netherlands	Sanofi-Synthelabo B.V. / Aventis Pharma B.V. Kampenringweg 45 D-E (toren D en E), 2803 PE GOUDA, The Netherlands	PREZAL	15 mg	Capsule	Oral use
		PREZAL	30 mg	Capsule	Oral use
Portugal	Seber Portuguesa Farmaceutica, SA Rua Norberto de Oliveira,1a 5 2675-130 Povoa de Santo Adriao, Portugal	OGASTO	15 mg	Capsule	Oral use
		OGASTO	30 mg	Capsule	Oral use
		OGASTO	15 mg	Oro-dispersible tablet	Oral use
		OGASTO	30 mg	Oro-dispersible tablet	Oral use
Spain	Almirall Prodesfarma, S.A. General Mitre, 151 08022 -Barcelona, Spain	OPIREN	15 mg	Capsule	Oral use
		OPIREN	30 mg	Capsule	Oral use
		BAMALITE	15 mg	Capsule	Oral use
		BAMALITE	30 mg	Capsule	Oral use
		OPIREN Frash	15 mg	Oro-dispersible tablet	Oral use
		OPIREN Frash	30 mg	Oro-dispersible tablet	Oral use
		BAMALITE Frash	15 mg	Oro-dispersible tablet	Oral use
		BAMALITE Frash	30 mg	Oro-dispersible tablet	Oral use
Sweden	Wyeth AB BOX 1822, 171 24 Solna, Sweden	LANZO	15 mg	Capsule	Oral use
		LANZO	30 mg	Capsule	Oral use
		LANZO	15 mg	Oro-dispersible tablet	Oral use

		LANZO	30 mg	Oro-dispersible tablet	Oral use
United Kingdom	John Wyeth & Brother Limited Trading as Wyeth Pharmaceuticals Huntercombe Lane South Taplow, Maidenhead Berkshire SL6 0PH UK	ZOTON	15 mg	Capsule	Oral use
		ZOTON	30 mg	Capsule	Oral use
		ZOTON	30 mg	Gastro-resistant granules for oral suspension	Oral use
		ZOTON FasTab	15 mg	Oro-dispersible Tablet	Oral use
		ZOTON FasTab	30 mg	Oro-dispersible Tablet	Oral use

Iceland	Wyeth AB BOX 1822, 171 24 Solna, Sweden	LANZO	15 mg	Capsule	Oral use
		LANZO	30 mg	Capsule	Oral use
		ZOTON	15 mg	Capsule	Oral use
		ZOTON	30 mg	Capsule	Oral use
		LANZO	15 mg	Oro-dispersible tablet	Oral use
		LANZO	30 mg	Oro-dispersible tablet	Oral use
Norway	Wyeth AB BOX 1822, 171 24 Solna, Sweden	LANZO	15 mg	Capsule	Oral use
		LANZO	30 mg	Capsule	Oral use
		LANZO	15 mg	Oro-dispersible tablet	Oral use
		LANZO	30 mg	Oro-dispersible tablet	Oral use

ANNEX II

SCIENTIFIC CONCLUSIONS AND GROUNDS FOR AMENDMENT OF THE SUMMARY OF PRODUCT CHARACTERISTICS, LABELLING AND PACKAGE LEAFLETS PRESENTED BY THE EMEA

SCIENTIFIC CONCLUSIONS

OVERALL SUMMARY OF THE SCIENTIFIC EVALUATION OF AGOPTON AND ASSOCIATED NAMES

Due to the fact that Agopton and associated names (lansoprazole) does not have the same Summary of Product Characteristics (SPC) in the various Member States in the European Union as a result of divergent national decisions, a harmonisation of the SPC for Agopton and associated names, throughout Europe has become necessary. Germany (referring Member State) identified the following issues, each affecting several sections of the SPC. These are:

1. Therapeutic Indications

- Treatment of NSAID-associated benign gastric and duodenal ulcers in patients requiring continued NSAID treatment
- Prophylaxis of NSAID-associated gastric ulcers, duodenal ulcers and relief of symptoms in patients requiring continued therapy
- Symptomatic gastroesophageal reflux disease

2. Posology and methods of administration

- Dosage recommendation for the eradication of H. pylori differences: inclusion of specific recommendations on the antibiotics to be used
- Dosage and dosing schedule of symptomatic gastroesophageal reflux disease.

3. Further issues: it was requested to present a harmonised SPC for all other relevant sections

Quality aspects do not form part of the current arbitration procedure.

1. 4.1 Therapeutic indications

- **Treatment of NSAID-associated gastric ulcers, duodenal ulcers and gastroduodenal erosions, and relief of the associated symptoms, in patients requiring continued NSAID treatment**

Gastric acid is central in the pathogenesis of gastroduodenal ulcers and acid inhibition has been shown to effectively heal NSAID-associated ulcers. In patients who continue to take NSAID medication healing is delayed.

Two pivotal studies for the support of the proposed indication in ulcer healing have been presented: Both of them were double-blind, positive-controlled, randomised, parallel group, multi-centre studies designed to evaluate the safety and efficacy of lansoprazole 15 mg and 30 mg o.d. in comparison to ranitidine 150 mg b.d. The efficacy was evaluated after 4 and 8 weeks treatment.

For healing of gastric ulcers, both the 15 and 30 mg dose were statistically superior to the ranitidine at both 4 and 8 weeks. However, at 4 weeks, the efficacy of the 15 mg dose was less than for the comparator at 8 weeks. Furthermore, at both timepoints, there was a trend for better efficacy of the 30 mg dose. Therefore the 15 mg dose cannot be recommended for healing of NSAID-associated gastric ulcers.

The data regarding healing of duodenal ulcers in one of the pivotal studies is limited (few patients) but support efficacy of both doses of lansoprazole 15 and 30 mg o.d.

As regards the relief of symptoms, this was examined in both studies through the use of diary cards and investigator interviews. The evaluation of the symptoms yielded less clear results than for the healing of the ulceration, and the results are inconsistent across the different symptoms/parameters and methods used to assess the symptoms.

The data from the 2 pivotal studies as well as supportive data from the open-label extension study and the comparative study with omeprazole and misoprostol, support the indication: “Treatment of NSAID associated benign gastric and duodenal ulcers in patients requiring continued NSAID treatment”. The studies support the use of lansoprazole 30 mg o.d for 4-8 weeks for this indication. Data concerning

the indications “relief of symptoms” and “healing of gastroduodenal erosions” are scarce and are not sufficient for approval of these indications.

- **Prophylaxis of NSAID-associated gastric ulcers, duodenal ulcers, gastroduodenal erosions, and prevention of the associated symptoms, in patients who require continued NSAID treatment**

For the prevention of NSAID associated ulceration, one pivotal study was presented. This study was a randomized, parallel-group, active- and placebo-controlled, multi-center, multinational study to evaluate the use of lansoprazole, misoprostol and placebo in the prevention of ulcers and erosions in patients continuing to take NSAIDs. The study duration was 12 weeks

While the results for the two doses of lansoprazole and for misoprostol are very similar, all three treatments were markedly better than placebo and this is confirmed by statistical analysis ($p<0.001$ for each active vs. placebo comparison). Lansoprazole (like misoprostol) is effective in reducing the risk of gastric or duodenal ulcers in patients who need to continue NSAIDs. This effect remains after adjustment for a range of covariates. No clinically relevant difference in ulcer prevention between the 15 and 30 mg dose of lansoprazole could be demonstrated. Only a small minority of patients developed duodenal ulcers

The studies presented by the MAH demonstrated efficacy of lansoprazole in the treatment and prevention of gastric ulceration associated with continued intake of NSAIDs. Limited data, well known-clinical facts about duodenal ulceration and an class effect of PPIs support the inclusion of duodenal ulcers into the indication.

Both the lansoprazole 15 and 30 mg dose are effective and the dosing recommendations proposed by the MAH are acceptable. However, prophylactic treatment should be recommended only for patients at high risk, see SPC for detailed proposal. The data do not support the indication “prevention of symptoms” nor “prophylaxis of gastroduodenal erosions”.

- **Symptomatic gastroesophageal reflux disease (4.1 and 4.2)**

Two pivotal randomised, double-blind, parallel-group trials and 5 supportive studies to evaluate the efficacy of lansoprazole for treatment of symptomatic gastroesophageal reflux disease were submitted. The overall relief of the primary symptoms (epigastric pain and heartburn) were assessed.

The submitted data for the indication “symptomatic gastroesophageal reflux disease” support this the indication. The recommended dose should be 15-30 mg o.d. with recommendations regarding further investigation, should the patient not respond within 4 weeks.

Different disease concepts for “symptomatic gastroesophageal reflux disease” and other “functional diseases” e.g. “dyspepsia”, are established throughout Europe and reflected in different labelling. It was agreed that the indication should only mention “symptomatic gastroesophageal reflux disease”.

2. Posology and methods of administration

- **Eradication of Helicobacter pylori**

Eradication of *H. pylori* has been shown to be a definitive cure for duodenum ulcer and most gastric ulcers. The Maastricht Consensus states that treatment regimens for eradication of H. pylori should be simple, well tolerated and achieve an eradication rate of over 80% on an intention to treat basis.

Lansoprazole 30 mg combined with clarithromycin 250 or 500 mg and amoxicillin 1g, or clarithromycin 250 and metronidazole 400-500 mg twice daily was associated with eradication rates meeting the above described requirements.

The use of a regimen including lansoprazole 30mg twice daily, amoxicillin 1g twice daily and metronidazole 400-500mg twice daily has also been examined. However lower eradication rates have been achieved with this regimen. This might be attributed to high rates of metronidazole resistence. It may be suitable for those who are unable to take clarithromycin as part of an eradication therapy, when local resistance rates to metronidazole are low. The treatment duration is most commonly 7 days but sometimes up to 14 days.

3. In addition the CHMP identified the additional points to be harmonised in the various SPC sections.

4.1 Therapeutic indications

- **Eradication and prevention of relapse of gastric ulcer and duodenal**

Two studies to support the indication prevention of duodenal ulcers were provided.

The objective of one study was to compare the efficacy and safety of lansoprazole 15mg qd with placebo in preventing the recurrence of duodenal ulceration in patients with a history of recently healed duodenal ulcer. There was no baseline stratification for H. pylori status, reflecting clinical practice at the time. The proportion remaining healed at 12 months in evaluable patients was 39% on placebo vs. 84 % on lansoprazole15 mg maintenance.

The second study examined the use of lansoprazole in the maintenance of healed ulcer (prevention of relapse) of duodenal or gastric ulcer disease resistant H2 blockers. The objective of this trial was to compare the efficacy /safety or lansoprazole 15/30mg to placebo in the prevention of duodenal ulcers in those with a history of duodenal, or gastric ulcer disease in those with a history of gasric ulcers. The time to first recurrence of duodenal ulcer was significantly longer for lansoprazole patients compared to placebo.

The submitted data needs to be viewed in the context of current clinical practice, which would mandate H. pylori screening and eradication therapy in the treatment of duodenal ulcers. As short-term antisecretory treatment combined with eradication therapy is known to be associated with significantly improved healing rates over antisecretory treatment alone, testing for and eradication of H. pylori would be considered mandatory. The submitted data on the use of maintenance antisecretory therapy to prevent duodenal ulcer recurrence predates the use of such eradication therapy.s.

4.2 Posology and methods of administration

- **Food interaction**

The MAH has provided three bioequivalence studies as background documentation on the effect of food intake on the bioavailability of lansoprazole. In two of the studies, lansoprazole (formulation) was given immediately after a meal. The AUC was reduced by about 50%. In the third study, no effect of food was observed when the food was taken 30 minutes after administration.

A restriction regarding food intake is necessary, since effects of food consumption on the pharmacokinetic profile has been observed. It can be expected that normally under fasting conditions gastric emptying of a formulation has taken place 30 minutes post-dose. This is reflected in the SPC.

- **Mixing the content of the “opened capsules” with food**

Studies have been performed investigating the effect of mixing the granules of lansoprazole with food. Although all treatments resulted in equivalent AUC of lansoprazole, it has to be noted that the studies were performed with certain brands of the different vehicles. The factor that would influence the bioavailability the most would be if the granules were mixed with a vehicle of pH>7. It is unlikely that the proposed vehicles, even if not of the same brand, would be of such pH and therefore affect the granule coating. This is reflected in the SPC under section 4.2 and 5.2.

4.2 Posology (in special populations)

- **Use in children**

A statement indicating the experience with the medicinal product in children is required under section 4.2 of the SPC.

Lansoprazole has not been marketed for use in children or adolescents in the EU. However, the pharmacokinetic and pharmacodynamic data as well as clinical data for the use of lansoprazole in children are available in the literature. The MAH proposed to include preliminary data in paediatric patients in the SPC. The CHMP requested, the MAH to submit a full review of the paediatric data and to make an adequate proposal for the treatment of children in the relevant sections of the SPC

The applicant answered the question on paediatric data with the filing of a complete paediatric data package.

The evaluation of the pharmacokinetics in children aged 10 weeks and above showed similar exposures in comparison to healthy adult volunteers receiving a 30 mg dose either with a body weight or body surface based dosing for babies. However, higher values for exposure will be expected in children below 1 year of age with the pharmaceutical forms that are commercially available. Higher exposure for lansoprazole was also seen in newborns and babies up to an age of approx. 10 weeks.

The clinical trials showed consistently gastric acid suppression and relief of symptoms in children and adolescents when treated with lansoprazole. However the trial design and the results of the studies were not adequate to recommend the use of lansoprazole in for the treatment of oesophagitis in children.

The clinical trials were all small, open and uncontrolled trials. Sub-optimal results were obtained for children 1-11 years of age and pharmacodynamic as well as the efficacy results make dosing recommendations difficult.

In conclusion, the efficacy data are considered too weak to support a paediatric indication of oesophagitis in children and adolescents. This is reflected in the SPC under 4.2.

The pharmacokinetic data of children and adolescents are summarised under section 5.2.

- **Liver impairment**

Three studies were submitted addressing the pharmacokinetics in lansoprazole in patients with different levels of (mild, moderate and severe) liver impairment

It was demonstrated that the total lansoprazole exposure is many-fold increased in patients with severe hepatic impairment.

The usually recommended dose in patients with normal hepatic function is 30 mg q.d. The safety of PPIs is generally considered high. However, the magnitude of increase in exposure that is acceptable depends on the available clinical safety data available on the exposures. Unless the applicant can show convincing data on satisfactory safety with the exposures obtained, it is recommended that a dose reduction of 50% is made. Further reductions are not practically possible and data may not allow simulations of PK/PD regarding the increase the dose-interval. This is reflected in section 4.2, 4.4 and 5.2 of the SPC.

- **4.3 Contraindication**

Due to a marked reduction in atazanavir trough concentrations observed during concomitant use of omeprazole, use of PPIs is contraindicated in the SPC for Rayataz (atazanavir). This is also reflected in the SPC for lansoprazole.

- **4.5 Interaction with other medicinal products and other forms of interaction**

One study of the interaction with phenytoin has been submitted. The effect of lansoprazole 60 mg q.d. for 9 days on the pharmacokinetics of phenytoin after a 250 mg i.v. dose was investigated. A very small statistically significant but clinically irrelevant effect was found. No marked changes were observed on an individual level.

The CHMP agrees that no information regarding the lansoprazole effects on phenytoin or carbamazepine is needed in the SPC. For the complete wording of section 4.5 please see attched SPC.

- **4.6 Pregnancy and lactation**

No data regarding of the use of lanzoprazole during preganancy and lactation has been provided. The following wording was agreed:

> For lansoprazole no clinical data on exposed pregnancies are available. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development. Therefore, the use of lansoprazole during pregnancy is not recommended.

Benefit/Risk consideration

Based on the documentation submitted by the MAH and the scientific discussion within the Committee, the CHMP considered that the benefit/risk ratio of Agopton and associated names is favourable for use relating to:

- Treatment of duodenal and gastric ulcer
- Treatment of reflux oesophagitis
- Prophylaxis of reflux oesophagitis
- Eradication of *Helicobacter pylori* (*H. pylori*) concurrently given with appropriate antibiotic therapy for treatment of *H.pylori* associated ulcers
- Treatment of NSAID-associated benign gastric and duodenal ulcers in patients requiring continued NSAID treatment
- Prophylaxis of NSAID-associated gastric ulcers and duodenal ulcers in patients at risk (see section 4.2) requiring continued therapy
- Symptomatic gastroesophageal reflux disease
- Zollinger-Ellison syndrome.

The divergences identified at the start of the referral have been resolved.

GROUNDS FOR AMENDMENTS OF THE SUMMARY OF PRODUCTS CHARACTERISTICS LABELLING AND PACKAGE LEAFLET

Whereas,

- the scope of the referral was the harmonisation of the Summary of Products Characteristics,
- the Summary of Products Characteristic, Labelling and Package Leaflet proposed by the Marketing Authorisation Holders has been assessed based on the documentation submitted and the scientific discussion within the Committee,

the CHMP has recommended the amendment of the Marketing Authorisations for which the Summary of Product Characteristics, Labelling and Package Leaflet is set out in Annex III of the CHMP Opinion for Agopton and associated names (see Annex I of the opinion).

ANNEX III

SUMMARY OF PRODUCT CHARACTERISTICS, LABELLING AND PACKAGE LEAFLET

Note: This SPC, labelling and package leaflet is the version that was annexed to the Commission Decision on this Article 30 referral for lansoprazole containing medicinal products. The text was valid at that time.

After the Commission Decision, the Member State competent authorities will update the product information as required. Therefore, this SPC, labelling and package leaflet may not necessarily represent the current text.

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Agopton and associated names (see Annex I) 15 mg capsules
Agopton and associated names (see Annex I) 30 mg capsules

[See Annex I - To be completed nationally]

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 15 mg of lansoprazole
Each capsule contains 30 mg of lansoprazole

Excipient(s): Each 15 mg capsule contains 29.9 mg of sucrose
Each 30 mg capsule contains 59.8 mg of sucrose

For a full list of excipients, see section 6.1.

[To be completed nationally]

3. PHARMACEUTICAL FORM

Agopton 15 mg: <colour> capsules. Each capsule contains <white to pale brownish white enteric-coated granules>.

Agopton 30 mg: <colour> capsules. Each capsule contains <white to pale brownish white enteric-coated granules>.

[To be completed nationally]

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

- Treatment of duodenal and gastric ulcer
- Treatment of reflux oesophagitis
- Prophylaxis of reflux oesophagitis
- Eradication of *Helicobacter pylori* (*H. pylori*) concurrently given with appropriate antibiotic therapy for treatment of *H.pylori*-associated ulcers
- Treatment of NSAID-associated benign gastric and duodenal ulcers in patients requiring continued NSAID treatment
- Prophylaxis of NSAID-associated gastric ulcers and duodenal ulcers in patients at risk (see section 4.2) requiring continued therapy
- Symptomatic gastroesophageal reflux disease
- Zollinger-Ellison syndrome.

4.2 Posology and method of administration

For optimal effect, Agopton should be taken once daily in the morning, except when used for *H. pylori* eradication when treatment should be twice a day, once in the morning and once in the evening. Agopton should be taken at least 30 minutes before food (see section 5.2). Capsules should be swallowed whole with liquid.

For patients with difficulty swallowing; studies and clinical practice suggest that the capsules may be opened and the granules mixed with a small amount of water, apple/tomato juice or sprinkled onto a small amount of soft food (e.g. yoghurt, apple puree) to ease administration. Capsules may also be opened and granules mixed with 40 ml of apple juice for administration through a nasogastric tube (see section 5.2). After preparing the suspension or mixture, the drug should be administered immediately.

Treatment of duodenal ulcer:
The recommended dose is 30 mg once daily for 2 weeks. In patients not fully healed within this time, the medication is continued at the same dose for another two weeks.

Treatment of gastric ulcer:
The recommended dose is 30 mg once daily for 4 weeks. The ulcer usually heals within 4 weeks, but in patients not fully healed within this time, the medication may be continued at the same dose for another 4 weeks.

Reflux oesophagitis:
The recommended dose is 30 mg once daily for 4 weeks. In patients not fully healed within this time, the treatment may be continued at the same dose for another 4 weeks.

Prophylaxis of reflux oesophagitis:
15 mg once daily. The dose may be increased up to 30 mg daily as necessary.

Eradication of *Helicobacter pylori:*
When selecting appropriate combination therapy consideration should be given to official local guidance regarding bacterial resistance, duration of treatment, (most commonly 7 days but sometimes up to 14 days), and appropriate use of antibacterial agents.

The recommended dose is 30 mg of Agopton twice daily for 7 days in combination with one of the following:
clarithromycin 250-500 mg twice daily + amoxicillin 1 g twice daily
clarithromycin 250 mg twice daily + metronidazole 400-500 mg twice daily

H. pylori eradication rates of up to 90%, are obtained when clarithromycin is combined with Agopton and amoxicillin or metronidazole.

Six months after successful eradication treatment, the risk of re-infection is low and relapse is therefore unlikely.

Use of a regimen including lansoprazole 30 mg twice daily, amoxicillin 1 g twice daily and metronidazole 400-500 mg twice daily has also been examined. Lower eradication rates were seen using this combination than in regimens involving clarithromycin. It may be suitable for those who are unable to take clarithromycin as part of an eradication therapy, when local resistance rates to metronidazole are low.

Treatment of NSAID associated benign gastric and duodenal ulcers in patients requiring continued NSAID treatment:
30 mg once daily for four weeks. In patients not fully healed the treatment may be continued for another four weeks. For patients at risk or with ulcers that are difficult to heal, a longer course of treatment and/or a higher dose should probably be used.

Prophylaxis of NSAID associated gastric and duodenal ulcers in patients at risk (such as age > 65 or history of gastric or duodenal ulcer) requiring prolonged NSAID treatment:
15 mg once daily. If the treatment fails the dose 30 mg once daily should be used.

Symptomatic gastro-oesophageal reflux disease:
The recommended dose is 15 mg or 30 mg daily. Relief of symptoms is obtained rapidly. Individual adjustment of dosage should be considered. If the symptoms are not relieved within 4 weeks with a daily dose of 30 mg, further examinations are recommended.

Zollinger-Ellison syndrome:
The recommended initial dose is 60 mg once daily. The dose should be individually adjusted and the treatment should be continued for as long as necessary. Daily doses of up to 180 mg have been used. If the required daily dose exceeds 120 mg, it should be given in two divided doses.

Impaired hepatic or renal function:

There is no need for a dose adjustment in patients with impaired renal function.

Patients with moderate or severe liver disease should be kept under regular supervision and a 50% reduction of the daily dose is recommended (see section 4.4 and 5.2).

Elderly:

Due to reduced clearance of lansoprazole in the elderly an adjustment of dose may be necessary based on individual requirements. A daily dose of 30 mg should not be exceeded in the elderly unless there are compelling clinical indications.

Children:

The use of Agopton is not recommended in children as clinical data are limited (see also section 5.2).

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients.

Lansoprazole should not be administered with atazanavir (see section 4.5).

4.4 Special warnings and precautions for use

In common with other anti-ulcer therapies, the possibility of malignant gastric tumour should be excluded when treating a gastric ulcer with lansoprazole because lansoprazole can mask the symptoms and delay the diagnosis.

Lansoprazole should be used with caution in patients with moderate and severe hepatic dysfunction (see sections 4.2 and 5.2).

Decreased gastric acidity due to lansoprazole might be expected to increase gastric counts of bacteria normally present in the gastrointestinal tract. Treatment with lansoprazole may lead to a slightly increased risk of gastrointestinal infections such as *Salmonella* and *Campylobacter*.

In patients suffering from gastro-duodenal ulcers, the possibility of *H. pylori* infection as an etiological factor should be considered.

If lansoprazole is used in combination with antibiotics for eradication therapy of *H.pylori*, then the instructions for the use of these antibiotics should also be followed.

Because of limited safety data for patients on maintenance treatment for longer than 1 year, regular review of the treatment and a thorough risk/benefit assessment should regularly be performed in these patients.

Very rarely cases of colitis have been reported in patients taking lansoprazole. Therefore, in the case of severe and/or persistent diarrhoea, discontinuation of therapy should be considered.

The treatment for the prevention of peptic ulceration of patients in need of continuous NSAID treatment should be restricted to high risk patients (e.g. previous gastrointestinal bleeding, perforation or ulcer, advanced age, concomitant use of medication known to increase the likelihood of upper GI adverse events [e.g. corticosteroids or anticoagulants], the presence of a serious co-morbidity factor or the prolonged use of NSAID maximum recommended doses).

<As Agopton contains sucrose, patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.>

[To be completed nationally]

4.5 Interaction with other medicinal products and other forms of interaction

Effects of lansoprazole on other drugs

Medicinal products with pH dependent absorption
Lansoprazole may interfere with the absorption of drugs where gastric pH is critical to bioavailability.

Atazanavir:
A study has shown that co-administration of lansoprazole (60 mg once daily) with atazanavir 400 mg to healthy volunteers resulted in a substantial reduction in atazanavir exposure (approximately 90% decrease in AUC and Cmax). Lansoprazole should not be co-administered with atazanavir (see section 4.3).

Ketoconazole and itraconazole:
The absorption of ketoconazole and itraconazole from the gastrointestinal tract is enhanced by the presence of gastric acid. Administration of lansoprazole may result in sub-therapeutic concentrations of ketoconazole and itraconazole and the combination should be avoided.

Digoxin:
Co-administration of lansoprazole and digoxin may lead to increased digoxin plasma levels. The plasma levels of digoxin should therefore be monitored and the dose of digoxin adjusted if necessary when initiating and ending lansoprazole treatment.

Medicinal products metabolised by P450 enzymes
Lansoprazole may increase plasma concentrations of drugs that are metabolised by CYP3A4. Caution is advised when combining lansoprazole with drugs which are metabolised by this enzyme and have a narrow therapeutic window.

Theophylline:
Lansoprazole reduces the plasma concentration of theophylline, which may decrease the expected clinical effect at the dose. Caution is advised when combining the two drugs.

Tacrolimus:
Co-administration of lansoprazole increases the plasma concentrations of tacrolimus (a CYP3A and P-gp substrate). Lansoprazole exposure increased the mean exposure of tacrolimus by up to 81%. Monitoring of tacrolimus plasma concentrations is advised when concomitant treatment with lanzoprazole is initiated or ended.

Medicinal products transported by P-glycoprotein
Lansoprazole has been observed to inhibit the transport protein, P-glycoprotein (P-gp) *in vitro*. The clinical relevance of this is unknown.

Effects of other drugs on lansoprazole

Drugs which inhibit CYP2C19
Fluvoxamine:
A dose reduction may be considered when combining lansoprazole with the CYP2C19 inhibitor fluvoxamine. The plasma concentrations of lansoprazole increase up to 4-fold.

Drugs which induces CYP2C19 and CYP3A4
Enzyme inducers affecting CYP2C19 and CYP3A4 such as rifampicin, and St John´s wort (*Hypericum perforatum*) can markedly reduce the plasma concentrations of lansoprazole.

Others
Sucralfate/Antacids:
Sucralfate/Antacids may decrease the bioavailability of lansoprazole. Therefore lansoprazole should be taken at least 1 hour after taking these drugs.

No clinically significant interactions of lansoprazole with nonsteroidal anti-inflammatory drugs have been demonstrated, although no formal interactions studies have been performed.

4.6 Pregnancy and lactation

Pregnancy:
For lansoprazole no clinical data on exposed pregnancies are available. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development.

Therefore, the use of lansoprazole during pregnancy is not recommended.

Lactation:
It is not known whether lansoprazole is excreted in human breast milk. Animal studies have shown excretion of lansoprazole in milk.

A decision on whether to continue/discontinue breast-feeding or to continue/discontinue therapy with lansoprazole should be made taking into account the benefit of breastfeeding to the child and the benefit of lansoprazole therapy to the woman.

4.7 Effects on ability to drive and use machines

Adverse drug reactions such as dizziness, vertigo, visual disturbances and somnolence may occur (see section 4.8). Under these conditions the ability to react may be decreased.

4.8 Undesirable effects

Frequencies are defined as common (> 1/100, < 1/10); uncommon (> 1/1,000, < 1/100); rare (>1/10,000, <1/1,000); very rare (<1/10,000).

	Common	Uncommon	Rare	Very rare
Blood and lymphatic system disorders		Thrombocytopenia, eosinophilia, leucopenia	Anaemia	Agranulocytosis, pancytopenia
Psychiatric disorders		Depression	Insomnia, hallucination, confusion	
Nervous system disorders	Headache, dizziness		Restlessness, vertigo, paresthesia, somnolence, tremor	
Eye disorders			Visual disturbances.	
Gastrointestinal disorders	Nausea, diarrhoea, stomach ache, constipation, vomiting, flatulence, dry mouth or throat		Glossitis, candidiasis of the oesophagus, pancreatitis, taste disturbances	Colitis, stomatitis
Hepatobiliary disorders	Increase in liver enzyme levels		Hepatitis, jaundice	
Skin and subcutaneous tissue disorders	Urticaria, itching, rash		Petechiae, purpura, hair loss, erythema multiforme, photosensitivity	Steven-Johnson syndrome, toxic epidermal necrolysis
Musculoskeletal and connective tissue disorders		Arthralgia, myalgia		
Renal and urinary disorders			Interstitial nephritis	
Reproductive system and breast disorders			Gynaecomastia	
General disorders and administration site conditions	Fatigue	Oedema	Fever, hyperhidrosis, angioedema, anorexia, impotence	Anaphylactic shock
Investigations				Increase in cholesterol and triglyceride levels, hyponatremia

4.9 Overdose

The effects of overdose on lansoprazole in humans are not known (although the acute toxicity is likely to be low) and, consequently, instruction for treatment cannot be given. However, daily doses of up to 180 mg of lansoprazole orally and up to 90 mg of lansoprazole intravenously have been administered in trials without significant undesirable effects.

Please refer to section 4.8 for possible symptoms of lansoprazole overdose.

In the case of suspected overdose the patient should be monitored. Lansoprazole is not significantly eliminated by haemodialysis. If necessary, gastric emptying, charcoal and symptomatic therapy is recommended.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Proton pump inhibitors, ATC code: A02BC03

Lansoprazole is a gastric proton pump inhibitor. It inhibits the final stage of gastric acid formation by inhibiting the activity of H^+/K^+ ATPase of the parietal cells in the stomach. The inhibition is dose-dependent and reversible, and the effect applies to both basal and stimulated secretion of gastric acid. Lansoprazole is concentrated in the parietal cells and becomes active in their acidic environment, whereupon it reacts with the sulphydryl group of H^+/K^+ATPase causing inhibition of the enzyme activity.

Effect on gastric acid secretion:
Lansoprazole is a specific inhibitor of the parietal cell proton pump. A single oral dose of lansoprazole inhibits pentagastrin-stimulated gastric acid secretion by about 80%. After repeated daily administration for seven days, about 90% inhibition of gastric acid secretion is achieved. It has a corresponding effect on the basal secretion of gastric acid. A single oral dose of 30 mg reduces basal secretion by about 70%, and the patients' symptoms are consequently relieved starting from the very first dose. After eight days of repeated administration the reduction is about 85%. A rapid relief of symptoms is obtained by one capsule (30 mg) daily, and most patients with duodenal ulcer recover within 2 weeks, patients with gastric ulcer and reflux oesophagitis within 4 weeks. By reducing gastric acidity, lansoprazole creates an environment in which appropriate antibiotics can be effective against *H. pylori.*

5.2 Pharmacokinetic properties

Lansoprazole is a racemate of two active enantiomers that are biotransformed into the active form in the acidic environment of the parietal cells. As lansoprazole is rapidly inactivated by gastric acid, it is administered orally in enteric-coated form(s) for systemic absorption.

Absorption and distribution

Lansoprazole exhibits high (80-90%) bioavailability with a single dose. Peak plasma levels occur within 1.5 to 2.0 hours. Intake of food slows the absorption rate of lansoprazole and reduces the bioavailabilty by about 50%. The plasma protein binding is 97%.

Studies have shown that granules from opened capsules give equivalent AUC as the intact capsule if the granules are suspended in a small amount of orange juice, apple juice, or tomato juice mixed with a tablespoon of apple or pear puree or sprinkled on a tablespoon of yoghurt, pudding or cottage cheese. Equivalent AUC has also been shown for granules suspended in apple juice administered through a naso-gastric tube.

Metabolism and elimination

Lansoprazole is extensively metabolised by the liver and the metabolites are excreted by both the renal and biliary route. The metabolism of lansoprazole is mainly catalysed by the enzyme CYP2C19. The enzyme CYP3A4 also contributes to the metabolism. The plasma elimination half-life ranges from 1 to 2 hours following single or multiple doses in healthy subjects. There is no evidence of accumulation following multiple doses in healthy subjects. Sulphone, sulphide and 5-hydroxyl derivatives of lansoprazole have been identified in plasma. These metabolites have very little or no antisecretory activity.

A study with ^{14}C labelled lansoprazole indicated that approximately one-third of the administered radiation was excreted in the urine and two-thirds was recovered in the faeces.

Pharmacokinetics in elderly patients

The clearance of lansoprazole is decreased in the elderly, with elimination half-life increased approximately 50% to 100%. Peak plasma levels were not increased in the elderly.

Pharmacokinetics in paediatric patients

The evaluation of the pharmacokinetics in children aged 1 –17 years of age showed a similar exposure as compared to adults with doses of 15 mg for those below 30 kg of weight and 30 mg for those above. The investigation of a dose of 17 mg/m^2 body surface or 1 mg/kg body weight also resulted in comparable exposure of lansoprazole in children aged 2-3 months up to one year of age compared to adults.

Higher exposure to lansoprazole in comparison to adults has been seen in infants below the age of 2-3 months with doses of both 1.0 mg/kg and 0.5 mg/kg body weight given as a single dose.

Pharmacokinetics in hepatic insufficiency

The exposure of lansoprazole is doubled in patients with mild hepatic impairment and much more increased in patients with moderate and severe hepatic impairment.

CYP2C19 poor metabolisers

CYP2C19 is subject to genetic polymorphism and 2-6 % of the population, called poor metabolisers (PMs), are homozygote for a mutant CYP2C19 allele and therefore lacks a functional CYP2C19 enzyme. The exposure of lansoprazole is several-fold higher in PMs than in extensive metabolisers (EMs).

5.3 Preclinical safety data

Preclinical data reveal no special hazards for humans based on conventional studies of safety pharmacology, repeated dose toxicity, toxicity to reproduction or genotoxicity.

In two rat carcinogenicity studies, lansoprazole produced dose-related gastric ECL cell hyperplasia and ECL cell carcinoids associated with hypergastrinaemia due to inhibition of acid secretion. Intestinal metaplasia was also observed, as were Leydig cell hyperplasia and benign Leydig cell tumours. After 18 months of treatment retinal atrophy was observed. This was not seen in monkeys, dogs or mice.

In mouse carcinogenicity studies dose-related gastric ECL cell hyperplasia developed as well as liver tumours and adenoma of rete testis.

The clinical relevance of these findings is unknown.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

[To be completed nationally]

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

[To be completed nationally]

6.4 Special precautions for storage

[To be completed nationally]

6.5 Nature and contents of container

Not all pack sizes may be marketed.

[To be completed nationally]

6.6 Special precautions for disposal and other handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

8. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

[To be completed nationally]

10. DATE OF REVISION OF THE TEXT

1. NAME OF THE MEDICINAL PRODUCT

Agopton and associated names (see Annex I) 15 mg oro-dispersible tablets
Agopton and associated names (see Annex I) 30 mg oro-dispersible tablets

[See Annex I - To be completed nationally]

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each oro-dispersible tablet contains 15 mg of lansoprazole
Each oro-dispersible tablet contains 30 mg of lansoprazole

Excipient(s): Each 15 mg oro-dispersible tablet contains 15 mg of lactose and 4.5 mg of aspartame
Each 30 mg oro-dispersible tablet contains 30 mg of lactose and 9.0 mg of aspartame

For a full list of excipients, see section 6.1.

[To be completed nationally]

3. PHARMACEUTICAL FORM

Agopton 15 mg: <colour> oro-dispersible tablet. Each oro-dispersible tablet contains <white to pale brownish white enteric-coated granules>.

Agopton 30 mg: <colour> oro-dispersible tablet. Each oro-dispersible tablet contains <white to pale brownish white enteric-coated granules>.

[To be completed nationally]

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

- Treatment of duodenal and gastric ulcer
- Treatment of reflux oesophagitis
- Prophylaxis of reflux oesophagitis
- Eradication of *Helicobacter pylori* (*H. pylori*) concurrently given with appropriate antibiotic therapy for treatment of *H.pylori*-associated ulcers
- Treatment of NSAID-associated benign gastric and duodenal ulcers in patients requiring continued NSAID treatment
- Prophylaxis of NSAID-associated gastric ulcers and duodenal ulcers in patients at risk (see section 4.2) requiring continued therapy
- Symptomatic gastroesophageal reflux disease
- Zollinger-Ellison syndrome.

4.2 Posology and method of administration

For optimal effect, Agopton should be taken once daily in the morning, except when used for H. pylori eradication when treatment should be twice a day, once in the morning and once in the evening. Agopton should be taken at least 30 minutes before food (see section 5.2). Agopton is strawberry flavoured and should be placed on the tongue and gently sucked. The tablet rapidly disperses in the mouth, releasing gastro-resistant microgranules which are swallowed with the patient's saliva. Alternatively, the tablet can be swallowed whole with a drink of water.

The orodispersible tablets can be dispersed in a small amount of water and administered via a naso-gastric tube or oral syringe.

Treatment of duodenal ulcer:
The recommended dose is 30 mg once daily for 2 weeks. In patients not fully healed within this time, the medication is continued at the same dose for another two weeks.

Treatment of gastric ulcer:
The recommended dose is 30 mg once daily for 4 weeks. The ulcer usually heals within 4 weeks, but in patients not fully healed within this time, the medication may be continued at the same dose for another 4 weeks.

Reflux oesophagitis:
The recommended dose is 30 mg once daily for 4 weeks. In patients not fully healed within this time, the treatment may be continued at the same dose for another 4 weeks.

Prophylaxis of reflux oesophagitis:
15 mg once daily. The dose may be increased up to 30 mg daily as necessary.

Eradication of *Helicobacter pylori:*
When selecting appropriate combination therapy consideration should be given to official local guidance regarding bacterial resistance, duration of treatment, (most commonly 7 days but sometimes up to 14 days), and appropriate use of antibacterial agents.

The recommended dose is 30 mg of Agopton twice daily for 7 days in combination with one of the following:
clarithromycin 250-500 mg twice daily + amoxicillin 1 g twice daily
clarithromycin 250 mg twice daily + metronidazole 400-500 mg twice daily

The *H. pylori* eradication results obtained when clarithromycin is combined with either amoxicillin or metronidazole give rates of up to 90%, when used in combination with Agopton.

Six months after successful eradication treatment, the risk of re infection is low and relapse is therefore unlikely.

Use of a regimen including lansoprazole 30 mg twice daily, amoxicillin 1 g twice daily and metronidazole 400-500 mg twice daily has also been examined. Lower eradication rates were seen using this combination than in regimens involving clarithromycin. It may be suitable for those who are unable to take clarithromycin as part of an eradication therapy, when local resistance rates to metronidazole are low.

Treatment of NSAID associated benign gastric and duodenal ulcers in patients requiring continued NSAID treatment:
30 mg once daily for four weeks. In patients not fully healed the treatment may be continued for another four weeks. For patients at risk or with ulcers that are difficult to heal, a longer course of treatment and/or a higher dose should probably be used.

Prophylaxis of NSAID associated gastric and duodenal ulcers in patients at risk (such as age > 65 or history of gastric or duodenal ulcer) requiring prolonged NSAID treatment:
15 mg once daily. If the treatment fails the dose 30 mg once daily should be used.

Symptomatic gastro-oesophageal reflux disease:
The recommended dose is 15 mg or 30 mg daily. Relief of symptoms is obtained rapidly. Individual adjustment of dosage should be considered. If the symptoms are not relieved within 4 weeks with a daily dose of 30 mg, further examinations are recommended.

Zollinger-Ellison syndrome:
The recommended initial dose is 60 mg once daily. The dose should be individually adjusted and the treatment should be continued for as long as necessary. Daily doses of up to 180 mg have been used. If the required daily dose exceeds 120 mg, it should be given in two divided doses.

Impaired hepatic or renal function:

There is no need for a dose adjustment in patients with impaired renal function.

Patients with moderate or severe liver disease should be kept under regular supervision and a 50% reduction of the daily dose is recommended (see section 4.4 and 5.2).

Elderly:

Due to reduced clearance of lansoprazole in the elderly an adjustment of dose may be necessary based on individual requirements. A daily dose of 30 mg should not be exceeded in the elderly unless there are compelling clinical indications.

Children:

The use of Agopton is not recommended in children as clinical data are limited (see also section 5.2.)

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients.

Lansoprazole should not be administered with atazanavir (see section 4.5).

4.4 Special warnings and precautions for use

In common with other anti-ulcer therapies, the possibility of malignant gastric tumour should be excluded when treating a gastric ulcer with lansoprazole because lansoprazole can mask the symptoms and delay the diagnosis.

Lansoprazole should be used with caution in patients with moderate and severe hepatic dysfunction (see sections 4.2 and 5.2).

Decreased gastric acidity due to lansoprazole might be expected to increase gastric counts of bacteria normally present in the gastrointestinal tract. Treatment with lansoprazole may lead to a slightly increased risk of gastrointestinal infections such as *Salmonella* and *Campylobacter*.

In patients suffering from gastro-duodenal ulcers, the possibility of *H. pylori* infection as an etiological factor should be considered.

If lansoprazole is used in combination with antibiotics for eradication therapy of *H.pylori*, then the instructions for the use of these antibiotics should also be followed.

Because of limited safety data for patients on maintenance treatment for longer than 1 year, regular review of the treatment and a thorough risk/benefit assessment should regularly be performed in these patients.

Very rarely cases of colitis have been reported in patients taking lansoprazole. Therefore, in the case of severe and/or persistent diarrhoea, discontinuation of therapy should be considered.

The treatment for the prevention of peptic ulceration of patients in need of continuous NSAID treatment should be restricted to high risk patients (e.g. previous gastrointestinal bleeding, perforation or ulcer, advanced age, concomitant use of medication known to increase the likelihood of upper GI adverse events [e.g. corticosteroids or anticoagulants], the presence of a serious co-morbidity factor or the prolonged use of NSAID maximum recommended doses).

<As Agopton contains lactose, patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.>

[To be completed nationally]

4.5 Interaction with other medicinal products and other forms of interaction

Effects of lansoprazole on other drugs

Medicinal products with pH dependent absorption
Lansoprazole may interfere with the absorption of drugs where gastric pH is critical to bioavailability.

Atazanavir:
A study has shown that co-administration of lansoprazole (60 mg once daily) with atazanavir 400 mg to healthy volunteers resulted in a substantial reduction in atazanavir exposure (approximately 90% decrease in AUC and Cmax). Lansoprazole should not be co-administered with atazanavir (see section 4.3).

Ketoconazole and itraconazole:
The absorption of ketoconazole and itraconazole from the gastrointestinal tract is enhanced by the presence of gastric acid. Administration of lansoprazole may result in sub-therapeutic concentrations of ketoconazole and itraconazole and the combination should be avoided.

Digoxin:
Co-administration of lansoprazole and digoxin may lead to increased digoxin plasma levels. The plasma levels of digoxin should therefore be monitored and the dose of digoxin adjusted if necessary when initiating and ending lansoprazole treatment.

Medicinal products metabolised by P450 enzymes
Lansoprazole may increase plasma concentrations of drugs that are metabolised by CYP3A4. Caution is advised when combining lansoprazole with drugs which are metabolised by this enzyme and have a narrow therapeutic window.

Theophylline:
Lansoprazole reduces the plasma concentration of theophylline, which may decrease the expected clinical effect at the dose. Caution is advised when combining the two drugs.

Tacrolimus:
Co-administration of lansoprazole increases the plasma concentrations of tacrolimus (a CYP3A and P-gp substrate). Lansoprazole exposure increased the mean exposure of tacrolimus by up to 81%. Monitoring of tacrolimus plasma concentrations is advised when concomitant treatment with lanzoprazole is initiated or ended.

Medicinal products transported by P-glycoprotein
Lansoprazole has been observed to inhibit the transport protein, P-glycoprotein (P-gp) *in vitro*. The clinical relevance of this is unknown.

Effects of other drugs on lansoprazole

Drugs which inhibit CYP2C19
Fluvoxamine:
A dose reduction may be considered when combining lansoprazole with the CYP2C19 inhibitor fluvoxamine. A study shows that the plasma concentrations of lansoprazole increase up to 4-fold.

Drugs which induces CYP2C19 and CYP3A4
Enzyme inducers affecting CYP2C19 and CYP3A4 such as rifampicin, and St John´s wort (*Hypericum perforatum*) can markedly reduce the plasma concentrations of lansoprazole.

Others
Sucralfate/Antacids:
Sucralfate/Antacids may decrease the bioavailability of lansoprazole. Therefore lansoprazole should be taken at least 1 hour after taking these drugs.

No clinically significant interactions of lansoprazole with nonsteroidal anti-inflammatory drugs have been demonstrated, although no formal interactions studies have been performed.

4.6 Pregnancy and lactation

Pregnancy:
For lansoprazole no clinical data on exposed pregnancies are available. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development.

Therefore, the use of lansoprazole during pregnancy is not recommended.

Lactation:
It is not known whether lansoprazole is excreted in human breast milk. Animal studies have shown excretion of lansoprazole in milk.

A decision on whether to continue/discontinue breast-feeding or to continue/discontinue therapy with lansoprazole should be made taking into account the benefit of breastfeeding to the child and the benefit of lansoprazole therapy to the woman.

4.7 Effects on ability to drive and use machines

Adverse drug reactions such as dizziness, vertigo, visual disturbances and somnolence may occur (see section 4.8). Under these conditions the ability to react may be decreased.

4.8 Undesirable effects

Frequencies are defined as common (> 1/100, < 1/10); uncommon (> 1/1,000, < 1/100); rare (>1/10,000, <1/1,000); very rare (<1/10,000).

	Common	Uncommon	Rare	Very rare
Blood and lymphatic system disorders		Thrombocytopenia, eosinophilia, leucopenia	Anaemia	Agranulocytosis, pancytopenia
Psychiatric disorders		Depression	Insomnia, hallucination, confusion	
Nervous system disorders	Headache, dizziness		Restlessness, vertigo, paresthesia, somnolence, tremor	
Eye disorders			Visual disturbances.	
Gastrointestinal disorders	Nausea, diarrhoea, stomach ache, constipation, vomiting, flatulence, dry mouth or throat		Glossitis, candidiasis of the oesophagus, pancreatitis, taste disturbances	Colitis, stomatitis
Hepatobiliary disorders	Increase in liver enzyme levels		Hepatitis, jaundice	
Skin and subcutaneous tissue disorders	Urticaria, itching, rash		Petechiae, purpura, hair loss, erythema multiforme, photosensitivity	Steven-Johnson syndrome, toxic epidermal necrolysis
Musculoskeletal and connective tissue disorders		Arthralgia, myalgia		
Renal and urinary disorders			Interstitial nephritis	
Reproductive system and breast disorders			Gynaecomastia	
General disorders and administration site conditions	Fatigue	Oedema	Fever, hyperhidrosis, angioedema, anorexia, impotence	Anaphylactic shock
Investigations				Increase in cholesterol and triglyceride levels, hyponatremia

4.9 Overdose

The effects of overdose on lansoprazole in humans are not known (although the acute toxicity is likely to be low) and, consequently, instruction for treatment cannot be given. However, daily doses of up to 180 mg of lansoprazole orally and up to 90 mg of lansoprazole intravenously have been administered in trials without significant undesirable effects.

Please refer to section 4.8 for possible symptoms of lansoprazole overdose.

In the case of suspected overdose the patient should be monitored. Lansoprazole is not significantly eliminated by haemodialysis. If necessary, gastric emptying, charcoal and symptomatic therapy is recommended.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Proton pump inhibitors, ATC code: A02BC03

Lansoprazole is a gastric proton pump inhibitor. It inhibits the final stage of gastric acid formation by inhibiting the activity of H^+/K^+ ATPase of the parietal cells in the stomach. The inhibition is dose-dependent and reversible, and the effect applies to both basal and stimulated secretion of gastric acid. Lansoprazole is concentrated in the parietal cells and becomes active in their acidic environment, whereupon it reacts with the sulphydryl group of H^+/K^+ATPase causing inhibition of the enzyme activity.

Effect on gastric acid secretion:
Lansoprazole is a specific inhibitor of the parietal cell proton pump. A single oral dose of lansoprazole inhibits pentagastrin-stimulated gastric acid secretion by about 80%. After repeated daily administration for seven days, about 90% inhibition of gastric acid secretion is achieved. It has a corresponding effect on the basal secretion of gastric acid. A single oral dose of 30 mg reduces basal secretion by about 70%, and the patients' symptoms are consequently relieved starting from the very first dose. After eight days of repeated administration the reduction is about 85%. A rapid relief of symptoms is obtained by one oro-dispersible tablet (30 mg) daily, and most patients with duodenal ulcer recover within 2 weeks, patients with gastric ulcer and reflux oesophagitis within 4 weeks. By reducing gastric acidity, lansoprazole creates an environment in which appropriate antibiotics can be effective against *H. pylori.*

5.2 Pharmacokinetic properties

Lansoprazole is a racemate of two active enantiomers that are biotransformed into the active form in the acidic environment of the parietal cells. As lansoprazole is rapidly inactivated by gastric acid, it is administered orally in enteric-coated form(s) for systemic absorption.

Absorption and distribution

Lansoprazole exhibits high (80-90%) bioavailability with a single dose. Peak plasma levels occur within 1.5 to 2.0 hours. Intake of food slows the absorption rate of lansoprazole and reduces the bioavailabilty by about 50%. The plasma protein binding is 97%.

Studies have shown that oro-dispersible tablets dispersed in a small amount of water and given via syringe directly into the mouth or administered via naso-gastric tube result in equivalent AUC compared to the usual mode of admnisistration.

Metabolism and elimination

Lansoprazole is extensively metabolised by the liver and the metabolites are excreted by both the renal and biliary route. The metabolism of lansoprazole is mainly catalysed by the enzyme CYP2C19. The enzyme CYP3A4 also contributes to the metabolism. The plasma elimination half-life ranges from 1 to 2 hours following single or multiple doses in healthy subjects. There is no evidence of accumulation following multiple doses in healthy subjects. Sulphone, sulphide and 5-hydroxyl derivatives of lansoprazole have been identified in plasma. These metabolites have very little or no antisecretory activity.

A study with ^{14}C labelled lansoprazole indicated that approximately one-third of the administered radiation was excreted in the urine and two-thirds was recovered in the faeces.

Pharmacokinetics in elderly patients

The clearance of lansoprazole is decreased in the elderly, with elimination half-life increased approximately 50% to 100%. Peak plasma levels were not increased in the elderly.

Pharmacokinetics in paediatric patients

The evaluation of the pharmacokinetics in children aged 1 –17 years of age showed a similar exposure as compared to adults with doses of 15 mg for those below 30 kg of weight and 30 mg for those above. The investigation of a dose of 17 mg/m^2 body surface or 1 mg/kg body weight also resulted in comparable exposure of lansoprazole in children aged 2-3 months up to one year of age compared to adults.

Higher exposure to lansoprazole in comparison to adults has been seen in infants below the age of 2-3 months with doses of both 1.0 mg/kg and 0.5 mg/kg body weight given as a single dose

Pharmacokinetics in hepatic insufficiency

The exposure of lansoprazole is doubled in patients with mild hepatic impairment and much more increased in patients with moderate and severe hepatic impairment.

CYP2C19 poor metabolisers

CYP2C19 is subject to genetic polymorphism and 2-6 % of the population, called poor metabolisers (PMs), are homozygote for a mutant CYP2C19 allele and therefore lacks a functional CYP2C19 enzyme. The exposure of lansoprazole is several-fold higher in PMs than in extensive metabolisers (EMs).

5.3 Preclinical safety data

Preclinical data reveal no special hazards for humans based on conventional studies of safety pharmacology, repeated dose toxicity, toxicity to reproduction or genotoxicity.

In two rat carcinogenicity studies, lansoprazole produced dose-related gastric ECL cell hyperplasia and ECL cell carcinoids associated with hypergastrinaemia due to inhibition of acid secretion. Intestinal metaplasia was also observed, as were Leydig cell hyperplasia and benign Leydig cell tumours. After 18 months of treatment retinal atrophy was observed. This was not seen in monkeys, dogs or mice.

In mouse carcinogenicity studies dose-related gastric ECL cell hyperplasia developed as well as liver tumours and adenoma of rete testis.

The clinical relevance of these findings is unknown.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

[To be completed nationally]

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

[To be completed nationally]

6.4 Special precautions for storage

[To be completed nationally]

6.5 Nature and contents of container

Not all pack sizes may be marketed.

[To be completed nationally]

6.6 Special precautions for disposal and other handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

8. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

[To be completed nationally]

10. DATE OF REVISION OF THE TEXT

1. NAME OF THE MEDICINAL PRODUCT

Agopton and associated names (see Annex I) 30 mg gastro-resistant granules for oral suspension

[See Annex I - To be completed nationally]

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each single dose sachet contains 30 mg of lansoprazole

Excipient(s): Each single dose sachet contains 25.248 g of sucrose and 24.64 g of mannitol.

For a full list of excipients, see section 6.1.

[To be completed nationally]

3. PHARMACEUTICAL FORM

Agopton 30 mg: Gastro-resistant granules for oral suspension. Each single dose sachet contains <fine pink granules containing white to off-white pellets>.

[To be completed nationally]

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

- Treatment of duodenal and gastric ulcer
- Treatment of reflux oesophagitis
- Prophylaxis of reflux oesophagitis
- Eradication of *Helicobacter pylori* (*H. pylori*) concurrently given with appropriate antibiotic therapy for treatment of *H.pylori*-associated ulcers
- Treatment of NSAID-associated benign gastric and duodenal ulcers in patients requiring continued NSAID treatment
- Prophylaxis of NSAID-associated gastric ulcers and duodenal ulcers in patients at risk (see section 4.2) requiring continued therapy
- Symptomatic gastroesophageal reflux disease
- Zollinger-Ellison syndrome.

4.2 Posology and method of administration

For optimal effect, Agopton should be taken once daily in the morning, except when used for *H. pylori* eradication when treatment should be twice a day, once in the morning and once in the evening. Agopton should be taken at least 30 minutes before food (see section 5.2). The contents of one sachet should be reconstituted by stirring into 30 ml (two tablespoons) of tap water, and swallowed immediately. When reconstituted in water the granules give a pink suspension with a strawberry flavour.

For patients requiring 15 mg lansoprazole daily, either Agopton 15 mg capsules or Agopton 15 mg oro-dispersible tablets should be used.

Treatment of duodenal ulcer:
The recommended dose is 30 mg once daily for 2 weeks. In patients not fully healed within this time, the medication is continued at the same dose for another two weeks.

Treatment of gastric ulcer:
The recommended dose is 30 mg once daily for 4 weeks. The ulcer usually heals within 4 weeks, but in patients not fully healed within this time, the medication may be continued at the same dose for another 4 weeks.

Reflux oesophagitis:
The recommended dose is 30 mg once daily for 4 weeks. In patients not fully healed within this time, the treatment may be continued at the same dose for another 4 weeks.

Prophylaxis of reflux oesophagitis:
15 mg once daily. The dose may be increased up to 30 mg daily as necessary.

Eradication of *Helicobacter pylori:*
When selecting appropriate combination therapy consideration should be given to official local guidance regarding bacterial resistance, duration of treatment, (most commonly 7 days but sometimes up to 14 days) and appropriate use of antibacterial agents.

The recommended dose is 30 mg of Agopton twice daily for 7 days in combination with one of the following:
clarithromycin 250-500 mg twice daily + amoxicillin 1 g twice daily
clarithromycin 250 mg twice daily + metronidazole 400-500 mg twice daily

H. pylori eradication rates of up to 90%, are obtained when clarithromycin is combined with Agopton and amoxicillin or metronidazole.

Six months after successful eradication treatment, the risk of re-infection is low and relapse is therefore unlikely.

Use of a regimen including lansoprazole 30 mg twice daily, amoxicillin 1 g twice daily and metronidazole 400-500 mg twice daily has also been examined. Lower eradication rates were seen using this combination than in regimens involving clarithromycin. It may be suitable for those who are unable to take clarithromycin as part of an eradication therapy, when local resistance rates to metronidazole are low.

Treatment of NSAID associated benign gastric and duodenal ulcers in patients requiring continued NSAID treatment:
30 mg once daily for four weeks. In patients not fully healed the treatment may be continued for another four weeks. For patients at risk or with ulcers that are difficult to heal, a longer course of treatment and/or a higher dose should probably be used.

Prophylaxis of NSAID associated gastric and duodenal ulcers in patients at risk (such as age > 65 or history of gastric or duodenal ulcer) requiring prolonged NSAID treatment:
15 mg once daily. If the treatment fails the dose 30 mg once daily should be used.

Symptomatic gastro-oesophageal reflux disease:
The recommended dose is 15 mg or 30 mg daily. Relief of symptoms is obtained rapidly. Individual adjustment of dosage should be considered. If the symptoms are not relieved within 4 weeks with a daily dose of 30 mg, further examinations are recommended.

Zollinger-Ellison syndrome:
The recommended initial dose is 60 mg once daily. The dose should be individually adjusted and the treatment should be continued for as long as necessary. Daily doses of up to 180 mg have been used. If the required daily dose exceeds 120 mg, it should be given in two divided doses.

Impaired hepatic or renal function:

There is no need for a dose adjustment in patients with impaired renal function.

Patients with moderate or severe liver disease should be kept under regular supervision and a 50% reduction of the daily dose is recommended (see section 4.4 and 5.2).

Elderly:

Due to reduced clearance of lansoprazole in the elderly an adjustment of dose may be necessary based on individual requirements. A daily dose of 30 mg should not be exceeded in the elderly unless there are compelling clinical indications.

Children:

The use of Agopton is not recommended in children as clinical data are limited (see also section 5.2).

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients.

Lansoprazole should not be administered with atazanavir (see section 4.5).

4.4 Special warnings and precautions for use

In common with other anti-ulcer therapies, the possibility of malignant gastric tumour should be excluded when treating a gastric ulcer with lansoprazole because lansoprazole can mask the symptoms and delay the diagnosis.

Lansoprazole should be used with caution in patients with moderate and severe hepatic dysfunction (see sections 4.2 and 5.2).

Decreased gastric acidity due to lansoprazole might be expected to increase gastric counts of bacteria normally present in the gastrointestinal tract. Treatment with lansoprazole may lead to a slightly increased risk of gastrointestinal infections such as *Salmonella* and *Campylobacter*.

In patients suffering from gastro-duodenal ulcers, the possibility of *H. pylori* infection as an etiological factor should be considered.

If lansoprazole is used in combination with antibiotics for eradication therapy of *H.pylori*, then the instructions for the use of these antibiotics should also be followed.

Because of limited safety data for patients on maintenance treatment for longer than 1 year, regular review of the treatment and a thorough risk/benefit assessment should regularly be performed in these patients.

Very rarely cases of colitis have been reported in patients taking lansoprazole. Therefore, in the case of severe and/or persistent diarrhoea, discontinuation of therapy should be considered.

The treatment for the prevention of peptic ulceration of patients in need of continuous NSAID treatment should be restricted to high risk patients (e.g. previous gastrointestinal bleeding, perforation

or ulcer, advanced age, concomitant use of medication known to increase the likelihood of upper GI adverse events [e.g. corticosteroids or anticoagulants], the presence of a serious co-morbidity factor or the prolonged use of NSAID maximum recommended doses).

<As Agopton contains sucrose, patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.>

[To be completed nationally]

4.5 Interaction with other medicinal products and other forms of interaction

Effects of lansoprazole on other drugs

Medicinal products with pH dependent absorption
Lansoprazole may interfere with the absorption of drugs where gastric pH is critical to bioavailability.

Atazanavir:
A study has shown that co-administration of lansoprazole (60 mg once daily) with atazanavir 400 mg to healthy volunteers resulted in a substantial reduction in atazanavir exposure (approximately 90% decrease in AUC and Cmax). Lansoprazole should not be co-administered with atazanavir (see section 4.3).

Ketoconazole and itraconazole:
The absorption of ketoconazole and itraconazole from the gastrointestinal tract is enhanced by the presence of gastric acid. Administration of lansoprazole may result in sub-therapeutic concentrations of ketoconazole and itraconazole and the combination should be avoided.

Digoxin:
Co-administration of lansoprazole and digoxin may lead to increased digoxin plasma levels. The plasma levels of digoxin should therefore be monitored and the dose of digoxin adjusted if necessary when initiating and ending lansoprazole treatment.

Medicinal products metabolised by P450 enzymes
Lansoprazole may increase plasma concentrations of drugs that are metabolised by CYP3A4. Caution is advised when combining lansoprazole with drugs which are metabolised by this enzyme and have a narrow therapeutic window.

Theophylline:
Lansoprazole reduces the plasma concentration of theophylline, which may decrease the expected clinical effect at the dose. Caution is advised when combining the two drugs.

Tacrolimus:
Co-administration of lansoprazole increases the plasma concentrations of tacrolimus (a CYP3A and P-gp substrate). Lansoprazole exposure increased the mean exposure of tacrolimus by up to 81%. Monitoring of tacrolimus plasma concentrations is advised when concomitant treatment with lanzoprazole is initiated or ended.

Medicinal products transported by P-glycoprotein
Lansoprazole has been observed to inhibit the transport protein, P-glycoprotein (P-gp) *in vitro*. The clinical relevance of this is unknown.

Effects of other drugs on lansoprazole

Drugs which inhibit CYP2C19
Fluvoxamine:
A dose reduction may be considered when combining lansoprazole with the CYP2C19 inhibitor fluvoxamine. The plasma concentrations of lansoprazole increase up to 4-fold.

Drugs which induces CYP2C19 and CYP3A4
Enzyme inducers affecting CYP2C19 and CYP3A4 such as rifampicin, and St John´s wort (*Hypericum perforatum*) can markedly reduce the plasma concentrations of lansoprazole.

Others
Sucralfate/Antacids:
Sucralfate/Antacids may decrease the bioavailability of lansoprazole. Therefore lansoprazole should be taken at least 1 hour after taking these drugs.

No clinically significant interactions of lansoprazole with nonsteroidal anti-inflammatory drugs have been demonstrated, although no formal interactions studies have been performed.

4.6 Pregnancy and lactation

Pregnancy:
For lansoprazole no clinical data on exposed pregnancies are available. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development.

Therefore, the use of lansoprazole during pregnancy is not recommended.

Lactation:
It is not known whether lansoprazole is excreted in human breast milk. Animal studies have shown excretion of lansoprazole in milk.

A decision on whether to continue/discontinue breast-feeding or to continue/discontinue therapy with lansoprazole should be made taking into account the benefit of breastfeeding to the child and the benefit of lansoprazole therapy to the woman.

4.7 Effects on ability to drive and use machines

Adverse drug reactions such as dizziness, vertigo, visual disturbances and somnolence may occur (see section 4.8). Under these conditions the ability to react may be decreased.

4.8 Undesirable effects

Frequencies are defined as common (> 1/100, < 1/10); uncommon (> 1/1,000, < 1/100); rare (>1/10,000, <1/1,000); very rare (<1/10,000).

	Common	Uncommon	Rare	Very rare
Blood and lymphatic system disorders		Thrombocytopenia, eosinophilia, leucopenia	Anaemia	Agranulocytosis, pancytopenia
Psychiatric disorders		Depression	Insomnia, hallucination, confusion	
Nervous system disorders	Headache, dizziness		Restlessness, vertigo, paresthesia, somnolence, tremor	
Eye disorders			Visual disturbances.	
Gastrointestinal disorders	Nausea, diarrhoea, stomach ache, constipation, vomiting, flatulence, dry mouth or throat		Glossitis, candidiasis of the oesophagus, pancreatitis, taste disturbances	Colitis, stomatitis
Hepatobiliary disorders	Increase in liver enzyme levels		Hepatitis, jaundice	
Skin and subcutaneous tissue disorders	Urticaria, itching, rash		Petechiae, purpura, hair loss, erythema multiforme, photosensitivity	Steven-Johnson syndrome, toxic epidermal necrolysis
Musculoskeletal and connective tissue disorders		Arthralgia, myalgia		
Renal and urinary disorders			Interstitial nephritis	
Reproductive system and breast disorders			Gynaecomastia	
General disorders and administration site conditions	Fatigue	Oedema	Fever, hyperhidrosis, angioedema, anorexia, impotence	Anaphylactic shock
Investigations				Increase in cholesterol and triglyceride levels, hyponatremia

4.9 Overdose

The effects of overdose on lansoprazole in humans are not known (although the acute toxicity is likely to be low) and, consequently, instruction for treatment cannot be given. However, daily doses of up to 180 mg of lansoprazole orally and up to 90 mg of lansoprazole intravenously have been administered in trials without significant undesirable effects.

Please refer to section 4.8 for possible symptoms of lansoprazole overdose.

In the case of suspected overdose the patient should be monitored. Lansoprazole is not significantly eliminated by haemodialysis. If necessary, gastric emptying, charcoal and symptomatic therapy is recommended.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Proton pump inhibitors, ATC code: A02BC03

Lansoprazole is a gastric proton pump inhibitor. It inhibits the final stage of gastric acid formation by inhibiting the activity of H^+/K^+ ATPase of the parietal cells in the stomach. The inhibition is dose-dependent and reversible, and the effect applies to both basal and stimulated secretion of gastric acid. Lansoprazole is concentrated in the parietal cells and becomes active in their acidic environment, whereupon it reacts with the sulphydryl group of H^+/K^+ATPase causing inhibition of the enzyme activity.

Effect on gastric acid secretion:
Lansoprazole is a specific inhibitor of the parietal cell proton pump. A single oral dose of lansoprazole inhibits pentagastrin-stimulated gastric acid secretion by about 80%. After repeated daily administration for seven days, about 90% inhibition of gastric acid secretion is achieved. It has a corresponding effect on the basal secretion of gastric acid. A single oral dose of 30 mg reduces basal secretion by about 70%, and the patients' symptoms are consequently relieved starting from the very first dose. After eight days of repeated administration the reduction is about 85%. A rapid relief of symptoms is obtained by one capsule (30 mg) daily, and most patients with duodenal ulcer recover within 2 weeks, patients with gastric ulcer and reflux oesophagitis within 4 weeks. By reducing gastric acidity, lansoprazole creates an environment in which appropriate antibiotics can be effective against *H. pylori.*

5.2 Pharmacokinetic properties

Lansoprazole is a racemate of two active enantiomers that are biotransformed into the active form in the acidic environment of the parietal cells. As lansoprazole is rapidly inactivated by gastric acid, it is administered orally in enteric-coated form(s) for systemic absorption.

Absorption and distribution

Lansoprazole exhibits high (80-90%) bioavailability with a single dose. Peak plasma levels occur within 1.5 to 2.0 hours. Intake of food slows the absorption rate of lansoprazole and reduces the bioavailabilty by about 50%. The plasma protein binding is 97%.

Metabolism and elimination

Lansoprazole is extensively metabolised by the liver and the metabolites are excreted by both the renal and biliary route. The metabolism of lansoprazole is mainly catalysed by the enzyme CYP2C19. The enzyme CYP3A4 also contributes to the metabolism. The plasma elimination half-life ranges from 1 to 2 hours following single or multiple doses in healthy subjects. There is no evidence of accumulation following multiple doses in healthy subjects. Sulphone, sulphide and 5-hydroxyl derivatives of lansoprazole have been identified in plasma. These metabolites have very little or no antisecretory activity.

A study with ^{14}C labelled lansoprazole indicated that approximately one-third of the administered radiation was excreted in the urine and two-thirds was recovered in the faeces.

Pharmacokinetics in elderly patients

The clearance of lansoprazole is decreased in the elderly, with elimination half-life increased approximately 50% to 100%. Peak plasma levels were not increased in the elderly.

Pharmacokinetics in paediatric patients

The evaluation of the pharmacokinetics in children aged 1 –17 years of age showed a similar exposure as compared to adults with doses of 15 mg for those below 30 kg of weight and 30 mg for those above. The investigation of a dose of 17 mg/m^2 body surface or 1 mg/kg body weight also resulted in comparable exposure of lansoprazole in children aged 2-3 months up to one year of age compared to adults.

Higher exposure to lansoprazole in comparison to adults has been seen in infants below the age of 2-3 months with doses of both 1.0 mg/kg and 0.5 mg/kg body weight given as a single dose.

Pharmacokinetics in hepatic insufficiency

The exposure of lansoprazole is doubled in patients with mild hepatic impairment and much more increased in patients with moderate and severe hepatic impairment.

CYP2C19 poor metabolisers

CYP2C19 is subject to genetic polymorphism and 2-6 % of the population, called poor metabolisers (PMs), are homozygote for a mutant CYP2C19 allele and therefore lacks a functional CYP2C19 enzyme. The exposure of lansoprazole is several-fold higher in PMs than in extensive metabolisers (EMs).

5.3 Preclinical safety data

Preclinical data reveal no special hazards for humans based on conventional studies of safety pharmacology, repeated dose toxicity, toxicity to reproduction or genotoxicity.

In two rat carcinogenicity studies, lansoprazole produced dose-related gastric ECL cell hyperplasia and ECL cell carcinoids associated with hypergastrinaemia due to inhibition of acid secretion. Intestinal metaplasia was also observed, as were Leydig cell hyperplasia and benign Leydig cell tumours. After 18 months of treatment retinal atrophy was observed. This was not seen in monkeys, dogs or mice.

In mouse carcinogenicity studies dose-related gastric ECL cell hyperplasia developed as well as liver tumours and adenoma of rete testis.

The clinical relevance of these findings is unknown.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

[To be completed nationally]

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

[To be completed nationally]

6.4 Special precautions for storage

[To be completed nationally]

6.5 Nature and contents of container

Not all pack sizes may be marketed.

[To be completed nationally]

6.6 Special precautions for disposal and other handling

No special requirements for disposal.

Directions for re-constituting suspension from sachets:

1. Add 30 ml (two tablespoons) of tap water to a glass
2. Empty the granules from one sachet into the glass
3. Stir well and drink immediately.

7. MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

8. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

[To be completed nationally]

10. DATE OF REVISION OF THE TEXT

LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

Agopton and associated names 15 mg capsules

[See Annex I - To be completed nationally]

lansoprazole

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each capsule contains lansoprazole 15 mg

3. LIST OF EXCIPIENTS

[To be completed nationally]

Also contains sucrose. See enclosed leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

[To be completed nationally]

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use

Do not crush or chew

Read the package leaflet before use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

9. SPECIAL STORAGE CONDITIONS

[To be completed nationally]

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

14. GENERAL CLASSIFICATION FOR SUPPLY

[To be completed nationally]

15. INSTRUCTIONS ON USE

[To be completed nationally]

16. INFORMATION IN BRAILLE

[To be completed nationally]

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER FOIL

1. NAME OF THE MEDICINAL PRODUCT

Agopton and associated names 15 mg capsules

[See Annex I - To be completed nationally]

lansoprazole

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

3. EXPIRY DATE

4. BATCH NUMBER

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

Agopton and associated names 30 mg capsules

[See Annex I - To be completed nationally]

lansoprazole

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each capsule contains lansoprazole 30 mg

3. LIST OF EXCIPIENTS

[To be completed nationally]

Also contains sucrose. See enclosed leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

[To be completed nationally]

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use

Do not crush or chew

Read the package leaflet before use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

9. SPECIAL STORAGE CONDITIONS

[To be completed nationally]

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

14. GENERAL CLASSIFICATION FOR SUPPLY

[To be completed nationally]

15. INSTRUCTIONS ON USE

[To be completed nationally]

16. INFORMATION IN BRAILLE

[To be completed nationally]

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER FOIL

1. NAME OF THE MEDICINAL PRODUCT

Agopton and associated names 30 mg capsules

[See Annex I - To be completed nationally]

lansoprazole

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

3. EXPIRY DATE

4. BATCH NUMBER

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

Agopton and associated names 15 mg oro-dispersible tablet

[See Annex I - To be completed nationally]

lansoprazole

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each oro-dispersible tablet contains lansoprazole 15 mg

3. LIST OF EXCIPIENTS

[To be completed nationally]

Also contains lactose and aspartame. See enclosed leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

[To be completed nationally]

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use

Do not crush or chew

Read the package leaflet before use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

9. SPECIAL STORAGE CONDITIONS

[To be completed nationally]

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

14. GENERAL CLASSIFICATION FOR SUPPLY

[To be completed nationally]

15. INSTRUCTIONS ON USE

[To be completed nationally]

16. INFORMATION IN BRAILLE

[To be completed nationally]

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER FOIL

1. NAME OF THE MEDICINAL PRODUCT

Agopton and associated names 15 mg oro-dispersible tablet

[See Annex I - To be completed nationally]

lansoprazole

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

3. EXPIRY DATE

4. BATCH NUMBER

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

Agopton and associated names 30 mg oro-dispersible tablet

[See Annex I - To be completed nationally]

lansoprazole

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each oro-dispersible tablet contains lansoprazole 30 mg

3. LIST OF EXCIPIENTS

[To be completed nationally]

Also contains lactose and aspartame. See enclosed leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

[To be completed nationally]

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use

Do not crush or chew

Read the package leaflet before use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

9. SPECIAL STORAGE CONDITIONS

[To be completed nationally]

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

14. GENERAL CLASSIFICATION FOR SUPPLY

[To be completed nationally]

15. INSTRUCTIONS ON USE

[To be completed nationally]

16. INFORMATION IN BRAILLE

[To be completed nationally]

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER FOIL

1. NAME OF THE MEDICINAL PRODUCT

Agopton and associated names 30 mg oro-dispersible tablet

[See Annex I - To be completed nationally]

lansoprazole

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

3. EXPIRY DATE

4. BATCH NUMBER

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING & SACHET

CARTON & SACHET

1. NAME OF THE MEDICINAL PRODUCT

Agopton and associated names 30 mg gastro-resistant granules for oral suspension

[See Annex I - To be completed nationally]

lansoprazole

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each single dose sachet contains lansoprazole 30 mg

3. LIST OF EXCIPIENTS

[To be completed nationally]

Also contains sucrose and mannitol (E421). See enclosed leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

[To be completed nationally]

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use

Do not crush or chew

Read the package leaflet before use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

9. SPECIAL STORAGE CONDITIONS

[To be completed nationally]

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

14. GENERAL CLASSIFICATION FOR SUPPLY

[To be completed nationally]

15. INSTRUCTIONS ON USE

[To be completed nationally]

16. INFORMATION IN BRAILLE

[To be completed nationally]

PACKAGE LEAFLET

PACKAGE LEAFLET: INFORMATION FOR THE USER

Agopton and associated names 15 mg capsules
Agopton and associated names 30 mg capsules
[See Annex 1- To be completed nationally]
Lansoprazole

<Prescription>

Read all of this leaflet carefully before you start taking this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor.

<OTC>

Read all of this leaflet carefully because it contains important information for you.

This medicine is available without prescription. However, you still need to take Agopton carefully to get the best results from it.

- Keep this leaflet. You may need to read it again.
- Ask you pharmacist if you need more information or advice.
- You must contact a doctor if your symptoms worsen or do not improve after 14 days.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT AGOPTON IS AND WHAT IT IS USED FOR

The active ingredient in Agopton is lansoprazole, which is a proton pump inhibitor. Proton pump inhibitors reduce the amount of acid that your stomach makes.

<For countries with OTC use and prescription use>

Agopton is indicated for use in:
- Treatment of heartburn and acid regurgitation

Your doctor may also prescribe Agopton for the following indications:
- Treatment of duodenal and stomach ulcer
- Treatment of inflammation in your oesophagus (reflux oesophagitis)

- Prevention of reflux oesophagitis
- Treatment of infections caused by the bacteria *Helicobacter pylori* when given in combination with antibiotic therapy
- Treatment or prevention of duodenal or stomach ulcer in patients requiring continued NSAID treatment (NSAID treatment is used against pain or inflammation)
- Treatment of Zollinger-Ellison syndrome.

<For countries with prescription use only>

Your doctor may prescribe Agopton for the following indications:
- Treatment of duodenal and stomach ulcer
- Treatment of inflammation in your oesophagus (reflux oesophagitis)
- Prevention of reflux oesophagitis
- Treatment of heartburn and acid regurgitation
- Treatment of infections caused by the bacteria Helicobacter pylori when given in combination with antibiotic therapy
- Treatment or prevention of duodenal or stomach ulcer in patients requiring continued NSAID treatment (NSAID treatment is used against pain or inflammation)
- Treatment of Zollinger-Ellison syndrome.

Your doctor may have prescribed Agopton for another indication or with a dose different from that which is written in this information leaflet. Please follow your doctor's instructions for taking your medicine.

2. BEFORE YOU TAKE AGOPTON

Do not take Agopton:

- if you are allergic (hypersensitive) to lansoprazole or any of the other ingredients of Agopton
- if you are taking a medicine containing the active substance atazanavir (used in the treatment of HIV).

Take special care with Agopton

Please tell your doctor if you have serious liver disease. The doctor may have to adjust your dosage.

Your doctor may perform or have performed an additional investigation called an endoscopy in order to diagnose your condition and/or exclude malignant disease.

If diarrhoea occurs during the treatment with Agopton contact your doctor immediately, as Agopton has been associated with a small increase in infectious diarrhoea.

If your doctor has given you Agopton in addition to other medicines intended for the treatment of *Helicobacter pylori* infection (antibiotics) or together with anti-inflammatory medicines to treat your pain or rheumatic disease: please also read the package leaflets of these medicines carefully.

If you take Agopton on a long-term basis (longer than 1 year) your doctor will probably keep you under regular surveillance. You should report any new and exceptional symptoms and circumstances whenever you see your doctor.

Taking other medicines

Please tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

In particular tell your doctor if you are taking medicines containing any of the following active substances as Agopton may affect the way these drugs work:
- ketoconazole, itraconazole, rifampicin (used to treat infections)
- digoxin (used to treat heart problems)
- theophylline (used to treat asthma)
- tacrolimus (used to prevent transplant rejection)
- fluvoxamine (used to treat depression and other psychiatric diseases)
- antacids (used to treat heartburn or acid regurgitation)
- sucralfate (used for healing ulcers)
- St John´s wort (*Hypericum perforatum*) (used to treat mild depression)

Taking Agopton with food and drink

For the best results from your medicines you should take Agopton at least 30 minutes before food.

Pregnancy and breast-feeding

If you are pregnant, breast-feeding or if there is a chance you might be pregnant ask your doctor for advice before taking this medicine.

Driving and using machines

Side effects such as dizziness, vertigo, tiredness and visual disturbances sometimes occur in patients taking Agopton. If you experience side effects like these you should take caution as your ability to react may be decreased.

You alone are responsible to decide if you are in a fit condition to drive a motor vehicle or perform other tasks that demand increased concentration. Because of their effects or undesirable effects, one of the factors that can reduce your ability to do these things safely is your use of medicines.
Descriptions of these effects can be found in other sections.
Read all the information in this leaflet for guidance.

Discuss with your doctor, nurse or pharmacist if you are unsure about anything.

Important information about some of the ingredients of Agopton

Agopton contains sucrose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

[To be completed nationally]

3. HOW TO TAKE AGOPTON

Swallow the capsule whole with a glass of water. If you find the capsules difficult to swallow your doctor may advise on alternative ways to take your medicine. Do not crush or chew these capsules or the content of an emptied capsule because this will stop them from working properly.

If you are taking Agopton once a day, try to take it at the same time each day. You may get best results if you take Agopton first thing in the morning.

If you are taking Agopton twice a day, you should have the first dose in the morning and the second dose in the evening.

<The packaging has been printed with the days of the week to help you keep track of the medicines you have already taken.>

[To be included nationally if applicable]

The dose of Agopton depends on your condition. The usual doses of Agopton for adults are given below. Your doctor will sometimes prescribe you a different dose and will tell you how long your treatment will last.

Treatment of heartburn and acid regurgitation: one 15 mg or 30 mg capsule for 4 weeks. If symptoms persist you should report to your doctor. If your symptoms are not relieved within 4 weeks, please contact your doctor.

Treatment of duodenal ulcer: one 30 mg capsule every day for 2 weeks

Treatment of stomach ulcer: one 30 mg capsule every day for 4 weeks

Treatment of inflammation in your oesophagus (reflux oesophagitis): one 30 mg capsule every day for 4 weeks

Long-term prevention of reflux oesophagitis: one 15 mg capsule every day, your doctor may adjust your dose to one 30 mg capsule every day.

Treatment of infection of *Helicobacter pylori*: The usual dose is one 30 mg capsule in combination with two different antibiotics in the morning and one 30 mg capsule in combination with two different antibiotics in the evening. Treatment will usually be every day for 7 days.

The recommended combinations of antibiotics are:
- 30 mg Agopton together with 250-500 mg clarithromycin and 1000 mg amoxicillin
- 30 mg Agopton together with 250 mg clarithromycin and 400-500 mg metronidazole

If you are being treated for infection because you have an ulcer, it is unlikely that your ulcer will return if the infection is successfully treated. To give your medicine the best chance of working, take it at the right time and **do not miss a dose.**

Treatment of duodenal or stomach ulcer in patients requiring continued NSAID treatment: one 30 mg capsule every day for 4 weeks.

Prevention of duodenal or stomach ulcer in patients requiring continued NSAID treatment: one 15 mg capsule every day, your doctor may adjust your dose to one 30 mg capsule every day.

Zollinger-Ellison syndrome: The usual dose is two 30 mg capsules every day to start with, then depending on how you respond to Agopton the dose that your doctor decides is best for you.

Agopton should not be given to children.

Take your medicine exactly as your doctor has told you. You should check with your doctor if you are not sure how to take your medicine.

If you take more Agopton than prescribed

If you take more Agopton than you have been told to, seek medical advice quickly <or quickly consult the Toxicological Information Service.>

[To be completed nationally - Statement and phone number to be inserted based on national requirement for information on a toxicological service.]

If you forget to take Agopton

If you forget to take a dose, take it as soon as your remember unless it is nearly time for your next dose. If this happens skip the missed dose and take the remaining capsules as normal. Do not take a double dose to make up for a forgotten capsule.

If you stop taking Agopton

Do not stop treatment early because your symptoms have got better. Your condition may not have been fully healed and may reoccur if you do not finish your course of treatment.

If you have any further questions on the use of this product, ask your doctor.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Agopton can cause side effects, although not everybody gets them.

The following side effects are common (occur in more than 1 in 100 patients):
- headache, dizziness
- diarrhoea, constipation, stomach pains, feeling or being sick, wind, dry or sore mouth or throat
- skin rash, itching
- changes in liver function test values
- tiredness.

The following side effects are uncommon (occur in less than 1 in 100 patients):
- depression
- joint or muscle pain
- fluid retention or swelling
- changes in blood cell counts.

The following side effects are rare (occur in less than 1 in 1000 patients):
- fever
- restlessness, drowsiness, confusion, hallucinations, insomnia, visual disturbances, vertigo
- a change in the way things taste, loss of appetite, inflammation of your tongue (glossitis)
- skin reactions such as burning or pricking feeling under the skin, bruising, reddening and excessive sweating
- sensitivity to light
- hair loss
- feelings of ants creeping over the skin (paresthesiae), trembling
- anaemia (paleness)
- kidney problems
- pancreatitis
- inflammation of the liver (may be seen as yellow skin or eyes)
- breast swelling in males, impotence
- candidiasis (fungal infection, may affect skin or the mucosa)
- angioedema; You should see your doctor immediately if you experience symptoms of angioedema, such as swollen face, tongue or pharynx, difficulty to swallow, hives and difficulties to breath.

The following side effects are very rare (occur in less than 1 in 10000 patients):

- severe hypersensitivity reactions including shock. Symptoms of a hypersensitivity reaction may include fever, rash, swelling and sometimes a fall in blood pressure
- inflammation of your mouth (stomatitis)
- colitis (bowel inflammation)
- changes in test values such as sodium, cholesterol and triglyceride levels
- very severe skin reactions with reddening, blistering, severe inflammation and skin loss.
- very rarely Agopton may cause a reduction in the number of white blood cells and your resistance to infection may be decreased. If you experience an infection with symptoms such as fever and serious deterioration of your general condition, or fever with local infection symptoms such as sore throat/pharynx/mouth or urinary problems you should see your doctor immediately. A blood test will be taken to check possible reduction of white blood cells (agranulocytosis).

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor.

5. HOW TO STORE AGOPTON

Keep out of the reach and sight of children.

Do not use Agopton after the expiry date which is stated on the blister and carton. The expiry date refers to the last day of that month.

[To be completed nationally]

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What Agopton contains

- The active substance is lansoprazole
- The other ingredients are

[To be completed nationally]

What Agopton looks like and contents of the pack

[To be completed nationally]

Marketing Authorisation Holder and Manufacturer

The marketing authorisation holder is:
<{Name and address}>
<{tel}>
<{fax}>
<{e-mail}>

The manufacturer is:
<{Name and address}>
<{tel}>
<{fax}>
<{e-mail}>

[To be completed nationally]

This medicinal product is authorised in the Member States of the EEA under the following names:

Austria:	AGOPTON
Belgium:	DAKAR, NIBITOR
Denmark:	LANZO
Finland:	LANZO
France:	LANZOR, OGAST
Germany:	AGOPTON, LANZOR
Greece:	LAPRAZOL
Hungary:	LANSONE
Iceland:	LANZO, ZOTON
Ireland:	ZOTON
Italy:	LANSOX, LANGAST, LIMPIDEX, ZOTON
Luxembourg:	DAKAR
Netherlands:	PREZAL
Norway:	LANZO
Portugal:	OGASTO
Spain:	BAMALITE, OPIREN
Sweden:	LANZO
United Kingdom:	ZOTON

This leaflet was last approved in {MM/YYYY}.

[To be completed nationally]

PACKAGE LEAFLET: INFORMATION FOR THE USER

Agopton and associated names 15 mg oro-dispersible tablets
Agopton and associated names 30 mg oro-dispersible tablets
[See Annex 1- To be completed nationally]
Lansoprazole

<Prescription>

Read all of this leaflet carefully before you start taking this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor.

<OTC>

<**Read all of this leaflet carefully because it contains important information for you.**

This medicine is available without prescription. However, you still need to take Agopton carefully to get the best results from it.
- Keep this leaflet. You may need to read it again.
- Ask your pharmacist if you need more information or advice.
- You must contact a doctor if your symptoms worsen or do not improve after 14 days.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT AGOPTON IS AND WHAT IT IS USED FOR

The active ingredient in Agopton is lansoprazole, which is a proton pump inhibitor. Proton pump inhibitors reduce the amount of acid that your stomach makes.

<For countries with OTC use and prescription use>

Agopton is indicated for use in:
- Treatment of heartburn and acid regurgitation

Your doctor may also prescribe Agopton for the following indications:
- Treatment of duodenal and stomach ulcer
- Treatment of inflammation in your oesophagus (reflux oesophagitis)
- Prevention of reflux oesophagitis

- Treatment of infections caused by the bacteria *Helicobacter pylori* when given in combination with antibiotic therapy
- Treatment or prevention of duodenal or stomach ulcer in patients requiring continued NSAID treatment (NSAID treatment is used against pain or inflammation)
- Treatment of Zollinger-Ellison syndrome.

<For countries with prescription use only>:

Your doctor may prescribe Agopton for the following indications:
- Treatment of duodenal and stomach ulcer
- Treatment of inflammation in your oesophagus (reflux oesophagitis)
- Prevention of reflux oesophagitis
- Treatment of heartburn and acid regurgitation
- Treatment of infections caused by the bacteria Helicobacter pylori when given in combination with antibiotic therapy
- Treatment or prevention of duodenal or stomach ulcer in patients requiring continued NSAID treatment (NSAID treatment is used against pain or inflammation)
- Treatment of Zollinger-Ellison syndrome.

Your doctor may have prescribed Agopton for another indication or with a dose different from that which is written in this information leaflet. Please follow your doctor's instructions for taking your medicine.

2. BEFORE YOU TAKE AGOPTON

Do not take Agopton:

- if you are allergic (hypersensitive) to lansoprazole or any of the other ingredients of Agopton
- if you are taking a medicine containing the active substance atazanavir (used in the treatment of HIV).

Take special care with Agopton

Please tell your doctor if you have serious liver disease. The doctor may have to adjust your dosage.

Your doctor may perform or have performed an additional investigation called an endoscopy in order to diagnose your condition and/or exclude malignant disease.

If diarrhoea occurs during the treatment with Agopton contact your doctor immediately, as Agopton has been associated with a small increase in infectious diarrhoea.

If your doctor has given you Agopton in addition to other medicines intended for the treatment of *Helicobacter pylori* infection (antibiotics) or together with anti-inflammatory medicines to treat your pain or rheumatic disease: please also read the package leaflets of these medicines carefully.

If you take Agopton on a long-term basis (longer than 1 year) your doctor will probably keep you under regular surveillance. You should report any new and exceptional symptoms and circumstances whenever you see your doctor.

Taking other medicines

Please tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

In particular tell your doctor if you are taking medicines containing any of the following active substances as Agopton may affect the way these drugs work:
- ketoconazole, itraconazole, rifampicin (used to treat infections)
- digoxin (used to treat heart problems)
- theophylline (used to treat asthma)
- tacrolimus (used to prevent transplant rejection)
- fluvoxamine (used to treat depression and other psychiatric diseases)
- antacids (used to treat heartburn or acid regurgitation)
- sucralfate (used for healing ulcers)
- St John´s wort (*Hypericum perforatum*) (used to treat mild depression)

Taking Agopton with food and drink

For the best results from your medicines you should take Agopton at least 30 minutes before food.

Pregnancy and breast-feeding

If you are pregnant, breast-feeding or if there is a chance you might be pregnant ask your doctor for advice before taking this medicine.

Driving and using machines

Side effects such as dizziness, vertigo, tiredness and visual disturbances sometimes occur in patients taking Agopton. If you experience side effects like these you should take caution as your ability to react may be decreased.

You alone are responsible to decide if you are in a fit condition to drive a motor vehicle or perform other tasks that demand increased concentration. Because of their effects or undesirable effects, one of the factors that can reduce your ability to do these things safely is your use of medicines.
Descriptions of these effects can be found in other sections.
Read all the information in this leaflet for guidance.

Discuss with your doctor, nurse or pharmacist if you are unsure about anything.

Important information about some of the ingredients of Agopton

Agopton contains lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

Agopton contains aspartame. Aspartame is a source of phenylalanine, which may be harmful for people with phenylketonuria.

[To be completed nationally]

3. HOW TO TAKE AGOPTON

Place the tablet on your tongue and suck gently. The tablet rapidly dissolves in the mouth, releasing microgranules which you should swallow without chewing. You can also swallow the tablet whole with a glass of water.

Your doctor might instruct you to take the tablet with a syringe, in case you have serious difficulties with swallowing.

The following instructions should be followed if administered via syringe:
It is important that the appropriateness of the selected syringe is carefully tested.

- Remove the plunger of the syringe (at least 5 ml syringe for the 15 mg tablet and 10 ml syringe for the 30 mg tablet)
- Put the tablet into the barrel
- Put the plunger back onto the syringe
- For the 15 mg tablet: Draw 4 ml tap water into the syringe
- For the 30 mg tablet: Draw 10 ml tap water into the syringe
- Invert the syringe and draw an additional 1 ml of air into it
- Shake the syringe gently for 10-20 seconds until the tablet is dispersed
- The contents can be emptied directly into the mouth
- Refill the syringe with 2-5 ml of tap water to flush the remnants out of the syringe into the mouth

If you are taking Agopton once a day, try to take it at the same time each day. You may get best results if you take Agopton first thing in the morning.

If you are taking Agopton twice a day, you should have the first dose in the morning and the second dose in the evening.

<The packaging has been printed with the days of the week to help you keep track of the medicines you have already taken.>

[To be included nationally if applicable]

The dose of Agopton depends on your condition. The usual doses of Agopton for adults are given below. Your doctor will sometimes prescribe you a different dose and will tell you how long your treatment will last.

Treatment of heartburn and acid regurgitation: one 15 mg or 30 mg oro-dispersible tablet for 4 weeks. If symptoms persist you should report to your doctor. If your symptoms are not relieved within 4 weeks, please contact your doctor.

Treatment of duodenal ulcer: one 30 mg oro-dispersible tablet every day for 2 weeks

Treatment of stomach ulcer: one 30 mg oro-dispersible tablet every day for 4 weeks

Treatment of inflammation in your oesophagus (reflux oesophagitis): one 30 mg oro-dispersible tablet every day for 4 weeks

Long-term prevention of reflux oesophagitis: one 15 mg oro-dispersible tablet every day, your doctor may adjust your dose to one 30 mg oro-dispersible tablet every day.

Treatment of infection of *Helicobacter pylori*: The usual dose is one 30 mg oro-dispersible tablet in combination with two different antibiotics in the morning and one 30 mg oro-dispersible tablet in combination with two different antibiotics in the evening. Treatment will usually be every day for 7 days.

The recommended combinations of antibiotics are:
- 30 mg Agopton together with 250-500 mg clarithromycin and 1000 mg amoxicillin
- 30 mg Agopton together with 250 mg clarithromycin and 400-500 mg metronidazole

If you are being treated for infection because you have an ulcer, it is unlikely that your ulcer will return if the infection is successfully treated. To give your medicine the best chance of working, take it at the right time and **do not miss a dose.**

Treatment of duodenal or stomach ulcer in patients requiring continued NSAID treatment: one 30 mg oro-dispersible tablet every day for 4 weeks.

Prevention of duodenal or stomach ulcer in patients requiring continued NSAID treatment: one 15 mg oro-dispersible tablet every day, your doctor may adjust your dose to one 30 mg oro-dispersible tablet every day.

Zollinger-Ellison syndrome: The usual dose is two 30 mg oro-dispersible tablet every day to start with, then depending on how you respond to Agopton the dose that your doctor decides is best for you.

Agopton should not be given to children.

Take your medicine exactly as your doctor has told you. You should check with your doctor if you are not sure how to take your medicine.

If you take more Agopton than prescribed

If you take more Agopton than you have been told to, seek medical advice quickly <or quickly consult the Toxicological Information Service.>

[To be completed nationally - Statement and phone number to be inserted based on national requirement for information on a toxicological service.]

If you forget to take Agopton

If you forget to take a dose, take it as soon as your remember unless it is nearly time for your next dose. If this happens skip the missed dose and take the remaining oro-dispersible tablets as normal. Do not take a double dose to make up for a forgotten oro-dispersible tablet.

If you stop taking Agopton

Do not stop treatment early because your symptoms have got better. Your condition may not have been fully healed and may reoccur if you do not finish your course of treatment.

If you have any further questions on the use of this product, ask your doctor.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Agopton can cause side effects, although not everybody gets them.

The following side effects are common (occur in more than 1 in 100 patients):
- headache, dizziness
- diarrhoea, constipation, stomach pains, feeling or being sick, wind, dry or sore mouth or throat
- skin rash, itching
- changes in liver function test values
- tiredness.

The following side effects are uncommon (occur in less than 1 in 100 patients):
- depression
- joint or muscle pain
- fluid retention or swelling
- changes in blood cell counts.

The following side effects are rare (occur in less than 1 in 1000 patients):
- fever
- restlessness, drowsiness, confusion, hallucinations, insomnia, visual disturbances, vertigo
- a change in the way things taste, loss of appetite, inflammation of your tongue (glossitis)
- skin reactions such as burning or pricking feeling under the skin, bruising, reddening and excessive sweating
- sensitivity to light
- hair loss
- feelings of ants creeping over the skin (paresthesiae), trembling
- anaemia (paleness)
- kidney problems
- pancreatitis
- inflammation of the liver (may be seen as yellow skin or eyes)
- breast swelling in males, impotence
- candidiasis (fungal infection, may affect skin or the mucosa)
- angioedema; You should see your doctor immediately if you experience symptoms of angioedema, such as swollen face, tongue or pharynx, difficulty to swallow, hives and difficulties to breath.

The following side effects are very rare (occur in less than 1 in 10000 patients):
- severe hypersensitivity reactions including shock. Symptoms of a hypersensitivity reaction may include fever, rash, swelling and sometimes a fall in blood pressure
- inflammation of your mouth (stomatitis)
- colitis (bowel inflammation)
- changes in test values such as sodium, cholesterol and triglyceride levels
- very severe skin reactions with reddening, blistering, severe inflammation and skin loss.
- very rarely Agopton may cause a reduction in the number of white blood cells and your resistance to infection may be decreased. If you experience an infection with symptoms such as fever and serious deterioration of your general condition, or fever with local infection symptoms such as sore throat/pharynx/mouth or urinary problems you should see your doctor immediately. A blood test will be taken to check possible reduction of white blood cells (agranulocytosis).

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor.

5. HOW TO STORE AGOPTON

Keep out of the reach and sight of children.

Do not use Agopton after the expiry date which is stated on the blister and carton. The expiry date refers to the last day of that month.

[To be completed nationally]

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What Agopton contains

- The active substance is lansoprazole
- The other ingredients are

[To be completed nationally]

What Agopton looks like and contents of the pack

[To be completed nationally]

Marketing Authorisation Holder and Manufacturer

The marketing authorisation holder is:
<{Name and address}>
<{tel}>
<{fax}>
<{e-mail}>

The manufacturer is:
<{Name and address}>
<{tel}>
<{fax}>
<{e-mail}>

[To be completed nationally]

This medicinal product is authorised in the Member States of the EEA under the following names:

Austria:	AGOPTON Rapid
Finland:	LANZO
Greece:	LAPRAZOL FasTab
Iceland:	LANZO
Ireland:	ZOTON FasTab
Italy:	LANSOX, LANGAST, LIMPIDEX, ZOTON
Norway:	LANZO
Portugal:	OGASTO
Spain:	BAMALITE Frash, OPIREN Frash
Sweden:	LANZO
United Kingdom:	ZOTON FasTab

This leaflet was last approved in {MM/YYYY}.

[To be completed nationally]

PACKAGE LEAFLET: INFORMATION FOR THE USER

Agopton and associated names 30 mg gastro-resistant granules for oral suspension
[See Annex 1- To be completed nationally]
Lansoprazole

<Prescription>

Read all of this leaflet carefully before you start taking this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor.

<OTC>

Read all of this leaflet carefully because it contains important information for you.

This medicine is available without prescription. However, you still need to take Agopton carefully to get the best results from it.

- Keep this leaflet. You may need to read it again.
- Ask you pharmacist if you need more information or advice.
- You must contact a doctor if your symptoms worsen or do not improve after 14 days.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT AGOPTON IS AND WHAT IT IS USED FOR

The active ingredient in Agopton is lansoprazole, which is a proton pump inhibitor. Proton pump inhibitors reduce the amount of acid that your stomach makes.

<For countries with OTC use and prescription use>

Agopton is indicated for use in:
- Treatment of heartburn and acid regurgitation

Your doctor may also prescribe Agopton for the following indications:
- Treatment of duodenal and stomach ulcer
- Treatment of inflammation in your oesophagus (reflux oesophagitis)

- Prevention of reflux oesophagitis
- Treatment of infections caused by the bacteria *Helicobacter pylori* when given in combination with antibiotic therapy
- Treatment or prevention of duodenal or stomach ulcer in patients requiring continued NSAID treatment (NSAID treatment is used against pain or inflammation)
- Treatment of Zollinger-Ellison syndrome.

<For countries with prescription use only>

Your doctor may prescribe Agopton for the following indications:
- Treatment of duodenal and stomach ulcer
- Treatment of inflammation in your oesophagus (reflux oesophagitis)
- Prevention of reflux oesophagitis
- Treatment of heartburn and acid regurgitation
- Treatment of infections caused by the bacteria Helicobacter pylori when given in combination with antibiotic therapy
- Treatment or prevention of duodenal or stomach ulcer in patients requiring continued NSAID treatment (NSAID treatment is used against pain or inflammation)
- Treatment of Zollinger-Ellison syndrome.

Your doctor may have prescribed Agopton for another indication or with a dose different from that which is written in this information leaflet. Please follow your doctor's instructions for taking your medicine.

2. BEFORE YOU TAKE AGOPTON

Do not take Agopton:

- if you are allergic (hypersensitive) to lansoprazole or any of the other ingredients of Agopton
- if you are taking a medicine containing the active substance atazanavir (used in the treatment of HIV).

Take special care with Agopton

Please tell your doctor if you have serious liver disease. The doctor may have to adjust your dosage.

Your doctor may perform or have performed an additional investigation called an endoscopy in order to diagnose your condition and/or exclude malignant disease.

If diarrhoea occurs during the treatment with Agopton contact your doctor immediately, as Agopton has been associated with a small increase in infectious diarrhoea.

If your doctor has given you Agopton in addition to other medicines intended for the treatment of *Helicobacter pylori* infection (antibiotics) or together with anti-inflammatory medicines to treat your pain or rheumatic disease: please also read the package leaflets of these medicines carefully.

If you take Agopton on a long-term basis (longer than 1 year) your doctor will probably keep you under regular surveillance. You should report any new and exceptional symptoms and circumstances whenever you see your doctor.

Taking other medicines

Please tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

In particular tell your doctor if you are taking medicines containing any of the following active substances as Agopton may affect the way these drugs work:
- ketoconazole, itraconazole, rifampicin (used to treat infections)
- digoxin (used to treat heart problems)
- theophylline (used to treat asthma)
- tacrolimus (used to prevent transplant rejection)
- fluvoxamine (used to treat depression and other psychiatric diseases)
- antacids (used to treat heartburn or acid regurgitation)
- sucralfate (used for healing ulcers)
- St John´s wort (*Hypericum perforatum*) (used to treat mild depression)

Taking Agopton with food and drink

For the best results from your medicines you should take Agopton at least 30 minutes before food.

Pregnancy and breast-feeding

If you are pregnant, breast-feeding or if there is a chance you might be pregnant ask your doctor for advice before taking this medicine.

Driving and using machines

Side effects such as dizziness, vertigo, tiredness and visual disturbances sometimes occur in patients taking Agopton. If you experience side effects like these you should take caution as your ability to react may be decreased.

You alone are responsible to decide if you are in a fit condition to drive a motor vehicle or perform other tasks that demand increased concentration. Because of their effects or undesirable effects, one of the factors that can reduce your ability to do these things safely is your use of medicines.
Descriptions of these effects can be found in other sections.
Read all the information in this leaflet for guidance.

Discuss with your doctor, nurse or pharmacist if you are unsure about anything.

Important information about some of the ingredients of Agopton

Agopton contains sucrose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

Agopton contains mannitol, which may have a mild laxative effect.

[To be completed nationally]

3. HOW TO TAKE AGOPTON

Add 30 ml (two tablespoons) of tap water to a glass. Empty the granules from one sachet into the glass. Stir well and drink immediately. When reconstituted in water Agopton is a pink suspension with a strawberry flavour.

If you are taking Agopton once a day, try to take it at the same time each day. You may get best results if you take Agopton first thing in the morning.

If you are taking Agopton twice a day, you should have the first dose in the morning and the second dose in the evening.

The dose of Agopton depends on your condition. The usual doses of Agopton for adults are given below. Your doctor will sometimes prescribe you a different dose and will tell you how long your treatment will last.

Treatment of heartburn and acid regurgitation: one 15 mg or 30 mg capsule for 4 weeks. If symptoms persist you should report to your doctor. If your symptoms are not relieved within 4 weeks, please contact your doctor.

Treatment of duodenal ulcer: one 30 mg capsule every day for 2 weeks

Treatment of stomach ulcer: one 30 mg capsule every day for 4 weeks

Treatment of inflammation in your oesophagus (reflux oesophagitis): one 30 mg capsule every day for 4 weeks

Long-term prevention of reflux oesophagitis: one 15 mg capsule every day, your doctor may adjust your dose to one 30 mg capsule every day.

Treatment of infection of *Helicobacter pylori*: The usual dose is one 30 mg capsule in combination with two different antibiotics in the morning and one 30 mg capsule in combination with two different antibiotics in the evening. Treatment will usually be every day for 7 days.

The recommended combinations of antibiotics are:
- 30 mg Agopton together with 250-500 mg clarithromycin and 1000 mg amoxicillin
- 30 mg Agopton together with 250 mg clarithromycin and 400-500 mg metronidazole

If you are being treated for infection because you have an ulcer, it is unlikely that your ulcer will return if the infection is successfully treated. To give your medicine the best chance of working, take it at the right time and **do not miss a dose.**

Treatment of duodenal or stomach ulcer in patients requiring continued NSAID treatment: one 30 mg capsule every day for 4 weeks.

Prevention of duodenal or stomach ulcer in patients requiring continued NSAID treatment: one 15 mg capsule every day, your doctor may adjust your dose to one 30 mg capsule every day.

Zollinger-Ellison syndrome: The usual dose is two 30 mg capsules every day to start with, then depending on how you respond to Agopton the dose that your doctor decides is best for you.

Agopton should not be given to children.

Take your medicine exactly as your doctor has told you. You should check with your doctor if you are not sure how to take your medicine.

If you take more Agopton than prescribed

If you take more Agopton than you have been told to, seek medical advice quickly <or quickly consult the Toxicological Information Service.>

[To be completed nationally - Statement and phone number to be inserted based on national requirement for information on a toxicological service.]

If you forget to take Agopton

If you forget to take a dose, take it as soon as your remember unless it is nearly time for your next dose. If this happens skip the missed dose and take the remaining capsules as normal. Do not take a double dose to make up for a forgotten capsule.

If you stop taking Agopton

Do not stop treatment early because your symptoms have got better. Your condition may not have been fully healed and may reoccur if you do not finish your course of treatment.

If you have any further questions on the use of this product, ask your doctor.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Agopton can cause side effects, although not everybody gets them.

The following side effects are common (occur in more than 1 in 100 patients):
- headache, dizziness
- diarrhoea, constipation, stomach pains, feeling or being sick, wind, dry or sore mouth or throat
- skin rash, itching
- changes in liver function test values
- tiredness.

The following side effects are uncommon (occur in less than 1 in 100 patients):
- depression
- joint or muscle pain
- fluid retention or swelling
- changes in blood cell counts.

The following side effects are rare (occur in less than 1 in 1000 patients):
- fever
- restlessness, drowsiness, confusion, hallucinations, insomnia, visual disturbances, vertigo
- a change in the way things taste, loss of appetite, inflammation of your tongue (glossitis)
- skin reactions such as burning or pricking feeling under the skin, bruising, reddening and excessive sweating
- sensitivity to light
- hair loss
- feelings of ants creeping over the skin (paresthesiae), trembling
- anaemia (paleness)
- kidney problems
- pancreatitis
- inflammation of the liver (may be seen as yellow skin or eyes)
- breast swelling in males, impotence
- candidiasis (fungal infection, may affect skin or the mucosa)

- angioedema; You should see your doctor immediately if you experience symptoms of angioedema, such as swollen face, tongue or pharynx, difficulty to swallow, hives and difficulties to breath.

The following side effects are very rare (occur in less than 1 in 10000 patients):
- severe hypersensitivity reactions including shock. Symptoms of a hypersensitivity reaction may include fever, rash, swelling and sometimes a fall in blood pressure
- inflammation of your mouth (stomatitis)
- colitis (bowel inflammation)
- changes in test values such as sodium, cholesterol and triglyceride levels
- very severe skin reactions with reddening, blistering, severe inflammation and skin loss.
- very rarely Agopton may cause a reduction in the number of white blood cells and your resistance to infection may be decreased. If you experience an infection with symptoms such as fever and serious deterioration of your general condition, or fever with local infection symptoms such as sore throat/pharynx/mouth or urinary problems you should see your doctor immediately. A blood test will be taken to check possible reduction of white blood cells (agranulocytosis).

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor.

5. HOW TO STORE AGOPTON

Keep out of the reach and sight of children.

Do not use Agopton after the expiry date which is stated on each sachet and the carton. The expiry date refers to the last day of that month.

[To be completed nationally]

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What Agopton contains

- The active substance is lansoprazole
- The other ingredients are

[To be completed nationally]

What Agopton looks like and contents of the pack

[To be completed nationally]

Marketing Authorisation Holder and Manufacturer

The marketing authorisation holder is:
<{Name and address}>
<{tel}>
<{fax}>
<{e-mail}>

The manufacturer is:
<{Name and address}>
<{tel}>
<{fax}>
<{e-mail}>

[To be completed nationally]

This medicinal product is authorised in the Member States of the EEA under the following names:

Ireland:	ZOTON
United Kingdom:	ZOTON

This leaflet was last approved in {MM/YYYY}.

[To be completed nationally]