ZANPROL 10MG TABLETS
(OMEPRAZOLE)

PL 00079/0660

UKPAR

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ZANPROL 10MG TABLETS
(OMEPRAZOLE)
PL 00079/0660

LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Glaxo Wellcome UK Limited (trading as ‘GlaxoSmithkline Consumer Healthcare’) a Marketing Authorisation (licence) for the medicinal product Zanprol 10mg Tablets (PL 10949/0370) on 26th June 2009. This is a P licensed medicine available only from pharmacies, under the supervision of a pharmacist.

Zanprol 10mg Tablets contain the active ingredient, omeprazole. Omeprazole belongs to a group of medicines called proton pump inhibitors, and works by preventing your stomach from producing too much acid.

Zanprol 10mg Tablets are used to give long lasting relief of acid reflux and heartburn. Heartburn and acid reflux are caused by stomach acid rising up the food pipe, resulting in a burning sensation in the chest and throat. This can be accompanied by a bitter taste in the mouth.

This application is a duplicate of a previously granted application for Dexcel Heartburn Relief 10mg Tablets (PL 14017/0069), authorised to Dexcel Pharma Limited on 19th January 2004. The test and reference products are identical.

No new or unexpected safety concerns arose from this application and it was therefore judged that the benefits of using Zanprol 10mg Tablets outweigh the risk; hence a Marketing Authorisation has been granted.

After a change of ownership was granted on 21st June 2010, the marketing authorisation holder changed to Beecham Group plc (PL 00079/0660).
ZANPROL 10MG TABLETS
(OMEPRAZOLE)

PL 00079/0660

SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the MHRA granted Glaxo Wellcome UK Limited (trading as ‘GlaxoSmithkline Consumer Healthcare’) a Marketing Authorisation for the medicinal product Zanprol 10mg Tablets (PL 10949/0370) on 26th June 2009. This is a P licensed medicine available only from pharmacies.

This application was submitted as a simple abridged ‘informed consent’ application according to article 10c of Directive 2001/83/EC (as amended), cross-referring to Dexcel Heartburn Relief 10mg Tablets (PL 14017/0069), authorised to Dexcel Pharma Limited on 19th January 2004.

Zanprol 10mg Tablets are indicated for the relief of reflux-like symptoms (e.g. heartburn) in patients aged 18 and over.

Omeprazole, a substituted benzimidazole, is a selective proton pump inhibitor which inhibits directly and in dose-dependent fashion the H+/K+-ATPase of the parietal cells of the stomach responsible for gastric acid secretion. By this selective intracellular attack, independently from membrane located receptors like histamine H2-, muscarine M1- or gastrinergic receptors, omeprazole belongs to an independent class of inhibitors which block the terminal secretion process. By its mode of action, omeprazole reduces not only basal but also stimulus-induced acid secretion, independently of the kind of stimulus. Omeprazole thus increases the pH-value and reduces the secretory volume.

Oral dosing with 20 mg omeprazole once daily produces inhibition of gastric acid secretion within 1-2 hours of the first dose. The maximum effect is achieved within 4 days of starting treatment after which the degree of inhibition remains constant. The mean decrease in pentagastrin-stimulated peak acid output twenty-four hours after dosing is about 70%.

Absorption of omeprazole takes place in the small intestine and is usually completed within 3-6 hours. The systemic bioavailability of omeprazole from a single oral dose is approximately 35%. Omeprazole is entirely metabolized, mainly in the liver.

No new data were submitted nor was it necessary for this simple application, as the data are identical to that of the previously granted cross-reference product. As the cross-reference product was granted prior to the introduction of current legislation, no PAR was generated for it.

After a change of ownership was granted on 21st June 2010, the marketing authorisation holder changed to Beecham Group plc (PL 00079/0660).
PHARMACEUTICAL ASSESSMENT

LICENCE NUMBER: PL 00079/0660
PROPRIETARY NAME: Zanprol 10mg Tablets
ACTIVE INGREDIENT/S: Omeprazole
COMPANY NAME: Glaxo Wellcome UK Limited
E.C. ARTICLE: Article 10c of Directive 2001/83/EC (as amended)
LEGAL STATUS: P

1. INTRODUCTION

This is a simple abridged application, submitted under Article 10c of Directive 2001/83/EC (as amended) for Zanprol 10mg Tablets. The proposed MA holder is ‘Glaxo Wellcome UK Limited’ (trading as ‘GlaxoSmithkline Consumer Healthcare’).

The reference product is Dexcel Heartburn Relief 10mg Tablets (PL 14017/0069), authorised to Dexcel Pharma Limited on 19th January 2004. The test and reference products are identical.

2. MARKETING AUTHORISATION APPLICATION FORM

2.1 Name(s)

The approved name of the product is Zanprol 10mg Tablets. The product has been named in line with current requirements and the product name is acceptable.

2.2 Strength, pharmaceutical form, route of administration, container and pack sizes

Zanprol 10mg Tablets are gastro-resistant tablets marketed in aluminium - aluminium blister strips, which are packaged with the Patient Information Leaflet (PIL) into cardboard outer cartons in pack sizes of 7, 14, and 28.

The approved shelf-life (2 years) and storage conditions (‘Do not store above 30°C’ and ‘Store in the original package’) are consistent with the details registered for the cross-reference product.

2.3 Legal status

The product is a P licensed medicine available only from pharmacies, under the supervision of a pharmacist

2.4 Marketing authorisation holder / Contact Persons / Company

The proposed Marketing Authorisation holder is ‘Glaxo Wellcome UK Limited, Stockley Park West, Uxbridge, Middlesex UB11 1BT, United Kingdom’; trading as ‘GlaxoSmithkline Consumer Healthcare, Brentford, TW8 9GS United Kingdom’.

The QP responsible for pharmacovigilance was stated and their CV included.
2.5 Manufacturers
The proposed manufacturing site is consistent with that registered for the cross-reference product and evidence of GMP compliance has been provided.

2.6 Qualitative and quantitative composition
The proposed composition is consistent with the details registered for the cross-reference product.

2.7 Manufacturing process
The proposed manufacturing process is consistent with the details registered for the cross-reference product and the maximum batch size is stated.

2.8 Finished product / shelf-life specification
The proposed finished product specification is in line with the details registered for the cross-reference product.

2.9 Drug substance specification
The proposed drug substance specification is consistent with the details registered for the cross-reference product.

2.10 TSE Compliance
The sodium stearyl fumarate has been confirmed as being of vegetable origin. A TSE Certificate of Suitability has been provided by the sodium stearate suppliers stating that the sodium stearate they provide meets the criteria described in the current version of the monograph ‘Products with risk of transmitting agents of animal spongiform encephalopathies’. The applicant has provided a declaration that milk used in the production of lactose monohydrate is sourced from healthy animals under the same conditions as that for human consumption.

3. EXPERT REPORTS
Satisfactory expert reports and curriculum vitae of experts were provided.

4. PRODUCT NAME & APPEARANCE
See 2.1 for details of the proposed product name. The appearance of the product (brownish-pink, capsule-shaped, film-coated tablets) is consistent with that of the cross-reference product.

5. SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)
The approved SmPC is consistent with the details registered for the cross-reference product.

6. PATIENT INFORMATION LEAFLET (PIL) / CARTON
PIL
The patient information leaflet has been prepared in the user tested format and in line with the details registered for the cross-reference product. The approved PIL is satisfactory.
Labelling

Colour mock-ups of the labelling have been provided and are satisfactory. The approved artwork is comparable to the artwork registered for the cross-reference product and complies with statutory requirements. In line with current legislation the applicant has included the name of the product in Braille on the outer packaging.

7. CONCLUSIONS

The grounds for this application are considered adequate. A Marketing Authorisation was, therefore, granted.
PRECLINICAL ASSESSMENT

This abridged application was submitted as a simple abridged application according to article 10c of Directive 2001/83/EC (as amended).

No new preclinical data have been supplied with this application and none are required for an application of this type. A preclinical expert report has been written by a suitably qualified person and is satisfactory.
CLINICAL ASSESSMENT

This abridged application was submitted as a simple abridged application according to article 10c of Directive 2001/83/EC (as amended).

As this is a piggy-back (‘informed consent’) application for PL 14017/0069, no new clinical data have been supplied with the application, and none are required for applications of this type. A clinical expert report has been written by a suitably qualified person and is satisfactory.
OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY
The data for this application are consistent with that previously assessed for the cross-reference product and as such have been judged to be satisfactory.

PRECLINICAL
No new preclinical data were submitted and none are required for an application of this type.

EFFICACY
Medicinal products containing omeprazole have been available in the UK for much more than ten years. Their use is well established with recognised efficacy and acceptable safety.

This application is identical to the previously granted application for Dexcel Heartburn Relief 10mg Tablets (PL 14017/0069, Dexcel Pharma Limited).

No new or unexpected safety concerns arise from this application.

PRODUCT LITERATURE
The approved SmPC, PIL and labelling are satisfactory and consistent with that for the cross-reference product.

A package leaflet has been submitted to the MHRA along with results of consultations with target patient groups ("user testing"), in accordance with Article 59 of Council Directive 2001/83/EC. The results indicate that the package leaflet is well-structured and organised, easy to understand and written in a comprehensive manner. The testing shows that patients/users are able to act upon the information that the leaflet contains.

The approved labelling artwork complies with statutory requirements. In line with current legislation, the name of the product in Braille appears on the outer packaging. The Marketing Authorisation Holder (MAH) has committed to submitting mock-ups for pack sizes 7 and 28 for assessment before those pack sizes are commercially marketed.

RISK BENEFIT ASSESSMENT
The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The applicant’s product is identical to the cross-reference product. Extensive clinical experience with omeprazole is considered to have demonstrated the therapeutic value of the active substance. The risk: benefit is, therefore, considered to be positive.
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Steps Taken for Assessment

1. The MHRA received the marketing authorisation application on 7th September 2004

2. Following standard checks and communication with the applicant the MHRA considered the application valid on 24th September 2004

3. Following assessment of the application the MHRA requested further information relating to the quality dossier on 18th February 2005

4. The applicant responded to the MHRA’s request, providing further information for the quality sections on 3rd August 2006

5. The application was determined on 26th June 2009
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STEPS TAKEN AFTER AUTHORISATION
Not applicable
SUMMARY OF PRODUCT CHARACTERISTICS
The UK Summary of Product Characteristics (SmPC) for the original granted licence Zanprol 10mg Tablets (PL 10949/0370) is as follows:

1. NAME OF THE MEDICINAL PRODUCT
Zanprol 10 mg Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Omeprazole 10 mg
For excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Gastro-resistant coated tablets.
Brownish-pink, capsule-shaped film-coated tablets.

4. CLINICAL PARTICULARS
4.1. Therapeutic indications
Relief of reflux-like symptoms (e.g. heartburn) in patients aged 18 and over.

4.2. Posology and method of administration
The tablets should be swallowed whole with plenty of liquid (e.g., water or fruit juice) prior to a meal. It is important that the tablets should not be crushed or chewed.

Initially the dosage is 20mg once daily.

Subsequently, symptomatic relief from heartburn can be achieved in some subjects by taking 10mg once daily, increasing to 20mg if symptoms return.

The lowest effective dose should always be used.

If no relief is obtained within two weeks then the patient should be referred to their doctor.

If continuous treatment for more than 4 weeks is required to relieve symptoms then the patient should be referred to their doctor.

4.3. Contraindications
Known hypersensitivity to omeprazole or to any of the other ingredients.

4.4. Special warnings and precautions for use
Decreased gastric acidity, due to any means - including proton-pump inhibitors - increases gastric counts of bacteria normally present in the gastrointestinal tract. Treatment with acid-reducing drugs leads to a slightly increased risk of gastrointestinal infections such as salmonella or campylobacter.

Special warnings and precautions for patients taking non-prescription indigestion or heartburn remedies:
Patients should be referred to their doctor if:
- They have had to take an indigestion or heartburn remedy continuously for 4 or more weeks in order to control their symptoms;
- They are aged over 45 years with new or recently changed symptoms;
- They have unintentional weight loss, anaemia, gastrointestinal bleeding, dysphagia, pain on swallowing, persistent vomiting or vomiting with blood, epigastric mass, previous gastric ulcer or surgery, jaundice or any other significant medical condition (including hepatic and renal impairment).
Patients with long-term recurrent symptoms of indigestion or heartburn should see their doctor at regular intervals. Patients aged over 45 years taking any “over the counter” (OTC, non-prescription) indigestion or heartburn remedy on a daily basis should inform their pharmacist or doctor.

Patients should not take another “acid suppressor” e.g. H₂ antagonist concomitantly.

Patients should consult their doctor before taking this product if they are due to have an endoscopy.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

The Patient Information Leaflet will contain advice that the tablets will not provide immediate relief of symptoms.

4.5. Interaction with other medicinal products and other forms of interaction

As with many indigestion and heartburn remedies, omeprazole may interact with other medications. Therefore, patients who are also taking other medications should first consult with either their pharmacist or doctor before taking omeprazole.

As omeprazole is metabolized in the liver through cytochrome P450 it can delay the elimination of diazepam, phenytoin and warfarin. Monitoring of patients receiving warfarin or phenytoin is recommended and a reduction of the warfarin or phenytoin dose may be necessary. However concomitant treatment with omeprazole 20 mg daily did not change the blood concentration of phenytoin in patients on continuous treatment with phenytoin. Similarly, concomitant treatment with omeprazole 20 mg daily did not change coagulation time in patients on continuous treatment with warfarin. Interactions with other medicinal products which are also metabolized via the cytochrome P-450 isoenzyme of group 2C cannot be excluded.

Due to the decreased intragastric acidity, the absorption of ketoconazole or itraconazole may be reduced during omeprazole treatment, as it is during treatment with other acid secretion inhibitors.

Concomitant use of omeprazole and cilostazol results in an increase in the plasma concentration of cilostazol, therefore concomitant use should be avoided. It is possible that omeprazole also increases the plasma-tacrolimus concentration, whereas voriconazole increases the plasma concentration of omeprazole.

Simultaneous treatment with omeprazole and digoxin in healthy subjects led to a 10% increase in the bioavailability of digoxin as a consequence of the increased intragastric pH.

Omeprazole as so far tested has no influence on the metabolism of the following substances: amoxycillin, antacids, quinidine, caffeine, ciclosporin, diclofenac, estradiol, lidocaine, metoprolol, naproxen, phenacetin, piroxicam, propranolol, quinidine, theophylline.

Treatment with omeprazole may cause false negative results in 13C-Urea breath tests.

Alcohol and food do not affect the absorption of omeprazole.

4.6. Pregnancy and lactation

This product should not be used during pregnancy or whilst breast feeding.

PREGNANCY

There is no evidence on the safety of omeprazole in human pregnancy. Animal studies have revealed no teratogenic effect, but reproduction studies have revealed reduced litter weights. Avoid in pregnancy, unless there is no safer alternative.
LACTATION

There is no information available on the passage of omeprazole into breast milk or its effects on the neonate. Breast-feeding should therefore be discontinued if the use of omeprazole is considered essential.

4.7. Effects on ability to drive and use machines

In rare cases, drowsiness has been reported. If affected patients should not drive or operate machinery.

4.8. Undesirable effects

Omeprazole is well tolerated and adverse reactions have generally been mild and reversible. The following have been reported as adverse events in clinical trials or reported from routine use but in many cases a relationship to treatment with omeprazole has not been established.

Skin and subcutaneous tissue disorders
Skin rash, urticaria and pruritus have been reported, usually resolving after discontinuation of treatment. In addition photosensitivity, bullous eruption, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, alopecia and increased sweating have been reported in isolated cases.

Musculoskeletal disorders
Arthritic and myalgic symptoms have been reported and have usually resolved when therapy is stopped.

Respiratory disorders
In isolated cases bronchospasm has been reported.

Gastrointestinal disorders
Diarrhoea has been reported and may be severe enough to require discontinuation of therapy. Constipation, abdominal pain, nausea/vomiting and flatulence have been reported. In isolated cases dry mouth, stomatitis and candidiasis have been reported.

Hepato-biliary disorders
Increases in liver enzyme levels have been observed. In isolated cases, encephalopathy in patients with pre-existing severe liver disease, hepatitis with or without jaundice and rarely hepatic failure.

Renal & urinary disorders
Interstitial nephritis which has resulted in acute renal failure has been reported in isolated cases.

Reproductive disorders
In isolated cases gynaecomastia and impotence have been reported.

Nervous system disorders
Headache has been reported which may be severe enough to require discontinuation of therapy. Rarely paraesthesia has also been reported. Taste disturbances have been reported in isolated cases.

Psychiatric disorders
In isolated cases reversible mental confusion, agitation, depression and hallucinations occurring predominantly in severely ill patients. Aggression has also been reported in isolated cases.

Disorders of the eye
In isolated cases blurred vision has been reported.

Haematological
In isolated cases leucopenia, thrombocytopenia, agranulocytosis, hyponatraemia and pancytopenia have been reported.
Disorders of the ear
Vertigo has been reported.

Disorders of the immune system
Anaphylactic shock and angioedema have been reported in isolated cases.

General disorders
Dizziness, light-headedness and feeling faint have been associated with treatment, but all usually resolve on cessation of therapy. Somnolence and insomnia have also been reported. In isolated cases peripheral oedema, malaise and fever have been reported.

4.9 Overdose
There is no information available on the effects of overdosage in man. Beside ventilatory and circulatory control according to general guidelines on the treatment of intoxication no further direct therapeutic measures are indicated. Single oral doses of omeprazole of up to 400 mg have not resulted in any severe symptoms; elimination remained first order and no specific treatment was needed.

5. PHARMACOLOGICAL PROPERTIES
5.1. Pharmacodynamic properties
Omeprazole, a substituted benzimidazole, is a selective proton pump inhibitor which inhibits directly and in dose-dependent fashion the H+/K+-ATPase of the parietal cells of the stomach responsible for gastric acid secretion. By this selective intracellular attack, independently from membrane located receptors like histamine H2-, muscarine M1- or gastrinergic receptors, omeprazole belongs to an independent class of inhibitors which block the terminal secretion process. By its mode of action, omeprazole reduces not only basal but also stimulus-induced acid secretion, independently of the kind of stimulus. Omeprazole thus increases the pH-value and reduces the secretory volume.

Oral dosing with 20 mg omeprazole once daily produces inhibition of gastric acid secretion within 1-2 hours of the first dose. The maximum effect is achieved within 4 days of starting treatment after which the degree of inhibition remains constant. The mean decrease in pentagastrin-stimulated peak acid output twenty-four hours after dosing is about 70%. During long-term treatment an increased frequency of gastric glandular cysts have been reported. These changes are a physiological consequence of pronounced inhibition of acid secretion. The cysts are benign and appear to be reversible. No other treatment related mucosal changes have been observed in patients treated continuously with omeprazole for periods of up to 5 years.

Site and Mechanism of Action: Omeprazole is a weak base and is concentrated and converted to the active form by protonation in the acid environment of the intracellular canaliculi within the parietal cell, where it inhibits the enzyme, H+/K+-ATPase - the proton pump. This effect on the final step of the gastric acid formation process is dose-dependent and provides for effective inhibition of both basal acid secretion and stimulated acid secretion irrespective of the stimulus. All pharmacodynamic effects observed are explained by the effect of omeprazole on acid secretion.

5.2. Pharmacokinetic properties
Absorption of omeprazole takes place in the small intestine and is usually completed within 3-6 hours. The systemic bioavailability of omeprazole from a single oral dose is approximately 35%. After repeated once-daily administration, the bioavailability increases to about 60%. Concomitant intake of food has no influence on bioavailability. The plasma protein binding of omeprazole is about 95%.

The average half-life of the terminal phase of the plasma concentration-time curve is approximately 40 minutes. There is no change in half-life during treatment. The inhibition of acid secretion is related to the area under the plasma concentration time-curve (AUC) but not to actual plasma concentration at a time.
Omeprazole is entirely metabolized, mainly in the liver. Identified metabolites in plasma are the sulphone, the sulphide and hydroxy-omeprazole; these metabolites have no significant effect on acid secretion. About 80% of the metabolites are excreted in the urine and the rest in the faeces. The two main urinary metabolites are hydroxy-omeprazole and the corresponding carboxylic acid.

The systemic bioavailability of omeprazole is not significantly altered in patients with reduced renal function. The area under the plasma concentration time-curve is increased in patients with impaired liver function, but no tendency to accumulation of omeprazole has been found.

Available data from children (1 year and older) suggest that the pharmacokinetics within the recommended doses is similar to those reported in adults. At steady state, lower plasma levels of omeprazole were seen in some children.

5.3. Preclinical safety data

Omeprazole is a well-established drug for which there are adequate published safety data. Preclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity or toxicity to reproduction.

Carcinogenic Potential: 2 years' carcinogenicity studies in rats (i.e., life-long treatment) showed development of ECL-cell-carcinoids; but rats which have been treated with high doses of omeprazole over a year have not shown any carcinoids in the later 1-year period. The mechanism for the build-up of the stomach carcinoids has been investigated very carefully and various studies lead to the conclusion that this is a secondary reaction due to the extreme increased serum gastrin levels of the rats during the treatment period. These changes are the result of sustained hypergastrinaemia secondary to acid inhibition and not from a direct effect of any individual drug. Similar development of ECL-cell-carcinoids was observed in rats subjected to partial fundectomy. ECL-cell-carcinoids were not seen in mice or dog studies.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core
lactose monohydrate
sodium starch glycollate
sodium stearate
sodium stearyl fumarate

Enteric Coating
hydroxypropyl methylcellulose (HPMC) acetate succinate
talc
triethyl citrate
monoethanolamine
sodium lauryl sulphate
Sepisperse AP-3527 (containing:
propylene glycol
titanium dioxide (E-171)
red iron oxide (E-172)
yellow iron oxide (E-172)
hydroxypropyl methylcellulose)

Polish
carnauba wax

6.2 Incompatibilities

Not applicable
6.3. **Shelf life**
2 years

6.4. **Special precautions for storage**
Store in the original package. Do not store above 30°C.

6.5. **Nature and contents of container**
Aluminium/aluminium blisters strips containing 7, 14 or 28 tablets, in a cardboard carton.

6.6. **Special precautions for disposal**
Not applicable.

7. **MARKETING AUTHORITY HOLDER**
GLAXO WELLCOME UK LTD.
Stockley Park West, Uxbridge
Middlesex UB11 1BT
United Kingdom

*trading as:*
GLAXOSMITHKLINE CONSUMER HEALTHCARE
Brentford, TW8 9GS United Kingdom

8. **MARKETING AUTHORIZATION NUMBER**
PL 10949/0370

9. **DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION**
26/06/2009

10. **DATE OF REVISION OF THE TEXT**
26/06/2009
PATIENT INFORMATION LEAFLET
The UK Patient Information Leaflet (PIL) for the original granted licence Zanprol 10mg Tablets (PL 10949/0370) is as follows:

Please read right through this leaflet before you start using this medicine. This medicine is available without prescription, but you still need to use Zanprol Tablets carefully to get the best results from them.
- Keep this leaflet you may need to read it again.
- If you have any questions, or if there is anything you do not understand, ask your pharmacist.

In this leaflet:
1. What Zanprol Tablets do
2. Check before you take Zanprol Tablets
3. How to take Zanprol Tablets
4. Possible side effects
5. How to store Zanprol Tablets
6. Further information

1. What Zanprol Tablets do
Zanprol Tablets are used to give long lasting relief of acid reflux and heartburn. Heartburn and acid reflux are caused by stomach acid rising up the food pipe, resulting in a burning sensation in the chest and throat. This can be accompanied by a bitter taste in the mouth. The active ingredient is omeprazole, a proton pump inhibitor which works by preventing your stomach from producing too much acid.

2. Check before you take Zanprol Tablets

Do not take Zanprol Tablets:
- If you have ever had an allergic reaction to omeprazole or to any of the other ingredients (listed in Section 6)
- If you are under 18 years.

Ask your doctor before you take this medicine:
- If you have had to take a heartburn or indigestion remedy continuously for 4 or more weeks to control your symptoms
- If you have kidney or liver problems
- If you are over 45 years with new or recently changed symptoms

- If you have unintended weight loss, anaemia, bleeding of the stomach, difficulty or pain on swallowing, persistent vomiting or vomiting blood, a lump in your stomach area, jaundice, or have previously had a gastric ulcer or stomach surgery
- If you regularly see your doctor for other conditions
- If you are due to have an endoscopy or undergo a 13C Urea breath test
- If you have been told by your doctor that you have an intolerance to some sugars.

Take special care with Zanprol Tablets

Do not drive or operate machinery if the tablets make you sleepy.
- If you have suffered from repeated heartburn or indigestion symptoms for some time, remember to see your doctor regularly.

If you are taking other medicines
Talk to your doctor or pharmacist before taking these tablets if you are taking any prescribed medicines; particularly diazepam (for anxiety), phenytoin (for epilepsy), tacrolimus (used for organ transplants), clopazol (for blood circulation problems) or warfarin (to thin the blood); digoxin (for the heart) and itaconazole, ketoconazole or voriconazole (for fungal infections).

Do not take any other ‘acid suppressors’ such as an H₂ antagonist (e.g., ranitidine) with Zanprol Tablets.

Pregnancy and breast feeding

Do not take Zanprol Tablets if you are pregnant or breast feeding.

3. How to take Zanprol Tablets
Take the tablets before a meal. The tablets should not be chewed or crushed; they should be swallowed whole. They will start to suppress acid in 1-2 hours, but will not give instant relief from acid reflux and heartburn. You should take the lowest dose that relieves your symptoms, and keep taking it for 3-4 days to achieve maximum results.
UKPAR Zanprol 10mg Tablets

Adults aged 18 years and over:

Initially swallow 2 tablets once daily with plenty of water.
If your symptoms improve, reduce the dose to 1 tablet daily.
If your symptoms come back, swallow 2 tablets once daily.

Do not take more than the recommended dose.

If you take too many tablets
Contact your doctor or casualty department.

Do not take Zanprol Tablets regularly for long periods
Ask your doctor:
• if your symptoms do not improve in 2 weeks
• if you have needed to take the tablets every day for 4 weeks
• if your symptoms come back shortly after you stop taking the tablets.

4. Possible side effects
Like all medicines, Zanprol Tablets can have side effects, but not everybody gets them:

Stop taking the medicine and tell your doctor if you experience:
• Very severe headache or diarrhoea.

The following side effects may occur.
Tell your doctor if you get them:
• Constipation, stomach ache, feeling or being sick and wind.
• Vertigo.
• Drowsiness or difficulty sleeping.

The following side effects are very rare.
Tell your doctor if you get them:
• Sensitivity to light.
• Swelling, soreness or dryness of the mouth or throat.
• Feeling confused (if you already have severe liver disease).
• Liver or kidney problems.
• Breast enlargement or impotence.
• Pins and needles or taste disorders.
• Confusion, anxiety, depression, hallucinations or aggression.
• Blurred vision.
• Blood disorders (tiredness, easy bruising, being more prone to infection).
• Severe allergic reactions with rash, swelling and shortness of breath.
• Wheezing.
• Swollen limbs or high fever.
• Hair loss or increased sweating.

The following side effects may occur but usually go away when you stop taking the medicine:
• Skin rash or itchy skin.
• Sore joints and muscles.
• Dizziness or feeling faint.

If you do get any side effects, even those not mentioned in this leaflet, tell your doctor or pharmacist.

5. How to store Zanprol Tablets
Keep out of the reach and sight of children.
Do not use this medicine after the 'EXP' date shown on the pack.
Do not store above 30°C. Store in the original package to protect from moisture.

6. Further information
Active ingredient Each gastro-resistant tablet contains Omeprazole 10 mg.
Other ingredients Lactose monohydrate, sodium starch glycolate, sodium stearate, sodium stearyl fumarate, hydroxypropyl methylcellulose (HPMC) acetate succinate, sepisperse AP-3527 (containing propylene glycol, titanium dioxide (E 171), red iron oxide (E 172), hydroxypropyl methylcellulose, yellow iron oxide (E 172)), talc, triethyl citrate, monoethanolamine, sodium laurilsulfate, camcaba wax.

Packs of Zanprol Tablets contain 7, 14 or 28 tablets (not all packs may be marketed).

The marketing authorisation holder is GlaxoSmithKline Consumer Healthcare, Brentford, TW8 9QS, U.K. and all enquiries should be sent to this address.

The manufacturer is Dexcel-Pharma Ltd,
1 Cottesbrooke Park, Heartlands Business Park,
Daventry, Northamptonshire, NN11 8YL.

This leaflet was last revised in December 2008.

Zanprol is a registered trade mark of the GlaxoSmithKline group of companies.

gsk GlaxoSmithKline
LABELLING

The UK labelling for the original granted licence Zanprol 10mg Tablets (PL 10949/0370) is as follows:

Carton – 14 tablets
Blister pack
Annex 1

Reference: PL 00079/0660 - 0003

Product: Zanprol 10mg Tablets

Marketing Authorisation Holder: Beecham Group plc

Active Ingredient(s): Omeprazole

Reason
To update sections 4.1-4.9, 5.1-5.3 and 6.1 of the SmPC in line with Article 30 of Directive 2001/83/EC for the medicinal product following a review by the European Medicines Agency. As a consequence, label and PIL have been updated.

Supporting Evidence
The Article 30 information, and proposed wording for the PIL, labels and SmPC

Evaluation
The SmPC, PIL and labels have been updated correctly to comply with Article 30 of Directive 2001/83/EC.

Conclusion
The updated SmPC sections and the updated PIL/labels are provided below.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
Zanprol 10 mg Tablets are indicated for the treatment of reflux symptoms (e.g. heartburn, acid regurgitation) in adults.

4.2 Posology and method of administration

Posology in adults
The recommended dose is 20 mg once daily for 14 days.

It might be necessary to take the tablets for 2-3 consecutive days to achieve improvement of symptoms.

The majority of patients achieve complete relief of heartburn within 7 days. Once complete relief of symptoms has occurred, treatment should be discontinued.

Special populations

Impaired renal function
Dose adjustment is not needed in patients with impaired renal function (see section 5.2).

Impaired hepatic function
Patients with impaired hepatic function should be advised by a doctor before taking Zanprol 10 mg Tablets (see section 5.2).

Elderly (> 65 years old)
Dose adjustment is not needed in the elderly (see section 5.2).

Method of administration
It is recommended to take Zanprol 10mg Tablets in the morning, swallowed whole with half a glass of water. The tablets must not be chewed or crushed.

For patients with swallowing difficulties
Break the tablet and disperse it in a spoonful of non-carbonated water - if so wished, mix with some fruit juices or applesauce. The dispersion should be taken immediately (or within 30 minutes). The dispersion should always be stirred just before drinking and rinsed down with half a glass of water. DO NOT USE milk or carbonated water. Do not chew.
4.3 Contraindications
Hypersensitivity to omeprazole, substituted benzimidazoles or to any of the other excipients.

Omeprazole like other proton pump inhibitors must not be used concomitantly with nelfinavir (see section 4.5).

4.4 Special warnings and precautions for use
In the presence of any alarm symptom (e.g. significant unintentional weight loss, recurrent vomiting, dysphagia, haematemesis or melena) and when gastric ulcer is suspected or present, malignancy should be excluded, as treatment may alleviate symptoms and delay diagnosis.

Co-administration of atazanavir with proton pump inhibitors is not recommended (see section 4.5). If the combination of atazanavir with proton pump inhibitor is judged unavoidable, close clinical monitoring (e.g. virus load) is recommended in combination with an increase in the dose of atazanavir to 400 mg with 100 mg of ritonavir, omeprazole 20 mg should not be exceeded.

Omeprazole is a CYP2C19 inhibitor. When starting or ending treatment with omeprazole, the potential for interactions with drugs metabolised through CYP2C19 should be considered. An interaction is observed between clopidogrel and omeprazole (see section 4.5). The clinical relevance of this interaction is uncertain. As a precaution, concomitant use of omeprazole and clopidogrel should be discouraged.

Zanprol Tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Treatment with proton pump inhibitors may lead to slightly increased risk of gastrointestinal infections such as Salmonella or Campylobacter (see section 5.1).

Patients with long-term recurrent symptoms of indigestion or heartburn should see their doctor at regular intervals. Especially, patients over 55 years taking any “over the counter” (OTC, non-prescription) indigestion or heartburn remedy on a daily basis should inform their pharmacist or doctor.

Patients should be instructed to consult a doctor if:
• They have had previous gastric ulcer or gastrointestinal surgery.
• They are on continuous symptomatic treatment of indigestion or heartburn for 4 or more weeks.
• They have jaundice or severe liver disease.
• They are aged over 55 years with new or recently changed symptoms.

Patients should not take omeprazole as a preventative medication.

4.5 Interaction with other medicinal products and other forms of interaction
Effects of omeprazole on the pharmacokinetics of other active substances
Active substances with pH dependent absorption
The decreased intragastric acidity during treatment with omeprazole might increase or decrease the absorption of active substances with a gastric pH dependent absorption.

Nelfinavir, atazanavir
The plasma levels of nelfinavir and atazanavir are decreased in case of co-administration with omeprazole.

Concomitant administration of omeprazole with nelfinavir is contraindicated (see section 4.3). Co-administration of omeprazole (40 mg once daily) reduced mean nelvinavir exposure by ca. 40% and the mean exposure of the pharmacologically active metabolite M8 was reduced by ca. 75-90%. The interaction may also involve CYP2C19 inhibition.
Concomitant administration of omeprazole with atazanavir is not recommended (see section 4.4). Concomitant administration of omeprazole (40 mg once daily) and atazanavir 300 mg/ritonavir 100 mg to healthy volunteers resulted in a 75% decrease of the atazanavir exposure. Increasing the atazanavir dose to 400 mg did not compensate for the impact of omeprazole on atazanavir exposure. The co-administration of omeprazole (20 mg once daily) with atazanavir 400 mg/ritonavir 100 mg to healthy volunteers resulted in a decrease of approximately 30% in the atazanavir exposure as compared to atazanavir 300 mg/ritonavir 100 mg once daily.

Digoxin
Concomitant treatment with omeprazole (20 mg daily) and digoxin in healthy subjects increased the bioavailability of digoxin by 10%. Digoxin toxicity has been rarely reported. However caution should be exercised when omeprazole is given at high doses in elderly patients. Therapeutic drug monitoring of digoxin should then be reinforced.

Clopidogrel
In a crossover clinical study, clopidogrel (300 mg loading dose followed by 75 mg/day) alone and with omeprazole (80 mg at the same time as clopidogrel) were administered for 5 days. The exposure to the active metabolite of clopidogrel was decreased by 46% (day 1) and 42% (Day 5) when clopidogrel and omeprazole were administered together. Mean inhibition of platelet aggregation (IPA) was diminished by 47% (24 hours) and 30% (Day 5) when clopidogrel and omeprazole were administered together. In another study it was shown that administering clopidogrel and omeprazole at different times did not prevent their interaction that is likely to be driven by the inhibitory effect of omeprazole on CYP2C19. Inconsistent data on the clinical implications of this PK/PD interaction in terms of major cardiovascular events have been reported from observational and clinical studies.

Other active substances
The absorption of posaconazole, erlotinib, ketoconazole and itraconazole is significantly reduced and thus clinical efficacy may be impaired. For posaconazole and erlotinib concomitant use should be avoided.

Active substances metabolised by CYP2C19
Omeprazole is a moderate inhibitor of CYP2C19, the major omeprazole metabolising enzyme. Thus, the metabolism of concomitant active substances also metabolised by CYP2C19, may be decreased and the systemic exposure to these substances increased. Examples of such drugs are R-warfarin and other vitamin K antagonists, cilostazol, diazepam and phenytoin.

Cilostazol
Omeprazole, given in doses of 40 mg to healthy subjects in a cross-over study, increased Cmax and AUC for cilostazol by 18% and 26% respectively, and one of its active metabolites by 29% and 69% respectively.

Phenytoin
Monitoring phenytoin plasma concentration is recommended during the first two weeks after initiating omeprazole treatment and, if a phenytoin dose adjustment is made, monitoring and a further dose adjustment should occur upon ending omeprazole treatment.

Unknown mechanism
Saquinavir
Concomitant administration of omeprazole with saquinavir/ritonavir resulted in increased plasma levels up to approximately 70% for saquinavir associated with good tolerability in HIV-infected patients.

Tacrolimus
Concomitant administration of omeprazole has been reported to increase the serum levels of tacrolimus. A reinforced monitoring of tacrolimus concentration as well as renal function (creatinine clearance) should be performed, and dosage of tacrolimus adjusted if needed.
Effects of other active substances on the pharmacokinetics of omeprazole

*Inhibitors of CYP2C19 and/or CYP3A4*

Since omeprazole is metabolised by CYP2C19 and CYP3A4, active substances known to inhibit CYP2C19 or CYP3A4 (such as clarithromycin and voriconazole) may lead to increased omeprazole serum levels by decreasing omeprazole’s rate of metabolism. Concomitant voriconazole treatment resulted in more than doubling of the omeprazole exposure. As high doses of omeprazole have been well-tolerated adjustment of the omeprazole dose is not generally required. However, dose adjustment should be considered in patients with severe hepatic impairment and if long-term treatment is indicated.

*Inducers of CYP2C19 and/or CYP3A4*

Active substances known to induce CYP2C19 or CYP3A4 or both (such as rifampicin and St. John’s wort) may lead to decreased omeprazole serum levels by increasing omeprazole’s rate of metabolism.

4.6 Pregnancy and lactation

Results from three prospective epidemiological studies (more than 1000 exposed outcomes) indicate no adverse effects of omeprazole on pregnancy or on the health of the foetus/newborn child. Omeprazole can be used during pregnancy.

Omeprazole is excreted in breast milk but is not likely to influence the child when therapeutic doses are used.

4.7 Effects on ability to drive and use machines

Zanprol is not likely to affect the ability to drive or use machines. Adverse drug reactions such as dizziness and visual disturbances may occur (see section 4.8). If affected patients should not drive or operate machinery.

4.8 Undesirable effects

The most common side effects (1-10% of patients) are headache, abdominal pain, constipation, diarrhoea, flatulence and nausea/vomiting.

The following adverse drug reactions have been identified or suspected in the clinical trials programme for omeprazole and post-marketing. None was found to be dose-related. Adverse reactions listed below are classified according frequency and System Organ Class (SOC). Frequency categories are defined according to the following convention: Very common (≥ 1/10), Common (≥ 1/100 to < 1/10), Uncommon (≥ 1/1,000 to < 1/100), Rare (≥ 1/10,000 to < 1/1,000), Very rare (< 1/10,000), Not known (cannot be estimated from the available data).

<table>
<thead>
<tr>
<th>SOC/frequency</th>
<th>Adverse reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood and lymphatic system disorders</td>
<td></td>
</tr>
<tr>
<td>Rare:</td>
<td>Leukopenia, thrombocytopenia</td>
</tr>
<tr>
<td>Very rare:</td>
<td>Agranulocytosis, pancytopenia</td>
</tr>
<tr>
<td>Immune system disorders</td>
<td></td>
</tr>
<tr>
<td>Rare:</td>
<td>Hypersensitivity reactions e.g. fever, angioedema and anaphylactic reaction/shock</td>
</tr>
<tr>
<td>Metabolism and nutrition disorders</td>
<td></td>
</tr>
<tr>
<td>Rare:</td>
<td>Hyponatraemia</td>
</tr>
<tr>
<td>Very rare:</td>
<td>Hypomagnesaemia</td>
</tr>
<tr>
<td>Psychiatric disorders</td>
<td></td>
</tr>
<tr>
<td>Uncommon:</td>
<td>Insomnia</td>
</tr>
<tr>
<td>Rare:</td>
<td>Agitation, confusion, depression</td>
</tr>
<tr>
<td>Very rare:</td>
<td>Aggression, hallucinations</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td></td>
</tr>
<tr>
<td>Common:</td>
<td>Headache</td>
</tr>
<tr>
<td>Uncommon:</td>
<td>Dizziness, paraesthesia, somnolence</td>
</tr>
<tr>
<td>Rare:</td>
<td>Taste disturbance</td>
</tr>
<tr>
<td>Eye disorders</td>
<td></td>
</tr>
</tbody>
</table>
4.9 Overdose

There is limited information available on the effects of overdose of omeprazole in humans. In the literature, doses up to 560 mg have been described, and occasional reports have been received when single doses have reached up to 2,400 mg omeprazole (120 times the usual recommended clinical dose). Nausea, vomiting, dizziness, abdominal pain, diarrhoea and headache have been reported. Also apathy, depression and confusion have been described in single cases.

The symptoms described in connection to omeprazole overdose have been transient, and no serious outcome has been reported. The rate of elimination was unchanged (first order kinetics) with increased doses. Treatment, if needed, is symptomatic.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Proton pump inhibitors, ATC code: A02BC01

Mechanism of action

Omeprazole, a racemic mixture of two enantiomers reduces gastric acid secretion through a highly targeted mechanism of action. It is a specific inhibitor of the acid pump in the parietal cell. It is rapidly acting and provides control through reversible inhibition of gastric acid secretion with once-daily dosing.

Omeprazole, is a weak base and is concentrated and converted to the active form in the highly acidic environment of the intracellular canaliculi within the parietal cell, where it inhibits the enzyme H^+/K^+-ATPase - the acid pump. This effect on the final step of the gastric acid formation process is dose-dependent and provides for highly effective inhibition of both basal acid secretion and stimulated acid secretion, irrespective of stimulus.

Pharmacodynamic effects

All pharmacodynamic effects observed can be explained by the effect of omeprazole on acid secretion.
**Effect on gastric acid secretion**

Oral dosing with omeprazole once daily provides for rapid and sustained inhibition of daytime and night-time gastric acid secretion with maximum effect being achieved within 4 days of treatment. With omeprazole 20 mg, a mean decrease of at least 80% in 24-hour intragastric acidity is then maintained in duodenal ulcer patients, with the mean decrease in peak acid output after pentagastrin stimulation being about about 70% 24 hours after dosing.

Oral dosing with omeprazole 20 mg maintains an intragastric pH of ≥ 3 for a mean time of 17 hours of the 24-hour period in duodenal ulcer patients.

As a consequence of reduced acid secretion and intragastric acidity, omeprazole dose-dependently reduces/normalizes acid exposure of the esophagus in patients with gastro-esophageal reflux disease.

The inhibition of acid secretion is related to the area under the plasma concentration-time curve (AUC) of omeprazole and not to the actual plasma concentration at a given time.

No tachyphylaxis has been observed during treatment with omeprazole.

**Other effects related to acid inhibition**

During long-term treatment gastric glandular cysts have been reported in a somewhat increased frequency. These changes are a physiological consequence of pronounced inhibition of acid secretion, are benign and appear to be reversible.

Decreased gastric acidity due to any means including proton pump inhibitors, increases gastric counts of bacteria normally present in the gastrointestinal tract. Treatment with acid-reducing drugs may lead to slightly increased risk of gastrointestinal infections such as Salmonella and Campylobacter.

Omeprazole, as all acid-blocking medicines, may reduce the absorption of vitamin B12 (cyanocobalamin) due to hypo- or achlorhydria. This should be considered in patients with reduced body stores or risk factors for reduced vitamin B12 absorption on long-term therapy.

### 5.2 Pharmacokinetic properties

**Absorption**

Omeprazole and omeprazole magnesium are acid labile and are therefore administered orally as enteric-coated granules in capsules or tablets. Absorption of omeprazole is rapid, with peak plasma levels occurring approximately 1-2 hours after dose. Absorption of omeprazole takes place in the small intestine and is usually completed within 3-6 hours. Concomitant intake of food has no influence on the bioavailability. The systemic availability (bioavailability) from a single oral dose of omeprazole is approximately 40%. After repeated once-daily administration, the bioavailability increases to about 60%.

**Distribution**

The apparent volume of distribution in healthy subjects is approximately 0.3 l/kg body weight. Omeprazole is 97% plasma protein bound.

**Metabolism**

Omeprazole is completely metabolised by the cytochrome P450 system (CYP). The major part of its metabolism is dependent on the polymorphically expressed CYP2C19, responsible for the formation of hydroxymeproprazole, the major metabolite in plasma. The remaining part is dependent on another specific isoform, CYP3A4, responsible for the formation of omeprazole sulphone. As a consequence of high affinity of omeprazole to CYP2C19, there is a potential for competitive inhibition and metabolic drug-drug interactions with other substrates for CYP2C19. However, due to low affinity to CYP3A4, omeprazole has no potential to inhibit the metabolism of other CYP3A4 substrates. In addition, omeprazole lacks an inhibitory effect on the main CYP enzymes.

Approximately 3% of the Caucasian population and 15-20% of Asian populations lack a functional CYP2C19 enzyme and are called poor metabolisers. In such individuals the metabolism of omeprazole is probably mainly catalysed by CYP3A4. After repeated once-
daily administration of 20 mg omeprazole, the mean AUC was 5 to 10 times higher in poor metabolisers than in subjects having a functional CYP2C19 enzyme (extensive metabolisers). Mean peak plasma concentrations were also higher, by 3 to 5 times. These findings have no implications for the posology of omeprazole.

Excretion
The plasma elimination half-life of omeprazole is usually shorter than one hour both after single and repeated oral once-daily dosing. Omeprazole is completely eliminated from plasma between doses with no tendency for accumulation during once-daily administration. Almost 80% of an oral dose of omeprazole is excreted as metabolites in the urine, the remainder in the faeces, primarily originating from bile secretion.

The AUC of omeprazole increases with repeated administration. This increase is dose-dependent and results in a non-linear dose-AUC relationship after repeated administration. This time- and dose-dependency is due to a decrease of first pass metabolism and systemic clearance probably caused by an inhibition of the CYP2C19 enzyme by omeprazole and/or its metabolites (e.g. the sulphone). No metabolite has been found to have any effect on gastric acid secretion.

Special populations
Impaired hepatic function
The metabolism of omeprazole in patients with liver dysfunction is impaired, resulting in an increased AUC. Omeprazole has not shown any tendency to accumulate with once-daily dosing.

Impaired renal function
The pharmacokinetics of omeprazole, including systemic bioavailability and elimination rate, are unchanged in patients with reduced renal function.

Elderly
The metabolism rate of omeprazole is somewhat reduced in elderly subjects (75-79 years of age).

5.3 Preclinical safety data
Gastric ECL-cell hyperplasia and carcinoids, have been observed in life-long studies in rats treated with omeprazole. These changes are the result of sustained hypergastrinaemia secondary to acid inhibition. Similar findings have been made after treatment with H2-receptor antagonists, proton pump inhibitors and after partial fundectomy. Thus, these changes are not from a direct effect of any individual active substance.

6 PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Core
lactose monohydrate
sodium starch glycollate
sodium stearate
sodium stearyl fumarate
Enteric Coating
hydroxypropyl methylcellulose (HPMC) acetate succinate
talc
triethyl citrate
monoethanolamine
sodium lauryl sulphate
Sepisperse AP-3527 [containing: propylene glycol, titanium dioxide (E-171), red iron oxide (E-172), yellow iron oxide (E-172) and hydroxypropyl methylcellulose]

Polish
carnauba wax
Please read right through this leaflet before you start using this medicine. This medicine is available without prescription, but you still need to use Zanprol Tablets carefully to get the best results from them.

Keep this leaflet as you may need to read it again.

If you have any questions, or if there is anything you do not understand, ask your pharmacist.

You must contact your 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 effect not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:
1. What Zanprol Tablets are and what are they used for
2. Before you take Zanprol Tablets
3. How to take Zanprol Tablets
4. Possible side effects
5. How to store Zanprol Tablets
6. Further information

1. What Zanprol Tablets are and what they are used for

Zanprol Tablets are given to long-lasting relief of acid reflux and heartburn. Zanprol Tablets contain the active substance omeprazole. It belongs to a group of medicines called 'proton pump inhibitors'. They work by reducing the amount of acid that your stomach produces.

Zanprol is used in adults for the short-term treatment of reflux symptoms (for example, heartburn, acid regurgitation).

Reflex is the backflow of acid from the stomach into the gullet ('oesophagus'), which may become inflamed and painful. This may cause you symptoms such as a painful burning sensation in the chest rising up to the throat (heartburn) and a sour taste in the mouth (acid regurgitation).

It may be necessary to take the tablets for 2-3 consecutive days to achieve improvement of symptoms.

2. Before you take Zanprol Tablets

Do not take Zanprol Tablets:

- If you are allergic (hypersensitive) to omeprazole or any of the other ingredients listed in Section 4.
- If you are allergic to medicines containing other proton pump inhibitors (e.g. pantoprazole, lansoprazole, rabeprazole, esomeprazole).
- If you are taking a medicine containing nevirapine (for HIV infection).

If you are not sure, talk to your doctor or pharmacist before taking Zanprol.

Take special care with Zanprol Tablets

Do not take Zanprol for more than 14 days without consulting a doctor. If you do not experience relief, or if you experience a worsening of symptoms, consult your doctor.

Zanprol may hide the symptoms of certain diseases. Therefore, if any of the following happen to you before you start taking Zanprol or while you are taking it, tell your doctor straight away.

- You lose a lot of weight for no reason and have problems swallowing.
- You get stomach pain or indigestion.
- You begin to vomit food or blood.
- You pass black stools (blood-stained stools).
- You experience severe or persistent diarrhoea, as omeprazole has been associated with a small increase in infectious diarrhoea.
- You have had previous gastric ulcer or gastrointestinal surgery.
- You are on continuous symptomatic treatment of indigestion or heartburn for 4 or more weeks.
- You continuously suffer from indigestion or heartburn for 4 or more weeks.
- You have jaundice or severe liver disease.
- You are aged over 55 years with new or recently changed symptoms.

Patients should not take omeprazole as a preventative medication.

Taking other medicines

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. This is because Zanprol can affect the way some medicines work and some medicines can have an effect on Zanprol.

Do not take Zanprol if you are taking a medicine containing nefilivir (used to treat HIV infection).

You should specifically tell your doctor or pharmacist if you are taking diazepam (used to treat anxiety, relax muscles or in epilepsy).

- Diazepam (used to treat anxiety, relax muscles or in epilepsy).
- Phenytoin (used in epilepsy).
- If you are taking phenytoin, your doctor will need to monitor you when you start or stop taking Zanprol.
- medicines that are used to thin your blood, such as warfarin or other vitamin K blockers. Your doctor may need to monitor you when you start or stop taking Zanprol.
- Rifampicin (used to treat tuberculosis).
- Atazanavir (used to treat HIV infection).
- Tacrolimus (used to treat diseases of organ transplantation).
- St John's wort (Hypericum perforatum) (used to treat mild depression).
- Glucocorticoids (used to treat intermittent claudication).
- Saquinavir (used to treat HIV infection).

Taking Zanprol with food and drink

You can take your tablets with food or on an empty stomach.

Pregnancy and breast feeding

Before taking Zanprol, tell your doctor or pharmacist if you are pregnant or planning to get pregnant. Your doctor will decide whether you can take Zanprol if you are breastfeeding.

Driving and using machines

Zanprol is not likely to affect your ability to drive or use any tools or machines. Side effects such as dizziness and visual disturbances may occur (see section 4). If affected, you should not drive or operate machinery.

Important information about some of the ingredients of Zanprol

Zanprol Tablets contain lactose monohydrate. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3. How to take Zanprol Tablets

Always take Zanprol exactly as described in this leaflet. You should check with your doctor or pharmacist if you are not sure.

The usual dose is two 10 mg tablets once a day for 14 days. Contact your doctor if you are not free from symptoms after this period.

It may be necessary to take the tablets for 2-3 consecutive days to achieve improvement of symptoms.

Taking this medicine

It is recommended that you take your tablets in the morning.

You can take your tablets with food or on an empty stomach.

Swallow your tablets whole with half a glass of water. Do not chew or crush the tablets.

What to do if you have trouble swallowing the tablets:

- Break the tablet and disperse it in a small amount of water (not fizzy), any acidic juice (e.g. apple,
United Kingdom Patent Office

UKPAR Zanprol 10mg Tablets

PL 00079/0660

Adults aged 18 years and over:

Initially swallow 2 tablets once daily with plenty of water. If your symptoms improve, reduce the dose to 1 tablet daily. If your symptoms come back, swallow 2 tablets once daily.

If you take more Zanprol than you should

If you take more Zanprol than recommended, talk to your doctor or pharmacist straight away.

If you forget to take Zanprol

If you forget to take a dose, take it as soon as you remember it. However, if it is almost time for your next dose, skip the missed dose. Do not take a double dose to make up for a forgotten dose.

4. Possible side effects

Like all medicines, Zanprol can have side effects, although not everybody gets them:

If you notice any of the following rare but serious side effects, stop taking Zanprol and consult a doctor immediately:

- Sudden wheezing, swelling of your lips, tongue and throat, or body, rash, fainting or difficulties in swallowing (severe allergic reaction).
- Reddening of the skin with blisters or peeling. There may also be severe blisters and bleeding in the lips, eyes, mouth, nose and genitals. This could be Stevens-Johnson syndrome or toxic epidermal necrolysis.
- Yellow skin, dark urine and tiredness which can be symptoms of liver problems.

Side effects may occur with certain frequencies, which are defined as follows:

Very common: affects more than 1 in 10
Common: affects 1 to 10 in 100
Uncommon: affects 1 to 10 in 1,000
Rare: affects 1 to 10 in 10,000
Very rare: affects less than 1 in 10,000

Not known: frequency cannot be estimated from the available data.

Other side effects include:

Common side effects

- Headache.
- Effects on your stomach or gut: diarrhoea, stomach pain, indigestion, wind, flatulence.
- Feeling sick (nausea) or being sick (vomiting).

Uncommon side effects

- Swelling of the feet and ankles.
- Disturbed sleep (insomnia).
- Dizziness, tingling feelings such as "pins and needles", feeling sleepy.
- Spinning feeling (vertigo).
- Changes in blood tests that check how the liver is working.
- Skin rash, lumpy rash (hives) and itchy skin.
- Generally feeling unwell and lacking energy.

Rare side effects

- Blood problems such as a reduced number of white cells or platelets. This can cause weakness, bruising or make infections more likely.
- Allergic reactions, sometimes very severe, including swelling of the lips, tongue and throat, fever, wheezing.
- Low levels of sodium in the blood. This may cause weakness, being sick (vomiting) and cramps.
- Feeling agitated, confused or depressed.
- Taste changes.
- Dry mouth.
- An inflammation of the inside of the mouth.
- An infection called "thrush" which can affect the gut and is caused by a fungus.
- Liver problems, including jaundice which can cause yellow skin, dark urine, and tiredness.
- Hair loss (alopecia).
- Skin rash on exposure to sunshine.
- Joint pains (arthralgia) or muscle pains (myalgia).
- Severe kidney problems (interstitial nephritis).
- Increased sweating.

Very rare side effects

- Changes in blood count including agranulocytosis (lack of white blood cells).
- Aggression.
- Seizures, feeling or hearing things that are not there (hallucinations).
- Severe liver problems leading to liver failure and inflammation of the brain.
- Sudden onset of a severe rash or blistering or peeling skin. This may be associated with a high fever and joint pains (erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis).
- Muscle weakness.
- Enlarged breast in men.
- Hemolytic anaemia.

Zanprol may in very rare cases affect the white blood cells leading to immune deficiency. If you have any infection with symptoms such as fever with a severely reduced general condition or fever with symptoms of a local infection such as pain in the neck, throat or mouth or difficulties in urinating, you must consult your doctor as soon as possible so that a lack of white blood cells (agranulocytosis) can be ruled out by a blood test. It is important for you to give information about your medicine at this time.

Do not be concerned by this list of possible side effects. You may not get any of them. If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. How to store Zanprol Tablets

- Keep out of the reach and sight of children.
- Do not use this medicine after the expiry date shown on the pack.
- Do not store above 30°C.
- Store in the original package to protect from moisture.
- 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

Active ingredient Each gastro-resistant tablet contains Omeprazole 10 mg.

Other ingredients Lactose monohydrate, sodium starch glycolate, sodium stearate, sodium stearyl fumarate, hydroxypropyl methylcellulose (HPMC) acetate succinate, sepiaspar AS-3527 containing propylene glycol, titanium dioxide (E 171), red iron oxide (E 126), hydroxypropyl methylcellulose, yellow iron oxide (E 172), talc, triethyl citrate, mononitroaniline, sodium laurylsulphate, carnauba wax.

Packs of Zanprol tablets contain 7, 14 or 28 tablets (not all packs may be marketed).

The marketing authorization holder is GlaxoSmithKline Consumer Healthcare, Brentford, TW8 9NS, U.K. and all enquiries should be sent to this address.

The manufacturer is Des installed Pharma Ltd., 7 Sapworth Way, Dayton Fields Industrial Estate, Daventry, Northamptonshire, NN11 8BP, U.K.

This leaflet was last revised in November 2011.

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Decision – Granted 13/03/2012