

**TRIMETHOPRIM 100MG TABLETS  
PL 17907/0092**

**TRIMETHOPRIM 200MG TABLETS  
PL 17907/0093**

**UKPAR**

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**TRIMETHOPRIM 100MG TABLETS  
PL 17907/0092**

**TRIMETHOPRIM 200MG TABLETS  
PL 17907/0093**

**LAY SUMMARY**

The MHRA today granted Bristol Laboratories Limited Marketing Authorisations (licences) for the medicinal products Trimethoprim 100mg Tablets (PL 17907/0092) and Trimethoprim 200mg Tablets (PL 17907/0093). These are prescription-only medicines (POM) for the treatment of susceptible infections caused by trimethoprim-sensitive organisms, including urinary and respiratory tract infections, and for the prophylaxis of recurrent urinary tract infections.

Trimethoprim Tablets contain the active ingredient trimethoprim, which is an antibacterial medicine.

The test product was considered the same as the original products Monotrim 100mg and 200mg Tablets (Solvay Healthcare) based on the bioequivalence study submitted and no new safety issues arose as a result of this study. No new or unexpected safety concerns arose from these applications and it was therefore judged that the benefits of taking Trimethoprim 100mg and 200mg Tablets outweigh the risks, hence Marketing Authorisations have been granted.

**TRIMETHOPRIM 100MG TABLETS  
PL 17907/0092**

**TRIMETHOPRIM 200MG TABLETS  
PL 17907/0093**

**SCIENTIFIC DISCUSSION**

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## **INTRODUCTION**

Based on the review of the data on quality, safety and efficacy, the UK granted marketing authorisations for the medicinal products Trimethoprim 100mg Tablets (PL 17907/0092) and Trimethoprim 200mg Tablets (PL 17907/0093) on 28<sup>th</sup> November 2006. The products are prescription-only medicines.

These are two strengths of Trimethoprim, submitted as abridged applications according to Article 10.1 of Directive 2001/83/EC, claiming essential similarity to the original products Monotrim 100mg and 200mg Tablets (Solvay Healthcare). The reference products have been authorised in the UK since March 1980 and so the 10-year period of data exclusivity has expired.

The products contain the active ingredient trimethoprim, a bacteriostatic antibiotic that interferes with the action of dihydrofolate reductase, inhibiting the synthesis of tetrahydrofolic acid (and thus synthesis of DNA nucleosides thymidine and uridine). Bacteria are unable to take up folic acid from the environment and are thus dependant on their own *de novo* synthesis, so inhibition of this system starves the bacteria of two bases necessary for DNA replication and transcription.

Trimethoprim 100mg and 200mg Tablets are indicated for the treatment of susceptible infections caused by trimethoprim-sensitive organisms, including urinary and respiratory tract infections, and for the prophylaxis of recurrent urinary tract infections.

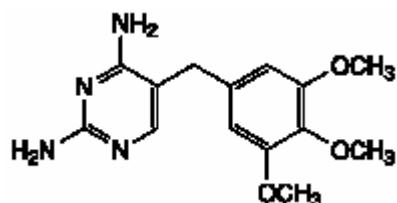
These applications were submitted at the same time and both depend on the bioequivalence study comparing the applicant's 200mg product with the reference product Monotrim 200mg Tablets (Solvay Healthcare). Consequently, all sections of this Scientific Discussion refer to both products.

## PHARMACEUTICAL ASSESSMENT

### DRUG SUBSTANCE

#### Trimethoprim

INN: Trimethoprim  
Chemical Name: 5-(3,4,5-Trimethoxybenzyl)pyrimidine-2,4,diamine  
CAS No: 738-70-5



Molecular formula: C<sub>14</sub>H<sub>18</sub>N<sub>4</sub>O<sub>3</sub>  
Molecular weight: 290.3

Physical form: White or yellowish white powder  
Solubility: Very slightly soluble in water, slightly soluble in alcohol

An appropriate specification based on the European Pharmacopoeia has been provided.

Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications.

Active trimethoprim is stored in appropriate packaging. The specifications and typical analytical test reports are provided and are satisfactory.

Batch analysis data are provided and comply with the proposed specification.

Satisfactory certificates of analysis have been provided for working standards used by the active substance manufacturer and finished product manufacturer during validation studies.

Appropriate stability data have been generated supporting a retest period of 60 months, with no specific storage instructions.

### DRUG PRODUCT

#### Other ingredients

Other ingredients consist of pharmaceutical excipients, namely lactose monohydrate, crospovidone, povidone K-25, industrial methylated spirit, purified water, sodium starch glycolate and magnesium stearate. Appropriate justification for the inclusion of each excipient has been provided.

All excipients used comply with their respective European Pharmacopoeial monograph, with the exception of industrial methylated spirit which complies with the British Pharmacopoeia monograph (in the absence of a Ph Eur monograph, this is acceptable). Satisfactory certificates of analysis have been provided for all excipients.

The only excipient used that contains material of animal or human origin is lactose monohydrate. 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.

There were no novel excipients used and no overages.

#### **Dissolution and impurity profiles**

Dissolution and impurity profiles for both strengths of drug product were found to be similar to those for the reference products.

#### **Manufacture**

A description and flow-chart of the manufacturing method has been provided.

In-process controls are appropriate considering the nature of the product and the method of manufacture. Process validation has been carried out on batches of each strength. The results are satisfactory.

#### **Finished product specification**

The finished product specification is satisfactory. Acceptance limits have been justified with respect to conventional pharmaceutical requirements and, where appropriate, safety. Test methods have been described and have been adequately validated, as appropriate. Batch data have been provided and comply with the release specification. Certificates of analysis have been provided for any working standards used.

#### **Container Closure System**

Product is packaged in either high density polyethylene (HDPE) containers or blisters composed of aluminium and polyvinyl chloride (PVC). Specifications and Certificates of Analysis for all packaging types used have been provided. These are satisfactory. All primary product packaging complies with EU legislation regarding contact with food. The product is packaged in sizes of 50 (100mg only), 100, 250 and 500 tablets for the HDPE containers and sizes of 14, 28, 56 and 84 tablets for the aluminium/PVC blister packs.

#### **Stability**

Finished product stability studies have been conducted in accordance with current guidelines. Based on the results, a shelf-life of 3 years has been set, which is satisfactory. Storage conditions are “Do not store above 25 degrees”, “Store in original container” and “Keep container tightly closed” for the HDPE containers, and “Do not store above 25 degrees” and “Store in original container” for the aluminium/PVC blisters.

#### **Conclusion**

It is recommended that Marketing Authorisations are granted for these applications.

The requirements for essential similarity of the proposed and reference products have been met with respect to qualitative and quantitative content of the active substance, pharmaceutical form and bioequivalence.

## **PRECLINICAL ASSESSMENT**

These applications for generic products claims essential similarity to Monotrim 100mg and 200mg Tablets (Solvay Healthcare), which have been licensed within the EEA for over 10 years.

No new preclinical data have been supplied with these applications and none are required for an application of this type.

## CLINICAL ASSESSMENT

### CLINICAL PHARMACOLOGY

#### General

Trimethoprim inhibits dihydrofolate reductase preventing the synthesis of tetrahydrofolic acid from dihydrofolic acid. It inhibits the nucleoprotein metabolism of micro-organisms.

Trimethoprim is readily absorbed from the gastro-intestinal tract and peak concentration in the circulation occurs at about three hours. About 45% is bound to plasma proteins. Tissue concentrations are reported to be higher than serum concentrations with particularly high concentrations in the kidneys and lungs. Concentrations in the CSF are about half those in blood. The half life is about 10–16 hours and 40–50% of the dose is excreted unchanged in the urine within 24 hours.

#### Pharmacokinetics - Bioequivalence study

A bioequivalence study was carried out comparing the 200 mg strength with the UK reference product from Solvay Healthcare Ltd.

This was an open-label, randomised, two treatment, crossover study in healthy men. There were 26 men enrolled and 24 analysed. Trimethoprim concentrations were analysed by HPLC with a detection limit of 0.03µg/ml. Samples were collected for 24 hours and the washout period was 7 days.

Parameter	Test Agent	Reference	90% CI
C <sub>max</sub> µg/ml	2.46	2.62	87-101%
T <sub>max</sub> hours	1.69	1.54	
AUC <sub>ss</sub> µg.h/ml	32.7	34.1	92-100%

#### Clinical Pharmacology - Clinical Assessor's Comments

The applicant appears to have demonstrated bioequivalence. It is claimed that pharmacokinetics are linear and it is, therefore, not necessary to study the lower dose.

### EFFICACY

Efficacy is reviewed in the Clinical Expert Report. The reference product is established and the application depends upon the ability to show bioequivalence with the reference product.

### SAFETY

Safety is reviewed in the Clinical Expert Report. The reference product is established and the application depends upon the ability to show bioequivalence with the reference product.

#### Post marketing surveillance

Not marketed.

### EXPERT REPORT

The expert report is written by a medically qualified pharmaceutical consultant and is satisfactory.



## **SUMMARY OF PRODUCT CHARACTERISTICS**

This is satisfactory.

## **PATIENT INFORMATION LEAFLET**

This is satisfactory.

## **CONCLUSIONS**

The applicant appears to have demonstrated bioequivalence. Marketing authorisations should be granted for these products.

## **OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT**

### **QUALITY**

The important quality characteristics of Trimethoprim 100mg and 200mg Tablets are well defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

### **PRECLINICAL**

No new preclinical data were submitted and none are required for applications of this type.

### **EFFICACY**

Bioequivalence has been demonstrated between the applicant's Trimethoprim 200mg Tablets and Monotrim 200mg Tablets (Solvay Healthcare). Given that linear kinetics apply between the 100mg and 200mg tablets, that proportional formulae for the capsules have been used and that similar dissolution results have been shown for the two strengths, a separate bioequivalence study using the 100mg tablets is not considered necessary.

No new or unexpected safety concerns arise from these applications.

The SPC, PIL and labelling are satisfactory and consistent with that for Monotrim tablets.

### **RISK BENEFIT ASSESSMENT**

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The bioequivalence study supports the claim that the applicant's products and the innovator products are interchangeable. Extensive clinical experience with trimethoprim is considered to have demonstrated the therapeutic value of the compound. The risk benefit is, therefore, considered to be positive.

**TRIMETHOPRIM 100MG TABLETS  
PL 17907/0092**

**TRIMETHOPRIM 200MG TABLETS  
PL 17907/0093**

**STEPS TAKEN FOR ASSESMENT**

1	The MHRA received the marketing authorisation applications on 3 <sup>rd</sup> February 2004
2	Following standard checks and communication with the applicant the MHRA considered the applications valid on 16 <sup>th</sup> February 2004
3	Following assessment of the applications the MHRA requested further information relating to the clinical dossiers on 3 <sup>rd</sup> September 2004, and further information relating to the quality dossiers on 19 <sup>th</sup> October 2004 and 15 <sup>th</sup> September 2005.
4	The applicant responded to the MHRA's requests, providing further information on 17 <sup>th</sup> September 2004 for the clinical sections, and again on 16 <sup>th</sup> June 2005 and 15 <sup>th</sup> September 2006 for the quality sections.
5	The applications were determined on 28 <sup>th</sup> November 2006

**TRIMETHOPRIM 100MG TABLETS**  
**PL 17907/0092**

**TRIMETHOPRIM 200MG TABLETS**  
**PL 17907/0093**

**STEPS TAKEN AFTER AUTHORISATION - SUMMARY**

<b>Date submitted</b>	<b>Application type</b>	<b>Scope</b>	<b>Outcome</b>

## SUMMARY OF PRODUCT CHARACTERISTICS

### 1 NAME OF THE MEDICINAL PRODUCT

Trimethoprim 100 mg Tablets

### 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 100 mg of Trimethoprim

For excipients, see 6.1

### 3 PHARMACEUTICAL FORM

Tablets

White circular, flat bevelled edged uncoated tablets with breakline dividing "TMP" and "100" on one side and plain on the other side.

### 4 CLINICAL PARTICULARS

#### 4.1 Therapeutic indications

Treatment of susceptible infections caused by trimethoprim-sensitive organisms including urinary and respiratory tract infections and for the prophylaxis of recurrent urinary tract infections.

Consideration should be given to official guidance regarding the appropriate use of antibacterial agents.

#### 4.2 Posology and method of administration

For oral administration

*Acute infections:*

*Adults and Children over 12 years:* 200 mg twice daily

*Children 6 years to 12 years:* 100 mg twice daily

The approximate dosage in children is 8 mg trimethoprim per kg body weight per day.

*Elderly:* Depending on kidney function, see special dosage schedule.

Treatment should continue for at least one week but not last longer than two weeks. The first dose can be doubled.

*Long-term treatment and prophylactic therapy:*

*Adults and children over 12 years:* 100 mg at night

The approximate dosage in children is 2 mg trimethoprim per kg body weight per day.

*Elderly:* Depending on kidney function, see special dosage schedule.

*Dosage advised where there is reduced kidney function:*

Creatinine clearance (ml/sec)	Plasma clearance (micromol/l)	Dosage advised
Over 0.45	Men < 250 Women < 175	Normal
0.25 – 0.45	Men 250 – 600 Women 175 – 400	Normal for three days then half dose
Under 0.25	Men > 600 Women > 400	Half the normal dose

Trimethoprim is removed by dialysis. However, it should not be administered to dialysis patients unless plasma concentrations can be estimated regularly.

#### 4.3 Contraindications

Pregnancy, trimethoprim hypersensitivity, blood dyscrasias, severe renal insufficiency where blood levels cannot be monitored.

#### 4.4 Special warnings and precautions for use

Caution should be exercised in the administration of trimethoprim to patients with actual or potential folate deficiency (e.g. elderly) and administration of folate supplement should be considered. Although an effect on folic acid metabolism is possible, interference with haematopoiesis rarely occurs at the recommended dose. If any such change is seen, folinic acid should reverse the effect. Elderly people may be more susceptible and a lower dose may be advisable. Regular haematological tests should be undertaken in long-term treatment.

In neonates, trimethoprim should be used under careful medical supervision. In patients with impairment of renal function, care should be taken to avoid accumulation.

This product contains the excipient lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactose deficiency or glucose-galactose malabsorption should not take this medicine.

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

Bone marrow depressants: Trimethoprim may increase the potential for bone marrow aplasia. Rifampicin may increase the elimination and shorten the elimination half-life of trimethoprim.

Phenytoin and digoxin: The patients should be carefully controlled as trimethoprim may increase the elimination half-life of phenytoin and digoxin. Ciclosporin may increase the nephrotoxicity of trimethoprim.

#### 4.6 Pregnancy and lactation

Pregnancy is a contraindication. Although trimethoprim is excreted in breast milk, lactation is not a contraindication for short-term trimethoprim therapy.

#### 4.7 Effects on ability to drive and use machines

None known

#### 4.8 Undesirable effects

Nausea, vomiting, and skin rashes have been reported in rare instances. These effects are generally mild and quickly reversible on withdrawal of the drug. Photosensitivity and allergic reactions including angioedema and anaphylaxis have been reported. Rarely, erythema multiforme and toxic epidermal necrolysis have occurred. Aseptic meningitis has been reported.

Rare cases of Stevens-Johnson syndrome have been reported following administration of trimethoprim. Isolated cases of myalgia have occurred. Trimethoprim may affect haematopoiesis.

#### 4.9 Overdose

Treatment of overdosage: Symptomatic treatment, gastric lavage and forced diuresis can be used. Depression of haematopoiesis by trimethoprim can be counteracted by intramuscular administration of calcium folinate.

### 5 PHARMACOLOGICAL PROPERTIES

#### 5.1 Pharmacodynamic properties

ATC code: J01EA01

Group: Anti-infectives for systemic use

Trimethoprim is an antimicrobial agent. The antimicrobial activity is due to selective inhibition of bacterial dihydrofolate reductase.

Trimethoprim is effective *in vitro* against Gram-positive and Gram-negative aerobic organisms, including enterobacteria – *E. coli*, *Proteus*, *Klebsiella pneumoniae*, *Streptococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Staphylococcus aureus*.

It is not active against *Mycobacterium tuberculosis*, *Neisseria gonorrhoeae*, *Pseudomonas aeruginosa*, *Treponema pallidum*, or anaerobic bacteria.

## 5.2 Pharmacokinetic properties

Absorption and half-life:

Trimethoprim is absorbed rapidly and almost completely following oral administration and maximal plasma concentrations are reached after 1-2 hours. Peak plasma concentrations of about 1 µg per ml have been reported after a single dose of 100 mg.

The half-life is about 10 hours in patients with normal renal function but up to 20-50 hours in anuric patients.

Distribution:

Trimethoprim is rapidly and widely distributed to various tissues and fluids, including kidneys, liver, spleen, bronchial secretions, saliva and prostatic tissue and fluid, and the tissue concentrations are generally higher than the plasma concentration.

Excretion:

Trimethoprim is predominantly excreted in the urine in unchanged form. Urinary concentrations are generally well above the MIC of common pathogens for more than 24 hours after the last dose.

## 5.3 Preclinical safety data

Not relevant (widely used in clinical practice)

# 6 PHARMACEUTICAL PARTICULARS

## 6.1 List of excipients

The tablet contains:  
lactose monohydrate  
povidone K-25  
crospovidone



sodium starch glycolate  
magnesium stearate

## **6.2 Incompatibilities**

Not applicable

## **6.3 Shelf life**

Blisters: 36 months  
HDPE tablet containers: 36 months

## **6.4 Special precautions for storage**

Blisters: Do not store above 25°C. Store in the original package.

HDPE Tablet containers: Do not store above 25°C. Store in the original container.  
Keep the container tightly closed.

## **6.5 Nature and contents of container**

HDPE tablet containers, pack sizes of 50, 100, 250 and 500 tablets.  
Al/PVC Blisters, pack sizes of 14, 28, 56 and 84 tablets.  
Not all pack sizes may be marketed.

## **6.6 Instructions for use and handling**

No special requirements

## **7. MARKETING AUTHORISATION HOLDER**

Bristol Laboratories Limited  
Unit 3, Canalside,  
Northbridge Road,  
Berkhamsted, Herts  
HP14 1EG, United Kingdom

## **8 MARKETING AUTHORISATION NUMBER**

PL 17907/0092

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE  
AUTHORISATION**

28/11/2006

**10 DATE OF REVISION OF THE TEXT**

28/11/2006

**1 NAME OF THE MEDICINAL PRODUCT**

Trimethoprim 200 mg Tablets

**2 QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each tablet contains 200 mg of Trimethoprim

For excipients, see 6.1

**3 PHARMACEUTICAL FORM**

Tablets

White circular, flat bevelled edged uncoated tablets with breakline dividing “TMP” and “200” on one side and plain on the other side.

**4 CLINICAL PARTICULARS****4.1 Therapeutic indications**

Treatment of susceptible infections caused by trimethoprim-sensitive organisms including urinary and respiratory tract infections and for the prophylaxis of recurrent urinary tract infections.

Consideration should be given to official guidance regarding the appropriate use of antibacterial agents.

**4.2 Posology and method of administration**

For oral administration

*Acute infections:*

*Adults and Children over 12 years:* 200 mg twice daily

*Children 6 years to 12 years:* 100 mg twice daily

The approximate dosage in children is 8 mg trimethoprim per kg body weight per day.

*Elderly:* Depending on kidney function, see special dosage schedule.

Treatment should continue for at least one week but not last longer than two weeks. The first dose can be doubled.

*Long-term treatment and prophylactic therapy:*

*Adults and children over 12 years:* 100 mg at night

The approximate dosage in children is 2 mg trimethoprim per kg body weight per day.

*Elderly:* Depending on kidney function, see special dosage schedule.

*Dosage advised where there is reduced kidney function:*

Creatinine clearance (ml/sec)	Plasma clearance (micromol/l)	Dosage advised
Over 0.45	Men < 250	Normal
	Women < 175	
0.25 – 0.45	Men 250 – 600	Normal for three days then half dose
	Women 175 – 400	
Under 0.25	Men > 600	Half the normal dose
	Women > 400	

Trimethoprim is removed by dialysis. However, it should not be administered to dialysis patients unless plasma concentrations can be estimated regularly.

### 4.3 Contraindications

Pregnancy, trimethoprim hypersensitivity, blood dyscrasias, severe renal insufficiency where blood levels cannot be monitored.

### 4.4 Special warnings and precautions for use

Caution should be exercised in the administration of trimethoprim to patients with actual or potential folate deficiency (e.g. elderly) and administration of folate supplement should be considered. Although an effect on folic acid metabolism is possible, interference with haematopoiesis rarely occurs at the recommended dose. If any such change is seen, folic acid should reverse the effect. Elderly people may be more susceptible and a lower dose may be advisable. Regular haematological tests should be undertaken in long-term treatment.

In neonates, trimethoprim should be used under careful medical supervision. In patients with impairment of renal function, care should be taken to avoid accumulation.

This product contains the excipient lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactose deficiency or glucose-galactose malabsorption should not take this medicine.

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

Bone marrow depressants: Trimethoprim may increase the potential for bone marrow aplasia. Rifampicin may increase the elimination and shorten the elimination half-life of trimethoprim.

Phenytoin and digoxin: The patients should be carefully controlled as trimethoprim may increase the elimination half-life of phenytoin and digoxin. Ciclosporin may increase the nephrotoxicity of trimethoprim.

#### **4.6 Pregnancy and lactation**

Pregnancy is a contraindication. Although trimethoprim is excreted in breast milk, lactation is not a contraindication for short-term trimethoprim therapy.

#### **4.7 Effects on ability to drive and use machines**

None known

#### **4.8 Undesirable effects**

Nausea, vomiting, and skin rashes have been reported in rare instances. These effects are generally mild and quickly reversible on withdrawal of the drug. Photosensitivity and allergic reactions including angioedema and anaphylaxis have been reported. Rarely, erythema multiforme and toxic epidermal necrolysis have occurred. Aseptic meningitis has been reported.

Rare cases of Stevens-Johnson syndrome have been reported following administration of trimethoprim. Isolated cases of myalgia have occurred. Trimethoprim may affect haematopoiesis.

#### **4.9 Overdose**

Treatment of overdose: Symptomatic treatment, gastric lavage and forced diuresis can be used. Depression of haematopoiesis by trimethoprim can be counteracted by intramuscular administration of calcium folinate.

### **5 PHARMACOLOGICAL PROPERTIES**

#### **5.1 Pharmacodynamic properties**

**ATC code:** J01EA01

**Group:** Anti-infectives for systemic use

Trimethoprim is an antimicrobial agent. The antimicrobial activity is due to selective inhibition of bacterial dihydrofolate reductase.

Trimethoprim is effective *in vitro* against Gram-positive and Gram-negative aerobic organisms, including enterobacteria – *E. coli*, *Proteus*, *Klebsiella pneumoniae*, *Streptococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Staphylococcus aureus*.

It is not active against *Mycobacterium tuberculosis*, *Neisseria gonorrhoeae*, *Pseudomonas aeruginosa*, *Treponema pallidum*, or anaerobic bacteria.

## 5.2 Pharmacokinetic properties

Absorption and half-life:

Trimethoprim is absorbed rapidly and almost completely following oral administration and maximal plasma concentrations are reached after 1-2 hours. Peak plasma concentrations of about 1 µg per ml have been reported after a single dose of 100 mg.

The half-life is about 10 hours in patients with normal renal function but up to 20-50 hours in anuric patients.

Distribution:

Trimethoprim is rapidly and widely distributed to various tissues and fluids, including kidneys, liver, spleen, bronchial secretions, saliva and prostatic tissue and fluid, and the tissue concentrations are generally higher than the plasma concentration.

Excretion:

Trimethoprim is predominantly excreted in the urine in unchanged form. Urinary concentrations are generally well above the MIC of common pathogens for more than 24 hours after the last dose.

## 5.3 Preclinical safety data

Not relevant (widely used in clinical practice)

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

The tablet contains:  
lactose monohydrate

povidone K-25  
crospovidone  
sodium starch glycolate  
magnesium stearate

## **6.2 Incompatibilities**

Not applicable

## **6.3 Shelf life**

Blisters: 36 months

HDPE tablet containers: 36 months

## **6.4 Special precautions for storage**

Blisters: Do not store above 25°C. Store in the original package.

HDPE Tablet containers: Do not store above 25°C. Store in the original container.  
Keep the container tightly closed.

## **6.5 Nature and contents of container**

HDPE tablet containers, pack sizes of 100, 250 and 500 tablets.

Al/PVC Blisters, pack sizes of 14, 28, 56 and 84 tablets.

Not all pack sizes may be marketed.

## **6.6 Instructions for use and handling**

No special requirements

## **7 MARKETING AUTHORISATION HOLDER**

Bristol Laboratories Limited  
Unit 3, Canalside,  
Northbridge Road,  
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HP14 1EG, United Kingdom

## **8 MARKETING AUTHORISATION NUMBER**

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**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE  
AUTHORISATION**

28/11/2006

**10 DATE OF REVISION OF THE TEXT**

28/11/2006



## PATIENT INFORMATION LEAFLET

### PATIENT INFORMATION LEAFLET

#### TRIMETHOPRIM TABLETS

#### Trimethoprim

#### What you should know about Trimethoprim Tablets

Please 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, please ask your doctor or pharmacist.
- This medicine has been prescribed for you personally and you should not pass it on to others. It may harm them, even if their symptoms are the same as yours.

#### What your Tablets Contain

Trimethoprim 100 mg Tablets are white circular, flat bevelled edged, uncoated tablets with a breakline dividing "TMP" and "100" on one side and plain on the other side.

Trimethoprim 200 mg Tablets are white circular, flat bevelled edged, uncoated tablets with a breakline dividing "TMP" and "200" on one side and plain on the other side.

Each tablet contains:

The active ingredient – trimethoprim 100 mg or 200 mg.

Other ingredients - lactose monohydrate, povidone K-25, cross povidone, sodium starch glycolate, and magnesium stearate.

Trimethoprim 100mg Tablets are packed in HDPE containers of 50, 100, 250 and 500 tablets or in blister packs of 14, 28, 56 and 84 tablets.

Trimethoprim 200mg Tablets are packed in HDPE containers of 100, 250 and 500 tablets or in blister packs of 14, 28, 56 and 84 tablets.

Not all pack sizes may be marketed.

#### Product Licence holder and manufacturer

Bristol Laboratories Ltd., Unit 3, Canalside, Northbridge Road, Berkhamsted, Herts, HP4 1EG, United Kingdom.

#### What Trimethoprim is used for

Trimethoprim is an antibacterial medicine. It is particularly active against certain types of bacteria which can cause urinary and chest infections. This medicine is sometimes prescribed for people who often suffer from urinary infections, to stop them getting an infection in the first place.

#### Before taking Trimethoprim Tablets

If you think the answer is yes for any of these questions, please tell your doctor or a pharmacist before you start taking your medicine.

- Are you pregnant, or do you think you could be?
- Have you had an allergic reaction to trimethoprim or any of the other ingredients before?
- Do you have a blood disorder?
- Do you have a severe kidney complaint?

If you are taking any anti-cancer preparations which depress bone marrow production, phenytoin (for epilepsy), digoxin (for a heart complaint), ciclosporin (for organ transplants or psoriasis), medicines for thinning the blood (eg warfarin), or an antibiotic called rifampicin, you doctor may wish to check your condition regularly. Trimethoprim and these other medicines can affect each other. Elderly patients and others who need extra folic acid in their diet may be given a low dose of trimethoprim.

If you are breast-feeding, talk to your doctor or pharmacist before taking trimethoprim.

This product contains the sugar lactose. If you have been told by your doctor that you have an intolerance to some sugars, check with your doctor before taking this medicinal product.

#### How to take Trimethoprim Tablets

Take trimethoprim exactly as directed by your doctor. If you do not understand these directions ask your pharmacist, nurse or doctor to explain them to you.

*For an infection:* for adults and children over 12, the usual dose is two 100 mg tablets or one 200 mg tablet taken twice a day (that is, every 12 hours).

For children aged 6 to 12 years, the usual dose is 100 mg tablet twice a day.  
For children aged 6 months to 5 years, the dose is half a 100 mg tablet twice a day.  
For elderly people with a kidney complaint, the doctor will decide what is the best dose to take.  
Treatment is for one to two weeks. Make sure you finish all the tablets prescribed to you. If you do not finish the tablets, the infection may come back or get worse.  
*For prevention of urinary infections:* for adults and children over 12, the usual dose is one 100 mg tablet at night. For children aged 6 to 12 years, the dose is half a 100 mg tablet at night.  
Treatment should continue for as long as your doctor feels it is needed.  
*Dialysis patients:* trimethoprim is removed by dialysis. Blood tests will be necessary to check your blood levels before and after dialysis.  
It is best to swallow the tablets with a drink of water.  
If you miss a dose, you should take it as soon as you remember, unless you suffer from a kidney complaint. In this case, ask your doctor or a pharmacist for advice.  
If someone takes an overdose of Trimethoprim Tablets, contact a doctor immediately or go to your nearest hospital casualty department. Take the pack with you to show to the doctor.

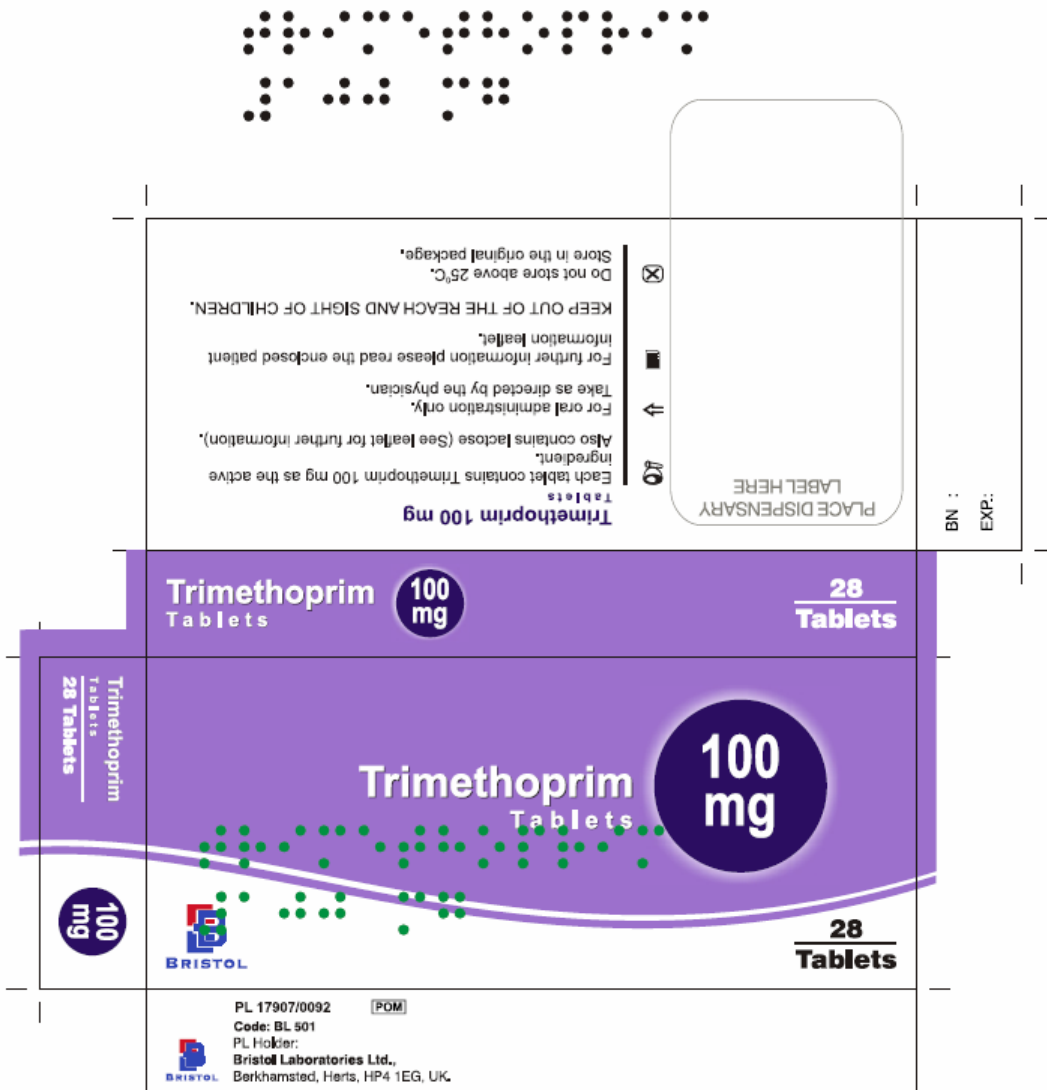
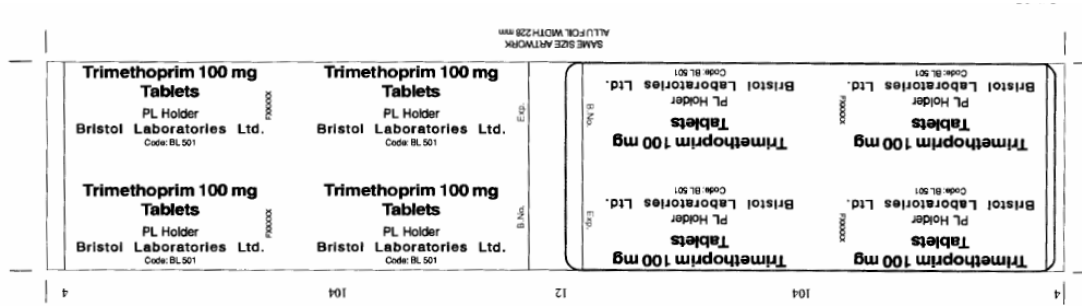
#### Possible side effects

As with all medicines, trimethoprim may cause side effects. Occasionally people taking this medicine get skin rashes (which may also appear to be abnormal sunburning when you have been out of doors, even on a cloudy day). Rarely, these are very serious and include mouth sores. If you get a rash and you are concerned, contact your doctor immediately.  
Inform your doctor if you develop any of the following: painful red blotches, widespread peeling skin, flu-like symptoms (fever, headache, stiff neck, vomiting).  
Very occasionally, people taking trimethoprim are sick or feel sick. Rarely, people have an allergic reaction, such as rash, itching, inflamed or reddened skin. Very rarely, this allergic reaction may be serious and could result in a fall in blood pressure, malaise (feeling unwell), facial oedema (a swelling of the face) and difficulty breathing. If you experience sudden wheeziness or difficulty in breathing, or swelling of the eyelids, lips, face or tongue, contact your doctor immediately.  
Aseptic meningitis has been reported as a very rare side effect.  
In isolated cases muscle pains can occur.  
Trimethoprim can affect your body's ability to make new blood cells. Your doctor will carry out blood tests if you take trimethoprim for a long time or if he thinks you are at special risk.  
If you think you have any other side effects not mentioned here, please tell your doctor or a pharmacist.

#### Where to keep Trimethoprim Tablets



Keep out of the reach and sight of children.  
Blisters: Do not store above 25°C. Store in the original package (Blister carton)  
Tablet containers: Do not store above 25°C. Store in the original container. Keep the container tightly closed.  
Unless your doctor tells you to, do not keep any Trimethoprim Tablets that you no longer need. Return any unused tablets back to your pharmacist. Do not take Trimethoprim Tablets after the expiry date as shown on the carton or label.  
**Remember**  
This medicine is for YOU. Only a doctor can prescribe it for you. Never give it to someone else. It may harm them even if they have the same symptoms as you.  
**Further information**  
This leaflet does not contain all the information about your medicine. If you have any questions or are not sure about anything, ask your doctor or pharmacist who has the information you need and will advise you.  
This leaflet was prepared in September 2005.

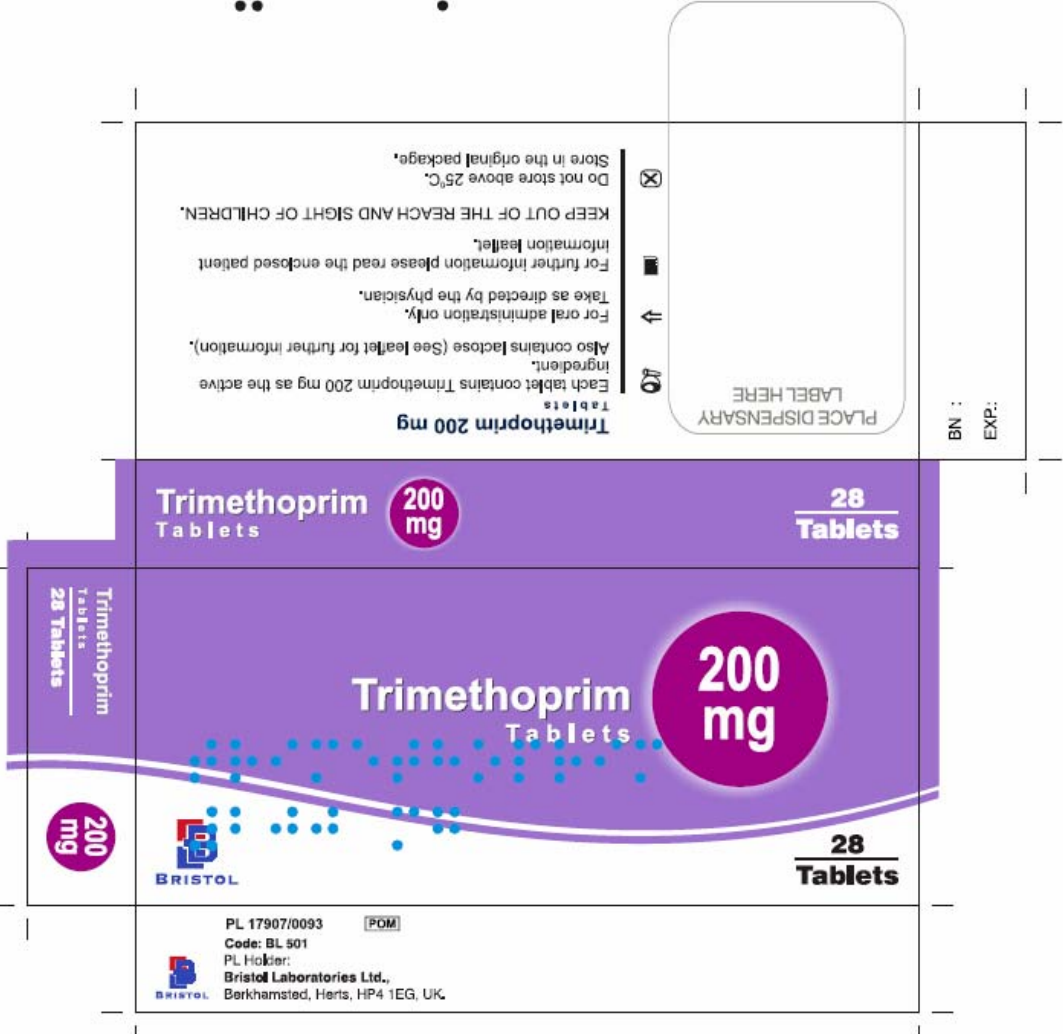
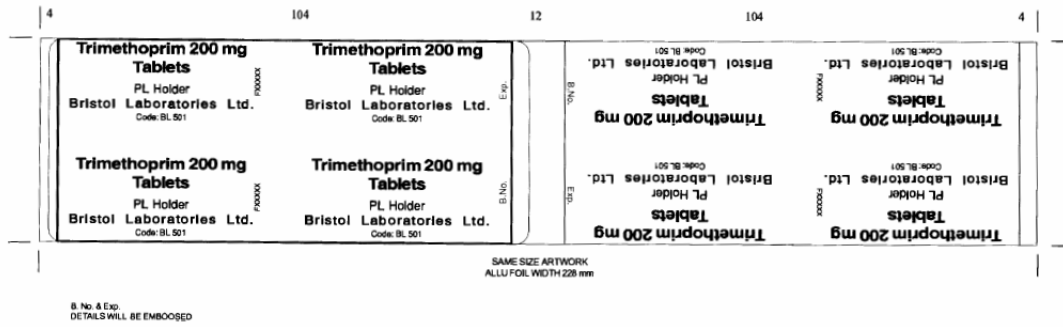
LABELLING



<p>Each tablet contains Trimethoprim 100 mg as the active ingredient. Also contains lactose.</p> <p>For oral administration only. Take as directed by the physician.</p> <p>Refer to the enclosed leaflet for further information.</p> <p><b>KEEP OUT OF THE REACH AND SIGHT OF CHILDREN.</b></p> <p>Do not store above 25°C. Store in the original container. Keep the container tightly closed.</p>	 <p><b>50</b> <b>Tablets</b></p> 	<div style="border: 1px solid black; width: 100%; height: 40px; margin-bottom: 5px;"></div> <p>BN : EXP :</p> <p>Code: BL 501</p> <p>PL 17907/0092 <span style="border: 1px solid black; padding: 2px;">POM</span></p> <p>PL Holder: <b>Bristol Laboratories Ltd.,</b> Berkhamsted, Herts, HP4 1EG, UK.</p> <p style="writing-mode: vertical-rl; transform: rotate(180deg);">LXXX</p>
<p><b>2655 C    274 C</b></p>	<p>Size : 110 X 30 mm</p>	



<p>Each tablet contains Trimethoprim 100 mg as the active ingredient. Also contains lactose.</p> <p>For oral administration only. Take as directed by the physician.</p> <p>Refer to the enclosed leaflet for further information.</p> <p><b>KEEP OUT OF THE REACH AND SIGHT OF CHILDREN.</b></p> <p>Do not store above 25°C. Store in the original container. Keep the container tightly closed.</p>	 <p><b>500</b> <b>Tablets</b></p> 	<div style="border: 1px solid black; width: 100%; height: 40px; margin-bottom: 5px;"></div> <p>BN : EXP :</p> <p>Code: BL 501</p> <p>PL 17907/0092 <span style="border: 1px solid black; padding: 2px;">POM</span></p> <p>PL Holder: <b>Bristol Laboratories Ltd.,</b> Berkhamsted, Herts, HP4 1EG, UK.</p> <p style="writing-mode: vertical-rl; transform: rotate(180deg);">LXXX</p>
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Each tablet contains Trimethoprim 200 mg as the active ingredient. Also contains lactose. For oral administration only. Take as directed by the physician. Refer to the enclosed leaflet for further information.

**KEEP OUT OF THE REACH AND SIGHT OF CHILDREN**

Do not store above 25°C. Store in the original container. Keep the container tightly closed.

**Trimethoprim Tablets 200 mg**

**100 Tablets**

BN :  
EXP :  
Code: BL 501  
PL 17907/0093 **POM**  
PL Holder: **Bristol Laboratories Ltd.**, Berkhamsted, Herts, HP4 1EG, UK.

LX000