AZITHROMYCIN 500MG TABLETS
PL 10622/0315

UKPAR

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LAY SUMMARY

On 25\textsuperscript{th} January 2011, the MHRA granted PLIVA Pharma Limited a Marketing Authorisation (licence) for the medicinal product Azithromycin 500mg Tablets (PL 10622/0315). This is a Pharmacy medicine (P).

The ingredient which makes this medicine work is a ‘macrolide’ antibiotic called azithromycin.

Azithromycin 500mg Tablets are used to treat a sexually transmitted infection (STI) called Chlamydia trachomatis in people aged 16 years or over, who have tested positive but have no symptoms and in treatment of their sexual partners.

No new or unexpected safety concerns arose from this application and it was, therefore, judged that the benefits of taking Azithromycin 500mg Tablets outweigh the risks; hence a Marketing Authorisation has been granted.
AZITHROMYCIN 500MG TABLETS
PL 10622/0315

SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the MHRA granted a marketing authorisation for the medicinal product Azithromycin 500mg Tablets (PL 10622/0315) to PLIVA Pharma Limited on the 25th January 2011. This is a Pharmacy medicine used in the treatment of confirmed asymptomatic *Chlamydia trachomatis* genital infection in individuals aged 16 years and over and the epidemiological treatment of their sexual partners.

This application was submitted as a simple abridged application according to Article 10c of Directive 2001/83/EC, cross-referring to Azithromycin 500mg Tablets (PL 10622/0164) also held by PLIVA Pharma Limited, which was granted a marketing authorisation on 17th May 2004.

No new data were submitted nor were they 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 Public Assessment Report (PAR) has been generated.

A pharmacovigilance system has been provided with this application and is satisfactory.

No environmental risk assessment has been undertaken, as this is not considered necessary. This is justified as it is not anticipated that the grant of this new marketing authorisation will result in an increase in the environmental exposure of the drug.

The applicant’s justification for absence of ERA is satisfactory.
PHARMACEUTICAL ASSESSMENT

LICENCE NO: PL 10622/0315
PROPRIETARY NAME: Azithromycin 500mg Tablets
COMPANY NAME: PLIVA Pharma Limited
E.C. ARTICLE: Article 10c of Directive 2001/83/EC
LEGAL STATUS: P

1 INTRODUCTION
This is a simple, informed consent application for Azithromycin 500mg Tablets, submitted under Article 10c of Directive 2001/83/EC. The application cross-refer to Azithromycin 500mg Tablets (PL 10622/0164), approved on 17th May 2004 to the marketing authorisation holder PLIVA Pharma Limited. The current application is considered valid.

2 MARKETING AUTHORISATION APPLICATION (MAA)
2.1 Name(s)
The proposed name of the product is Azithromycin 500mg Tablets. The product has been named in line with current requirements.

2.2 Strength, pharmaceutical form, route of administration, container and pack sizes
The product contains the active ingredient azithromycin dihydrate.

The product is packed in Blister (PVC/Al foil) with a pack size of 2 tablets. Specification and Certificate of Analysis for all packaging components used have been provided and are satisfactory. The packaging and pack size are the same as those for the reference product.

The proposed shelf life is 36 months, with the storage conditions ‘Store below 25°C’, ‘Keep in a dry place’ and ‘Store in the original packaging’. The shelf-life and storage conditions are identical to those of the reference product and are satisfactory.

2.3 Legal status
The product is a Pharmacy medicine (P).

2.4 Marketing authorisation holder/Contact Persons/Company
The proposed Marketing Authorisation holder is PLIVA Pharma Ltd, Vision House, Bedford Road, Petersfield, Hampshire, GU32 3QB

The Qualified Person (QP) responsible for pharmacovigilance is stated and a Curriculum Vitae (CV) is included.

2.5 Manufacturers
The proposed manufacturing sites are the same as those registered for the reference product and evidence of Good Manufacturing Practice compliance has been provided.
2.6 Qualitative and quantitative composition
The proposed composition is consistent with the details registered for the reference product.

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

2.8 Finished product/shelf-life specifications
The proposed finished product and shelf-life specifications are in line with the details registered for the reference product.

2.9 Drug substance specification
The proposed drug substance specification conforms to the current United States Pharmacopoeia monograph for azithromycin dihydrate, and is in-line with that for the reference product.

European Directorate for the Quality of Medicines (EDQM) Certificates of Suitability for the manufacturer of azithromycin dihydrate has been provided. The active substance manufacturer is in line with that for the reference product.

2.10 TSE Compliance
No materials of human or animal origin have been used in the manufacture of this product. This is consistent with the reference product.

2.11 Bioequivalence
No bioequivalence data are required to support this informed consent application, as the proposed product is manufactured to the same formula utilising the same process as the reference product Azithromycin 500mg Tablets (PL 10622/0164).

3 EXPERT REPORT
The applicant has included detailed expert reports of the application. Signed declarations and copies of the experts’ CVs are enclosed for the quality, non-clinical and clinical experts. All are considered to have sufficient experience for their responsibilities.

4 PRODUCT NAME & APPEARANCE
See 2.1 for details of the proposed product name. The appearance of the product is identical to that of the reference product.

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

6 PATIENT INFORMATION LEAFLET (PIL)/LABELLING
The patient information leaflet has been prepared in line with the details registered for the reference product.
The Marketing Authorisation Holder has committed to submit a PIL user testing on the basis that the application is to undergo change of ownership following licence grant.

7. CONCLUSIONS
The data submitted with the application is acceptable. The grant of a marketing authorisation is recommended.
PRECLINICAL ASSESSMENT

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

No new clinical data have been supplied with this application and none are required for an application of this type.
OVERALL CONCLUSION AND BENEFIT RISK ASSESSMENT

QUALITY
The data for this application are consistent with those previously assessed for the 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
This application is identical to the previously granted application for Azithromycin 500mg Tablets (PL 10622/0164), granted to PLIVA Pharma Limited on the 17th May 2004.

Pharmaceutical preclinical and clinical expert statements have been provided, together with CVs showing the experts are appropriately qualified. The experts confirm that the product is identical in composition, manufacture and pharmaceutical characteristics to the respective reference product and that there are no toxicological or clinical issues.

No new or unexpected safety concerns arise from this application.

The SmPC, PIL and labelling are satisfactory and consistent with those for the reference product.

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 reference product. Extensive clinical experience with azithromycin dihydrate is considered to have demonstrated the therapeutic values of the compounds. The risk benefit is, therefore, considered to be positive.
**STEPS TAKEN FOR ASSESSMENT**

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SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Azithromycin 500mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each film-coated tablet contains 500 mg azithromycin as dihydrate.
For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Film-coated tablets.
Azithromycin 500mg Tablets are light blue, oval, biconvex tablets imprinted with PLIVA on one side and 500 on the other side.

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
Treatment of confirmed asymptomatic Chlamydia trachomatis genital infection in individuals aged 16 years and over and the epidemiological treatment of their sexual partners.
Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and method of administration
A single 1g (2 x 500mg tablets) dose.
It is not necessary to alter the dose in elderly.

4.3 Contraindications
Azithromycin is contraindicated in patients with known hypersensitivity to azithromycin or any macrolide antibiotic, or to any of the excipients.
Relative for Azithromycin sold as a Pharmacy Medicine.
Symptomatic infection.
Symptoms suggestive of other STIs e.g. any unusual genital or anal swellings or lesions.
Children aged under 16 years.
Renal or hepatic impairment.
History of cardiac disease.
Individuals receiving ciclosporin, digoxin, ergotamine, terfenadine, theophylline, disopyramide, rifabutin and coumarin anticoagulant therapy, such as warfarin.
Individuals receiving azithromycin for treatment of other infections.
Pregnancy and breast feeding.

4.4 Special warnings and precautions for use
As with erythromycin and other macrolides, rare serious allergic reactions including angioneurotic oedema and anaphylaxis (rarely fatal), have been reported with azithromycin (see section 4.8 Undesirable Effects). Some of these reactions with azithromycin have resulted in recurrent symptoms and required a longer period of observation and treatment.
Vomiting: To reduce the risk of vomiting, advise the individual to take the dose before bed and at least 2hrs after food or drink. If vomiting occurs after taking the dose pharmacist advice should be sought.
Oral contraception: if vomiting or diarrhoea occurs whilst taking Azithromycin 500mg tablets, refer to the oral contraceptive’s instructions for measures to minimise the risk of contraception failure.
Diarrhoea/pseudomembranous colitis caused by Clostridium difficile has occurred. Due to this, patients with diarrhoea should be carefully monitored.

4.5 Interaction with other medicinal products and other forms of interaction
In individuals receiving azithromycin and antacids, azithromycin should be taken at least 1 hour before or 2 hours after the antacid.
Nelfinavir:
Co-administration of 1200 mg azithromycin and steady state nelfinavir (750 mg 3 times daily) resulted in a mean decrease of AUC of 16% for nelfinavir, an increase of AUC of
azithromycin of 113%, and an increase of Cmax of 136%. Dose adjustment is not necessary, but the increased potential for known side-effects of azithromycin should be considered.

CYP3A4:
Although azithromycin does not seem to inhibit the enzyme CYP3A4, possible inhibition of this enzyme cannot be excluded. Consequently, caution is advised when given in combination with pimozide and other drugs with a narrow therapeutic window and a metabolism catalysed by CYP3A4.
Due to interaction, Azithromycin 500mg tablets are contraindicated if individual is concomitantly taking any of the following medications (see also section 4.3 Contraindications):

Ciclosporin:
Some of the related macrolide antibiotics interfere with the metabolism of ciclosporin. In the absence of conclusive pharmacokinetic studies or data investigating the potential for an interaction between azithromycin and ciclosporin, Azithromycin 500 mg tablets are contraindicated.

Coumarin-Type Oral Anticoagulants:
In a pharmacodynamic interaction study, azithromycin did not alter the anticoagulant effect of a single 15mg dose of warfarin administered to healthy volunteers. There have been reports received in the post-marketing period of potentiated anticoagulation subsequent to co-administration of azithromycin and coumarin-type oral anticoagulants. Although a causal relationship has not been established, Clamelle 500mg tablets are contraindicated.

Digoxin:
Some of the macrolide antibiotics have been reported to impair the metabolism of digoxin (in the gut) in some individuals. Since there is a possibility of raised digoxin levels, Azithromycin 500 mg tablets are contraindicated.

Disopyramide:
Some of the related macrolide antibiotics have been reported to increase serum disopyramide levels, which can result in ventricular fibrillation.

Ergot derivatives:
Because of the theoretical possibility of ergotism, azithromycin and ergot derivatives should not be co-administered.

Rifabutin:
Co-administration of azithromycin and rifabutin did not affect the serum concentrations of either drug. Neutropenia was observed in subjects receiving concomitant treatment of azithromycin and rifabutin. Although neutropenia has been associated with the use of rifabutin, a causal relationship to combination with azithromycin has not been established.

Terfenadine:
There is a theoretical risk of serious dysrhythmias due to prolongation of QTc interval.

Theophylline:
Theophylline levels may be increased in patients taking azithromycin.

4.6 Pregnancy and lactation
Azithromycin 500 mg Tablets are contraindicated during pregnancy and lactation.

4.7 Effects on ability to drive and use machines
Azithromycin has the potential to cause dizziness and somnolence. If affected, the individual should not drive or operate machinery.
4.8 Undesirable effects

Azithromycin is well tolerated with a low incidence of side effects. The most commonly reported adverse events are gastrointestinal in nature.

Infections and infestations

Rare (≥1/10,000 to ≤1/1,000):
- candidiasis

Blood and lymphatic system disorders

Rare (≥1/10,000 to ≤1/1,000):
- neutropenia - transient mild reductions in neutrophil counts have occasionally been observed in clinical trials, however a causal relationship has not been confirmed

Thrombocytopenia

Psychiatric system disorders

Rare (≥1/10,000 to ≤1/1,000):
- aggressiveness, restlessness, anxiety and nervousness

Nervous system disorders

Uncommon (1/1,000 to ≤1/100):
- dizziness, vertigo, convulsions (as seen with other macrolides), headache, somnolence, taste and smell perversion, syncope.

Rare (≥1/10,000 to ≤1/1,000):
- paraesthesia, hyperactivity, asthenia, insomnia

Ear and labyrinth disorders

Rare (≥1/10,000 to ≤1/1,000):
- Hearing impairment has been reported with macrolide antibiotics. There have been rare reports of hearing impairment, including hearing loss, deafness and tinnitus in some patients receiving azithromycin. Many of these have been associated with prolonged use of high doses in investigational studies. In those cases where follow-up information was available, the majority of these events were reversible.

Cardiac disorders

Rare (≥1/10,000 to ≤1/1,000):
- palpitations and arrhythmias including ventricular tachycardia (as seen with macrolides) have been reported. There have been rare reports of QT prolongation and torsades de pointes, especially in patients at risk for prolonged cardiac repolarisation (see section 4.3 Contraindications).

Vascular disorders

Rare (≥1/10,000 to ≤1/1,000):
- hypotension

Gastrointestinal disorders

Common (≥1/100 to <1/10):
- nausea, vomiting, diarrhoea, (rarely resulting in dehydration) abdominal discomfort (pain/cramps)

Uncommon (1/1,000 to ≤1/100):
- loose stools, flatulence, digestive disorders, anorexia, dyspepsia

Rare (≥1/10,000 to ≤1/1,000):
- constipation, discoloration of tongue, pancreatitis, pseudomembranous colitis.

Hepatobiliary disorders

Rare (≥1/10,000 to ≤1/1,000):
- abnormal liver function, including hepatitis and cholestatic jaundice, as well as rare cases of hepatic necrosis and hepatic failure

Skin and subcutaneous tissue disorders

Uncommon (≥1/1,000 to ≤1/100):
- allergic reactions including pruritus and rash

Rare (≥1/10,000 to ≤1/1,000):
- serious allergic reactions including photosensitivity, oedema, urticaria, angioneurotic oedema, serious skin reactions such as erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis.

Musculoskeletal, connective tissue and bone disorders

Uncommon (≥1/1,000 to ≤1/100):
- arthralgia

Renal and urinary disorders

Rare (≥1/10,000 to ≤1/1,000):

interstitial nephritis and acute renal failure have been reported.

**Reproductive system and breast disorders**

Uncommon (≥1/1,000 to ≤1/100):
- vaginitis

**General disorders**

Rare (≥1/10,000 to ≤1/1,000):
- anaphylaxis (see section 4.4 Warnings and Special Precautions for Use), fatigue, malaise

### 4.9 Overdose

Adverse events experienced in higher than recommended doses were similar to those seen at normal doses. In the event of overdosage, general symptomatic and supportive measures are indicated as required.

### 5 PHARMACOLOGICAL PROPERTIES

#### 5.1 Pharmacodynamic properties

**ATC code:** J01FA10

**Mode of action:**

Azithromycin is an azalide, a subclass of the macrolide antibiotics. The mode of action of azithromycin is based upon suppression of bacterial RNA-dependent protein synthesis, by reversibly binding to the 23S ribosomal RNA in the 50S subunit of the ribosomes.

**Mechanism of resistance:**

Stable resistance to azithromycin has not been described for *Chlamydia trachomatis*. In vitro evidence to date indicates that whilst certain point mutations in the 23S rRNA gene may lead to decreased sensitivity to macrolides, including azithromycin, such strains seem to carry a prohibitive physiological cost which may make their maintenance in the wild (i.e. dissemination in clinical cases) presently unlikely.

**Breakpoints:**

Chlamydiae are obligate intra-cellular pathogens. Determination of sensitivity/ resistance to antibiotics in vitro requires a cell culture technique which is inappropriate for routine monitoring of resistance. The complexity of the chlamydial life cycle is such that a universally agreed method for determining minimal inhibitory concentrations and breakpoints of antibiotics is not available. Comparative activity of antibiotics on chlamydia can be compared within a laboratory using the same method. Qualitative results can be compared between laboratories, but caution is required when applying numerical values to comparative data in this setting.

The prevalence of acquired resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.

Stable resistance to azithromycin has not been described for *Chlamydia trachomatis*.

#### 5.2 Pharmacokinetic properties

**Absorption**

Azithromycin is well absorbed following oral administration and rapidly passes from serum to tissues and various organs. After a single 500 mg oral dose of azithromycin, 37% of the drug is absorbed, and a peak plasma concentration (0.41 µg/ml) is achieved in 2-3 hours.

**Distribution**

Azithromycin is widely distributed throughout the body, achieving high tissue concentration (up to 50 times higher than observed concentration in plasma). Volume of distribution is approximately 31 l/kg.

Azithromycin is rapidly distributed to a wide range of tissues and achieves high tissue concentrations ranging between 1 and 9 µg/ml, depending on the tissue. Therapeutic concentrations of azithromycin are maintained in tissues for five to seven days after the ingestion of last oral dose.

Azithromycin achieves very high intracellular concentrations in phagocytic cells and exhibits very good intracellular activity.
**Excretion**
Plasma terminal elimination half-life closely reflects the tissue depletion half-life of 2-4 days. Biliary excretion of azithromycin is a major route of elimination. Approximately 50% biliary excretion is in the form of unchanged compound. The other half are 10 metabolites formed by N- and O-demethylation, by hydroxylation of desosamine and aglycone rings, and by cleavage of the cladinose conjugate. Comparison of HPLC and microbiological assay suggests that metabolites play no part in the microbiological activity of azithromycin. Approximately 6% of administered dose is excreted in urine.

In elderly volunteers (> 65 years), slightly higher (30%) AUC values were seen than in younger volunteers (< 45 years), but this is not considered clinically significant and hence no dose adjustment is recommended.

5.3 Preclinical safety data
In higher-dose animal studies azithromycin has been noted to cause reversible phospholipidosis, generally without discernible toxicological consequences.

6 PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Core:
- Calcium hydrogen phosphate, anhydrous
- Hypromellose
- Maize starch
- Pregelatinised starch
- Microcrystalline cellulose
- Sodium laurylsulfate
- Magnesium stearate

Film-coating:
- Hypromellose
- Colour Indigotin (E132)
- Titanium dioxide (E171)
- Polysorbate 80
- Talc

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
36 months.

6.4 Special precautions for storage
Store below 25 °C. in a dry place, in original packaging

6.5 Nature and contents of container
Blisters (PVC/Al foil) packed in a carton box containing 2 tablets.

6.6 Special precautions for disposal
There are no special instructions for use and handling.

7 MARKETING AUTHORISATION HOLDER
PLIVA Pharma Ltd.
Vision House
Bedford Road
Petersfield
Hampshire, GU32 3QB

8 MARKETING AUTHORISATION NUMBER(S)
PL10622/0315
PATIENT INFORMATION LEAFLET

Azithromycin 500mg Tablets

Read all of this leaflet carefully because it contains important information for you.
This medicine is available without prescription. However, you still need to take Azithromycin
500 mg Tablets carefully to get the best results from it.

- Keep this leaflet. You may need to read it again.
- 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.
- Ask your pharmacist if you need more information or advice.
- You must contact a doctor or specialist if you develop symptoms.

In this leaflet:
1. What Azithromycin 500mg Tablets are and what they are used for
2. Before you take Azithromycin 500mg Tablets
3. How to take Azithromycin 500mg Tablets
4. Possible side effects?
5. How to store Azithromycin 500mg Tablets
6. Further information
7. Important information about Chlamydia and other sexual health advice

1. What Azithromycin 500mg Tablets are and what they are used for

The ingredient which makes this medicine work is a ‘macrolide’ antibiotic called azithromycin.
Azithromycin 500 mg Tablets are used to treat the sexually transmitted infection (STI) called
Chlamydia trachomatis in people aged 18 years or over, who have tested positive but have
no symptoms and in treatment of their sexual partners.

To buy Azithromycin 500 mg Tablets you must have had a positive Chlamydia test result and
have no symptoms or be a sexual partner of someone who has had a positive Chlamydia test
result, and have no symptoms. If you have symptoms contact your pharmacist for advice.

2. Before you take Azithromycin 500mg Tablets

Do not take Azithromycin 500 mg Tablets but see a doctor instead if you:
- are allergic to azithromycin, other ‘macrolide’ antibiotics or any ingredient in the product
  (see section 6)
- are under 16 years of age
- have tested positive and also have symptoms of Chlamydia such as
  – pain when urinating or having sex
  – unusual vaginal discharge (in women) or discharge from penis (in men)
  – bleeding after sex or between periods (in women)
  – pain below your belly button (in women) or in your testicles (in men)
- symptoms suggestive of other STIs, such as unusual lumps, bumps, blisters or sores
  around the genital or anal area
- are or may be pregnant or are breast feeding
- have liver, kidney or heart problems.

Do not take Azithromycin 500 mg Tablets if you are taking any of these other medicines:
- ergotamine or dihydroergotamine (for migraine or poor blood flow)
- warfarin (to thin the blood)
- disopyramide (for irregular heart beat)
- rifabutin (for tuberculosis)
- ciclosporin (to help prevent rejection of transplanted organs, or for use in arthritis or skin
  problems)
- digoxin (for heart disorders)
theophylline (for asthma)
• terfenadine (for hayfever or allergies)
• azithromycin for any other infections e.g. chest, sinusus, ear, skin.

You can still take Azithromycin 500 mg Tablets but may need to take extra care if you are taking these medicines:
• oral contraceptives (the ‘pill’) – if you get sickness or diarrhoea whilst taking Azithromycin 500 mg Tablets your ‘pill’ may not prevent you becoming pregnant. You will need to read the ‘pill’ instruction leaflet to take the right action. Do not have sex, even with a condom, for seven days after taking Azithromycin 500 mg Tablets (see section 3).
• indigestion remedies – take Azithromycin 500 mg Tablets at least 1 hour before or 2 hours after the indigestion remedy. Azithromycin 500 mg Tablets will not work as well if both are taken too close together.
• pemiscide (for mental illness)
• nefinavir (for HIV infection)

If you are taking an regular medication and are unsure, check with your doctor or pharmacist.

Driving and operating machinery:
Azithromycin 500 mg Tablets can cause dizziness and sleepiness. Make sure you are not affected before you drive or operate machinery.

3. How to take Azithromycin 500mg Tablets.
The pack contains two tablets. Take both tablets together as a single dose with a glass of water before you go to bed and at least 2 hours after food or any other drink besides water. If you are sick (vomit) within 3 hours of taking your dose, they might not work properly, so ask your pharmacist or doctor for advice.

You should not delay treatment. If you have to wait before taking them, see section 5 for storage conditions.

After treatment
• Contact your doctor, Genito-Urinary Medicine (GUM) clinic or community sexual health clinic if you think you have come into contact with Chlamydia again or if symptoms develop.
• Ensure any sexual partners are also tested and treated before you have sex with them, otherwise you are at risk of catching Chlamydia again.
• If you, or your partner, have been treated for Chlamydia do not have sex (oral, vaginal, anal or using sex toys), even with a condom for 7 days after taking Azithromycin 500 mg Tablets.

4. Possible Side Effects
Like many medicines, Azithromycin 500 mg Tablets may occasionally cause side effects. However, this is usually with longer courses of azithromycin treatment. Do not be alarmed by this list, you may not experience any of them. If you are worried speak to your pharmacist.

Contact your doctor or nearest casualty department immediately if you have a rare but serious allergic reaction such as swelling of the body, face, lips or throat. Very occasionally, these effects may be severe causing shortness of breath, shock or collapse.

Tell your doctor if you notice any of the following side effects or notice any other effects not listed:
• Common (occurs in less than 1 in 10 users):
  • feeling or being sick, diarrhoea or stomach ache
• Uncommon (occurs in less than 1 in 100 users):


- dizziness, 'spinning' sensation, fits, headache, fainting, changes in taste and smell, wind, poor appetite, indigestion, painful joints, vaginal inflammation (you might feel soreness), dryness, rash, itchy rash (pruritis).

- Rare (occurs in less than 1 in 1,000 users):
  - thrush (candidiasis), increase in nosebleeds, bruising, sore throat or infections (signs of changes in blood cells), aggression, restlessness, hyperactivity, anxiety, difficulty sleeping, nervousness, pins and needles, poor hearing, ringing in the ears, deafness, palpitations, irregular or racing heart beat, feeling faint due to a drop in blood pressure, constipation, tongue discolouration, feeling tired or unwell, weakness or loss of strength, sensitivity to sunlight, inflammation of the pancreas (pancreatitis), inflammation of the lining of large intestine (pseudomembranous colitis; you might get diarrhoea, stomach cramps, fever, blood in the stools). Changes in liver function or jaundice (yellowing of the skin or whites of the eyes), liver damage, failure or inflammation (fatigue, weakness, loss of appetite, weight loss, abdominal pain, fever). 
  - Severe but rare skin conditions such as erythema multiforme (raised, red patches on the skin which may blister), Stevens Johnson Syndrome (more severe form of erythema multiforme) or toxic epidermal necrolysis (red painful rash that looks like a scald and may cause peeling of the skin). Kidney failure or inflammation (increased need to urinate at night, muscle twitching and cramps, loss of appetite, feeling or being sick, unpleasant taste in mouth).

You can help make sure that medicines remain as safe as possible by reporting any unwanted side effects via the internet at www.yellowcard.gov.uk; alternatively you can call Freephone 0800 100 3362 (available between 10am to 2pm Monday to Friday) or fill in a paper form available from your local pharmacy.

5. How to store Azithromycin 500mg Tablets.
   - Keep in a secure place out of the reach and sight of children.
   - Store below 25°C (room temperature) in the original package.
   - Do not use after the expiry date shown on the pack.

6. Further information

What Azithromycin 500mg Tablets contain

- Each tablet contains 500mg of azithromycin (the active ingredient that makes the tablet work).
- The tablets also contain calcium hydrogen phosphate (anhydrous), hypromellose, maize starch, pregelatinised starch, microcrystalline cellulose, sodium lauryl sulfate, magnesium stearate, polysorbate 80, talc, indigo blue (E132) and titanium dioxide (E171).

7. More about Chlamydia and other important sexual health advice

What is it?

Chlamydia is an extremely common sexually transmitted infection (STI) caused by a bacteria called Chlamydia trachomatis which is found in the semen and vaginal fluids of men and women who have the infection. It infects the neck of the womb (cervix) in women, the tube that drains the bladder of urine (urethra) and the back passage (rectum) in both women and men.

Chlamydia affects between 1 in 10 and 1 in 100 people and is most common in people aged 16 to 25 years.

How do you get it?

Chlamydia is easily passed from one person to another through sexual contact.
The infection is most commonly spread through:
- unprotected vaginal, anal or oral sex
- sharing sex toys if you don’t wash them or cover them with a new condom each time they’re used.

It can also be passed on fingers to your eyes after touching the genital area.

A mother can also pass the infection to her baby during childbirth.

Are there any symptoms?
Chlamydia is a ‘silent’ condition; as many as 70% of infected individuals have no symptoms, so it can stay hidden for many months or years. Those who do have symptoms may have any of the following:

In women: unusual vaginal discharge, a need to pass urine more often, pain when passing urine or during sexual intercourse, pain below the belly button or bleeding between periods or after sex

In men: pain and/or burning when passing urine, discharge from the penis, irritation at the tip of the penis or swelling and pain in the testicles.

In men and women: if the infection is in the rectum, there are rarely any symptoms but it may cause discomfort and discharge.

If you have symptoms or you think you may have another infection, consult your doctor or local GUM clinic or community sexual health clinic for further investigation and treatment.

Why is treatment important?
It is very important to get treated for Chlamydia. If left untreated the infection can spread to other parts of the body and develop into more serious problems such as:

In women:
- pelvic inflammatory disease which can seriously affect the womb or fallopian tubes
- scarring or damage to the fallopian tubes causing pain or infertility (problems getting pregnant)
- increased risk of ectopic pregnancies (when pregnancy develops outside the womb)
- infection in the liver, causing pain and inflammation.

In men:
- painful infection in the testicles and possible reduced fertility.

In men and women:
- rarely, inflammation of the joints (reactive arthritis). This is sometimes accompanied by inflammation of the urethra and the eye, when it is known as Reiter’s syndrome.

Each time you have Chlamydia you are at increased risk of serious problems. If you have already had Chlamydia in the last 6 months you should see a doctor.

If left untreated you can also infect your partner.

Can it be prevented?
Use a condom during sex to reduce the risk of getting or passing on not just Chlamydia, but other sexually shared infections, such as HIV, syphilis and gonorrhoea.

If you, or your partner have been treated for Chlamydia do not have sex (oral, vaginal, anal or using sex toys), even with a condom for 7 days after taking Azithromycin 500 mg Tablets, otherwise you can become re-infected. Avoid using sex toys. If you do share them, wash them or cover them with a new condom before anyone else uses them.
Other important sexual health advice
Using a condom will help reduce your risk of getting or passing on Chlamydia and other sexually shared infections (STIs).

If you have tested positive for Chlamydia, you are also at higher risk of other STIs. It is important that you visit your GUM clinic or community sexual health clinic to be tested for these. Your pharmacist can tell you how to go about this.

If you have tested positive for Chlamydia, then it is important that your current sexual partner and any previous, but recent partners are also tested and treated. They should also receive advice from a healthcare professional. There are a number of ways that partners can be contacted confidentially; your pharmacist can tell you how to go about this. You are strongly advised to tell your partner(e), but it is not compulsory.

Marketing Authorisation Holder and Manufacturer
Marketing Authorisation Holder is:

Manufacturer is:
Pliva Krakow Zaklady Farmaceutyczne S.A., ul. Mogilska 80, 31-546 Krakow, Poland

This leaflet was last revised in March 2010
PL 10622/0315
LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

1. NAME OF THE MEDICINAL PRODUCT

Azithromycin 500 mg Tablets

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains 500 mg azithromycin (as dihydrate)

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Tablets

2

This pack contains one complete treatment course.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral Use

Please read the enclosed package leaflet before use.

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

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

WARNING: Do not exceed the stated dose

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C in the original packaging
10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Pliva Pharma Limited, Petersfield, GU32 3Q8

12. MARKETING AUTHORISATION NUMBER(S)

PL 10622/0315

13. BATCH NUMBER

LOT:

14. GENERAL CLASSIFICATION FOR SUPPLY

P

15. INSTRUCTIONS ON USE

For treatment of Chlamydia in people 16 years and older who have tested positive but have no symptoms.

Also for the treatment of their sexual partners.

DOSE: Adults and adolescents 16 years and older:

Take both tablets together as a single dose.

DO NOT TAKE if you: are allergic to azithromycin or any of the ingredients of the tablet have symptoms of Chlamydia or other STIs have liver, kidney or heart problems are pregnant or breast feeding are under 16 years old are taking certain prescribed medicines

For further information please read the enclosed leaflet

16. INFORMATION IN BRAILLE

Azithromycin 500 mg Tablets
MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

1. NAME OF THE MEDICINAL PRODUCT
Azithromycin 500 mg tablets

2. NAME OF THE MARKETING AUTHORISATION HOLDER
Pliva Pharma Ltd.

3. EXPIRY DATE
EXP:

4. BATCH NUMBER
LOT:

5. OTHER