SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Erythroped A Tablets.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablets contains active substance Erythromycin as Erythromycin Ethylsuccinate Ph. Eur. 500mg/tablet

Excipient(s) with known effect
sodium starch glycollate
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablets.

4.1 Therapeutic indications

For the prophylaxis and treatment of infections caused by erythromycin-sensitive organisms (see section 5.1).

- Upper Respiratory Tract infections: tonsillitis, peritonsillar abscess, pharyngitis, laryngitis, sinusitis, secondary infections in influenza and common colds
- Lower Respiratory Tract infections: tracheitis, acute and chronic bronchitis, pneumonia (lobar pneumonia, bronchopneumonia, primary atypical pneumonia), bronchiectasis, Legionnaire's disease
- Ear infection: otitis media and otitis externa, mastoiditis
- Oral infections: gingivitis, Vincent's angina
- Eye infections: blepharitis
- Skin and soft tissue infections: boils and carbuncles, paronychia, abscesses, pustular acne, impetigo, cellulitis, erysipelas
- Gastrointestinal infections: cholecystitis, staphylococcal enterocolitis
- Prophylaxis: peri- and post-operative trauma, burns, rheumatic fever.
- Other infections: osteomyelitis, urethritis, gonorrhoea, syphilis, lymphogranuloma venereum, diphtheria, prostatitis, scarlet fever

4.2 Posology and method of administration

Posology

Adults and children over 8 years: For mild to moderate infections 2g daily in divided doses. Up to 4g daily in severe infections.

Elderly: No special dosage recommendations.

Paediatric population
Note: For younger children, infants and babies, erythromycin suspensions is normally recommended. The recommended dose for children age 2 – 8, for mild to moderate infections, is 1 g daily in divided doses. The recommended dose for infants and babies, for mild to moderate infections, is 500 mg daily in divided doses. For severe infections doses may be doubled.

Method of administration
For oral administration

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Erythromycin is contraindicated in patients taking simvastatin, tolterodine, mizolastine, amisulpride, astemizole, terfenadine, domperidone, cisapride or pimozide.

Erythromycin should not be given to patients with a history of QT prolongation (congenital or documented acquired QT prolongation) or ventricular cardiac arrhythmia, including torsades de pointes (see section 4.4 and 4.5).

Erythromycin should not be given to patients with electrolyte disturbances (hypokalaemia, hypomagnesaemia due to the risk of prolongation of QT interval).

Erythromycin is contraindicated with ergotamine and dihydroergotamine.

Concomitant administration of erythromycin and lomitapide is contraindicated (see section 4.5)

4.4 Special warnings and precautions for use

Erythromycin is excreted principally by the liver, so caution should be exercised in administering the antibiotic to patients with impaired hepatic function or concomitantly receiving potentially hepatotoxic agents. Hepatic dysfunction including increased liver enzymes and/or cholestatic hepatitis, with or without jaundice, has been infrequently reported with erythromycin.

Pseudomembranous colitis has been reported with nearly all antibacterial agents, including macrolides, and may range in severity from mild to life-threatening (see section.4.8). Clostridium difficile-associated diarrhoea (CDAD) has been reported with use of nearly all antibacterial agents including erythromycin and may range in severity from mild diarrhoea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon, which may lead to overgrowth of C. difficile. CDAD must be considered in all patients who present with diarrhoea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

As with other macrolides, rare serious allergic reactions, including acute generalised exanthematous pustulosis (AGEP) have been reported. If an allergic reaction occurs, the drug should be discontinued, and appropriate therapy should be instituted. Physicians should be aware that reappearance of the allergic symptoms may occur when symptomatic therapy is discontinued.

Cardiovascular Events:
Prolongation of the QT interval, reflecting effects on cardiac repolarisation imparting a risk of developing cardiac arrhythmia and torsades de pointes, have been seen in patients treated with macrolides including erythromycin (see sections 4.3, 4.5 and 4.8). Fatalities have been reported.

Erythromycin should be used with caution in the following;
- Patients with coronary artery disease, severe cardiac insufficiency, conduction disturbances or clinically relevant bradycardia.
- Patients concomitantly taking other medicinal products associated with QT prolongation (see section 4.3 and 4.5).
- Elderly patients may be more susceptible to drug- associated effects on the QT interval (see section 4.8).

Epidemiological studies investigating the risk of adverse cardiovascular outcomes with macrolides have shown variable results. Some observational studies have identified a rare short term risk of arrhythmia, myocardial infarction and cardiovascular mortality associated with macrolides including erythromycin. Consideration of these findings should be balanced with treatment benefits when prescribing erythromycin.

Carefully consider the balance of benefits and risks before prescribing erythromycin for any patients taking hydroxychloroquine or chloroquine, because of the potential for an increased risk of cardiovascular events and cardiovascular mortality (see section 4.5).

There have been reports suggesting erythromycin does not reach the foetus in adequate concentrations to prevent congenital syphilis. Infants born to women treated during pregnancy with oral erythromycin for early syphilis should be treated with an appropriate penicillin regimen.

There have been reports that erythromycin may aggravate the weakness of patients with myasthenia gravis.

Erythromycin interferes with the fluorometric determination of urinary catecholamines.

Rhabdomyolysis with or without renal impairment has been reported in seriously ill patients receiving erythromycin concomitantly with statin.

Paediatric population

There have been reports of infantile hypertrophic pyloric stenosis (IHPS) occurring in infants following erythromycin therapy. Epidemiological studies including data from meta-analyses suggest a 2-3-fold increase in the risk of IHPS following exposure to erythromycin in infancy. This risk is highest following exposure to erythromycin during the first 14 days of life. Available data suggests a risk of 2.6% (95% CI: 1.5 -4.2%) following exposure to erythromycin during this time period. The risk of IHPS in the general population is 0.1-0.2%. Since erythromycin may be used in the treatment of conditions in infants which are associated with significant mortality or morbidity (such as pertussis or chlamydia), the benefit of erythromycin therapy needs to be weighed against the potential risk of developing IHPS. Parents should be informed to contact their physician if vomiting or irritability with feeding occurs.

Erythroped A Tablets contains sodium starch glycollate.
This medicine contains less than 1mmol sodium (23 mg) per tablet, that is to say essentially 'sodium- free'.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant use of erythromycin with terfenadine or astemizole is likely to result in an enhanced risk of cardiotoxicity with these drugs. The concomitant use of erythromycin with either astemizole or terfenadine is therefore contraindicated.

The metabolism of terfenadine and astemizole is significantly altered when either are taken concomitantly with erythromycin. Rare cases of serious cardiovascular events have been observed, including Torsades de pointes, other ventricular arrhythmias and cardiac arrest. Death has been reported with the terfenadine / erythromycin combination.

Mizolastine has a weak potential to prolong QT interval and has not been associated with arrhythmias, however, the metabolism of mizolastine is inhibited by erythromycin, therefore concomitant use should be avoided.

Elevated cisapride levels have been reported in patients receiving erythromycin and cisapride concomitantly. This may result in QT prolongation and cardiac arrhythmias including ventricular tachycardia, ventricular fibrillation and Torsades de pointes. Similar effects have been

observed with concomitant administration of pimozide and clarithromycin, another macrolide antibiotic.

Concurrent use of erythromycin and ergotamine or dihydroergotamine has been associated in some patients with acute ergot toxicity characterised by the rapid development of severe peripheral vasospasm and dysaesthesia.

Increases in serum concentrations of the following drugs metabolised by the cytochrome P450 system may occur : when administered concurrently with erythromycin: acenocoumarol, alfentanil, astemizole, bromocriptine, carbamazepine, cilostazol, cyclosporin, digoxin, dihydroergotamine, disopyramide, ergotamine, hexobarbitone, methylprednisolone, midazolam, omeprazole, phenytoin, quinidine, rifabutin, sildenafil, tacrolimus, terfenadine, domperidone, theophylline, triazolam, valproate, vinblastine, antifungals e.g fluconazole, ketoconazole and itraconazole and warfarin. Appropriate monitoring should be undertaken and dosage should be adjusted as necessary. Erythromycin has been reported to decrease the clearance of zopiclone and thus may increase the pharmacodynamic effects of this drug

When oral erythromycin is given concurrently with theophylline, there is also a significant decrease in erythromycin serum concentrations. The decrease could result in subtherapeutic concentrations of erythromycin.

There have been reports of increased anticoagulant effects when erythromycin and oral anticoagulants (e.g. warfarin, rivaroxaban) are used concomitantly.

Observational data have shown that co-administration of azithromycin with hydroxychloroquine in patients with rheumatoid arthritis is associated with an increased risk of cardiovascular events and cardiovascular mortality. Because of the potential for a similar risk with other macrolides when used in combination with hydroxychloroquine or chloroquine, careful consideration should be given to the balance of benefits and risks before prescribing erythromycin for any patients taking hydroxychloroquine or chloroquine.

Concomitant administration of erythromycin with lomitapide is contraindicated due the potential for markedly increased transaminases (see section 4.3).

Corticosteroids: Caution should be exercised in concomitant use of erythromycin with systemic and inhaled corticosteroids that are primarily metabolised by CYP3A due to the potential for increased systemic exposure to corticosteroids. If concomitant use occurs, patients should be closely monitored for systemic corticosteroid undesirable effects.

Hydroxychloroquine and chloroquine: Erythromycin should be used with caution in patients receiving these medicines known to prolong the QT interval due to the potential to induce cardiac arrhythmia and serious adverse cardiovascular events.

4.6 Fertility, pregnancy and lactation

Pregnancy
The available epidemiological studies on the risk of major congenital malformations with use of macrolides including erythromycin during pregnancy provide conflicting results. Some observational studies in humans have reported cardiovascular malformations after exposure to medicinal products containing erythromycin during early pregnancy.

Erythromycin has been reported to cross the placental barrier in humans, but foetal plasma levels are generally low.

There is a large amount of data from observational studies performed in several countries on exposure to erythromycin during pregnancy, compared to no antibiotic use or use of another antibiotic during the same period (>24,000 first trimester exposures). While most studies do not suggest an association with adverse fetal effects such as major congenital malformations, cardiovascular malformations or miscarriage, there is limited epidemiological evidence of a small increased risk of major congenital malformations, specifically cardiovascular malformations following first trimester exposure to erythromycin.

Therefore, erythromycin should only be used during pregnancy if clinically needed and the benefit of treatment is expected to outweigh any small increased risks which may exist.

Breast-feeding
Erythromycin can be excreted into breast-milk. Caution should be exercised when administering erythromycin to lactating mothers due to reports of infantile hypertrophic pyloric stenosis in breast-fed infants.

There have been reports that maternal macrolide antibiotics exposure within 7 weeks of delivery may be associated with a higher risk of infantile hypertrophic pyloric stenosis (IHPS).

Fertility
No data available

4.7 Effects on ability to drive and use machines

No data available.

4.8 Undesirable effects

The list of undesirable effects shown below is presented by system organ class, MedDRA preferred term, and frequency using the following frequency conventions:

Rare (≥1/10,000 to <1/1,000)

Very rare (<1/10,000)

Not known (cannot be estimated from the available data)

System Organ Class	Frequency	Adverse reactions
Immune system disorders	Not known	Allergic reactions (rare and mild) although anaphylaxis has occurred.
Eye disorders	Not known	Mitochondrial optic neuropathy
Ear and labyrinth disorders	Not known	*Reversible hearing loss
Cardiac disorders	Very rare	**Cardiac arrhythmias
	Not known	Cardiac arrest, ventricular fibrillation
Gastrointestinal disorders	Not known	Infantile hypertrophic pyloric stenosis Nausea, abdominal discomfort, vomiting and diarrhoea
Hepatobiliary disorders	Not known	Hepatic dysfunction, hepatitis
Skin and subcutaneous tissue disorders	Rare	Stevens-Johnson syndrome, toxic epidermal necrolysis, mild eruptions to erythema multiforme
	Not known	Acute generalised exanthematous pustulosis (AGEP)
Investigations	Not known	Abnormal liver function tests

* Associated with doses of erythromycin usually greater than 4g per day has been reported.
** There have been isolated reports of chest pain, dizziness and palpitations, however, a cause and effect relationship has not been established.

There are no reports implicating erythromycin products with abnormal tooth development, and only rare reports of damage to the blood, kidneys or central nervous system.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Symptoms
Hearing loss, severe nausea, vomiting and diarrhoea.

Treatment
Gastric lavage, general supportive measures.

5 PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic Properties

Pharmacotherapeutic group: Antibacterials for systemic use, ATC code: J01FA01

Mechanism of action
Erythromycin exerts its antimicrobial action by binding to the 50S ribosomal sub-unit of susceptible microorganisms and suppresses protein synthesis. Erythromycin is usually active against most strains of the following organisms both in vitro and in clinical infections:

Gram positive bacteria - *Listeria monocytogenes, Corynebacterium diphtheriae* (as an adjunct to antitoxin), Staphylococci spp, Streptococci spp (including Enterococci).
Gram negative bacteria - *Haemophilus influenzae, Neisseria meningitidis, Neisseria gonorrhoeae, Legionella pneumophila, Moraxella (Branhamella) catarrhalis, Bordetella pertussis,* Campylobacter spp.
Mycoplasma - *Mycoplasma pneumoniae, Ureaplasma urealyticum.*
Other organisms - *Treponema pallidum,* Chlamydia spp, Clostridia spp, L-forms, the agents causing trachoma and *lymphogranuloma venereum.*

Note: The majority of strains of Haemophilus influenzae are susceptible to the concentrations reached after ordinary doses.

Susceptibility testing breakpoints:

EUCAST clinical MIC breakpoints for erythromycin (Version 14.0, valid from 2024-01-01):

Pathogen	Susceptible (mg/L)	Resistant (mg/L)
Staphylococcus spp.	≤1	>1
Streptococcus groups A,B,C andG	≤ 0.25	> 0.25
Streptococcus pneumoniae	≤ 0.25	> 0.25
Viridans group streptococci	IE*	IE*
Haemophilus influenzae	Note[1)]	Note[1)]
Moraxella catarrhalis	≤ 0.25	> 0.25
Listeria monocytogenes	≤ 1	> 1
Campylobacter jejuni	≤ 4	> 4

Campylobacter coli	≤ 8	> 8
Corynebacterium diphtheriae and C. ulcerans	≤ 0.06	>0.06
Kingella kingae	≤ 0.5	>0.5
Bacillus spp. *except B. anthracis*	≤ 0.5	>0.5

1) Clinical evidence for the efficacy of macrolides in H. influenza respiratory infections is conflicting due to high spontaneous cure rates. Should there be a need to test any macrolide against this species, the epidemiological cut-offs (ECOFFS) should be used to detect strains with acquired resistance. The ECOFF for erythromycin is 16 mg/l.

**"IE" indicates that there is insufficient evidence that the species in question is a good target for therapy with the drug. A MIC with a comment but without an accompanying S, I or R categorisation may be reported.*

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 known and the utility of the agent in at least some types of infections is questionable.

5.2 Pharmacokinetic properties

Absorption
Erythromycin ethylsuccinate is less susceptible than erythromycin to the adverse effect of gastric acid. It is absorbed from the small intestine. Peak blood levels normally occur within 1 hour of dosing of erythromycin ethylsuccinate granules. Doses may be administered 2, 3 or 4 times a day.

Distribution
It is widely distributed throughout body tissues.

Biotransformation
Little metabolism occurs and only about 5% is excreted in the urine

Elimination
The elimination half-life is approximately two hours. It is excreted principally by the liver.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Calcium hydrogen phosphate, sodium starch glycollate, starch maize, povidone, magnesium stearate, hydroxypropyl methylcellulose, polyethylene glycol, titanium dioxide, quinoline yellow (E 104), sorbic acid.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

2 years

6.4 Special precautions for storage

None.

6.5 Nature and contents of container

Polypropylene bottles of 50, 100 or 500 tablets.
Blister: PVC/aluminium of 4 or 28 tablets.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements

7 MARKETING AUTHORISATION HOLDER

Amdipharm UK Limited

Dashwood House,

69 Old Broad Street,

London, EC2M 1QS**,** United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 20072/0040

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

19 May 1995

10 DATE OF REVISION OF THE TEXT

01/05/2024