SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Ery-Max 200 mg granules for oral suspension, sachet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 sachet contains erythromycin ethylsuccinate equivalent to 200 mg erythromycin.

Excipients with known effect:
1 sachet of granules for oral suspension contains sucrose 792 mg.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Granules for oral suspension, sachet

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Pneumonia caused by *Mycoplasma pneumoniae, Chlamydophila psittaci* (ornithosis) or *Chlamydophila pneumoniae* (TWAR). Whooping cough. Diphtheria. Urogenital infections caused by *Chlamydophila trachomatis*. Conjunctivitis and pneumonia in newborns caused by *Chlamydophila trachomatis*.

For the following indications, Ery-Max should be reserved for patients with penicillin hypersensitivity or where penicillin is unsuitable for other reasons: Pharyngotonsillitis. Acute otitis media. Community-acquired pneumonia. Skin and soft tissue infections.

4.2 Posology and method of administration

Children < 4 kg:
The dose is calculated individually.

Children 4–35 kg:
30–50 mg/kg body weight per day, divided into 2 doses.

Adults and children > 35 kg:
1 g twice daily.
If gastrointestinal problems occur, it is recommended to divide the daily dose into 3 or 4 administrations.

The contents of one 200 mg sachet correspond to 5 ml oral suspension at 40 mg/ml.

Example of dosing when administered twice daily

Weight	*Dosage*
4-12 kg	1 sachet x 2
13-22 kg	2 sachets x 2
23-35 kg	3 sachets x 2

Good absorption is achieved when taken immediately before a meal.

Ery-Max granules for oral suspension, sachet, is intended as an emergency pack and is particularly suitable for children.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
Known hypersensitivity to macrolides. Concomitant medication with terfenadine, astemizole, cisapride, disopyramide, domperidone, and pimozide; ergot alkaloids (such as ergotamine and dihydroergotamine).
Ery-Max should not be used concurrently with simvastatin, atorvastatin, lovastatin, and lomitapide (see section 4.5).
Erythromycin should not be given to patients with a history of QT prolongation (congenital, familial (unless excluded by ECG), or documented acquired QT prolongation) or ventricular cardiac arrhythmia, including torsades de pointes (see sections 4.4 and 4.5).
Erythromycin should not be given to patients with electrolyte disturbances (hypokalemia, hypomagnesemia) due to the risk of QT interval prolongation.

4.4 Special warnings and precautions for use

Since erythromycin is mainly excreted via the liver, caution is recommended in patients with impaired liver function.

There have been reports that erythromycin may worsen symptoms in patients with myasthenia gravis.

Diarrhea/pseudomembranous colitis caused by *Clostridioides difficile* can occur. Patients with diarrhea should therefore be monitored closely.

Cardiovascular events
Prolongation of the QT interval, reflecting effects on cardiac repolarization that increase the risk of developing arrhythmias and torsades de pointes, has been observed in patients treated with macrolides, including erythromycin (see sections 4.3, 4.5, and 4.8).

<u>Erythromycin should be used with caution in the following cases:</u>
Patients with coronary artery disease, severe heart failure, conduction system disorders, or clinically relevant bradycardia.
Patients taking other medications associated with QT prolongation (see sections 4.3 and 4.5).
Epidemiological studies investigating the risk of adverse cardiovascular outcomes with macrolides have shown varying results. Some observational studies have identified a rare, short-term risk of arrhythmia, myocardial infarction, and cardiac mortality related to macrolides, including erythromycin. These findings should be weighed against the benefits of treatment when prescribing erythromycin.

Ery-Max should not be used during and for two weeks after treatment with CYP3A4 inducers (such as *rifampicin, phenytoin, carbamazepine, phenobarbital, St. John's wort*). Concomitant treatment with these

medicines may likely result in subtherapeutic levels of erythromycin and thereby pose a risk of treatment failure (see section 4.5).

Ery-Max is an inhibitor of CYP3A4 and should only be used under special circumstances when treating with other medicines metabolized by CYP3A4 (see section 4.5).

Cases of infantile hypertrophic pyloric stenosis (IHPS) in infants after treatment with erythromycin have been reported (see section 4.8 Adverse Reactions). Epidemiological studies, including data from meta-analyses, suggest a 2–3-fold increase in the risk of IHPS after exposure to erythromycin in infants. This risk is highest after exposure to erythromycin during the first 14 days of life. Available data indicate a risk of 2.6 % (95 % CI: 1.5–4.2 %) after exposure to erythromycin during this period. The risk of IHPS in the general population is 0.1–0.2 %. Since erythromycin may be used to treat conditions in infants associated with significant mortality and morbidity (such as pertussis and chlamydia), the benefits of erythromycin treatment should be weighed against the potential risk of developing IHPS. Parents should be advised to contact a doctor if vomiting or irritability during feeding occurs.

As with other macrolides, rare severe allergic reactions, including acute generalized exanthematous pustulosis (AGEP), have been reported. If an allergic reaction occurs, the drug should be discontinued, and appropriate treatment initiated. Physicians must be aware that allergic symptoms may recur when symptomatic treatment is stopped.

Ery-Max contains sucrose and sodium
Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.
The oral suspension contains sugar; therefore, careful and regular tooth brushing is important.
Ery-Max contains less than 1 mmol (23 mg) sodium per sachet, that is to say essentially “sodium-free.”

4.5 Interaction with other medicinal products and other forms of interaction

Medicinal products that can prolong the QT interval:

Experimental and epidemiological studies indicate that erythromycin treatment could trigger torsades de pointes syndrome in patients treated with terfenadine, as erythromycin strongly inhibits the metabolism of *terfenadine*. This combination is contraindicated.

Elevated levels of *cisapride* have been reported in patients receiving concomitant medication with erythromycin. This may result in QT interval prolongation and cardiac arrhythmia, including ventricular tachycardia, ventricular fibrillation, and torsades de pointes.

Similar symptoms have been observed in patients taking *disopyramide* and erythromycin simultaneously and can be expected in patients taking domperidone, astemizole, and pimozide. Concomitant use of *astemizole, cisapride, domperidone, disopyramide,* and *pimozide* is contraindicated.

Caution is warranted when Ery-Max is administered to patients treated with other medicinal products that may prolong the QT interval.

Erythromycin may inhibit the metabolism of *quinidine,* resulting in increased plasma concentrations. An increase in C_{max} by approximately 40% was observed in healthy volunteers in one study. A case report indicates that the combination triggered torsades de pointes. Monitoring of quinidine serum levels should be considered during concomitant treatment with erythromycin.

Hydroxychloroquine and chloroquine: Erythromycin should be used with caution in patients receiving these medicines, which are known to prolong the QT interval, due to the risk of inducing cardiac arrhythmia and serious cardiovascular adverse effects.

Effect of Ery-Max on other medicinal products:

Erythromycin is an inhibitor of CYP3A4 and the transport protein P-glycoprotein. The degree of inhibition with different CYP3A4 substrates is difficult to predict. Therefore, Ery-Max should not be used during treatment with medicines that are CYP3A4 substrates unless plasma concentrations of the CYP3A4 substrate, effect, or adverse reactions can be closely monitored. A dose reduction may be necessary for other medicines metabolized by CYP3A4, and combination with erythromycin should be undertaken with caution. Alternatively, treatment with the CYP3A4 substrate should be discontinued during treatment with Ery-Max.

Erythromycin inhibits the metabolism of several HMG-CoA reductase inhibitors and increases plasma concentrations of these medicines. Erythromycin also increases serum concentration of simvastatin acid (fivefold). Rhabdomyolysis, associated with elevated plasma concentrations, has rarely occurred during concomitant treatment with *clarithromycin* and *lovastatin* or *simvastatin*. Ery-Max should not be used concurrently with simvastatin, *atorvastatin,* and lovastatin. Treatment with these medicines should be discontinued during treatment with Ery-Max. Concomitant administration of erythromycin and *lomitapide* is contraindicated due to the risk of markedly increased transaminases (see section 4.3).

Preoperative treatment with erythromycin may prolong and enhance the effect of *alfentanil* due to inhibited metabolism. This interaction is not seen with sufentanil.

Erythromycin inhibits the metabolism of single doses of *alprazolam*, indicating that this benzodiazepine is metabolized by CYP3A4. Plasma concentration of alprazolam increased by approximately 50%.

A case report suggests that erythromycin may inhibit the metabolism of benzodiazepines (*clozapine*, *triazolam*), resulting in markedly increased plasma concentrations. In healthy volunteers pre-treated with erythromycin, absorption of *zopiclone* was faster, resulting in higher plasma concentrations and a more pronounced hypnotic effect compared with controls.

In patients treated with erythromycin, clearance of intravenous midazolam was reduced by approximately 50% compared with controls, with increased plasma levels as a result, likely due to inhibited metabolism via CYP3A4. In such patients, the midazolam dose should be reduced by half. The effect of erythromycin on plasma levels of orally administered midazolam is expected to be even greater due to reduced first-pass metabolism.

Two case reports describe plasma levels of *bromocriptine* during maintenance therapy increasing by about 50% after erythromycin was introduced, with enhanced clinical effect.

It has later been confirmed in experimental studies that erythromycin increases the bioavailability of bromocriptine threefold, resulting in enhanced effects. Adjustment of the bromocriptine dose may be necessary.

When erythromycin is administered concomitantly, the bioavailability of *buspirone* (single oral dose) increases sixfold. This is likely due to inhibited metabolism of buspirone via CYP3A4. During combination therapy, the buspirone dose should be reduced accordingly.

Many case reports and observations in healthy volunteers indicate that erythromycin inhibits the metabolism of *ciclosporin*, with a risk of toxic plasma levels unless its concentration is closely monitored.

In six cases (three of which were children), treatment with erythromycin was confirmed to increase whole blood concentrations of tacrolimus up to twofold, likely due to inhibited metabolism via CYP3A4. Dose adjustment based on tacrolimus concentration monitoring is recommended. Erythromycin is expected to inhibit the metabolism of sirolimus, resulting in increased plasma levels.

Concomitant use of erythromycin and *digoxin* may lead to elevated plasma concentrations of digoxin. Monitoring of serum levels should be considered when starting or discontinuing erythromycin. Dose adjustment may be necessary.

When erythromycin and *fexofenadine* are administered together, plasma concentrations of fexofenadine increase two- to threefold, likely due to increased absorption.

Erythromycin treatment results in a reduction in *carbamazepine* clearance by approximately 20%, leading to increased plasma levels. Three case reports in children have described toxic plasma concentrations of carbamazepine after initiation of erythromycin. Plasma carbamazepine levels should therefore be monitored during combination therapy.

Erythromycin reduces metabolic clearance of *methylprednisolone*, resulting in enhanced effects.

Case reports suggest that the vasospastic adverse effects of ergot alkaloids (*dihydroergotamine, ergotamine*) after oral administration may be intensified by concomitant treatment with erythromycin. This is likely related to increased bioavailability of dihydroergotamine. The combination is contraindicated.
Data indicate that erythromycin inhibits the metabolism of *sildenafil*. A starting dose of 25 mg sildenafil should be considered.

Erythromycin treatment may result in increased plasma levels of *theophylline*, likely due to inhibited metabolism. In one study, serum erythromycin levels decreased simultaneously. During combination therapy, plasma theophylline levels should be monitored to avoid toxic concentrations (dose reduction). Additionally, a negative interaction study has been published. A very pronounced metabolic interaction with a threefold increase in plasma theophylline concentrations has been described in a patient treated with both erythromycin and ciprofloxacin.

Tramadol is metabolized via CYP3A4, and erythromycin may therefore inhibit its metabolism.

Erythromycin may inhibit the metabolism of warfarin and rivaroxaban, resulting in enhanced effects.

Vinblastine, vincristine, vindesine, and vinorelbine appear to be metabolized by CYP3A4. Therefore, their metabolism may be inhibited by CYP3A4 inhibitors such as erythromycin.

Corticosteroids
Caution should be exercised when erythromycin is used concomitantly with systemic and inhaled corticosteroids that are primarily metabolized by CYP3A, due to the risk of increased systemic exposure to corticosteroids. If concomitant use occurs, patients should be closely monitored for systemic corticosteroid adverse effects.

When erythromycin and felodipine were administered together, C_{max} and AUC of felodipine increased approximately 2.5-fold.

Effects of other medicinal products on the pharmacokinetics of erythromycin:

Erythromycin is metabolized by the enzyme CYP3A4. Therefore, strong inhibitors of this enzyme may inhibit erythromycin metabolism, resulting in elevated plasma concentrations.
Medicines that induce CYP3A4 (such as *rifampicin, rifabutin, phenytoin, carbamazepine, phenobarbital, St. John's wort*) can induce the metabolism of erythromycin. This may result in subtherapeutic levels of erythromycin and reduced efficacy. Induction gradually decreases over two weeks after discontinuation of treatment with CYP3A4 inducers. Ery-Max should not be used during and for two weeks after treatment with CYP3A4 inducers.

Cimetidine may inhibit the metabolism of erythromycin, resulting in elevated plasma concentrations.

Several cases of erythromycin toxicity have been described in liver-transplanted patients treated with ciclosporin.

4.6 Fertility, pregnancy and lactation

Pregnancy
Available epidemiological studies on the risk of serious congenital malformations with the use of macrolides, including erythromycin, during pregnancy provide conflicting results. Some observational studies in humans have reported cardiovascular malformations following exposure to medicines containing erythromycin during early pregnancy.
In reproductive toxicology studies with other macrolides that, like erythromycin, are potent hERG channel blockers, embryonic death and malformations (including cardiovascular defects and cleft palate) have been induced.
Mechanistic studies show that substances that are potent hERG channel blockers cause cardiovascular defects and embryonic death by inducing arrhythmia in the embryo. Erythromycin should not be used by women planning pregnancy or during pregnancy unless absolutely necessary.

Breastfeeding
Erythromycin passes into breast milk, but the risk of effects on the infant appears unlikely at therapeutic doses.

4.7 Effects on ability to drive and use machines

Ery-Max has no observable effect on the ability to drive and use machines.

4.8 Undesirable effects

Approximately 5–15% of treated patients can be expected to experience adverse reactions. The most common are transient gastrointestinal disturbances (abdominal pain and nausea), particularly at high doses. These symptoms may decrease if the dose is taken with food.

Adverse reactions are listed below by organ system classification and frequency.
The frequency of adverse reactions is expressed as follows:
Very common (>1/10); common (>1/100, <1/10); uncommon (>1/1 000, <1/100); rare (>1/10 000, <1/1 000); very rare (<1/10 000); not known (cannot be estimated from available data).

Organ system	**Frequency**	**Adverse reactions**
Immune system disorders:	Rare	Anaphylactic reactions.

Ear and labyrinth disorders:	Rare	Reversible hearing loss.
Cardiac disorders:	Rare Not known	Arrhythmia. QTc interval prolongation, torsades de pointes, cardiac arrest, ventricular fibrillation.
Gastrointestinal disorders:	Common Not known	Abdominal pain, nausea, diarrhea. Infantile hypertrophic pyloric stenosis, pseudomembranous colitis.
Hepatobiliary disorders:	Rare	Intrahepatic cholestasis, elevated liver enzyme values.
Skin and subcutaneous tissue disorders:	Common Uncommon Not known	Rash. Urticaria. Acute generalized exanthematous pustulosis (AGEP), erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis.
Investigations:	Rare	Increased bilirubin.

Fungal overgrowth in the oral cavity and genital area may occur.

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 national reporting system listed in Appendix V.

4.9 Overdose

Toxicity: Erythromycin has low acute toxicity. According to case reports, administration of 3 g erythromycin to a 3-year-old who received activated charcoal and 3.5 g to a 7-year-old, caused no symptoms.

Symptoms: Nausea, vomiting, diarrhea, reversible hearing loss, possible hallucinations, possible pancreatitis. Allergic reactions and liver impairment may occur.

Treatment: Gastric emptying and activated charcoal if justified. Symptomatic treatment.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Macrolide antibiotics, ATC code: J01FA01

The antibacterial effect is exerted through binding to the bacterial ribosomes. Erythromycin's interference with translation leads to inhibition of protein synthesis. This causes disintegration of both the bacterial interior and its envelope, ultimately resulting in bacterial lysis. The effect of erythromycin is mainly bacteriostatic.

Antibacterial spectrum

Susceptible	Streptococci and pneumococci *Staphylococcus aureus* and coagulase-negative staphylococci *Arcanobacterium haemolyticum* *Corynebacterium diphtheriae* *Moraxella catarrhalis* *Bordetella pertussis* *Campylobacter* *Chlamydophila trachomatis, pneumoniae,* and *psittaci* *Mycoplasma pneumoniae* *Ureaplasma urealyticum* *Clostridium perfringens*
Intermediate	*Haemophilus influenzae*
Resistant	Enterococci *Pasteurella multocida* Gram-negative enteric bacteria Pseudomonas *Clostridium difficile* Anaerobic gram-negative rods *Mycoplasma hominis*

Resistance occurs (1–10%) in beta-hemolytic streptococci, pneumococci, and *Staphylococcus aureus*. Resistance is common (>10%) in coagulase-negative staphylococci.

Mechanisms of resistance: Modification of the binding site on the ribosome is one cause of resistance development to erythromycin. Most gram-negative rods have natural resistance due to poor penetration through the cell wall.

Cross-resistance: Cross-resistance occurs between all macrolides and azithromycin. Some cross-resistance also occurs between macrolides and clindamycin.

Development of resistance: Erythromycin resistance in streptococci and pneumococci is uncommon in Sweden but common in certain parts of the rest of Europe.

The resistance situation varies geographically, and information on local resistance patterns should be obtained from the local microbiology laboratory.

Breakpoints for susceptibility testing
The interpretation criteria for MIC (minimum inhibitory concentration) in susceptibility testing have been established by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) for erythromycin and are listed here: https://www.ema.europa.eu/documents/other/minimum-inhibitory-concentration-mic-breakpoints_en.xlsx

5.2 Pharmacokinetic properties

Ery-Max oral suspension is an aqueous suspension containing erythromycin ethylsuccinate, which after absorption is hydrolyzed to free, active erythromycin. The absorption of erythromycin ethylsuccinate in Ery-Max oral suspension is lower than that of erythromycin base in Ery-Max capsules; therefore, a higher dose of the biologically inactive ester must be administered to achieve equivalent plasma concentrations of erythromycin. Maximum serum concentrations are reached after 0.5–1 hour. Protein binding for pure erythromycin base is 65%. Erythromycin crosses the blood-brain barrier to a limited extent. Excretion occurs mainly via the liver and bile. Only a small amount is excreted via urine. Erythromycin can therefore be administered at an unchanged dose to patients with impaired renal function.

5.3 Preclinical safety data

There are no preclinical data of relevance for the safety assessment beyond what has already been considered in the Summary of Product Characteristics.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

1 sachet of granules for oral suspension contains: sucrose, magnesium aluminum silicate, sodium citrate, sodium carmellose, cherry flavor.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

After reconstitution, the oral suspension is stable for 14 days at 2°C–8°C and for 5 days at a maximum of 25°C.

6.4 Special precautions for storage

The reconstituted oral suspension should be stored at 2°C–8°C.

6.5 Nature and contents of container

Sachets in a box, 20 sachets.

6.6 Special precautions for disposal and other handling

The contents of a 200 mg sachet correspond to 5 ml oral suspension at 40 mg/ml. The sachet is cut open or torn on one side. The contents is mixed with some water (20–30 ml).

7. MARKETING AUTHORISATION HOLDER

To be completed nationally

8. MARKETING AUTHORISATION NUMBER(S)

To be completed nationally

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

To be completed nationally

10. DATE OF REVISION OF THE TEXT

2026-02-17