Summary of Product Characteristics (SmPC)

1. Name of the medicinal product
Lincomycin Capsules, 500mg

2. Qualitative and quantitative composition
Each capsule contains 500mg Lincomycin

3. Pharmaceutical form
Capsules

4. Clinical particulars

4.1 Therapeutic indications

Lincomycin has been shown to be effective in the treatment of the following infections when caused by susceptible strains of gram positive aerobes such as streptococci, pneumococci, and staphylococci, or by susceptible anaerobic bacteria.

Upper respiratory infections including tonsillitis, pharyngitis, otitis media, sinusitis, scarlet fever and as adjuvant therapy for diphtheria. Effectiveness in the treatment of mastoiditis would be anticipated.

Lower respiratory infections including acute and chronic bronchitis and pneumonia.

Skin and soft tissue infections including cellulitis, furuncles, abscesses, impetigo, acne and wound infections. Conditions like erysipelas, lymphadenitis, paronychia (panaritium), mastitis and cutaneous gangrene, should, if caused by susceptible organisms, respond to lincomycin therapy.

Bone and joint infections including osteomyelitis and septic arthritis.

Septicemia and endocarditis. Selected cases of septicemia and/or endocarditis due to susceptible organisms have responded well to lincomycin. However, bactericidal drugs are often preferred for these infections.

Bacillary dysentery Although Shigella is resistant to lincomycin in vitro (MIC approximately 200-400 mcg/mL), lincomycin has been effective in its treatment due to the very high levels of lincomycin attained in the bowel (approximately 3000-7000 mcg/gram of stool).

4.2 Posology and method of administration
Adults

- Severe infections: 500 mg every 8 hours
- Very severe infections: 500 mg every 6 hours
- To achieve an optimal absorption, it is recommended to ingest nothing save water for a period of one to two hours before and after administration of lincomycin.

Dosage in Children (over 1 month of age)

30 mg/kg/day divided into 3 or 4 equal doses.

More severe infections: 60 mg/kg/day divided into 3 or 4 equal doses.

For optimal absorption, it is recommended that nothing be given by mouth for a period of 1 to 2 hours before or after oral administration of lincomycin.

Dosage in Patients with Diminished Hepatic or Renal Function

In patients with impaired hepatic function or impaired renal function, lincomycin's serum half-life is increased. Consideration should be given to decreasing the frequency of administration of lincomycin in patients with impaired hepatic or renal function

When therapy with lincomycin is required in individuals with severe impairment of renal function, an appropriate dose is 25% to 30% of that recommended for patients with normally functioning kidneys.

Beta-hemolytic Streptococcal Infections

Treatment should be continued for at least 10 days.

Incompatibilities

Lincomycin is physically incompatible with novobiocin and kanamycin.

It should be stressed that the determinations of compatibility and incompatibility are only physical observations not chemical determinations. No adequate clinical evaluations of the safety and efficacy of these combinations have been performed so far.

Method of administration

For oral administration.

4.3 Contraindications

Lincomycin is contraindicated in patients previously found sensitive to lincomycin or clindamycin or to any other component of the product.

4.4 Special warnings and precautions for use

If anaphylactic reactions or severe skin reactions occur, lincomycin administration should be discontinued and an appropriate therapy should be initiated (see section 4.8. UNDESIRABLE EFFECTS).

Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including lincomycin, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of C difficile.

C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of C. difficile cause increased morbidity and mortality, as these

infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.
Cases of mild colitis may subside following discontinuation of treatment with lincomycin. Moderate to severe cases should promptly be managed with the administration of fluids, electrolyte solutions and proteins (if indicated).
Antiperistaltic drugs, such as opioids and diphenoxylate with atropine, could prolong and/or worsen the situation. Vancomycin has been shown to be effective in the treatment of pseudomembranous colitis caused by Clostridium difficile. The usual adult dose is 0.5–2 g daily of oral vancomycin, divided into three to four administrations for 7-10 days.
Cholestyramine and colestipol resins bind vancomycin in vitro. If both a resin and vancomycin are to be administered concurrently, it is advisable to separate the time of administration of each drug. However, all the other causes responsible for colitis should also be considered.

Currently available data show that elderly or weakened patients may tolerate less well diarrhea; if these patients need to be treated with Lincomycin Capsules, they should be carefully monitored for any changes in bowel frequency.
Lincomycin Capsules should be prescribed with caution in patients with history of gastrointestinal disorders, especially colitis and in atopic individuals.
During a long-term therapy, periodical checks of liver and kidney functions and complete blood count should be performed. The serum half-life of lincomycin increases in patients with impaired liver or renal function. In such patients, a reduced frequency of administration of lincomycin should be considered. In particular, since adequate clinical data are not yet available, it should be advisable to avoid the use of Lincomycin Capsules in patients with pre-existing liver disease, unless special clinical circumstances indicate so.
Though it seems that lincomycin passes into the cephalorachidian fluid, its levels in cephalorachidian fluid may be inadequate for the treatment of meningitis. Therefore, the drug should not be used in the management of this condition.
Lincomycin has been shown to have neuromuscular blocking properties that could enhance the action of other neuromuscular blocking agents. Therefore, lincomycin should be used with caution in the treatment of patients receiving these drugs.

4.5 Interaction with other medicinal products and other forms of interaction
Lincomycin has been shown to have neuromuscular blocking properties that may enhance the action of other neuromuscular blocking agents. Therefore, lincomycin should be used with caution in patients receiving such agents(Especially clindamycin).

4.6 Pregnancy and lactation
Pregnancy
There are limited data on the use of lincomycin in pregnant women. In woman, lincomycin crosses the placenta reaching, at cord level, serum levels of 25% with respect to maternal serum levels. There is no significant accumulation at amniotic fluid level. The progeny of 302 patients treated with lincomycin at different stages of pregnancy did not show an increase in congenital anomalies or developmental delays compared to a control group up to 7 years after birth.

Lincomycin should only be used during pregnancy if strictly necessary.

Breastfeeding
Lincomycin is excreted into the mother's milk in concentrations of 0.5 to 2.4 mcg/mL.

4.7 Effects on ability to drive and use machines
No studies were conducted to determine the effect of lincomycin on ability to drive and use machines.

4.8 Undesirable effects

System organ class	Very common (≥1/10)	Common (≥1/100 to<1/10)	Uncommon (≥1/1,000 to<1/100)	Rare (≥1/10,000 to<1/1,000)	Very rare (<1/10,000)	Frequency not known (cannot be estimated from the available data)
Infections and infestations			Vaginal infection			Pseudomembranous colitis, colitis from Clostridium difficile (see section 4.4)
Blood and lymphatic system disorders						Pancytopoenia, agranulocytosis, aplastic anaemia, neutropoenia, leukopoenia, thrombocytopoenic purpura
Immune system disorders						Anaphylactic reactions, angio-oedema, serum sickness
Cardiac disorders						Cardiopulmonary arresta
Vascular disorders						Hypotensionb, thrombophlebitisc
Gastrointestinal disorders		Diarrhoea, nausea, vomiting				Oesophagitisd, abdominal discomfort
Hepatobiliary disorders						Jaundice, abnormal liver function tests
Skin and subcutaneous tissue disorders			Skin rash, urticaria	Itching		Toxic epidermal necrolysis, Steven-Johnson syndrome, acute generalized exanthematous pustulosis, bullous dermatitis, exfoliative dermatitis, erythema multiforme
General						Sterile injection-site

disorders and administration site conditions						abscesse, injection-site induratione, injection-site paine, injection-site irritatione

a Rare cases have been reported after excessively rapid intravenous administration.
b After parenteral administration, particularly after excessively rapid administration.
c Event reported with intravenous injection.
d Event reported with preparation for oral use.
e Reported with intramuscular injection.

Other adverse events:
Gastrointestinal disorders: Glossitis, stomatitis, enterocolitis, pruritus ani.
Renal and urinary disorders: Although no direct relationship between treatment with lincomycin and renal damage has been established, renal dysfunction as evidenced by elevation of blood urea levels, oliguria and/or proteinuria has been observed in a few cases.
Ear and labyrinth disorders: Instances of vertigo and tinnitus have occasionally been reported.
If allergic reactions should occur, therapy should be discontinued and standard emergency treatment (adrenaline, corticosteroids, antihistamines) should be started.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization of the medicinal product is important, as it allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions.

4.9 Overdose
Hemodialysis or peritoneal dialysis does not effectively remove lincomycin from the blood.

5. Pharmacological properties

5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Antibacterial agents for systemic use. Lincosamides.
ATC code: J01FF02.

Mode of Action:
Lincomycin is an antibiotic produced by fermentation of Streptomyces lincolnensis. Lincomycin inhibits bacterial protein synthesis by binding to the 50S subunit of the bacterial ribosome. Lincomycin is predominantly bacteriostatic in vitro. The antibacterial activity of lincomycin appears to best correlate with the length of time the concentration of active ingredient remains above the MIC of the infecting organism.

Mechanism of Resistance
Cross resistance between lincomycin and clindamycin is complete. Resistance in staphylococci and streptococci is most often due to methylation of specific nucleotides in the 23S RNA of the 50S ribosomal subunit, which can determine cross resistance to macrolides and streptogramins

B (MLSB phenotype). Macrolide-resistant isolates of these organisms should be tested for inducible resistance to lincomycin/clindamycin using the D zone test.

Methodology for determining in vitro susceptibility to lincomycin
Susceptibility testing should be conducted using standardized laboratory methods, such as those described by the Clinical and Laboratory Standards Institute (CLSI) or the European Committee on Antimicrobial Susceptibility Testing (EUCAST). Because CLSI and EUCAST have not established susceptibility breakpoints for lincomycin, clindamycin should be tested instead. Resistance to lincosamides may be inducible by macrolides in macrolide-resistant staphylococci, Streptococcus pneumoniae, and beta-hemolytic streptococci. Macrolide-resistant isolates of these organisms should be screened for inducible clindamycin resistance using the D-zone test or other standard methodology.

CLSI dilution and disk diffusion susceptibility interpretive criteria for clindamycin

Organism	Susceptibility Interpretive Criteria					
	Minimal Inhibitory Concentrations (MIC in µg/mL)			Disk Diffusion (Zone Diameters in mm)		
	S	I	R	S	I	R
Staphylococcus spp.	≤0.5	1–2	≥4	≥21	15–20	≤14
Streptococcus pneumoniae, β-hemolytic streptococci and viridans group streptococci	≤0.25	0.5	≥1	≥19	16–18	≤15
Anaerobic Bacteria	≤2	4	≥8	NA	NA	NA
Disk content 2 µg. MIC interpretive criteria for anaerobes are based on agar dilution. NA=not applicable.						

The validity of both the dilution and disk diffusion test methods should be verified using quality control (QC) strains, as indicated by CLSI. Acceptable limits when testing clindamycin against these organisms are listed in the table below.

Quality control ranges for clindamycin susceptibility tests (CLSI)

Organism	**Minimum Inhibitory Concentration Range (MIC in µg/mL)**	**Disk Diffusion Range (Zone Diameters in mm)**
Staphylococcus aureus ATCC 29213	0.06–0.25	NA
Staphylococcus aureus ATCC 25923	NA	24–30
Streptococcus pneumoniae ATCC 49619	0.03–0.12	19–25
Bacteroides fragilis ATCC 25285	0.5–2	NA
Bacteroides thetaiotaomicron ATCC 29741	2–8	NA
Eggerthella lenta	0.06–0.25	NA

ATCC 43055		
MIC ranges for anaerobic bacteria are based on agar dilution.		
NA=Not applicable		
ATCC® is a registered trademark of the American Type Culture Collection		

EUCAST dilution and disk diffusion susceptibility interpretive criteria for clindamycin[94]

Organism	**Minimal Inhibitory Concentrations (MIC in µg/mL)**		**Disk Diffusion (Zone Diameters in mm)**	
	S	**R**	**S**	**R**
Staphylococcus spp.	≤0.25	>0.5	≥22	<19
Streptococcus groups A, B, C, G	≤0.5	>0.5	≥17	<17
Streptococcus pneumoniae	≤0.5	>0.5	≥19	<19
Viridans group streptococci	≤0.5	>0.5	≥19	<19
Gram-positive anaerobes (except *Clostridium difficile*)	≤4	--	NA	NA
Gram-negative anaerobes	≤4	--	NA	NA
Disk content 2 µg. MIC interpretive criteria for anaerobes are based on agar dilution. NA=not applicable.				

Quality control ranges for clindamycin susceptibility tests (EUCAST)

Organism	**Minimum Inhibitory Concentration Range (MIC in µg/mL)**	**Disk Diffusion Range (Zone Diameters in mm)**
Staphylococcus aureus ATCC 29213	0.06–0.25	23-29
Streptococcus pneumoniae ATCC 49619	0.03–0.12	22-28
NA=Not applicable		
ATCC® is a registered trademark of the American Type Culture Collection		

Antibacterial Spectrum

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. Lincomycin is cross-resistant with clindamycin. A decrease in clindamycin/lincomycin susceptibility over time has been noted in particular among methicillin-resistant Staphylococcus aureus and in some species of *Clostridium*.

Organisms that are commonly susceptible to lincomycin include:

Aerobic and facultative gram-positive bacteria:

- *Staphylococcus aureus* (methicillin-susceptible strains only); *Streptococcus pneumoniae*; Streptococcus pyogenes; viridans group streptococci; *Corynebacterium diphtheriae*.

Anaerobic and microaerophilic bacteria:

- *Clostridium perfringens; Clostridium tetani; Propionibacterium acnes*.

5.2 Pharmacokinetic properties

Oral administration of a single 500 mg dose of lincomycin in the fasting state produces an average peak serum level of 5.3 μg/mL at 2 hours post-dose. Administration immediately after a meal reduces oral absorption.

Intramuscular administration of a single dose of 600 mg of lincomycin produces average peak serum levels of 11.6 μg/mL at 60 minutes and maintains therapeutic levels for 17 to 20 hours for most susceptible gram-positive organisms. Urinary excretion after this dose ranges from 1.8 to 24.8 percent (mean: 10.3 percent).

A two hour intravenous infusion of 600 mg of lincomycin achieves average peak serum levels of 15.9 μg/mL and yields therapeutic levels for 14 hours for most susceptible gram-positive organisms. Urinary excretion ranges from 4.9 to 23.3 percent (mean: 15.1 percent).

The biological half-life after intramuscular administration is approximately 5 hours. The serum half-life of lincomycin may be prolonged in patients with severe impairment of renal function compared to patients with normal renal function.79 In patients with abnormal hepatic function, serum half-life may be two-fold longer than in patients with normal hepatic function.80 Hemodialysis and peritoneal dialysis are not effective in removing lincomycin from the serum.

Tissue level studies indicate that bile is an important route of excretion. Significant levels have been demonstrated in the majority of body tissues. Although lincomycin appears to diffuse into cerebrospinal fluid (CSF), levels of lincomycin in the CSF appear inadequate for the treatment of meningitis.

5.3 Preclinical safety data

Nonclinical data from conventional studies on repeated administration toxicity, genotoxicity, carcinogenesis, and reproductive and developmental toxicity have not identified any particular risks to humans. No developmental toxicity was observed when doses greater than 6x the maximum recommended human dose (MRHD) were administered to pregnant rats during the organogenesis period. No effects on fertility were observed in rats administered lincomycin at 1.2x the MRHD.

6. Pharmaceutical particulars

6.1 List of excipients

Magnesium stearate
Talc

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Three years.

6.4 Special precautions for storage

Store in a dark and dry place below 30℃.

KEEP MEDICINES OUT OF REACH OF CHILDREN.

6.5 Nature and contents of container

4 Capsules/Blister of PVC-ALU, 3Blisters/Box.

7. Marketing authorisation holder

Applicant name: DANNYFAITH PHARMACY LIMITED.
Address: 23, OSENI STREET, LAWANSON, SURULERE, LAGOS, NIGERIA