

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

NGC Cotrimoxazole suspension

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml contains 40 mg Trimethoprim and 200 mg Sulfamethoxazole.

Excipients with known effect:

For the full list of excipients, see section 6.1,

3 PHARMACEUTICAL FORM

Oral suspension

A pink, banana flavoured suspension.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

NGC Cotrimoxazole Suspension is indicated in children aged 12 years and under (infants (>6 weeks to <2 years old) and children (>2 to <12 years old) for the treatment of the following infections when owing to sensitive organisms (see section 5.1):

- **Respiratory tract infections and Ear Nose and throat infection:** acute and chronic bronchitis (prophylaxis and treatment), bronchiectasis, lung abscess, lobar, and broncho-pneumonia, pneumocystis carinii pneumonia, otitis media, sinusitis.

- **Urinary tract infections:** urethritis, cystitis, pyelonephritis, pyelitis, prostatitis, male and female gonorrhoea,

- **Gastro-intestinal tract infections:** caused by salmonella typhi and paratyphi including the chronic carrier state; bacillary dysentery and cholera.

- **Skin infection abscesses, wound infection**

- **Other bacterial infections:** acute and chronic osteomyelitis, acute brucellosis, septicaemia.

4.2 Posology and method of administration

Posology

Standard dosage recommendations for acute infections

The standard dosage for children is equivalent to approximately 6 mg trimethoprim and 30 mg sulfamethoxazole per kg body weight per day, given in two equally divided doses. The schedules for children are according to the child's age and provided in the table below:

STANDARD DOSAGE	
Age	Paediatric Suspension
6 to 12 years	10 ml every 12 hours
6 months to 5 years	5 ml every 12 hours
6 weeks to 5 months	2.5 ml every 12 hours

Age Paediatric Suspension

6 to 12 years 10 ml every 12 hours (2 teaspoonful)

6 months to 5 years 5 ml every 12 hours (1 teaspoonful)

6 weeks to 5 months 2.5 ml every 12 hours ($\frac{1}{2}$ teaspoonful)

Treatment should be continued until the patient has been symptom free for two days; acute infections will require treatment for at least 5 days. If clinical improvement is not evident after 7 days therapy, the patient should be reassessed.

As an alternative to standard dosage for acute uncomplicated lower urinary tract infections, short-term therapy of 1 to 3 days' duration has been shown to be effective.

Impaired hepatic function:

No data are available relating to dosage in patients with impaired hepatic function.

Impaired renal function:

Dosage recommendation:

Adults (>18 years old) and children over 12 years old (>12 to < 18 years old):

Creatinine Clearance (ml/min)	Recommended Dosage
>30	10 ml every 12 hours
15 to 30	5 ml every 12 hours
<15	Not recommended

No information is available for children aged 12 years and under with renal failure. See section 5.2 for the pharmacokinetics in the paediatric population with normal renal function of both components of trimethoprim-sulfamethoxazole.

Method of administration

Oral

It may be preferable to take NGC Cotrimoxazole suspension with some food or drink to minimise the possibility of gastrointestinal disturbances.

4.3 Contraindications

NGC Cotrimoxazole suspension is contraindicated in patients with:

- hypersensitivity to the active substance(s) sulphonamides, trimethoprim or to any of the excipients listed in section 6.1.
- severe renal insufficiency where repeated measurements of the plasma drug concentration cannot be performed.
- severe impairment of liver function.
- a history of drug-induced immune thrombocytopenia with use of trimethoprim and/or sulphonamides.
- acute porphyria.

-NGC Cotrimoxazole suspension should not be given to infants during the first 6 weeks of life or premature babies.

-Pregnant mothers at end of pregnancy and breastfeeding mothers

G6PD deficiency patients.

4.4 Special warnings and precautions for use

Complete blood counts are necessary in the event of prolonged treatment.

Fatalities, although very rare, have occurred due to severe reactions including Stevens-Johnson syndrome, toxic epidermal necrolysis, fulminant hepatic necrosis, agranulocytosis, aplastic anaemia, other blood dyscrasias and hypersensitivity of the respiratory tract.

Life threatening adverse reaction

- Life-threatening cutaneous reactions Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) and drug reaction with eosinophilia with systemic symptoms (DRESS) have been reported with the use of Cotrimoxazole suspension.

- Patients should be advised of the signs and symptoms and monitored closely for skin reactions. The highest risk for occurrence of SJS or TEN is within the first weeks of treatment and for DRESS the risk of occurrence is in the first two to eight weeks after drug administration.

If symptoms or signs of SJS, TEN (e.g. progressive skin rash often with blisters or mucosal lesions) or DRESS (e.g. fever, eosinophilia, rash, lymphadenopathy, abnormal blood/liver function test and/or visceral organ involvement) are present, NGC Cotrimoxazole suspension treatment should be discontinued (see section 4.8).

Haemophagocytic lymphohistiocytosis (HLH)

Cases of HLH have been reported very rarely in patients treated with co-trimoxazole. HLH is a life-threatening syndrome of pathologic immune activation characterised by clinical signs and symptoms of an excessive systemic inflammation (e.g. fever, hepatosplenomegaly, hypertriglyceridaemia, hypofibrinogenaemia, high serum ferritin, cytopenias and haemophagocytosis).

Patients who develop early manifestations of pathologic immune activation should be evaluated immediately. If diagnosis of HLH is established, co-trimoxazole treatment should be discontinued.

Respiratory toxicity

Very rare, severe cases of respiratory toxicity, sometimes progressing to Acute Respiratory Distress Syndrome (ARDS), have been reported during co-trimoxazole treatment. The onset of pulmonary signs such as cough, fever, and dyspnoea in association with radiological signs of pulmonary infiltrates, and deterioration in pulmonary function may be preliminary signs of ARDS. In such circumstances, co-trimoxazole should be discontinued and appropriate treatment given.

Elderly patients

Particular care is always advisable when treating elderly patients because, as a group, they are more susceptible to adverse reactions and more likely to suffer serious effects as a result particularly when complicating conditions exist, e.g. impaired kidney and/or liver function and/or concomitant use of other drugs.

Patients with renal impairment

For patients with known renal impairment special measures should be adopted (see section 4.2).

Urinary output

An adequate urinary output should be maintained at all times. Evidence of crystalluria in vivo is rare, although sulphonamide crystals have been noted in cooled urine from treated patients. In patients suffering from hypoalbuminaemia the risk may be increased.

Folate

Regular monthly blood counts are advisable when NGC Cotrimoxazole suspension is given for long periods, or to folate deficient patients or to the elderly; since there exists a possibility of asymptomatic changes in haematological laboratory indices due to lack of available folate. Supplementation with folic acid may be considered during treatment but this should be initiated with caution due to possible interference with antimicrobial efficacy (see section 4.5).

Patients with glucose-6-phosphate dehydrogenase deficiency

In glucose-6-phosphate dehydrogenase (G-6-PD) deficient patients, haemolysis may occur.

Patients with severe atopy or bronchial asthma

NGC Cotrimoxazole suspension should be given with caution to patients with severe atopy or bronchial asthma.

Treatment of streptococcal pharyngitis due to Group A beta-haemolytic streptococci

NGC Cotrimoxazole suspension should not be used in the treatment of streptococcal pharyngitis due to Group A β -haemolytic streptococci; eradication of these organisms from the oropharynx is less effective than with penicillin.

Phenylalanine metabolism

Trimethoprim has been noted to impair phenylalanine metabolism but this is of no significance in phenylketonuric patients on appropriate dietary restriction.

Patients with or at risk of porphyria

The administration of NGC Cotrimoxazole suspension to patients known or suspected to be at risk of porphyria should be avoided. Both trimethoprim and sulphonamides (although not specifically sulfamethoxazole) have been associated with clinical exacerbation of porphyria.

Patients with hyperkalaemia and hyponatraemia

Close monitoring of serum potassium and sodium is warranted in patients at risk of hyperkalaemia and hyponatraemia.

Metabolic acidosis

NGC Cotrimoxazole suspension has been associated with metabolic acidosis when other possible underlying causes have been excluded. Close monitoring is always advisable when metabolic acidosis is suspected.

Patients with serious haematological disorders

Except under careful supervision NGC Cotrimoxazole suspension should not be given to patients with serious haematological disorders (see section 4.8).

4.5 Interaction with other medicinal products and other forms of interaction

Diuretics (thiazides): in elderly patients concurrently receiving diuretics, mainly thiazides, there appears to be an increased risk of thrombocytopenia with or without purpura.

Pyrimethamine: occasional reports suggest that patients receiving pyrimethamine at doses in excess of 25 mg weekly may develop megaloblastic anaemia should trimethoprim-sulfamethoxazole be prescribed concurrently.

Zidovudine: in some situations, concomitant treatment with zidovudine may increase the risk of haematological adverse reactions to trimethoprim-sulfamethoxazole. If concomitant treatment is necessary, consideration should be given to monitoring of haematological parameters.

Lamivudine: administration of trimethoprim/sulfamethoxazole 160 mg/800 mg causes a 40% increase in lamivudine exposure because of the trimethoprim component. Lamivudine has no effect on the pharmacokinetics of trimethoprim or sulfamethoxazole.

Warfarin: trimethoprim-sulfamethoxazole has been shown to potentiate the anticoagulant activity of warfarin via stereo-selective inhibition of its metabolism. Sulfamethoxazole may displace warfarin from plasma-albumin protein-binding sites in vitro. Careful control of the anticoagulant therapy during treatment with NGC Cotrimoxazole suspension is advisable.

Phenytoin: trimethoprim-sulfamethoxazole prolongs the half-life of phenytoin and if co-administered the prescriber should be alert for excessive phenytoin effects. Close monitoring of the patient's condition and serum phenytoin levels are advisable.

Interaction with sulphonylurea hypoglycaemic agents is uncommon but potentiation has been reported.

Rifampicin: concurrent use of rifampicin and NGC Cotrimoxazole suspension results in a shortening of the plasma half-life of trimethoprim after a period of about one week. This is not thought to be of clinical significance.

Cyclosporin: reversible deterioration in renal function has been observed in patients treated with trimethoprim and sulfamethoxazole and cyclosporin following renal transplantation.

Digoxin: concomitant use of trimethoprim with digoxin has been shown to increase plasma digoxin levels in a proportion of elderly patients.

Hyperkalaemia: caution should be exercised in patients taking any other drugs that can cause hyperkalaemia, for example ACE inhibitors, angiotensin receptor blockers and potassium-sparing diuretics such as spironolactone. Concomitant use of trimethoprim-sulfamethoxazole (co-trimoxazole) may result in clinically relevant hyperkalaemia.

Azathioprine: There are conflicting clinical reports of interactions, resulting in serious haematological abnormalities, between azathioprine and trimethoprim-sulfamethoxazole.

Methotrexate: trimethoprim-sulfamethoxazole may increase the free plasma levels of methotrexate. If Cotrimoxazole is considered appropriate therapy in patients receiving other anti-folate drugs such as methotrexate, a folate supplement should be considered (see section 4.4).

Repaglinide: trimethoprim may increase the exposure of repaglinide which may result in hypoglycaemia.

Folinic acid: folinic acid supplementation has been shown to interfere with the antimicrobial efficacy of trimethoprim-sulfamethoxazole. This has been observed in *Pneumocystis jirovecii* pneumonia prophylaxis and treatment.

Contraceptives: oral contraceptive failures have been reported with antibiotics. The mechanism of this effect has not been elucidated. Women on treatment with antibiotics should temporarily use a barrier method in addition to the oral contraceptive, or choose another method of contraception.

Interaction with laboratory tests:

Trimethoprim interferes with assays for serum methotrexate when dihydrofolate reductase from *Lactobacillus casei* is used in the assay. No interference occurs if methotrexate is measured by radio-immune assay.

Trimethoprim may interfere with the estimation of serum/plasma creatinine when the alkaline picrate reaction is used. This may result in overestimation of serum/plasma creatinine of the order of 10%.

Functional inhibition of the renal tubular secretion of creatinine may produce a spurious fall in the estimated rate of creatinine clearance.

4.6 Fertility, pregnancy and lactation

Pregnancy

NGC Co-Trimoxazole should not be used in pregnancy, particularly in the first trimester, unless clearly necessary. Folate supplementation should be considered if NGC Cotrimoxazole is used in pregnancy

Breast Feeding:

Trimethoprim and sulfamethoxazole are excreted in breast milk. Administration of NGC Cotrimoxazole suspension should be avoided in late pregnancy and in lactating mothers where the mother or infant has, or is at particular risk of developing, hyperbilirubinaemia. Additionally, administration of NGC Cotrimoxazole suspension should be avoided in infants younger than eight weeks in view of the predisposition of young infants to hyperbilirubinaemia.

4.7 Effects on ability to drive and use machines

Effects on the ability to drive and operate machinery in patients taking this medicine have not been studied.

4.8 Undesirable effects

As NGC Cotrimoxazole suspension contains trimethoprim and a sulphonamide the type and frequency of adverse reactions associated with such compounds are expected to be consistent with extensive historical experience.

Data from large published clinical trials were used to determine the frequency of very common to rare adverse events. Very rare adverse events were primarily determined from post-marketing experience data and therefore refer to reporting rate rather than a "true" frequency. In addition, adverse events may vary in their incidence depending on the indication.

The following convention has been used for the classification of adverse events in terms of frequency:

Very common $\geq 1/10$,

Common $\geq 1/100$ and $< 1/10$,

Uncommon $\geq 1/1000$ and $< 1/100$,

Rare $\geq 1/10,000$ and $< 1/1000$,

Very rare $< 1/10,000$

Not known: cannot be estimated from the available data.

System Organ Class	Frequency	Side effects
Infections and infestations	Common	Overgrowth fungal.
Blood and lymphatic system disorders	Very rare	Leucopenia, neutropenia, thrombocytopenia, agranulocytosis, anaemia megaloblastic, aplastic anaemia, haemolytic anaemia, methaemoglobinaemia, eosinophilia, purpura, haemolysis in certain susceptible G-6-PD deficient patients.
Immune system disorders	Very rare	Serum sickness, anaphylactic reactions, allergic myocarditis, hypersensitivity vasculitis resembling Henoch-Schoenlein purpura, periarteritis nodosa, systemic lupus erythematosus. Severe hypersensitivity reactions associated with PJP* including rash, pyrexia, neutropenia, thrombocytopenia, hepatic enzyme increased, rhabdomyolysis, hyperkalaemia, hyponatraemia.
Metabolism and nutrition disorders	Very common	Hyperkalaemia.
	Very rare	Hypoglycaemia, hyponatraemia, decreased appetite, metabolic acidosis.
Psychiatric disorders	Very rare	Depression, hallucination.
	Not known	Psychotic disorder.
Nervous system disorders	Common	Headache.
	Very rare	Meningitis aseptic*, seizure, neuropathy peripheral, ataxia, dizziness.
Ear and labyrinth disorders	Very rare	Vertigo, tinnitus
Eye disorders	Very rare	Uveitis.
Respiratory, thoracic and mediastinal disorders	Very rare	Cough*, dyspnoea*, lung infiltration.*
Gastrointestinal disorders	Common	Nausea, diarrhoea.
	UnCommon	Vomiting.
	Very rare	Glossitis, stomatitis, pseudomembranous colitis, pancreatitis.
Hepatobiliary disorders	Very rare	Jaundice cholestatic *, hepatic necrosis*, transaminases increased; blood bilirubin increased.

Skin and subcutaneous tissue disorders*	Common	Rash.
	Very rare	Photosensitivity reaction, angioedema, dermatitis exfoliative, fixed drug eruption, erythema multiforme, Stevens-Johnson syndrome (SJS)*, toxic epidermal necrolysis (TEN)*, Acute generalised exanthematous pustulosis (AGEP).
	Not Known	Drug reaction with eosinophilia and systemic symptoms (DRESS)*, Acute febrile neutrophilic dermatosis (Sweet's syndrome)
Musculoskeletal and connective tissue disorders	Very rare	Arthralgia, myalgia.
Renal and urinary disorders	Very rare	Renal impairment (sometimes reported as renal failure), tubulointerstitial nephritis.
General disorders and administration site conditions	Very rare	Pyrexia.

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: [ADR e-Reporting Form](#) online

4.9 Overdose

Symptoms

Nausea, vomiting, dizziness and confusion are likely signs/symptoms of overdose. Bone marrow depression has been reported in acute trimethoprim overdose.

Management

Dependent on the status of renal function administration of fluids is recommended if urine output is low.

Both trimethoprim and active sulfamethoxazole are moderately dialysable by haemodialysis. Peritoneal dialysis is not effective.

In cases of known, suspected or accidental overdose, stop therapy.

Acidification of the urine will increase the elimination of trimethoprim. Inducing diuresis plus alkalinisation of urine will enhance the elimination of sulfamethoxazole. Alkalinisation will reduce the rate of elimination of trimethoprim. Calcium folinate (5 to 10 mg/day) will reverse any folate deficiency effect of trimethoprim on the bone marrow should this occur. General supportive measures are recommended.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antibacterials for systemic use – sulfonamides and trimethoprim

ATC code: J01EE01

Mechanism of action

Sulfamethoxazole competitively inhibits the utilisation of para-aminobenzoic acid in the synthesis of dihydrofolate by the bacterial cell resulting in bacteriostasis. Trimethoprim reversibly inhibits bacterial dihydrofolate reductase (DHFR), an enzyme active in the folate metabolic pathway converting dihydrofolate to tetrahydrofolate. Depending on the conditions the effect may be bactericidal. Thus, trimethoprim and sulfamethoxazole block two consecutive steps in the biosynthesis of purines and therefore nucleic acids essential to many bacteria. This action produces marked potentiation of activity in vitro between the two agents.

Trimethoprim binds to plasmodial DHFR but less tightly than to the bacterial enzyme. The affinity of trimethoprim for mammalian DHFR is some 50,000 times less than for the corresponding bacterial enzyme.

Pharmacodynamic effects

The majority of common pathogenic bacteria are sensitive in vitro to trimethoprim and sulfamethoxazole at concentrations well below those reached in blood, tissue fluids and urine after the administration of recommended doses. In common with other antimicrobial agents in vitro activity does not necessarily imply that clinical efficacy had been demonstrated. These organisms include:

Gram Negative
Brucella spp. Citrobacter spp. Escherichia coli (including ampicillin-resistant strains) Haemophilus ducreyi Haemophilus influenzae (including ampicillin-resistant strains) Klebsiella/Enterobacter spp. Legionella pneumophila Morganella morganii (previously Proteus morganii) Neisseria spp. Proteus spp. Providencia spp.(including previously Proteus rettgeri) Certain Pseudomonas spp. except aeruginosa Salmonella spp. including S. typhi and paratyphi. Serratia marcescens. Shingella spp. Vibrio cholerae Yersinia spp.
Gram positive
<i>Listeria monocytogenes.</i> <i>Nocardia spp.</i> <i>Staphylococcus aureus.</i> <i>Staphylococcus epidermidis and saprophyticus</i> <i>Enterococcus faecalis.</i> <i>Streptococcus pneumoniae.</i> <i>Streptococcus viridans.</i>

Many strains of Bacteroides fragilis are sensitive. Some strains of Campylobacter fetus subsp. Jejuni and chlamydia are sensitive without evidence of synergy. Some varieties of non-tuberculous

mycobacteria are sensitive to sulfamethoxazole but not trimethoprim. Mycoplasmas, Ureaplasma urealyticum, Mycobacterium tuberculosis and Treponema pallidum are insensitive.

Satisfactory sensitivity testing is achieved only with recommended media free from inhibitory substances especially thymidine and thymine.

5.2 Pharmacokinetic properties

Absorption:

After oral administration trimethoprim - sulfamethoxazole are rapidly and nearly completely absorbed. The presence of food does not appear to delay absorption. Peak levels in the blood occur between one and four hours after ingestion and the level attained is dose related. Effective levels persist in the blood for up to 24 hours after a therapeutic dose. Steady state levels in adults are reached after dosing for 2-3 days. Neither component has an appreciable effect on the concentrations achieved in the blood by the other.

Distribution:

Approximately 50% of trimethoprim in the plasma is protein bound. Tissue levels of trimethoprim are generally higher than corresponding plasma levels, the lungs and kidneys showing especially high concentrations. Trimethoprim concentrations exceed those in plasma in the case of bile, prostatic fluid and tissue, saliva, sputum and vaginal secretions. Levels in the aqueous humor, breast milk, cerebrospinal fluid, middle ear fluid, synovial fluid and tissue (interstitial) fluid are adequate for antibacterial activity. Trimethoprim passes into amniotic fluid and foetal tissues reaching concentrations approximating those of maternal serum. Approximately 66% of sulfamethoxazole in the plasma is protein bound. The concentration of active sulfamethoxazole in amniotic fluid, aqueous humour, bile, cerebrospinal fluid, middle ear fluid, sputum, synovial fluid and tissue (interstitial) fluid is of the order of 20-50% of the plasma concentration.

Metabolism:

Renal excretion of intact sulfamethoxazole accounts for 15-30% of the dose. This drug is more extensively metabolised than trimethoprim, via acetylation, oxidation or glucuronidation. Over a 72-hour period, approximately 85% of the dose can be accounted for in the urine as unchanged drug plus the major (N4-acetylated) metabolite.

Elimination:

The principal route of excretion of trimethoprim is renal and approximately 50% of the dose is excreted in the urine within 24 hours as unchanged drug. Several metabolites have been identified in the urine. Urinary concentration of trimethoprim varies widely.

The principal route of excretion of sulfamethoxazole is renal; between 15% and 30% of the dose recovered in the urine is in the active form.

Special patient populations

Renal impairment

The elimination half-life of trimethoprim is increased by a factor of 1.5-3.0 when the creatinine clearance is less than 10mL/minute. When the creatinine clearance falls below 30 mL/min the dosage of Cotrimoxazole should be reduced (see section 4.2).

Hepatic impairment

Caution should be exercised when treating patients with severe hepatic impairment as there may be changes in the absorption and biotransformation of trimethoprim and sulfamethoxazole.

Older patients

In older patients, a slight reduction in renal clearance of sulfamethoxazole but not trimethoprim has been observed.

Paediatric population

The pharmacokinetics in the paediatric population with normal renal function of both components of Cotrimoxazole, trimethoprim and sulfamethoxazole are age dependent. Elimination of trimethoprim - sulfamethoxazole is reduced in neonates, during the first two months of life, thereafter both trimethoprim and sulfamethoxazole show a higher elimination with a higher body clearance and a shorter elimination half-life. The differences are most prominent in young infants (> 1.7 months up to 24months) and decrease with increasing age, as compared to young children (1 year up to 3.6 years), children (7.5 years and < 10years) and adults (see section 4.2).

5.3 Preclinical safety data

At doses in excess of the recommended human therapeutic dose, trimethoprim and sulfamethoxazole have been reported to cause cleft palate and other foetal abnormalities in rats, findings typical of a folate antagonist. Effects with trimethoprim were preventable by co-administration of dietary folate. In rabbits, foetal loss was seen at doses of trimethoprim in excess of human therapeutic doses

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sorbitol

Carmoisine Red

Carboxy methyl Cellulose

Polysorbate 80 (Tween 80)

Sucrose (granulated sugar)

Banana essence

Aerosil 200

Methyl Paraben

Propyl Paraben

De-mineralized water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 30°C.

Keep the bottle in the outer carton in order to protect from light.

Once opened: use within 6 weeks

6.5 Nature and contents of container

Amber Pet bottles, with White Plain Cap and polypropylene plastic cup. Bottles of 50ml in outer carton.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

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

7 MARKETING AUTHORISATION HOLDER

SYGEN PHARMACEUTICAL LTD

KM38 LAGOS ABEOKUTA EXPRESSWAY

SANGO OTA

OGUN STATE

NIGERIA

8 MARKETING AUTHORISATION NUMBER

NAFDAC NO: 04-2659

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Not reported

10 DATE OF REVISION OF THE TEXT

06-06- 2024