SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Cefotaxime Medo 1 gr

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Cefotaxime Medo 1 gr contains 1 g cefotaxime as cefotaxime sodium.

Excipient with known effect: sodium.

1 g cefotaxime contains approximately 48 mg (2.09 mmol) of sodium.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for solution for injection or infusion

The powder is white or slightly yellow, and when reconstituted with water for injection gives a straw coloured solution. Any variation in the intensity of colour of the freshly prepared solution is not indicative of change in potency or safety.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Properties: Cefotaxime Medo 1 gr is a broad-spectrum bactericidal cephalosporin antibiotic. Cefotaxime Medo 1 gr is exceptionally active in vitro against Gram-negative organisms sensitive or resistant to first or second-generation cephalosporins. It is similar to other cephalosporins in activity against Gram-positive organisms.

Indication: Cefotaxime Medo 1 gr is indicated in the treatment of the following infections either before the infecting organism has been identified or when caused by bacteria of established sensitivity:

- **Septicaemias**
- **Respiratory Tract Infections** such as acute and chronic bronchitis, bacterial pneumonia, infected bronchiectasis, lung abscess and post-operative chest infections.
- **Urinary Tract Infections** such as acute and chronic pyelonephritis, cystitis and asymptomatic bacteriuria.
- **Soft Tissue Infections** such as cellulitis, peritonitis and wound infections.
- **Bone and Joint Infections** such as osteomyelitis, septic arthritis.

- **Obstetric and Gynaecological Infections** such as pelvic inflammatory disease.
- **Gonorrhoea** particularly when penicillin has failed or is unsuitable.
- **Other Bacterial Infections**, such as meningitis and other sensitive infections suitable for parenteral antibiotic therapy.

Prophylaxis:

Prophylaxis of infections in patients with reduced resistance.

Pre-operative prophylaxis in patients who are at increased risk from infection.

The administration of cefotaxime Medo 1 gr prophylactically may reduce the incidence of certain post-operative infections in patients undergoing surgical procedures that are classified as contaminated or potentially contaminated or in clean operations where infections would have serious effects.

Protection is best ensured by achieving adequate local tissue concentrations at the time contamination is likely to occur.

Cefotaxime Medo 1 gr should therefore be administered immediately prior to surgery and if necessary continued in the immediate post-operative period.

Administration should usually be stopped within 24 hours since continuing use of any antibiotic in the majority of surgical procedures does not reduce the incidence of subsequent infection.

BACTERIOLOGY:

The following organisms have shown in vitro sensitivity to Cefotaxime Medo 1 gr.

GRAM POSITIVE:

Staphylococci, including coagulase-positive, coagulase-negative and penicillinase-producing strains.

Beta-haemolytic and other streptococci such as Streptococcus mitis (viridans) (many strains of enterococci, e.g. Streptococcus faecalis, are relatively resistant).

Streptococcus (Diplococcus) pneumoniae.

Clostridium spp.

GRAM NEGATIVE:

Escherichia coli., Haemophilus influenzae including ampicillin-resistant strains.

Klebsiella spp., Proteus spp. (both indole positive and indole negative)., Enterobacter spp., Neisseria spp. (including β-lactamase producing strains of N. gonorrhoea)., Salmonella spp. (including S. typhi)., Shigella spp., Providencia spp., Serratia spp., Citrobacter spp.

Cefotaxime Medo 1 gr has frequently exhibited useful in vitro activity against Pseudomonas and Bacteroides species although some strains of Bacteroides fragilis are resistant.

There is in vitro evidence of synergy between Cefotaxime Medo 1 gr and aminoglycoside antibiotics such as gentamicin against some species of Gram-negative bacteria including some strains of

Pseudomonas. No in vitro antagonism has been noted. In severe infections caused by Pseudomonas spp. the addition of an aminoglycoside antibiotic may be indicated.

4.2. Posology and method of administration

Posology

Cefotaxime Medo 1 gr may be administered intravenously or by slow injection or infusion or intramuscularly. The dosage, route and frequency of administration should be determined by the severity of infection, the sensitivity of causative organisms and condition of the patient. Therapy may be initiated before the results of sensitivity tests are known.

***Adults*:**

The recommended dosage for mild to moderate infections is 1 g 12 hourly. However, dosage may be varied according to the severity of the infection, sensitivity of causative organisms and condition of the patient. Therapy may be initiated before the results of sensitivity tests are known.

In severe infections dosage may be increased up to 12 g daily given in 3 or 4 divided doses. For infections caused by sensitive *Psuedomonas* spp. daily doses of greater than 6 g will usually be required.

Dosage in Gonorrhea: A single injection of 1 g may be administered intramuscularly or intravenously.

Children:

The usual dosage range is 100-150 mg/kg/day in 2 to 4 divided doses. However, in very severe infections doses of up to 200 mg/kg/day may be required.

Neonates:

The recommended dosage is 50 mg/kg/day in 2 to 4 divided doses. In severe infections 150-200mg/kg/day, in divided doses, have been given.

Dosage in Renal Impairment:

Because of extra-renal elimination, it is only necessary to reduce the dosage of Cefotaxime Medo 1 gr in severe renal failure (GFR <5 ml/min = serum creatinine approximately 751 micromol/l). After an initial loading dose of 1 g, daily dose should be halved without change in the frequency of dosing, i.e.,

1 g in 12 hourly becomes 0.5 g 12 hourly, 1 g 8 hourly becomes 0.5 g 8 hourly, 2 g 8 hourly becomes 1 g 8 hourly, etc. As in all other patients, dosage may require further adjustment according to the course of the infection and the general condition of the patient.

Method of administration:

Intravenous and Intramuscular

Intravenous administration (Injection or infusion):

For Intravenous injection, reconstitute cefotaxime Medo 1 gr with Water for Injection as given in the *Dilution Table*.

Shake well until dissolved and then withdraw the entire contents of the vial into the syringe and use immediately.

Dilution Table:

Vial Size	*Diluent to be added*	*Approximate volume*
1 g	4 ml	4.5 ml

For intermittent I.V. injections, the solution must be injected over a period of 3 to 5 minutes. During post-marketing surveillance, potentially life-threatening arrhythmia has been reported in a very few patients who received rapid intravenous administration of cefotaxime through a central venous catheter.

Intravenous infusion: Cefotaxime Medo 1 gr may be administered by *intravenous infusion*:

- 1-2 g are dissolved in 40-100 ml of Water for Injection or in the infusion fluids listed under section 6.6.

The prepared infusion may be administered over 20-60 minutes. To produce an infusion using vials with an infusion connector, remove the safety cap and directly connect the infusion bag. The needle in the closure will automatically pierce the vial stopper. Pressing the infusion bag will transfer solvent into the vial. Reconstitute by shaking the vial and finally, transfer the reconstituted solution back to the infusion bag ready for use.

Cefotaxime and aminoglycosides should not be mixed in the same syringe or infusion fluid.

Intramuscular administration:

For intramascular injection Cefotaxime Medo 1gr should be dissolved in 4 ml Water for Injections and then administered by deep intragluteal injection. Pain on I.M. injection can be avoided by

dissolving Cefotaxime Medo 1gr in 4 ml lidocaine solution 1%. An intravascular injection should be avoided because lidocaine can cause restlessness, tachycardia, conduction disturbances, vomiting and convulsions following intravascular administration. (See 4.3 contraindications) It is advisable not to inject a volume greater than 4 ml on one side. If the daily dose exceeds 2 g, or more than two daily injections are required, the dose should be administered intravenously.

For instructions on dilution of the medicinal product before administration, see section 6.6.

4.3. Contraindications

Hypersensitivity to the active substance, to cephalosporin antibiotics or to any of the excipients listed in section 6.1.
Allergic cross-reactions can exist between penicillins and cephalosporins (see section 4.4).
Cefotaxime reconstituted with lidocaine is contraindicated in patients with:

- Known history of hypersensitivity to lidocaine or other local anesthetics of the amide type
- Non-paced heart block
- Severe heart failure
- Administration by the intravenous route
- Infants aged less than 30 months of age

4.4. Special warnings and precautions for use

As with other antibiotics, the use of cefotaxime, especially if prolonged, may result in overgrowth of non-susceptible organisms. Repeated evaluation of the patient's condition is essential. If superinfection occurs during therapy, appropriate measures should be taken (see section 4.8).

Anaphylactic reactions
Serious, including fatal hypersensitivity reactions have been reported in patients receiving cefotaxime (see sections 4.3 and 4.8).
If a hypersensitivity reaction occurs, treatment must be stopped.
The use of cefotaxime is strictly contra-indicated in subjects with a previous history of immediate-type hypersensitivity to cephalosporins.
Since cross allergy exists between penicillins and cephalosporins, use of the latter should be undertaken with extreme caution in penicillin sensitive subjects.

Serious bullous reactions

Cases of serious bullous skin reactions like Stevens-Johnson syndrome or toxic epidermal necrolysis have been reported with cefotaxime (see section 4.8). Patients should be advised to contact their doctor immediately prior to continuing treatment if skin and/or mucosal reactions occur.

Clostridium difficile associated disease (e.g. pseudomembranous colitis)

Diarrhea, particularly if severe and/or persistent, occurring during treatment or in the initial weeks following treatment, may be symptomatic of *Clostridium difficile* associated disease (CDAD). CDAD may range in severity from mild to life threatening, the most severe form of which is pseudo-membranous colitis.

The diagnosis of this rare but possibly fatal condition can be confirmed by endoscopy and/or histology. It is important to consider this diagnosis in patients who present with diarrhoea during or subsequent to the administration of cefotaxime.

If a diagnosis of pseudomembranous colitis is suspected, cefotaxime should be stopped immediately and appropriate specific antibiotic therapy should be started without delay. *Clostridium difficile* associated disease can be favoured by faecal stasis. Medicinal products that inhibit peristalsis should not be given.

Blood disorders

Leukopenia, neutropenia and, more rarely, bone marrow failure, pancytopenia or agranulocytosis may develop during treatment with cefotaxime. For treatment, courses lasting longer than 7-10 days, the blood white cell count should be monitored and treatment stopped in the event of neutropenia.

Some cases of eosinophilia and thrombocytopenia, rapidly reversible on stopping treatment, have been reported. Cases of haemolytic anemia have also been reported (see section 4.8).

Patients with renal insufficiency

The dosage should be modified according to the creatinine clearance calculated.

Caution should be exercised if cefotaxime is administered together with aminoglycosides or other nephrotoxic drugs (see section 4.5). Renal function must be monitored in these patients, the elderly, and those with pre-existing renal impairment.

Neurotoxicity

High doses of beta-lactam antibiotics, including cefotaxime, particularly in patients with renal insufficiency, may result in encephalopathy (e.g. impairment of consciousness, abnormal movements and convulsions) (see section 4.8).

Patients should be advised to contact their doctor immediately prior to continuing treatment if such reactions occur.

Precautions for administration

During post-marketing surveillance, potentially life-threatening arrhythmia has been reported in a very few patients who received rapid intravenous administration of cefotaxime through a central venous catheter. The recommended time for injection or infusion should be followed (see section 4.2).

See section 4.3 for contraindications for cefotaxime when reconstituted with lidocaine.

Effects on Laboratory Tests

As with other cephalosporins a positive Coombs' test has been found in some patients treated with cefotaxime. This phenomenon can interfere with the cross-matching of blood. Urinary glucose testing with non-specific reducing agents may yield false-positive results. This phenomenon is not seen when a glucose-oxydase specific method is used.

Sodium intake

Cefotaxime Medo 1 g vial contains approximately 48 mg (2.09 mmol) sodium per dose, equivalent to 2.4% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

4.5. Interactions with other medicinal products and other forms of interaction

Probenecid interferes with the renal tubular transfer of cephalosporins, thereby delaying their excretion and increasing their plasma concentrations.

As with other cephalosporins, cefotaxime may potentiate the nephrotoxic effects of nephrotoxic drugs such as aminoglycosides or potent diuretics (e.g. furosemide). Renal function must be monitored (see section 4.4).

4.6. Fertility, pregnancy and lactation

Pregnancy

The safety of cefotaxime has not been established in human pregnancy.
Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity.
There are, however, no adequate and well controlled studies in pregnant women.
Cefotaxime crosses the placental barrier. Therefore, cefotaxime should not be used during pregnancy unless the anticipated benefit outweighs any potential risks.

Breast-feeding

Cefotaxime passes into human breast milk.

Effects on the physiological intestinal flora of the breast-fed infant leading to diarrhoea, colonisation by yeast-like fungi, and sensitisation of the infant cannot be excluded. Therefore, a decision must be made whether to discontinue breast-feeding or to discontinue therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

4.7. Effects on ability to drive and use machines

In the case of side effects such as dizziness, the patient's ability to concentrate and to react properly may be impaired. In such cases, patients should refrain from driving cars and using machines. High doses of cefotaxime, particularly in patients with renal insufficiency, may cause encephalopathy (e.g. impairment of consciousness, abnormal movements and convulsions) (see section 4.8). Patients should be advised not to drive or operate machinery if any such symptoms occur.

4.8. Undesirable effects

System organ class	*Very Common (≥1/10)*	*Uncommon (≥1/1,000 to <1/100)*	*Rare (≥1/10,000 to <1/1,000)*	*Very rare (<1/10,000)*	*Not known (cannot be estimated from available data)*
Infections and infestations					Superinfection (see section 4.9)
Blood and the lymphatic system disorders		Leukopenia Eosinophilia Thrombocytopenia			Bone marrow failure Pancytopenia Neutropenia Agranulocytosis (see section 4.4) Haemolytic anaemia
Immune system disorders		Jarisch-Herxheimer reaction			Anaphylactic reactions Angioedema Bronchospas

System organ class	*Very Common (≥1/10)*	*Uncommon (≥1/1,000 to <1/100)*	*Rare (≥1/10,000 to <1/1,000)*	*Very rare (<1/10,000)*	*Not known (cannot be estimated from available data)*
					m Anaphylactic shock
Nervous system disorders		Convulsions (see section 4.4)			Headache Dizziness Encephalopathy (e.g. impairment of consciousness, abnormal movements) (see section 4.4)
Cardiac disorders					Arrhythmia following rapid bolus infusion through central venous catheter
Gastrointestinal disorders		Diarrhea			Nausea Vomiting Abdominal pain Pseudomembranous colitis (see section 4.4)
Hepatobiliary disorders		Increase in liver enzymes (ALAT,			Hepatitis* (sometimes with jaundice)

System organ class	*Very Common (≥1/10)*	*Uncommon (≥1/1,000 to <1/100)*	*Rare (≥1/10,000 to <1/1,000)*	*Very rare (<1/10,000)*	*Not known (cannot be estimated from available data)*
		ASAT, LDH, gamma-GT and/or alkaline phosphatase) and/or bilirubin			
Skin and subcutaneous tissue disorders		Rash Pruritus Urticaria			Erythema multiforme Stevens-Johnson syndrome Toxic epidermal necrolysis (see section 4.4) Acute generalised exanthematous pustulosis (AGEP)
Renal and Urinary disorders		Decrease in renal function/ increase of creatinine (particularly when co-prescribed with aminoglycosides)			Acute renal failure (see section 4.4) Interstititial nephritis

System organ class	*Very Common (≥1/10)*	*Uncommon (≥1/1,000 to <1/100)*	*Rare (≥1/10,000 to <1/1,000)*	*Very rare (<1/10,000)*	*Not known (cannot be estimated from available data)*
General disorders and administration site conditions	*For IM formulations*: Pain at the injection site	Fever Inflammatory reactions at the injection site, including phlebitis/ thrombophlebitis			*For IM formulations (where lidocaine is used for reconstitution)*: Systemic reactions to lidocaine

*postmarketing experience

Jarisch-Herxheimer reaction

For the treatment of borreliosis, a Jarisch-Herxheimer reaction may develop during the first days of treatment.

The occurrence of one or more of the following symptoms has been reported after several week's treatment of borreliosis: skin rash, itching, fever, leucopenia, increase in liver enzymes, difficulty of breathing, joint discomfort.

Hepatobiliary disorders

Increase in liver enzymes (ALAT, ASAT, LDH, gamma-GT and/or alkaline phosphatase) and/or bilirubin have been reported. These laboratory abnormalities may rarely exceed twice the upper limit of the normal range and elicit a pattern of liver injury, usually cholestatic and most often asymptomatic.

Superinfection:

As with other antibiotics, the use of cefotaxime, especially if prolonged, may result in overgrowth of non-susceptible organisms. Repeated evaluation of the patient's condition is essential. If superinfection occurs during therapy, appropriate measures should be taken.

For IM Formulations

Since the solvent contains lidocaine, systemic reactions to lidocaine may occur, especially in the event of inadvertent intravenous injection or injection into highly vascularised tissue or in the event of an overdose.

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. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form https://sideeffects.health.gov.il

4.9. Overdose

Symptoms

Symptoms of overdose may largely correspond to the profile of side effects.

There is a risk of reversible encephalopathy in cases of administration of high doses of b-lactam antibiotics including cefotaxime.

Management

In case of overdose, cefotaxime must be discontinued, and supportive treatment initiated, which includes measures to accelerate elimination, and symptomatic treatment of adverse reactions (e.g. convulsions).

No specific antidote exists. Serum levels of cefotaxime can be reduced by haemodialysis or peritoneal dialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Antibacterials for systemic use, ATC code: J01DD01

Cefotaxime is a broad-spectrum bactericidal cephalosporin antibiotic. Cefotaxime is exceptionally active in vitro against Gram-negative organisms sensitive or resistant to first or second-generation cephalosporins. It is similar to other cephalosporins in activity against Gram-positive bacteria.

Bacteriology:

The following organisms have shown in vitro sensitivity to cefotaxime.

Gram Positive

Staphylococci, including coagulase-positive, coagulase-negative and penicillinase producing strains.

Beta-haemolytic and other streptococci such as *Streptococcus mitis* (*viridans*) (many strains of enterococci, e.g. *Streptococcus faecalis*, are relatively resistant).
Streptococcus (*Diplococcus*) *pneumonia*.
Clostridium spp.

Gram Negative
Escherichia coli.
Haemophilius influenzae including ampicillin resistant strains.
Klebsiella spp.
Proteus spp. (both indole positive and indole negative).
Enterobacter spp.
Neisseria spp. (including B-lactamase producing strains of *N. gonorrhoea*).
Salmonella spp. (including *Sal. Typhi*).
Shigella spp.
Providencia spp.
Serratia spp.
Citrobacter spp.

Cefotaxime has frequently exhibited useful *in vitro* activity against *Pseudomonas* and *Bacteroides* species although some strains of *Bacteroides fragilis* are resistant.

There is *in vitro* evidence of synergy between cefotaxime and aminoglycoside antibiotics such as gentamicin against some species of Gram-Negative bacteria including some strains of *Pseudomonas*. No *in vitro* antagonism has been noted. In severe infections cause by *Pseudomonas* spp. the addition of an aminoglycoside antibiotic may be indicated.

5.2. Pharmacokinetic properties

After a 1000 mg intravenous bolus, mean peak plasma concentrations of cefotaxime usually range between 81 and 102 μg/ml. Doses of 500 mg and 2000 mg produce plasma concentrations of 38 and 200 μg/ml, respectively. There is no accumulation following administration of 1000 mg intravenously or 500 mg intramuscularly for 10 or 14 days.

The apparent volume of distribution at steady-state of cefotaxime is 21.6 L/1.73 m2 after 1 g intravenous 30 minute infusion.

Concentrations of cefotaxime (usually determined by non-selective assay) have been studied in a wide range of human body tissues and fluids. Cerebrospinal fluid concentrations are low when the meninges are not inflamed, but are between 3 and 30 μg/ml in children with meningitis.

Cefotaxime usually passes the blood-brain barrier in levels above the MIC of common sensitive pathogens when the meninges are inflamed. Concentrations (0.2-5.4 μg/ml), inhibitory for most Gram-negative bacteria, are attained in purulent sputum, bronchial secretions and pleural fluid after doses of 1 or 2 g. Concentrations likely to be effective against most sensitive organisms are similarly attained in female reproductive organs, otitis media effusions, prostatic tissue, interstitial fluid, renal tissue, peritoneal fluid and gall bladder wall, after usual therapeutic doses. High concentrations of cefotaxime and desacetyl-cefotaxime are attained in bile.

Cefotaxime is partially metabolised prior to excretion. The principle metabolite is the microbiologically active product, desacetyl-cefotaxime. Most of a dose of cefotaxime is excreted in the urine about 60% as unchanged drug and a further 24% as desacetyl-cefotaxime. Plasma clearance is reported to be between 260 and 390 ml/minute and renal clearance 145 to 217 ml/minute.

After intravenous administration of cefotaxime to healthy adults, the elimination half-life of the parent compound is 0.9 to 1.14 hours and that of the desacetyl metabolite, about 1.3 hours.

In neonates the pharmacokinetics are influenced by gestational and chronological age, the half-life being prolonged in premature and low birth weight neonates of the same age.

In severe renal dysfunction the elimination half-life of cefotaxime itself is increased minimally to about 2.5 hours, whereas that of desacetyl-cefotaxime is increased to about 10 hours. Total urinary recovery of cefotaxime and its principal metabolite decreases with reduction in renal function.

5.3. Preclinical safety data

Not applicable.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

None.

6.2. Incompatibilities

Prolonged use of an anti-infective may result in the development of superinfection due to organisms resistant to that anti-infective.
Aminoglycosides are incompatible with cephalosporins in parenteral mixtures.

6.3. Shelf life

Unopened: The expiry date of the product is indicated on the packaging materials.

Reconstituted solution: twenty four (24) hours.
Satisfactory potency is maintained for twenty four (24) hours when stored refrigerated with the following intravenous infusion fluids:

- Water for injection
- 0.9% Sodium chloride
- Dextrose 5 %
- 5% Dextrose and 0.9% Sodium chloride
- Ringer's lactated solution

From a microbiological point of view, reconstituted solution for intramuscular or intravenous administration should be used immediately upon reconstitution .If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would not be longer than 24 hours at 2 to 8^0C unless reconstitution/dilution (etc) has taken place in controlled and validated aseptic conditions.
Any unused solution remaining must be discarded at twenty four hours.

6.4. Special precautions for storage

Unopened: Store below 25°C. Keep the vial in the outer carton, in order to protect from light..
Reconstituted solutions should preferably be used immediately upon reconstitution.
For storage conditions after reconstitution of the medicinal product, see section 6.3.

Cefotaxime is also compatible with Lignocaine 1% injection, but freshly prepared solutions only must be used.
Cefotaxime is also compatible with metronidazole infusion (500 mg/100 ml) and both will maintain potency when refrigerated for up to 24 hours.

6.5. Nature and contents of container

Clear type I glass vials, sealed with a grey bromobutyl rubber stopper and aluminium cap. Vials are cartonned in packs of 10with an instruction leaflet.

6.6. Special precautions for disposal

Reconstitution of the vials should be done with suitable aseptic precautions. From a microbiological point of view, reconstituted solution for intramuscular or intravenous administration should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8°C.
Infusion solutions, as specified in section 6.3, should not be stored for more than twenty-four hours. Any unused solution should be discarded. Before use, examine solutions for evidence of particles, any such solutions should not be used.Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

A.L. Medi-Market Ltd., 3 Hakatif St., Emek Hefer Industrial Park, 3877701

8. MANUFACTURER

Medochemie Ltd (Factory C), 2, Michael Erakleous, Agios Athanassios Industrial Area, 4101 Agios Athanassios, Limassol, Cyprus

9. MARKETING AUTHORISATION NUMBERS

167-79-36007-00

10. DATE OF REVISION OF THE TEXT

Revised in November 2021 according to MoHs guidelines