SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

MOCLAV 0,6, 500 mg/100 mg, Powder for solution for injections

MOCLAV 1,2, 1 000 mg/200 mg, Powder for solution for injections

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each MOCLAV 0,6 vial contains 500 mg amoxicillin (as sodium salt) and 100 mg clavulanic acid (as potassium salt)

Each MOCLAV 1,2 vial contains 1000 mg amoxicillin (as sodium salt) and 200 mg clavulanic acid (as potassium salt)

Excipient(s) with known effect:

The sodium content of each MOCLAV 0,6 vial is 30 mg (1,3 mmol)

The potassium content of each MOCLAV 0,6 vial is 19 mg (0,5 mmol) which at less than 39 mg (1 mmol) is considered essentially 'potassium free'.

The sodium content of each MOCLAV 1,2 vial is 60 mg (2,6 mmol)

The potassium content of each MOCLAV 1,2 vial is 38 mg (0,97 mmol) which at less than 39 mg (1 mmol) is considered essentially 'potassium free'.

Sugar-free

For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Powder for solution for injections

A white or almost white powder

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

MOCLAV is indicated for the treatment of infections caused by amoxicillin resistant organisms producing β-lactamases sensitive to clavulanic acid:

- upper respiratory tract infections, such as sinusitis, otitis media, tonsillitis caused by *Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis* and *Streptococcus pyogenes* sensitive to MOCLAV.
- lower respiratory tract infections, such as bronchitis (caused by amoxicillin-resistant β-lactamase producing *Escherichia coli, Haemophilus influenzae* and *Haemophilus para-influenzae*), bronchopneumonia sensitive to MOCLAV.
- urinary tract infections, such as cystitis, urethritis, pyelonephritis caused by *Enterobacteriaceae* (mainly *Escherichia coli*), *Staphylococcus saprophyticus* and *Enterococcus* species.
- skin and soft tissue infections caused by methicillin susceptible *Staphylococcus aureus*, *Streptococcus pyogenes* and *Bacteroides species* sensitive to MOCLAV.

MOCLAV will also be effective in the treatment of infections caused by amoxicillin-sensitive organisms at the appropriate amoxicillin dosage since in this situation the clavulanic acid component does not contribute to the therapeutic effect.

4.2 Posology and method of administration

Posology

For infections caused by amoxicillin sensitive organisms the dosage is that approved for amoxicillin as the clavulanic acid component does not contribute to the therapeutic effect.

Adult (intravenous):

For severe infections of the respiratory tract, urinary tract and skin and soft tissue requiring parenteral therapy initially one MOCLAV 1,2 vial can be administered intravenously 6 to 8 hourly by intravenous injection (2 minutes) or intravenous infusion (30 minutes) until condition settles. If no response has occurred within 48 hours therapy must be reviewed.

Intravenous treatment with MOCLAV should not be extended beyond 10 days without review and the total daily administration of clavulanic acid should not exceed 800 mg. Treatment can be continued with tablets, containing amoxicillin and clavulanic acid, at the recommended dose orally where appropriate after a satisfactory therapeutic response has been obtained.

AMOXICILLIN-SENSITIVE ORGANISMS				
PRODUCT	**UPPER RESPIRATORY TRACT INFECTIONS**	**LOWER RESPIRATORY TRACT INFECTIONS**	**URINARY TRACT INFECTIONS**	**SKIN AND SOFT TISSUE INFECTIONS**
ADULTS:				
MOCLAV 1,2	1 vial [1)] 6-8 hourly	1 vial [1)] 6-8 hourly	1 vial [1)] 6-8 hourly	1 vial [1)] 6-8 hourly
MOCLAV 0,6	2 vials [1)] 6-8 hourly	2 vials [1)] 6-8 hourly	2 vials [1)] 6-8 hourly	2 vials [1)] 6-8 hourly

AMOXICILLIN-RESISTANT ORGANISMS				
PRODUCT	**UPPER RESPIRATORY TRACT INFECTIONS (otitis media)** ***H. influenzae*** ***H. para influenzae***	**LOWER RESPIRATORY TRACT INFECTIONS (bronchitis)** ***H. influenzae*** ***H. para influenzae***	**URINARY TRACT INFECTIONS** ***E. coli*** ***Klebsiella pneumoniae***	**SKIN AND SOFT TISSUE INFECTIONS** ***Staphylococcus aureus***
ADULTS:				

MOCLAV 1,2	1 vial [1)] 6-8 hourly	1 vial [1)] 6-8 hourly	1 vial [1)] 6-8 hourly	1 vial [1)] 6-8 hourly
MOCLAV 0,6	2 vials [1)] 6-8 hourly	2 vials [1)] 6-8 hourly	2 vials [1)] 6-8 hourly	2 vials [1)] 6-8 hourly

1) Intravenous therapy should not be continued for longer than 10 days.

Special populations

Patients with renal impairment

As both the amoxicillin and clavulanic acid components of MOCLAV are excreted by the kidneys, accumulation of both may occur in patients with renal insufficiency. In these cases, monitoring of the serum levels and a reduction in the number of administrations of the suggested dosage may be required. Dosing adjustments are based on the maximum recommended level of amoxicillin.

Experience in a limited number of patients with varying degrees in renal insufficiency suggests that the following schedule of dosage based on the creatinine clearance of the patient, may be used as a guideline:

Creatinine Clearance	**Dosage**
> 30 ml/min	no dosage adjustment
10-30 ml/min	1,2 g MOCLAV immediately and 600 mg 12 hourly
< 10 ml/min	1,2 g MOCLAV immediately and 600 mg 24 hourly

Paediatric population

The safety and efficacy of MOCLAV in children have not been established. MOCLAV is contraindicated in children (see section 4.3)

Method of administration:

For intravenous use only.

Note: MOCLAV vials are not suitable for intramuscular or subcutaneous administration.

The reconstituted vials can be administered intravenously by injection (2 minutes) or slow intravenous infusion (30 minutes). Infusion should be completed within the period of stability of MOCLAV infusions after reconstitution and dilution as reflected in section 6.3. The contents of the vials must be used within 20 minutes and thereafter any unused material discarded.

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

4.3 Contraindications

- MOCLAV is contraindicated in patients with known hypersensitivity to penicillin's, amoxicillin and cephalosporins or to any of the excipients listed in section 6.1.
- Safety and efficacy in children have not been established with the parenteral forms of MOCLAV.
- MOCLAV is contraindicated in patients with a previous history of MOCLAV associated jaundice/hepatic dysfunction.

4.4 Special warnings and precautions for use

Before initiating therapy with MOCLAV, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins or other beta-lactam medicines (see sections 4.3 and 4.8). There have been reports of individuals with a history of penicillin hypersenstitivity who have experienced severe reaction when treated with cephaolosporins.

Serious and occasionally fatal hypersensitivity reactions (including anaphylaphylactoid and severe cutaneous adverse reactions) have been reported in patients on penicillin therapy. Hypersensitivity reactions can also progress to Kounis syndrome, a serious allergic reaction that can result in myocardial infarction (see section 4.8). Although anaphylaxis is more frequent following parenteral therapy, it has occurred in patients on oral penicillins. These reactions are more likely to occur in individuals with a history of penicillin hypersensitivity and/or a history of sensitivity to multiple

allergens and in atopic individuals.

If an allergic reaction occurs, MOCLAV should be discontinued and the appropriate therapy instituted which may include epinephrine (adrenaline), corticosteroids and antihistamines.

In the case that an infection is proven to be due to an amoxicillin-susceptible organisms(s) then consideration should be given to switching from amoxicillin/clavulanic acid to amoxicillin in accordance with official guidance.

This presentation of MOCLAV may not be suitable for use when there is a high risk that the presumptive pathogens have resistance to beta-lactam medicines that is not mediated by beta-lactamases susceptible to inhibition by clavulanic acid. As no specific data for T>MIC are available and the data for comparable oral presentations are borderline, this presentation (without additional amoxicillin) may not be suitable for the treatment of penicillin-resistant *S. pneumoniae.*

Convulsions may occur in patients with impaired renal function or in those receiving high doses (see section 4.8).

MOCLAV should be avoided if infectious mononucleosis is suspected since the occurrence of a morbilliform rash has been assocociated with this condition following the use of amoxicillin.

Concomitant use of allopurinol during treatment with amoxicillin can increase the likelihood of allergic skin reactions.

Prolonged use may also result in overgrowth of non-susceptible organisms. The possibility of superinfections with mycotic or bacterial pathogens should be kept in mind during therapy. If superinfections occur (usually involving *Aerobacter, Pseudomonas* or *Candida*), the medicine should be discontinued and/or appropriate therapy instituted.

The occurrence at the treatment initiation of a feverish generalised erythema associated with pustula may be a symptom of acute generalised exanthemous pustulosis (AGEP) (see section 4.8). This reaction requires MOCLAV discontinuation and contraindicates any subsequent administration of amoxicillin.

MOCLAV should be used with caution in patients with evidence of hepatic impairment (see section 4.3 and 4.8)

Changes in liver function tests have been observed in some patients receiving amoxicillin/clavulanic acid as in MOCLAV. Hepatic events, such as transient hepatitis and cholestatic jaundice, have been reported predominantly in males and elderly patients and may be associated with prolonged treatment. These events have been reported in children. In all populations, signs and symptoms usually occur during or shortly after treatment but in some cases may not become apparent until several weeks after treatment has ceased. These are usually reversible. Hepatic events may be severe, and in extremely rare circumstances deaths have been reported. These have almost always occurred in patients with serious underlying disease or taking concomitant medications known to have the potential for hepatic effects (see section 4.8).

Antibiotic-associated colitis has been reported with nearly all antibacterial medicines including amoxicillin and may range in severity from mild to life threatening (see section 4.8). Therefore, it is important to consider this diagnosis in patients who present with diarrhoea during or subsequent to

the administration of any antibiotics. Should antibiotic-associated colitis occur, amoxicillin/clavulanic acid should immediately be discontinued, a medical practitioner be consulted, and an appropriate therapy initiated. Anti-peristaltic medicines are contraindicated in this situation.

Periodic assessment of organ system functions, including renal, hepatic and haematopoietic function is advisable during prolonged therapy.

Prolongation of prothrombin time has been reported in patients receiving amoxicillin/clavulanic acid as in MOCLAV and oral anticoagulants. Appropriate monitoring should be undertaken when anticoagulants are prescribed concomitatnly. Adjustments in the dose of oral anticoagulants may be necessary to maintain the desired level of anticoagulation (see sections 4.5 and 4.8).

In patients with moderate or severe renal impairment, MOCLAV dosage should be adjusted according to the degree of impiarment (see section 4.2).

In patients with reduced urine output crystalluria (including acute renal injury) has been observed, predominantly with parenteral therapy. During the administration of high doses of amoxicillin, it is advisable to maintain adequate fluid intake and urinary output in order to reduce the possibility of amoxicillin crystalluria. In patients with bladder catheters, a regular check of patency should be maintained (see section 4.8 and 4.9).

MOCLAV should not be mixed with aminoglycosides in the same syringe or giving set, as substantial inactivation of the aminoglycosides can result.

MOCLAV should be given with caution to patients with lymphatic leukaemia since they are especially susceptible to amoxicillin induced skin rashes.

Effects on laboratory tests

During treatment with amoxicillin, enzymatic glucose oxidase methods should be used whenever testing for the presence of glucose in urine because false positive results may occur with non-enzymatic methods.

The presence of clavulanic acid in amoxicillin-clavulanate may cause a non-specific binding of IgG and albumin by red cell membranes leading to a false positive Coombs test (antiglobulin test).

There have been reports of positive test results in patients receiving amoxicillin/clavulanic acid who were subsequently found to be free of *Aspergillus* infection. Therefore, positive test results in patients receiving MOCLAV should be interpreted cautiously and confirmed by other diagnostic methods.

MOCLAV 0,6 Powder for solution for injections

This medicine contains 30 mg (1,3 mmol) of sodium per vial, equivalent to 1,5 % of the WHO recommended maximum daily intake of 2 g sodium for an adult. To be taken into consideration by patients on a controlled sodium diet.

This medicine contains 19 mg (0,5 mmol) of potassium which is less than 1 mmol (39 mg) per vial or bottle. This is considered essentially as 'potassium-free'.

MOCLAV 1,2 Powder for solution for injections

This medicine contains 60 mg (2,6 mmol) of sodium per vial or bottle, equivalent to 3 % of the WHO recommended maximum daily intake of 2 g sodium for an adult. To be taken into consideration by patients on a controlled sodium diet.

This medicine contains 38 mg (0,97 mmol) of potassium which is less than 1 mmol (39 mg) per vial or bottle. This is considered to be 'potassium-free'. However, this can be taken in consideration by patients with reduced kidney function or patients on a controlled potassium diet.

4.5 Interaction with other medicines and other forms of interaction

Probenecid

Concomitant use of probenecid is not recommended. Probenecid decreases the renal tubular secretion of amoxicillin but does not affect clavulanic acid excretion. Concomitant use with MOCLAV may result in increased and prolonged blood levels of amoxicillin but not of clavulanic acid.

Oral anticoagulants

Oral anticoagulants and penicillin antibiotics have been widely used in practice without reports of interaction. However, in the literature there are cases of increased international normalised ratio in patients maintained on warfarin and prescribed a course of amoxicillin. If co-administration is necessary, the prothrombin time or international normalised ratio should be carefully monitored with the addition or withdrawal of MOCLAV. Moreover, adjustments in the dose of oral anticoagulants may be necessary (see section 4.4 and 4.8).

Methotrexate

Penicillins may reduce the excretion of methotrexate causing a potential increase in toxicity.

Aminoglycosides

MOCLAV should not be mixed with aminoglycosides in the same syringe or giving set, as substantial inactivation of the aminoglycosides can result.

Mycophenolate mofetil

In patients receiving mycophenolate mofetil, reduction in pre-dose concentration of the active metabolite mycophenolic acid (MPA) of approximately 50 % has been reported following commencement of oral amoxicillin plus clavulanic acid. The change in pre-dose level may not accurately represent changes in overall MPA exposure. Therefore, a change in the dose of mycophenolate mofetil should not normally be necessary in the absence of clinical evidence of graft dysfunction. However, close clinical monitoring should be performed during the combination and

shortly after antibiotic treatment.

Allopurinol

The concomitant administration of allopurinol and ampicillin substantially increases the incidence of rashes in patients receiving both medicines as compared to patients receiving ampicillin alone. It is not known whether this potentiation of ampicillin rashes is due to allopurinol or the hyperuricaemia present in these patients (see section 4.4). There is no data on MOCLAV, and allopurinol administered concomitantly.

Alcohol

No information is available about the concurrent use of MOCLAV and alcohol. However, the ingestion of alcohol whilst being treated with some other beta-lactam antibiotics has precipitated a disulfiram-like reaction in some patients. Therefore, the ingestion of alcohol should be avoided during and for several days after treatment with MOCLAV.

Oral contraceptives

Following administration of ampicillin to pregnant woman a transient decrease in plasma concentration of total conjugate oestriol, oestriol-glucuronide, conjugated oestrone and oestradiol has been noted. This effect may also occur with MOCLAV leading to lower oestrogen re-absorption and reduced efficacy of combined oral contraceptives.

Resistant organisms

The use of MOCLAV may lead to the selection of resistant strains of organisms and sensitivity testing should, therefore, be carried out whenever possible, to demonstrate the appropriateness of therapy.

4.6 Fertility, pregnancy and lactation

Pregnancy

Safety in pregnancy has not been established.

In women with pre-term, premature rupture of the foetal membrane (pPROM), it was reported that prophylactic treatment with amoxicillin-clavulanate may be associated with an increased risk of necrotising enterocolitis in neonates.

Breastfeeding

Both amoxicillin and clavulanic acid are excreted into breast milk (nothing is known of the effects of clavulanic acid on the breast-fed infant). Mothers on treatment with MOCLAV should not breastfeed their infants.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. However, undesirable effects may occur (e.g. allergic reactions, dizziness, convulsions), which may influence the ability to drive and use machines (see section 4.8).

4.8 Undesirable effects

a) Summary of safety profile

The most frequent adverse drug reactions are diarrhoea, nausea and vomiting.

b) Tabulated summary of adverse reactions

System organ class	**Frequency**	**Adverse Reaction**
Infections and Infestations	Frequent	Mucocutaneous candidiosis (including vaginitis, stomatitis, glossitis)
	Frequency unknown	Overgrowth of non-susceptible organisms
Blood and lymphatic system disorders	Less frequent	Reversible leukopenia (including neutropenia), thrombocytopenia

	Frequency unknown	Reversible agranulocytosis, haemolytic anaemia, prolongation of bleeding time and prothrombin time (see section 4.4)
Immune system disorders	Frequency unknown	Angioedema, anaphylaxis, serum sickness-like syndrome, hypersensitivity vasculitis (see section 4.3 and 4.4)
Nervous system disorders	Less frequent	Dizziness, headache
	Frequency unknown	Convulsions (see section 4.4), aseptic meningitis
Cardiac disorders	Frequency unknown	Kounis syndrome
Vascular disorders	Less frequent	Thrombophlebitis at the site of injection
Gastrointestinal disorders	Frequent	Diarrhoea[1)]
	Less frequent	Nausea[1)], vomiting, indigestion, gastritis
	Frequency unknown	Antibiotic-associated colitis including pseudomembranous colitis and haemorrhagic colitis (see section 4.4)
Hepato-biliary disorders	Less frequent	Rises in AST and/or ALT2)
	Frequency unknown	Hepatitis[3)], cholestatic jaundice[3)]
Skin and subcutaneous tissue disorders[4)]	Less frequent	Skin rash, pruritus, urticaria, erythema multiforme
	Frequency unknown	Stevens-Johnson syndrome, toxic epidermal necrolysis, bullous exfoliative-dermatitis, acute

		generalised exanthemous pustulosis (AGEP), drug reaction with eosinophilia and systemic symptoms (DRESS) (see section 4.4), linear IgA disease.
Renal and urinary disorders	Frequency unknown	Interstitial nephritis, crystalluria (including acute renal injury) (see section 4.9)

[1)] The incidence and severity of adverse effects, particularly nausea and diarrhoea, increased with the higher recommended dose and can be minimised by administering MOCLAV at the start of a meal. In addition, as these symptoms are especially related to the potassium clavulanate component, where these gastrointestinal symptoms occur and a higher concentration of amoxicillin is required, consideration should be given to administering the additional amoxicillin separately.

[2)] A moderate rise in AST and/or ALT has been noted in patients treated with beta-lactam class antibiotics, but the significance of these findings is unknown.

[3)] Hepatic events may be severe and fatal. Signs and symptoms usually occur during or shortly after treatment but in some cases may not become apparent until several weeks after treatment has ceased. These events have been noted with other penicillins and cephalosporins (see section 4.4).

[4)] If any hypersensitivity dermatitis reaction occurs, treatment should be discontinued.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

4.9 Overdose

Gastrointestinal symptoms and disturbance of the fluid and electrolyte balances may be evident. Amoxicillin crystalluria, in some cases leading to renal failure, has been observed (see section 4.4). Convulsions may occur in patients with impaired renal function or in those receiving high doses. Amoxicillin has been reported to precipitate in bladder catheters, predominantly after intravenous administration of large doses. A regular check of patency should be maintained (see section 4.4).

Treatment of intoxication.

Gastrointestinal symptoms may be treated symptomatically, with attention to the water/electrolyte balance. MOCLAV can be removed from the circulation by haemodialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 20.1.2 Penicillins

Pharmacotherapeutic group: Combinations of penicillins, including beta-lactamase inhibitors

ATC class: J01CR02

Mechanism of action

Bactericidal action - The amoxicillin component of the formulations exert a bactericidal action against many strains of Gram-positive and Gram-negative organisms. The clavulanic acid component has very little bactericidal action. It does however, by inactivation of susceptible beta-lactamases, protect amoxicillin from degradation by a large number of beta-lactamase enzymes produced by penicillin resistant strains of organisms.

Potassium clavulanate has been shown *in vitro* to be an irreversible inhibitor of beta-lactamases.

Inherently resistant organisms

Aerobic Gram-negative micro-organisms

Acinetobacter sp.

Citrobacter freundii

Enterobacter sp.

Legionella pneumophila

Morganella morganii

Providencia spp.

Pseudomonas sp.

Serratia sp.

Stenotrophomonas maltophilia

Other micro-organisms

Chlamydia trachomatis

Chlamydophila pneumoniae

Chlamydophila psittaci

Coxiella burnetti

Mycoplasma pneumoniae

5.2 Pharmacokinetic properties

Absorption:

The pharmacokinetics of amoxicillin and clavulanic acid are closely allied. Doubling the dose virtually doubles the peak serum level.

Distribution:

About 25 % of total plasma clavulanic acid and 18 % of total plasma amoxicillin is bound to protein. The apparent volume of distribution is around 0,3-0,4 L/kg for amoxicillin and around 0,2 L/kg for clavulanic acid.

Following intravenous administration, both amoxicillin and clavulanic acid have been found in gall bladder, abdominal tissue, skin, fat, muscle tissues, synovial and peritoneal fluids, bile and pus.

Amoxicillin does not adequately distribute into the cerebrospinal fluid.

Both amoxicillin and clavulanic acid have been shown to cross the placental barrier (see section 4.6).

Biotransformation:

Amoxicillin is partly excreted in the urine as the inactive penicilloic acid in quantities equivalent to up to 10 to 25 % of the initial dose. Clavulanic acid is extensively metabolised in man, and eliminated in urine and faeces, and as carbon dioxide in expired air.

Elimination:

The major route of elimination for amoxicillin is via the kidney, whereas for clavulanic acid it is by both renal and non-renal mechanisms.

Amoxicillin/clavulanic acid has a mean elimination half-life of approximately one hour and a mean total clearance of approximately 25 L/h in healthy subjects. Approximately 60 to 70 % of the amoxicillin and approximately 40 to 65 % of the clavulanic acid are excreted unchanged in urine during the first 6 h after administration of a single 500/100 mg or a single 1000/200 mg bolus intravenous injection. Various studies have found the urinary excretion to be 50-85 % for amoxicillin and between 27-60 % for clavulanic acid over a 24 hour period. In the case of clavulanic acid, the largest amount of drug is excreted during the first 2 hours after administration.

Co-administration of probenecid has little effect on the excretion of the clavulanic acid component of the formulation.

Characteristics in specific groups of subjects or patients

Renal impairment

The total serum clearance of amoxicillin/clavulanic acid decreases proportionately with decreasing

renal function. The reduction in drug clearance is more pronounced for amoxicillin than for clavulanic acid, as a higher proportion of amoxicillin is excreted via the renal route. Doses in renal impairment must therefore prevent undue accumulation of amoxicillin while maintaining adequate levels of clavulanic acid (see section 4.2).

Hepatic impairment

Hepatically impaired patients should be dosed with caution and hepatic function monitored at regular intervals.

Age

The elimination half-life of amoxicillin is similar for children aged around 3 months to 2 years and older children and adults. For very young children (including preterm newborns) in the first week of life the interval of administration should not exceed twice daily administration due to immaturity of the renal pathway of elimination. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

None.

6.2 Incompatibilities

MOCLAV solutions should not be mixed with:

- dextrose solution
- sodium bicarbonate solution for injection
- protein hydrolysates or other proteinaceous fluids
- blood or plasma
- intravenous lipids.

If prescribed concomitantly with an aminoglycoside, the antibiotics should not be mixed in the syringe, intravenous fluid container or giving set because loss of activity of the aminoglycoside can occur under these conditions.

However, the reconstituted solution may be injected into the drip tubing of infusion fluids containing glucose, bicarbonate and dextran over a period of 3-4 minutes.

This medicine must not be mixed with other medicines except those mentioned in section 6.6.

6.3 Shelf life

Powder in vials or bottles

3 years.

In-use storage conditions and shelf-life

MOCLAV 0,6 can be reconstituted by dissolving in 10 ml Water for Injections B.P. The contents of the vials must be used within 20 minutes below 25 °C and thereafter any unused material discarded.

MOCLAV 1,2 can be reconstituted by dissolving in 20 ml Water for Injections B.P. The contents of the vials must be used within 20 minutes below 25 °C and thereafter any unused material discarded.

Diluted for intravenous infusion

Chemical and physical in-use stability for MOCLAV 0,6 has been demonstrated for the reconstituted solution for 2-4 hours infusion for 60 minutes if stored at 25 °C. From a microbiological point of view, the reconstituted and diluted solution (1 reconstituted vial in a minimum volume of 50 ml of infusion fluid) 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, unless reconstitution/dilution has taken place in controlled and validated aseptic conditions.

Chemical and physical in-use stability for MOCLAV 1,2 has been demonstrated for 2-4 hours at if stored at 25 °C. From a microbiological point of view, the reconstituted and diluted solution (1 reconstituted vial in a minimum volume of 100 ml of infusion fluid) 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, unless reconstitution/dilution has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

Store at or below 30 ˚C.

For storage conditions after reconstitution of the medicine, see section 6.3.

6.5 Nature and contents of container

MOCLAV 0,6 Powder for solution for injections:

Clear 20 mL moulded glass vial (Type II) with halogenated butyl rubber stopper and flip-off caps (Aluminum-plastic combination caps).

Packs of 10 vial/tray/box, 12 boxes /carton.

MOCLAV 1,2 Powder for solution for injections:

Clear 20 mL moulded glass vial (Type II) with halogenated butyl rubber stopper and flip-off caps (Aluminum-plastic combination caps).

Packs of 10 vial/tray/box, 12 boxes /carton.

6.6 Special precautions for disposal and other handling

For single use only. Discard any unused solution.

The reconstitution/dilution is to be made under aseptic conditions. The solution is to be inspected visually for particulate matter and discoloration prior to administration. The solution should only be used if the solution is clear and free from particles.

Preparation of solutions for intravenous injection

MOCLAV 0,6 can be reconstituted by dissolving in 10 ml Water for Injections B.P.

MOCLAV 1,2 can be reconstituted by dissolving in 20 ml Water for Injections B.P.

When a diluent is added a transient pink colouration or slight opalescence will be observed whereafter, a pale yellow fluid.

MOCLAV for bolus injection should be administered within 20 min of reconstitution.

If reconstituted with sterile water for injection and maintained at room temperature (25 °C), infusions should be completed within the times stated in the following table:

Intravenous infusion	Stability period at 25°C
Water for Injection Ph.Eur.	4 hours
0,9 % w/v Sodium Chloride Intravenous Infusion (9 mg/mL)	4 hours
Compound Sodium Chloride Injection 1959 (Ringer's)	2 hours
Compound Sodium Lactate Intravenous Infusion (Ringer-Lactate:Hartmann's)	2 hours
0,3 % *w/v* Potassium Chloride and 0,9 % *w/v* Sodium Chloride Intravenous Infusion (3 mg/mL and 9 mg/mL)	2 hours

For MINI-BAG™ PLUS:

Alternatively, if minibags of sodium chloride 0,9 % *m/v* are to be used, the stability results obtained

with MOCLAV indicated that 600 mg per 50 ml or 1,2 g per 100 ml bag is suitable. Using a MINI-BAG™ PLUS unit containing 50 ml or 100 ml physiological saline, the appropriate volume of sodium chloride solution may be transferred from the MINI-BAG™ PLUS unit bag into an MOCLAV 0,6 or MOCLAV 1,2 vial respectively, and then back into the bag after dissolution. When the latter method is used the permissible time between preparation of the solution and completion of the infusion is reduced from 4 hours to 3 hours.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Ando Pharma (Pty) Ltd.

73 Keurboom Crescent

Plattekloof

Cape Town

8. REGISTRATION NUMBER(S)

MOCLAV 0,6, 500 mg/100 mg, Powder for solution for injections - 56/20.1.2/1137

MOCLAV 1,2, 1 000 mg/200 mg, Powder for solution for injections - 56/20.1.2/1138

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

22 April 2025

10. DATE OF REVISION OF THE TEXT