**SCHEDULING STATUS:**

S4

## 1. NAME OF THE MEDICINE

**SEPTAPEN 250** (Capsules)

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITON:

**SEPTAPEN 250**

Each hard gelatine capsules containing flucloxacillin sodium equivalent to 250 mg flucloxacillin.

Sugar free.

For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

**SEPTAPEN 250** capsules are black/red size “2” hard gelatine capsules.

## 4. CLINICAL PARTICULARS

### 4.1 THERAPEUTIC INDICATIONS:

Infections caused by susceptible gram-positive organisms, including beta-lactamase producing staphylococci and streptococci:

- Skin and soft tissue infections
- Infected wounds and burns
- Otitis media
- Urinary tract infections
- Respiratory tract infections caused by penicillinase-producing organisms.
- Orthopaedic infections

- Septicaemia
- Meningitis
- Endocarditis
- Enterocolitis

**4.2 POSOLOGY AND METHOD OF ADMINISTRATION**

**Posology**

**Adults**

The usual adult dose is to take 1 capsule 4 times a day preferably 1 hour before meals.

**Severe infections**

Up to 8 g daily in divided doses, six to eight hourly, one hour before meals for endocarditis, osteomyelitis, skin, and soft tissue infections.

**Special populations**

*Renal impairment:*

For patients with a creatinine clearance value < 10 mL / min, consider a dose reduction or extension of dose interval. For patients with a creatinine clearance value > 10 mL / min, no dose adjustment is necessary.

*Paediatric population*

**SEPTAPEN 250** is indicated for adults and must not be prescribed to children. Safety and efficacy has not been established in children.

**Method of administration**

Should be taken one hour before meals.

**4.3 CONTRAINDICATIONS:**

- Hypersensitivity to flucloxacillin sodium or other beta-lactam antibiotics (e.g. penicillins, cephalosporins) or to any of the excipients listed in section 6.1.Flucloxacillin is contraindicated in patients with a previous history of flucloxacillin associated jaundice / hepatic dysfunction.
- Not to be used topically in the eye.

**4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE:**

- **Feverish Generalised Erythema**

  The occurrence at the treatment initiation of a feverish generalised erythema associated with pustules may be a symptom of acute generalised exanthematous pustulosis (AGEP) (see section 4.8). In case of AGEP diagnosis, flucloxacillin should be discontinued and any subsequent administration of flucloxacillin contraindicated.

- **Impaired Renal Function**

  The use of flucloxacillin (like other penicillins) in patients with renal impairment does not usually require dosage reduction. In the presence of severe renal failure (creatinine clearance less than 10 mL/min), however, a reduction in dose or an extension of dose interval should be considered because of the risk of neurotoxicity.

- **Patients on Dialysis**

  Flucloxacillin is not significantly removed by dialysis and so no supplementary dosages need to be administered either during or at the end of the dialysis period.

- **Previous hypersensitivity reactions to β-lactams**

  Before initiating therapy with flucloxacillin, attention should be paid to possible cross-sensitivity with other p-lactam antibiotics e.g. Cephalosporins. Cross-sensitivity between penicillins and cephalosporins is well documented. Serious and occasionally fatal

hypersensitivity reactions (anaphylaxis) have been reported in patients receiving β-lactam antibiotics. Although anaphylaxis is more frequent following parenteral therapy, it has occurred in patients on oral therapy. These reactions are more likely to occur in individuals with a history of β-lactam hypersensitivity.

If anaphylaxis occurs flucloxacillin should be discontinued and the appropriate therapy instituted. Serious anaphylactic reactions may require immediate emergency treatment with adrenaline (epinephrine). Ensure adequate airway and ventilation and give 100 % oxygen. IV crystalloids, hydrocortisone, antihistamine, and nebulised bronchodilators may also be required.

- **Patients taking Paracetamol**

  Caution is advised when flucloxacillin is administered concomitantly with paracetamol due to the increased risk of high anion gap metabolic acidosis (HAGMA). Patients at high risk of HAGMA are in particular those with severe renal impairment, sepsis, or malnutrition especially if the maximum daily doses of paracetamol are used.

  After co-administration of flucloxacillin and paracetamol, a close monitoring is recommended in order to detect the appearance of acid-base disorders, namely HAGMA, including the search of urinary 5-oxoproline.

  If flucloxacillin is continued after cessation of paracetamol, it is advisable to ensure that there are no signals of HAGMA, as there is a possibility of flucloxacillin maintaining the clinical picture of HAGMA (see section 4.5).

- **Newborns**

  Special caution is essential in the newborn because of the risk of hyperbilirubinaemia. Studies have shown that, at high dose following parenteral administration, flucloxacillin can

displace bilirubin from plasma protein binding sites, and may therefore predispose to kernicterus in a jaundiced baby. In addition, special caution is essential in the newborn because of the potential for high serum levels of flucloxacillin due to a reduced rate of renal excretion.

During prolonged treatments (e.g. osteomyelitis, endocarditis), regular monitoring of hepatic and renal functions is recommended.

- **Impaired Hepatic Function**

Hepatitis and cholestatic jaundice have been reported. These reactions are related neither to the dose nor to the route of administration. Flucloxacillin should be used with caution in patients with evidence of hepatic dysfunction, patients > 50 years or patients with underlying disease all of whom are at increased risk of hepatic reactions. The onset of these hepatic effects may be delayed for up to two months post-treatment. In several cases, the course of the reactions has been protracted and lasted for some months. In very rare cases, a fatal outcome has been reported (see section 4.8).

As for other penicillins contact with the skin should be avoided as sensitisation may occur. Patients with a known history of allergy are more likely to develop a hypersensitivity reaction.

Prolonged use of an anti-infective agent may occasionally result in overgrowth of non-susceptible organisms. Gastro-intestinal upsets (e.g. nausea, colic, diarrhoea) have been reported. As with other penicillins, pseudomembranous colitis has been reported.

## 4.5 INTERACTION WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTION

- Probenecid and sulfinpyrazone slow down the excretion of flucloxacillin by decreasing tubular secretion.

- Other drugs, such as piperacillin, which are excreted via renal tubular secretion, may interfere with flucloxacillin elimination.
- Oral typhoid vaccine may be inactivated by flucloxacillin.
- Flucloxacillin reduces the excretion of methotrexate which can cause methotrexate toxicity.
- Flucloxacillin may reduce the response to sugammadex.
- There are cases of altered international normalised ratio (INR) in patients taking warfarin and prescribed a course of flucloxacillin. If co-administration is necessary, the prothrombin time or international normalised ratio should be carefully monitored during addition or withdrawal of flucloxacillin.
- Bacteriostatic drugs may interfere with the bactericidal action of flucloxacillin.
- Caution should be taken when flucloxacillin is used concomitantly with paracetamol as concurrent intake has been associated with high anion gap metabolic acidosis, especially in patients with risk factors. (See section 4.4.)
- Flucloxacillin causes subtherapeutic levels of Voriconazole.

## 4.6 FERTILITY, PREGNANCY AND LACTATION

### Pregnancy

Safety and efficacy has not been established in pregnant women taking **SEPTAPEN 250**.

**SEPTAPEN 250** should not be used by pregnant women.

### Breastfeeding

Safety and efficacy has not been established in women who are breastfeeding and taking **SEPTAPEN 250**. **SEPTAPEN 250** should not be used by women who are breastfeeding.

## 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. Patients should be instructed that if they experience sedation or dizziness, they should avoid potentially hazardous tasks such as driving or operating machinery.

## 4.8 UNDESIRABLE EFFECTS

| System organ class | Frequent | Less frequent | Frequency Unknown |
|---|---|---|---|
| **Blood and lymphatic system disorders** | | Neutropenia (including agranulocytosis) and thrombocytopenia. These are reversible when treatment is discontinued. Eosinophilia, haemolytic anaemia. | |
| **Immune system disorders** | | Angioedema, anaphylactic shock (exceptional with oral administration) (see Section 4.4), angioneurotic oedema. If any hypersensitivity reaction occurs, the treatment should be discontinued. (See also | |

| | | | |
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| | | Skin and subcutaneous tissue disorders). | |
| **Metabolism and nutrition disorders** | | Very rare case of high anion gap metabolic acidosis, when flucloxacillin is used concomitantly with paracetamol, generally in the presence of risk factors (see section 4.4.) | |
| **Gastrointestinal disorders** | Minor gastrointestinal disturbances. | | |
| **Hepatobiliary disorders** | | Hepatitis and cholestatic jaundice.<br>(See Section 4.4).<br>Changes in liver function laboratory test results (reversible when treatment is discontinued).These reactions are related neither to the dose nor to | |

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|---|---|---|---|---|
| | | the route of administration.<br>Hepatitis and cholestatic jaundice may be delayed for up to two months post-treatment; in several cases the course of the reactions has been protracted and lasted for some months. Hepatic events may be severe and in very rare circumstances a fatal outcome has been reported. Most reports of deaths have been in patients ≥50 years and inpatients with serious underlying disease.<br>There is evidence that the risk of flucloxacillin induced liver injury is increased in subjects carrying the HLA - | | |

| | | | |
|---|---|---|---|
| | | B*5701allele. Despite this strong association, only 1 in 500-1000 carriers will develop liver injury. Consequently, the positive predictive value of testing the HLA-B*5701 allele for liver injury is very low (0.12%) and routine screening for this allele is not recommended. | |
| **Skin and subcutaneous tissue disorders** | | Rash, urticaria and purpura.<br>Erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis.<br>(See also Immune system disorders). | AGEP – acute generalized exanthematous pustulosis (see section 4.4) |
| **Musculoskeletal and connective tissue disorders** | | Arthralgia and myalgia sometimes develop more than 48 hours after the start of the treatment. | |

| | | | |
|---|---|---|---|
| **Renal and urinary disorders** | | Interstitial nephritis. This is reversible when treatment is discontinued. | |
| **General disorders and administration site conditions** | | Fever sometimes develops more than 48 hours after the start of the treatment. | |

**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. Healthcare professionals are asked to report any suspected adverse reactions to SAHPRA via the "6.04 Adverse Drug Reaction Reporting Form", found online under SAHPRA's publications:

https://www.sahpra.org.za/Publications/Index/8

**4.9 OVERDOSE**

If encountered, gastro-intestinal symptoms and disturbances of the fluid and electrolyte balance may be evident. They may be treated symptomatically with attention to the water/electrolyte balance. Flucloxacillin cannot be removed from the circulation by haemodialysis.

**5. PHARMACOLOGICAL PROPERTIES**

**5.1 PHARMACODYNAMIC PROPERTIES**

Pharmacological Classification/ Category and Class: A 20.1.2 Penicillin

Flucloxacillin is a semi-synthetic, penicillinase-stable penicillin derived from 6-amino-penicillanic acid.

**Bacteriology**

Flucloxacillin exhibits bacterial activity against all Gram-positive organisms (with the exception of Strep. faecalis) e.g. haemolytic streptococci, staphylococci, Streptococcus pneumoniae and N. gonorrhoeae.

Flucloxacillin anti-staphylococcal activity is not affected by penicillinase and as Flucloxacillin is active against virtually all strains of Staph. aureus (methicillin-resistant strains being the only exception), it is primarily indicated in the treatment of staphylococcal infections.

The minimum inhibitory concentrations of benzylpenicillin against staphylococci are lower than those of flucloxacillin except in the case of the penicillinase- producing staphylococci.

***Resistant organisms***

Group D (Enterococcus faecalis) staphylococci

Methicillin-resistant staphylococci

**5.2 Pharmacokinetic properties**

**Absorption**

Flucloxacillin is very well absorbed orally. A single 250 mg oral dose achieves an average peak serum level virtually equal to that achieved by an equivalent IM injection. The peak serum level is achieved half to one hour after administration.

Flucloxacillin should be taken 1 hour before meals to ensure that maximum absorption is achieved.

**Excretion**

Approximately 60% of an oral dose and 90% of an intramuscular and intravenous dose of Flucloxacillin is excreted unchanged in the active form into the urine within 6 hours.

**Probenecid**

Even higher Flucloxacillin serum levels may be achieved after oral administration in patients with normal renal function by the simultaneous administration of a renal blocking agent such as probenecid. Probenecid should not be given in the presence of abnormal renal function.

**5.3 PRECLINICAL SAFETY DATA**

Not available.

**6. PHARMACEUTICAL PARTICULARS**

**6.1 LIST OF EXCIPIENTS**

Magnesium stearate.

*Size 2 black/red hard gelatine capsule components:*

Black oxide, erythrosine, gelatine, red oxide, titanium dioxide

**6.2 INCOMPATIBILITIES**

N/A

**6.3 SHELF LIFE**

HDPE containers: 24 months

PRP pouches: 15 months from packing

**6.4 SPECIAL PRECAUTIONS FOR STORAGE**

Store at or below 25 ºC.

Store in the original container. Keep tightly closed.

Keep out of the sight and reach of children.

**6.5 NATURE AND CONTENTS OF CONTAINER**

Amber glass bottles containing 20 or 100 capsules.

20's, 40's and 100's printed Alu/LDPE patient ready packs.

PP or HDPE Securitainers containing 20 or 100 capsules.

Not all pack sizes may be marketed.

**6.6 SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING**

No special requirements.

**7. HOLDER OF CERTIFICATE OF REGISTRATION**

Innovata Pharmaceuticals (Pty) Ltd

Crownwood Office Park,

Block D, Ground floor

100 Northern Parkway

Ormonde

Johannesburg

2091

**8. REGISTRATION NUMBER**

A 29/20.1.2/0550

**9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

08 February 1999

**10. DATE OF REVISION OF THE TEXT**

09/05/2024

**SKEDULERINGSTATUS:**

S4

## 1. NAAM VAN DIE MEDISYNE

**SEPTAPEN 250** (Kapsules)

## 2. KWALITATIEWE EN KWANTITATIEWE SAMESTELLING:

**SEPTAPEN 250**

Elke harde gelatien kapsule bevat flukloksasillien natrium ekwivalent aan 250 mg flukloksasillien.

Suiker-vry.

Vir die volledige lys van eksipiënte, sien afdeling 6.1.

## 3. FARMASEUTIESE VORM

**SEPTAPEN 250** kapsules is swart/rooi grootte “2” harde gelatien kapsules.

## 4. KLINIESE BESONDERHEDE

### 4.1 TERAPEUTIESE INDIKASIES:

Infeksies veroorsaak deur gevoelige gram-positiewe organismes, insluitend beta-laktamase produserende stafilokokke en streptokokke:

- Vel- en sagte weefselinfeksies
- Besmette wonde en brandwonde
- Otitis media
- Urienweginfeksies
- Lugweginfeksies veroorsaak deur penisillinase-produserende organismes.
- Ortopediese infeksies

- Septisemie
- Meningitis
- Endokarditis
- Enterokolitis

**4.2 POSOLOGIE EN METODE VAN TOEDIENING**

**Posologie**

**Volwassenes**

Die gewone volwasse dosis is 1 kapsule wat 4 keer per dag geneem word, verkieslik 1 uur voor maaltye.

**Ernstige infeksies**

Tot 8 g per dag in verdeelde doserings, ses tot agt uurliks, een uur voor maaltye vir endokarditis, osteomiëlitis, vel- en sagte weefsel-infeksies.

**Spesiale bevolkings**

*Renale inkorting:*

Vir pasiënte met ‘n kreatinien-opruiming waarde < 10 mL / min, oorweeg ‘n dosisafname of verlenging van doseringsinterval. Vir pasiënte met ‘n kreatinien-opruiming waarde > 10 mL / min is geen doseringsaanpassing nodig nie.

*Pediatriese bevolking*

**SEPTAPEN 250** is aangedui vir volwassenes en moet nie voorgeskryf word vir kinders nie.

Veiligheid en effektiwiteit is nog nie vasgestel by kinders nie.

**Metode van toediening**

Moet geneem word een uur voor maaltye.

**4.3 KONTRA-INDIKASIES:**

- Hipersensitiwiteit vir flukloksasillien natrium of ander beta-laktam antibiotika (bv. penisilliene, kefalosporiene) of vir enige van die eksipiënte aangedui in afdeling 6.1. Flukloksasillien is teenaangedui by pasiënte met ‘n vorige geskiedenis van flukloksasillien-geassosieerde geelsug / hepatiese disfunksie.
- Moenie topikaal in die oë gebruik word nie.

**4.4 SPESIALE WAARSKUWINGS EN VOORSORGMAATREËLS VIR GEBRUIK:**

- **Koorsagtige Algemene Eriteem**

  Die voorkoms aan die begin van behandeling van ‘n koorsagtige algemene eriteem geassosieer met pustules kan ‘n simptoom wees van akute algemene eksantemateuse pustulose (AGEP) (sien afdeling 4.8). Ingeval van AGEP diagnose, moet flukloksasillien onttrek word en enige daaropvolgende toediening van fluklosasillien is teenaangedui.

- **Ingekorte Renale Funksie**

  Die gebruik van flukloksasillien (soos ander penisilliene) by pasiënte met renale inkorting vereis nie gewoonlik doseringsafname nie. In die teenwoordigheid van ernstige nierversaking (kreatinienopruiming van minder as 10 mL/min), maar ‘n afname in dosis of ‘n verlenging van doseringsinterval moet oorweeg word, weens die risiko van neurotoksisiteit.

- **Pasiënte op Dialise**

  Flukloksasillien word nie beduidend verwyder deur dialise nie en dus word geen aanvullende doserings benodig om toegedien te word gedurende of aan die einde van die dialise periode nie.

- **Vorige hipersensitiwiteitsreaksies tot β-laktams**

  Voor begin van terapie met flukloksasillien moet aandag gegee word aan moontlik kruis-sensitiwiteit met ander p-laktam antibiotika bv. kefalosporiene. Kruis-sensitiwiteit tussen

penisilliene en kefalosporiene is goed gedokumenteer. Ernstige en soms noodlottige hipersensitiewe reaksies (anafilakse) is gerapporteer by pasiënte wat β-laktam antibiotika ontvang. Alhoewel anafilakse meer dikwels voorkom na parenterale terapie, het dit voorgekom by pasiënte op orale terapie. Hierdie reaksies kom waarskynlik meer dikwels voor by individue met ‘n geskiedenis van β-laktam hipersensitiwiteit.

Indien anafilakse voorkom, moet flukloksasillien onttrek word en die toepaslike terapie ingestel word. Ernstige anafilaktiese reaksies kan onmiddellike nood-behandeling vereis met adrenalien (epinefrien). Maak seker van voldoende lugweg en ventilasie en dien 100 % suurstof toe. IV kristalloïede, hidrokortisoon, antihistamien en genebuliseerde brongodilators kan ook nodig wees.

- **Pasiënte wat Parasetamol neem**

  Omsigtigheid word aanbeveel wanneer flukloksasillien toegedien word saam met parasetamol weens die verhoogde risiko van hoë anion gap metaboliese asidose asidose (HAGMA). Pasiënte wat ‘n hoë risiko van HAGMA het, is dié in besonder met ernstige renale inkorting, sepsis, of wanvoeding, veral indien die maksimum daaglikse doserings van parasetamol gebruik was.

  Na meegaande toediening van flukloksasillien en parasetamol, word ‘n noukeurige monitering aanbeveel om die voorkoms van suur-basis afwykings te bespeur, naamlik HAGMA, insluitend die naspeur van urinêre 5-oksoprolien.

  Indien daar met flukloksasillien voortgegaan word na die staak van parasetamol, word dit aanbeveel om seker te maak dat daar geen tekens is van HAGMA nie, omdat daar ‘n moontlikheid is dat fluklosasillien die kliniese beskrywing van HAGMA behou (sien afdeling 4.5).

- **Pasgeborenes**

  Spesiale omsigtigheid is belangrik by pasgeborenes weens die risiko van hiperbilirubinemie. Studies het gewys dat by hoë doserings van parenterale toediening, kan flukloksasillien die bilirubien verplaas vanaf plasmaproteïen-binding situs en kan dus geneig wees tot kernikterus in ‘n geelsug baba. Addisioneel, is omsigtigheid nodig by die pasgeborene weens die potensiaal vir hoë serumvlakke van flukloksasillien weens ‘n afname in tempo van renale ekskresie.

  Gedurende verlengde behandelings (bv. osteomiëlitis, endokarditis), word gereëlde monitering van hepatiese en renale funksies aanbeveel.

- **Belemmerde Hepatiese Funksie**

  Hepatitis en cholestatiese geelsug is gerapporteer. Hierdie reaksies is nòg verwant aan die dosering nòg aan die roete van toediening. Flukloksasillien moet omsigtig gebruik word by pasiënte met bewys van hepatiese disfunksie, pasiënte > 50 jaar of pasiënte met onderliggende siekte, alles met ‘n toename in risiko van hepatiese reaksies. Die aanvang van hierdie hepatiese effekte kan vertraag word vir tot twee maande na behandeling. In etlike gevalle was die verloop van die reaksies langdurig en het voortgeduur vir etlike maande. In baie rare gevalle was ‘n noodlottige uitkoms gerapporteer (sien afdeling 4.8).

  Soos met ander penisilliene moet kontak met die vel vermy word omdat oorgevoeligheid kan voorkom.

  Pasiënte met ‘n bekende geskiedenis van allergie is meer geneig om ‘n hipersensitiwiteitsreaksie te ontwikkel.

Verlengde gebruik van ‘n anti-infektiewe middel kan soms tot gevolg hê in oorgroei van nie-gevoelige organismes. Gastroïntestinale gevoeligheid (bv. naarheid, koliek, diarree) is gerapporteer. Soos met ander penisilliene is pseudomembraneuse kolitis gerapporteer.

## 4.5 INTERAKSIE MET ANDER MEDISYNES EN ANDER VORMS VAN INTERAKSIE

- Probenesied en sulfienpirasoon vertraag die ekskresie die flukloksasillien deur verminderde tubulêre sekresie.
- Ander medisynes, soos piperasillien, wat uitgeskei word deur renale tubulêre sekresie, kan inmeng met fluklosasillien eliminasie.
- Orale tifoïed vaksiene kan onaktief gemaak word deur flukloksasillien.
- Flukloksasillien verminder die ekskresie van metotreksaat wat metotreksaat-toksisiteit kan veroorsaak.
- Flukloksasillien kan die respons tot sugammedeks verminder.
- Daar is gevalle van veranderde “international normalised ratio (INR)” by pasiënte wat warfarien neem en ‘n kursus van flukloksasillien voorgeskryf word. Indien gesamentlike toediening nodig is, moet die protrombientyd of “international normalised ratio” omsigtig gemonitor word gedurende toevoeging of onttrekking van flukloksasillien.
- Bakteriostatiese medisynes kan inmeng met die bakterisidele werking van flukloksasillien.
- Omsigtigheid is nodig wanneer flukloksasillien gebruik word saam met parasetamol omdat meegaande inname geassosieer was met hoë anion gap metaboliese asidose, veral by pasiënte met risiko faktore. (Sien afdeling 4.4)
- Flukloksasillien veroorsaak subterapeutiese vlakke van vorikonasool.

## 4.6 FERTILITEIT, SWANGERSKAP EN LAKTASIE

### Swangerskap

Veiligheid en effektiwiteit is nog nie vasgestel by swanger vrouens wat **SEPTAPEN 250** neem nie.

**SEPTAPEN 250** moet nie gebruik word deur swanger vrouens nie.

### Borsvoeding

Veiligheid en effektiwiteit is nog nie vasgestel by vrouens wat borsvoed en **SEPTAPEN 250** neem nie. **SEPTAPEN 250** moet nie gebruik word by vrouens wat borsvoed nie.

## 4.7 EFFEKTE OP VERMOË OM TE BESTUUR EN MASJINERIE TE GEBRUIK

Geen studies omtrent die effekte op die vermoë om te bestuur en masjinerie te gebruik is gedoen nie. Pasiënte moet ingelig word dat indien hulle kalmering of duiseligheid ondervind, moet hulle potensiële gevaarlike take vermy soos bestuur of masjinerie te hanteer.

## 4.8 ONGEWENSTE EFFEKTE

| **Sisteem orgaan klas** | **Dikwels** | **Minder dikwels** | **Frekwensie onbekend** |
|---|---|---|---|
| **Bloed- en limfatiese sisteemafwykings** | | Neutropenie (insluitend agranulositose) en trombositopenie. Hierdie is omkeerbaar wanneer behandeling gestaak word. Esinofilie, hemolitiese anemie. | |

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| **Immuunstelsel-afwykings** | | Angio-edeem, anafilaktiese skok (behalwe met orale toediening) (sien afdeling 4.4), angioneurotiese edeem.<br>Indien enige hipersensitiwiteitsreaksie voorkom, moet die behandeling gestaak word. (Sien ook Vel- en subkutaneuse weefselafwykings). | | |
| **Metabolisme en voedingsafwykings** | | Baie rare gevalle van hoë anion gap metaboliese asidose, wanneer flukloksasillien gebruik word saam met parasetamol, gewoonlik in die teenwoordigeid van risiko faktore (sien afdeling 4.4.) | | |

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| **Gastroïntestinale afwykings** | Mindere gastroïntestinale versteurings. | | |
| **Hepatobiliêre afwykings** | | Hepatitis en cholestatiese geelsug.<br>(Sien afdeling 4.4).<br>Veranderinge in lewerfunksie laboratorium toets resultate (omkeerbaar wanneer behandeling gestaak word). Hierdie reaksies is nie verwant aan die dosis of die roete van toediening nie.<br>Hepatitis en cholestatiese geelsug kan vertraag word tot twee maande na behandeling; in etlike gevalle was die koers van die reaksies verleng en het aangehou vir sommige vir sommige | |

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| | | maande. Hepatiese voorvalle kan ernstig wees en kan in baie rare omstandighede was noodlottige voorkoms gerapporteer. Die meeste verslae van sterftes was by pasiënte ≥ 50 jaar en by pasiënte met ernstige onderliggende siekte. Daar is bewys dat die risiko van flukloksasillien-geïnduseerde lewerskade toeneem by dié pasiënte met die HLA - B*5701allele. Ten spyte van hierdie sterk assosiasie, sal slegs 1 in 500-1000 draers lewerskade ontwikkel. Konsekwent is die positiewe voorspelbare waarde van toets van die | | |

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|---|---|---|---|
| | | HLA-B*5701 allele vir lewerskade baie laag (0.12 %) en roetine keuring vir hierdie allele word nie aanbeveel nie. | |
| **Vel- en subkutaneuse weefselafwykings** | | Uitslag, urtikarie en purpura.<br>Erythema multiforme, Stevens-Johnson se sindroom en toksiese epidermale nekrolise.<br>(Sien ook Immuunstelsel-afwykings). | AGEP – akute algemene eksantemateuse algemene pustulose (sien afdeling 4.4) |
| **Muskuloskeletale en bindweefsel-afwykings** | | Artralgie en mialgie ontwikkel soms meer as 48 uur na die begin van behandeling. | |
| **Renale en urinêre afwykings** | | Interstisiële nefritis. Dit is omkeerbaar wanneer behandeling gestaak word. | |

| | | | |
|---|---|---|---|
| **Algemene afwykings en toediening situs toestande** | | Koors ontwikkel soms meer as 48 uur na die begin van behandeling. | |

**Rapporteer van vermoedelike ongunstige reaksies**

Rapporteer van vermoedelike ongunstige reaksies na goedkeuring van die medisyne is belangrik. Dit laat toe vir volgehoue monitering van die voordeel/risiko balans van die medisyne. Gesondheidsorg professionele persone word versoek om enige vermoedelike ongunstige reaksies te rapporteer aan SAHPRA via die “6.04 Adverse Drug Reaction Reporting Form”, wat aanlyn gevind word onder SAHPRA se publikasies: https://www.sahpra.org.za/Publications/Index/8

**4.9 OORDOSERING**

Indien dit voorkom kan gastroïntestinale simptome en versteurings van die vloeistof en elektroliet balans duideliker wees. Hulle kan simptomaties behandel word met oplettendheid tot die water/elektroliet balans. Fluklosasillien kan nie uit die sirkulasie verwyder word deur hemodialise nie.

**5. FARMAKOLOGIESE EIENSKAPPE**

**5.1 FARMAKODINAMIESE EIENSKAPPE**

Farmakologiese Klassifikasie/ Kategorie en Klas: A 20.1.2 Penisilliene

Flukloksasillien is ‘n semi-sintetiese, penisillinase-stabiele penisillien afgelei van 6-amino-penisillanase suur.

**Bakteriologie**

Flukloksasillien wys bakteriële aktiwiteit teen alle Gram-positiewe organismes (met die uitsondering van *Strep. faecalis*) bv. hemolitiese streptokokke, stafilokokke, *Streptococcus pneumoniae* en *N. gonorrhoeae.*

Flukloksasillien anti-stafilokokkale aktiwiteit word nie beïnvloed deur penisillinase nie en omdat flukloksasillien aktief is teen amper alle soorte van *Staph. aureus* (metisillien-weerstandige soorte wat die enigste uitsondering is), word dit hoofsaaklik aangedui by die behandeling van stafilokokkale infeksies.

Die minimum inhiberende konsentrasies van bensielpenisillien teen stafilokokke is laer as die van flukloksasillien behalwe in die geval van die penisillinase-produserende stafilokokke.

***Weerstandige organismes***

Groep D (*Enterococcus faecalis*) stafilokokke

Metisillien-weerstandige stafilokokke

**5.2 Farmakokinetiese eienskappe**

**Absorpsie**

Flukloksasillien word oraal goed geabsorbeer. ‘n Enkel 250 mg orale dosis bereik ‘n gemiddelde piek serumvlak virtueel gelyk aan die wat bereik word deur ‘n ekwivalente IM-inspuiting. Die piek serumvlak word bereik ‘n half tot een uur na toediening.

Flukloksasillien moet geneem word 1 uur voor maaltye om seker te maak dat die maksimum absorpsie bereik word.

**Ekskresie**

Ongeveer 60 % van ‘n orale dosis en 90 % van ‘n intramuskulêre en intraveneuse dosering van flukloksasillien word onveranderd uitgeskei in die aktiewe vorm in die uriene binne 6 ure.

**Probenesied**

Selfs hoër flukloksasillien serumvlakke kan bereik word na orale toediening by pasiënte met normale nierfunksie deur die gelyktydige toediening van ‘n renaal blokker-middel soos probenesied. Probenesied moet nie toegedien word in die teenwoordigheid van abnormale nierfunksie nie.

**5.3 VOORKLINIESE VEILIGHEIDSDATA**

Nie beskikbaar nie.

**6. FARMASEUTIESE BESONDERHEDE**

**6.1 LYS VAN EKSIPIËNTE**

Magnesiumstearaat.

*Grootte 2 swart/rooi harde gelatien kapsule komponente:*

Swart oksied, eritrosien, gelatien, rooi oksied, titaniumdioksied.

**6.2 ONVERENIGBAARHEDE**

N/A

**6.3 RAAKLEEFTYD**

HDPE houers: 24 maande

PRP sakkies: 15 maande vanaf verpakking

**6.4 SPESIALE VOORSORGMAATREËLS VIR BERGING**

Berg by of benede 25 ºC.

Berg in die oorspronklike houer. Hou dig toe.

Hou buite die sig en bereik van kinders.

**6.5 AARD EN INHOUD VAN HOUERS**

Bruin glas bottels bevattende 20 of 100 kapsules.

20's, 40's en 100's gedrukte Alu/LDPE pasiënt-gereed pakkies.

PP of HDPE Securitainers bevattende 20 of 100 kapsules.

Nie alle pakgroottes mag bemark word nie.

**6.6 SPESIALE VOORSORGMAATREËLS VIR WEGGOOI EN ANDER HANTERING**

Geen spesiale vereistes nie.

**7. HOUER VAN SERTIFIKAAT VAN REGISTRASIE**

Innovata Pharmaceuticals (Pty) Ltd

Crownwood Office Park,

Block D, Ground floor

100 Northern Parkway

Ormonde

Johannesburg

2091

**8. REGISTRASIENOMMER**

A 29/20.1.2/0550

**9. DATUM VAN EERSTE GOEDKEURING/HERNUWING VAN DIE GOEDKEURING**

08 Februarie 1999

**10. DATUM VAN REVISIE VAN DIE TEKS**

09/05/2024