SCHEDULING STATUS

S4

PROPRIETARY NAME (AND DOSAGE FORM)

FLUCLOXACILLIN 250mg OETHMAAN (Capsule)

COMPOSITION

Each capsule contains flucloxacillin sodium equivalent to 250 mg flucloxacillin.
Sugar free.
Excipients: Colloidal anhydrous silica, gelatine, iron oxide black, iron oxide red, iron oxide yellow, magnesium stearate and titanium dioxide.

PHARMACOLOGICAL CLASSIFICATION

A 20.1.2 Penicillins

PHARMACOLOGICAL ACTION

Pharmacodynamic properties:

Flucloxacillin is a semi-synthetic isoxazolyl penicillin which is resistant to hydrolysis by staphylococcal penicillinase. Flucloxacillin exhibits bactericidal activity against Gram-positive organisms, particularly penicillinase producing strains of *Staphylococcus aureus*.

Pharmacokinetic properties:

Absorption: Flucloxacillin is rapidly but incompletely absorbed from the gastrointestinal tract. 30 – 50 % is absorbed and a peak serum concentration of 6 - 10 mcg/ml is attained 1 hour after administration of a 250 mg oral dose. Absorption is more efficient when flucloxacillin is taken on an empty stomach and should preferably be administered one hour before or two hours after meals to ensure better absorption. 94 % of flucloxacillin is plasma protein bound.

Elimination: 50 – 65 % of flucloxacillin is excreted unchanged by the kidney in the first six hours after a conventional oral dose. The half-life of flucloxacillin is 0,7 – 1,3 hours when creatinine clearance is > 50 ml/min.

INDICATIONS

FLUCLOXACILLIN 250mg OETHMAAN is indicated for the treatment of infections caused by penicillinase producing staphylococci.

CONTRAINDICATIONS

FLUCLOXACILLIN 250mg OETHMAAN is contraindicated in patients with hypersensitivity to penicillins, any other beta-lactam antibiotics, or any of the capsule ingredients.

WARNINGS AND SPECIAL PRECAUTIONS

Before initiating therapy with FLUCLOXACILLIN 250mg OETHMAAN, careful enquiry should be made concerning previous hypersensitivity reactions with beta-lactam antibiotics (see **"CONTRAINDICATIONS"**).

FLUCLOXACILLIN 250mg OETHMAAN is associated rarely with an increased risk of hepatitis and cholestatic jaundice. In some patients, almost always those with serious underlying hepatic disease, fatalities have occurred. The onset of hepatic adverse effects may be delayed for up to 2 months after stopping treatment, and is not related to the dose or to the route. Older patients and those receiving treatment for more than 2 weeks are at increased risk. FLUCLOXACILLIN 250mg OETHMAAN should not be used in patients with a history of hepatic dysfunction related to its use, and should be used only with caution in patients with evidence of other hepatic impairment.

FLUCLOXACILLIN 250mg OETHMAAN has been associated with acute attacks of porphyria and is considered unsafe in porphyric patients.

Special precautions:

FLUCLOXACILLIN 250mg OETHMAAN should be used with caution in patients with a known history of allergies.

The use of this antibiotic may lead to the appearance of resistant strains of organisms, and sensitivity testing should therefore be carried out whenever possible to ensure the appropriateness of the therapy.

Effects on ability to drive and use machines:

Adverse effects on the ability to drive or operate machinery have not been observed.

INTERACTIONS

Concurrent use of other hepatotoxic medicines with FLUCLOXACILLIN 250mg OETHMAAN may increase the potential for hepatotoxicity.

Probenecid decreases the renal tubular secretion of penicillins when used concurrently. This effect results in increased and prolonged serum concentrations, prolonged elimination half-life, and increased risk of toxicity.

PREGNANCY AND LACTATION

Pregnancy:

The safety of FLUCLOXACILLIN 250mg OETHMAAN for use in human pregnancy has not been established. FLUCLOXACILLIN 250mg OETHMAAN should be used in pregnancy only if the potential benefit outweighs the risk to the foetus.

Lactation:

FLUCLOXACILLIN 250mg OETHMAAN is distributed into human breast milk. Although significant problems have not been documented, the use of FLUCLOXACILLIN 250mg OETHMAAN by nursing mothers may lead to sensitisation, diarrhoea, candidiasis and skin rash in the infant.

DOSAGE AND DIRECTIONS FOR USE

Usual adult dose:

250 mg every six hours, one hour before meals.

Patients with renal impairment:

Patients with impaired renal function do not generally require a reduction in dose unless the impairment is severe.

SIDE EFFECTS

The following side effects have been reported:

Infections and infestations:

More frequent: Oral candidiasis, vaginal candidiasis.

Blood and lymphatic system disorders:

The following side effects have been reported but their frequencies are unknown: Agranulocytosis, leukopenia or neutropenia.

Immune system disorders:

Less frequent: Anaphylaxis, allergic reactions presenting as a pruritic skin rash, an erythematous skin reaction or urticaria, fever, eosinophilia, joint pains, angioneurotic oedema, or exfoliative dermatitis.

Should an allergic or anaphylactic reaction occur, FLUCLOXACILLIN 250mg OETHMAAN should be discontinued and the appropriate treatment instituted.

The following side effects have been reported but their frequencies are unknown: Erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis.

Metabolism and nutrition disorders:

The following side effects have been reported but their frequencies are unknown: Disturbances of electrolyte balance. Acute attacks of porphyria (see **"WARNINGS AND SPECIAL PRECAUTIONS"**).

Nervous system disorders:

More frequent: Headache.

The following side effect has been reported but its frequency is unknown: Seizures.

Gastrointestinal disorders:

More frequent: Diarrhoea, nausea, vomiting.

The following side effects have been reported but their frequencies are unknown: Heartburn, colic, pruritus ani, *Clostridium difficile* colitis.

Hepato-biliary disorders:

The following side effects have been reported but their frequencies are unknown: Hepatotoxicity, hepatitis and cholestatic jaundice (see **"WARNINGS AND SPECIAL PRECAUTIONS"**).

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

Treatment is symptomatic and supportive. FLUCLOXACILLIN 250mg OETHMAAN is not removed from the circulation to a significant degree by hemodialysis.

IDENTIFICATION

Size 2, caramel and black coloured hard gelatin capsule filled with white to almost white granular powder.

PRESENTATION

20, 28 and 40 capsules packed in opaque white PVC/silver aluminium foil blister strips packed in cardboard cartons.
20 and 40 capsules packed in aluminium laminated Patient-Ready-Packs (PRP) pouch.
100 capsules packed in securitainers.

STORAGE INSTRUCTIONS

Store in a dry place, at or below 25 °C.
Do not remove the blister from the carton until required for use.
KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER

44/20.1.2/0816

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

Oethmaan Biosims (Pty) Ltd
14 Komatie Road
Emmarentia
Johannesburg, 2195

DATE OF PUBLICATION OF THE PACKAGE INSERT

Date of registration: 06 March 2014

SKEDULERINGSTATUS

S4

EIENDOMSNAAM (EN DOSEERVORM)

FLUCLOXACILLIN 250mg OETHMAAN (Kapsule)

SAMESTELLING

Elke kapsule bevat natriumflukloksasillien ekwivalent aan 250 mg flukloksasillien.
Suikervry.
Ander bestanddele is: Kolloïdale anhidriese silika, gelatien, swart ysteroksied, rooi ysteroksied, geel ysteroksied, magnesiumstearaat en titaniumdioksied.

FARMAKOLOGIESE KLASSIFIKASIE

A 20.1.2 Penisilliene

FARMAKOLOGIESE WERKING

Farmakodinamiese eienskappe:

Flukloksasillien is 'n semi-sintetiese isoksazoliel penisillien wat weerstandig is teen hidrolise van stafilokokkale penisillinase. Flukloksasillien openbaar bakteriedodende aktiwiteit teenoor Gram-positieve organismes, veral penisillinase produserende stamme van *Staphylococcus aureus*.

Farmakokinetiese eienskappe:

Absorpsie: Flukloksasillien word vinnig, maar onvolledig uit die gastro-intestinale kanaal geabsorbeer. 30 – 50 % word geabsorbeer en piek serumkonsentrasies van 6 - 10 mcg/ml word 1 uur na toediening van 'n 250 mg mondelikse dosis bereik. Absorpsie is meer effektief wanneer flukloksasillien op 'n leë maag geneem word en moet verkieslik 'n uur voor of twee ure na 'n maaltyd geneem word om beter absorpsie te verseker. 94 % van flukloksasillien is plasmaproteïengebonde.

Eliminasie: 50 – 65 % flukloksasillien word onveranderd in die eerste ses ure na 'n konvensionele mondelikse dosis deur die niere uitgeskei. Die halfleeftyd van flukloksasillien is 0,7 – 1,3 uur wanneer kreatinienopruiming > 50 ml/min is.

INDIKASIES

FLUCLOXACILLIN 250mg OETHMAAN word aangedui vir die behandeling van infeksies wat veroorsaak word deur penisillinase produserende stafilokokki.

KONTRA-INDIKASIES

FLUCLOXACILLIN 250mg OETHMAAN is teenaagedui by pasiënte met 'n hipersensitiwiteit vir penisilliene, enige ander beta-laktaam antibiotika, of enige van die kapsule bestanddele.

WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS

Alvorens terapie met FLUCLOXACILLIN 250mg OETHMAAN geïnisieer word, moet versigtig ondersoek ingestel word rakende vorige hipersensitiwiteitsreaksies met beta-laktaam antibiotika (sien **"KONTRA-INDIKASIES"**).

FLUCLOXACILLIN 250mg OETHMAAN word selde met 'n verhoogde risiko van hepatitis en cholestatiese geelsug geassosieer. In sommige pasiënte, amper altyd die met ernstige onderliggende hepatiese siektes, het sterftes voorgekom. Die begin van hepatiese newe-effekte mag tot 2 maande nadat behandeling gestaak is, vertraag wees en dit is nie verwant aan die dosis of die toedieningsroete nie. Ouer pasiënte en die wat behandeling vir langer as twee weke ontvang, is 'n verhoogde risiko. FLUCLOXACILLIN 250mg OETHMAAN moet nie by pasiënte met 'n geskiedenis van hepatiese disfunksie gebruik word wat verband hou met die gebruik daarvan nie, en moet slegs met versigtigheid gebruik word by pasiënte met bewys van ander hepatiese inkorting.

FLUCLOXACILLIN 250mg OETHMAAN is geassosieer met akute aanvalle van porfirie en word as onveilig geag in pasiënte met porfirie.

Spesiale voorsorgmaatreëls:

FLUCLOXACILLIN 250mg OETHMAAN moet met versigtigheid by pasiënte met 'n geskiedenis van allergieë gebruik word.

Die gebruik van hierdie antibiotika mag tot die verskyning van weerstandige stamme van organismes lei, en sensitiwiteitstoetse moet dus uitgevoer word wanneer nodig om die toepaslikheid van die behandeling te verseker.

Uitwerking op vermoë om motor te bestuur en masjinerie te gebruik:

Nadelige uitwerking op die vermoë om te bestuur of masjinerie te gebruik is nog nie waargeneem nie.

INTERAKSIES

Die potensiaal vir hepatotoksisiteit mag verhoog met die gelyktydige gebruik van ander hepatotoksiese medisyne saam met FLUCLOXACILLIN 250mg OETHMAAN.

Probenesied verminder die renale tubulêre sekresie van penisilliene met gelyktydige gebruik. Hierdie effek lei tot verhoogde en verlengde serumkonsentrasies, verlengde eliminasie halfleeftyd, en verhoogde toksisiteitsrisiko.

SWANGERSKAP EN LAKTASIE

Swangerskap:

Veiligheid van FLUCLOXACILLIN 250mg OETHMAAN in menslike swangerskap is nog nie bevestig nie. FLUCLOXACILLIN 250mg OETHMAAN moet net tydens swangerskap gebruik word indien die potensiële voordeel die risiko aan die fetus oortref.

Laktasie:

FLUCLOXACILLIN 250mg OETHMAAN word in menslike borsmelk uitgeskei. Alhoewel beduidende probleme nog nie gedokumenteer is nie, mag die gebruik van FLUCLOXACILLIN 250mg OETHMAAN deur vroue wat borsvoed, tot sensitisasie, diaree, kandidiase en veluitslag in die baba lei.

DOSIS EN GEBRUIKSAANWYSINGS

Gewone volwasse dosis:

250 mg elke ses ure, een uur voor maaltye.

Pasiënte met nierinkorting:

Pasiënte met ingekorte nierfunksie benodig nie gewoonlik 'n verlaagde dosis nie, tensy die inkorting ernstig is.

NEWE-EFFEKTE

Die volgende newe-effekte is aangemeld:

Infeksies en infestasies:

Meer dikwels: Orale kandidiase, vaginale kandidiase.

Bloed- en limfatiesestelsel versteurings:

Die volgende newe-effekte is aangemeld, maar die frekwensie is onbekend: Agranulositose, leukopenie of neutropenie.

Immuunstelselversteurings:

Minder dikwels: Anafilakse, allergiese reaksies in die vorm van 'n pruritiese veluitslag, 'n eritemateuse velreaksie of urtikarie, koors, eosinofilie, gewrigspyne, angioneurotiese edeem of eksfoliatiewe dermatitis.

In die geval van 'n allergiese of anafilaktiese reaksie moet FLUCLOXACILLIN 250mg OETHMAAN dadelik gestaak word en die nodige behandeling toegepas word.

Die volgende newe-effekte is aangemeld, maar die frekwensie is onbekend: Erythema multiforme, Stevens-Johnson sindroom, toksiese epidermale nekrolise.

Metabolisme en voedselversteurings:

Die volgende newe-effekte is aangemeld, maar die frekwensie is onbekend: Elektrolietbalans versteurings. Akute aanvalle van porfirie (sien **"WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS"**).

Senuweestelselversteurings:

Meer dikwels: Hoofpyn.

Die volgende newe-effekte is aangemeld, maar die frekwensie is onbekend: Stuipe.

Gastro-intestinale versteurings:

Meer dikwels: Diaree, naarheid, braking.

Die volgende newe-effekte is aangemeld, maar die frekwensie is onbekend: Sooibrand, koliek, pruritus ani, *Clostridium difficile kolitis.*

Hepatiese- en bilière versteurings:

Die volgende newe-effekte is aangemeld, maar die frekwensie is onbekend: Hepatotoksisiteit, hepatitis en cholestatiese geelsug (sien **"WAARSKUWINGS EN SPESIALE VOORSORG-MAATREËLS"**).

BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VIR DIE BEHANDELING DAARVAN

Behandeling is simptomaties en ondersteunend. FLUCLOXACILLIN 250mg OETHMAAN word nie tot 'n beduidende mate deur hemodialise uit die sirkulasie verwyder nie.

IDENTIFIKASIE

Grootte 2, karamel en swart gekleurde harde gelatienkapsule, gevul met wit tot amper wit granulêre poeier.

AANBIEDING

20, 28 en 40 kapsules verpak in ondeursigtige wit PVC/silwer aluminiumfoeliestulpstroke in kartonhouers.
20 en 40 kapsules verpak in aluminium-gelamineerde Pasiënt-Gereed-Pakke-sakkie.
100 kapsules verpak in securitainers.

BERGINGSAANWYSINGS

Bewaar in 'n droë plek, teen of benede 25 °C.
Moenie die stulpverpakking uit die karton verwyder voordat dit vir gebruik benodig word nie.
HOU BUITE BEREIK VAN KINDERS.

REGISTRASIENOMMER

44/20.1.2/0816

NAAM EN BESIGHEIDSADRES VAN DIE HOUER VAN DIE REGISTRASIESERTIFIKAAT

Oethmaan Biosims (Pty) Ltd
Komatieweg 14
Emmarentia, 2195

DATUM VAN PUBLIKASIE VAN HIERDIE VOUBILJET

Datum van registrasie: 06 Maart 2014