SCHEDULING STATUS:

S3

PROPRIETARY NAME (AND DOSAGE FORM):
Defulide 40 (Tablets)

COMPOSITION:
Each tablet contains 40 mg furosemide. Sugar free.

PHARMACOLOGICAL CLASSIFICATION:
A 18.1 - Diuretics.

PHARMACOLOGICAL ACTION:
Defulide 40 exerts its diuretic action by virtue of its saluretic properties. Experimental evidence has proved that furosemide acts by reducing the reabsorption of sodium and water at the levels of the proximal convoluted tubule, ascending limb of Henle's loop and the distal convoluted tubule. **Defulide 40** thus acts through the tubule, and it is today believed that the action of furosemide on the Loop of Henle is the most important action on the nephron. In situations where other methods of treatment fail to induce diuresis, it is often possible, with **Defulide 40,** to increase the excretion of sodium and water, even when the glomerular filtration rate is markedly impaired. **Defulide 40** lowers pathologically raised blood pressure levels, but does not affect normal values. With **Defulide 40** administration, the onset of action is rapid, usually within half-an-hour. Peak action is usually achieved after 2 hours, and the duration of action of the drug is 4 - 5 hours.

INDICATIONS:
a. Ascites due to cirrhosis of the liver, mechanical obstruction or cardiac failure.
b. To prevent oliguria from progressing to complete anuria.
c. Cardiac oedema.
d. Hypertension of mild to moderate degree.
e. Oedema occurring during the last three months of pregnancy - pre-eclamptic toxaemia and eclampsia. (See "**WARNINGS")**
f. Peripheral oedema due to mechanical obstruction or changes in the walls of the veins.

CONTRAINDICATIONS:
Patients who exhibit hypersensitivity to furosemide. In hepatic coma and in states of electrolyte depletion. **Defulide 40** is contraindicated if increasing azotaemia and oliguria occur during treatment of severe progressive renal disease. Lactating women.

WARNINGS:
During pregnancy, **Defulide 40** should be administered with great caution and only in carefully selected cases for short periods of time. Concomitant therapy with cephaloridine may result in nephrotoxicity.

DOSAGE AND DIRECTIONS FOR USE:
Adults Initial Dose: One to three tablets.
Maintenance: Half to one tablet daily.
Or: As prescribed by the physician.

SIDE EFFECTS AND SPECIAL PRECAUTIONS:
i) Various forms of dermatitis including urticaria and exfoliative dermatitis, pruritis, paraesthesia, blurring of vision, yellow vision, dizziness, pancreatitis, photosensitivity, postural hypotension, headache, nausea, vomiting or diarrhoea may occur.
ii) Anaemia, leucopenia, aplastic anaemia and thrombocytopenia (with purpura) may occur. Agranulocytosis has occurred.
iii) Asymptomatic hyperuricaemia can occur and gout may be precipitated.
iv) Alterations in glucose tolerance tests with abnormalities of the fasting and 2 hour post-prandial sugar have been observed, and cases of precipitation of diabetes mellitus have been reported.
v) **Defulide 40** may lower the serum calcium levels and cases of tetany have been reported.
vi) Excessive diuresis may result in dehydration and reduction in blood volume, with circulatory collapse and the possibility of vascular thrombosis and embolism, particularly in elderly patients. The excessive loss of potassium in patients receiving cardiac glycosides may precipitate digitalis toxicity. Care should be taken in patients receiving potassium depleting steroids.
vii) Electrolyte disturbance. Hypokalaemia may be reduced with a potassium-rich diet. If it already exists before the commencement of treatment which is particularly likely to occur in cases of cirrhosis - the serum potassium should be restored to normal by potassium supplements and, if necessary, by the administration of sodium and chloride. Because of its strong natriuretic effect, **Defulide 40** may cause a decrease in the sodium level, particularly when the oedema is corrected rapidly. Electrolyte depletion may manifest itself by weakness, dizziness, lethargy, leg cramps, anorexia, vomiting and/or mental confusion.

Hepatic dysfunction, cholestatic jaundice and paraesthesia have been reported. Tinnitus and deafness may occur in particular during rapid high-dose parenteral furosemide therapy. Deafness may be permanent particularly if furosemide has been given to patients taking ototoxic medication. **Defulide 40** increases the urinary excretion of calcium. Renal stone formation has been reported when furosemide has been used to treat preterm infants. It should be used with care in patients with prostatic hypertrophy or impairment of micturition. **Defulide 40** may enhance the nephrotoxicity of cephalosporin antibiotics such as cephalothin and of aminoglycoside antibiotics. It can also enhance the ototoxcity of aminoglycoside antibiotics. Concurrent administration of phenytoin or indomethacin may reduce the clinical effects of **Defulide 40. Defulide 40** should be used with caution in patients with impaired hepatic function since it may increase the risk of hepatic encephalopathy. It should be used with caution in patients with renal impairment. **Defulide 40** may enhance the toxicity of digitalis glycosides by depleting serum potassium concentrations. It may enhance the neuromuscular blocking action of competitive muscle relaxants, such as tubocurarine. It may enhance the effects of antihypertensive agents. The potassium depleting effect of furosemide may be enhanced by corticosteroids, corticotrophin, or carbenoxolone. Concomitant administration of **Defulide 40** and lithium is generally not recommended since the association may lead to toxic blood concentrations of lithium. Blood-glucose concentrations should be monitored in patients taking antidiabetic agents as requirements may change.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:
See **"SIDE EFFECTS"** above. Treatment is symptomatic and supportive.

IDENTIFICATION:
White to off-white, round, flat bisected tablets with bevelled edges.

PRESENTATION:
Securitainers containing 28, 30,100,250 or 500 tablets. PVC/PVDC/Aluminium blister packs containing strips of 28 or 30 tablets each in a unit carton.

STORAGE INSTRUCTIONS:
Store below 25 °C. Protect from light.
KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER:
Y/18.1/135

NAME AND BUSINESS ADDRESS OF HOLDER OF THE CERTIFICATE OF REGISTRATION:
Trinity Pharma (Pty) Ltd.
106 16th Road
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DATE OF PUBLICATION OF THIS PACKAGE INSERT:
31 August 1990

TRINITY PHARMA

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CIPPI_01/22

SKEDULERINGSTATUS:

S3

EIENDOMSNAAM (EN DOSEERVORM):
Defulide 40 (Tablette)
SAMESTELLING:
Elke tablet bevat 40 mg furosemied. Suikervry.

FARMAKOLOGIESE KLASSIFIKASIE:
A 18.1 - Diuretika.

FARMAKOLOGIESE WERKING:
Defulide 40 se diuretiese werking word uitgeoefen vanweë sy saluretiese eienskappe. Eksperimente het bewys dat furosemied werk deur die herabsorbering van natrium en water te verminder in die proksimale gekronkelde buisie, die stygende deel van die Henle-lus en die distale gekronkelde buisie. **Defulide 40** werk dus deur die buisie, en daar word tans aanvaar dat die werking van furosemied in die Henle-lus, die belangrikste op die nefron is. In omstandighede waar ander metodes van behandeling nie daarin kon slaag om diurese te induseer nie, is dit dikwels moontlik om die uitskeiding van natrium en water met furosemied te verhoog selfs wanneer die glomerulêre filtrasietempo merkbaar aangetas is. **Defulide 40** verlaag patologiese verhoogde bloeddrukvlakke, maar het geen uitwerking op normale waardes nie. Wanneer **Defulide 40** toegedien word, is die aanvang van werking vinnig, gewoonlik binne 'n halfuur. Optimale werking word gewoonlik na 2 ure verkry en die tydperk van werking is 4 - 5 uur.

INDIKASIES:
a. Askites as gevolg van lewersirrose, meganiese obstruksie of hartversaking.
b. Om te voorkom dat oligurie oorgaan na algehele anurie.
c. Hartedeem.
d. Hipertensie van ligte tot matige graad.
e. Edeem wat voorkom gedurende die laaste drie maande van swangerskap - pre-eklamptiese toksemie en eklampsie. (Sien **"WAARSKUWINGS")**
f. Perifere edeem as gevolg van meganiese obstruksie of veranderings in die bloedvaatwande.

KONTRA-INDIKASIES:
Pasiënte wat hipersensitiwiteit is vir furosemied. By lewerkoma en in gevalle van elektrolietverlies. **Defulide 40** word teenaangedui indien asotemie en oligurie ontstaan gedurende die behandeling van progressiewe niersiekte. Moeders wat borsvoed.

WAARSKUWINGS:
By swangerskap moet **Defulide 40** tablette toegedien word met die grootse versigtigheid en slegs in uitgesoekte gevalle vir kort periodes. Meegaande terapie met kefaloridien kan lei tot nefrotosisiteit.

DOSIS EN GEBRUIKSAANWYSINGS:
Volwassenes Aanvangsdosis: Een tot drie tablette.
Daarna: 'n Halwe tot een tablet per dag.
Of: Soos deur die geneesheer voorgeskryf.

NEWE-EFFEKTE EN SPESIALE VOORSORGMAATREËLS:
i) Verskeie vorms van dermatitis, insluitende urtikarie en eksfoliatiewe dermatitis, pruritis, parastesie, versteuring van gesigsvermoë, geelvisie, duiseligheid, pankreatitis, fotosensitiwiteit, posturale hipotensie, hoofpyn, naarheid, braking of diarree kan voorkom.
ii) Anemie, leukopenie, aplastiese anemie en trombositopenie (met binnehuidbloeding) kan voorkom. Agranulositose het al voorgekom.
iii) Asimptomatiese hiperurisemie kan voorkom en jig kan gepresipiteer word.
iv) Veranderings in glukosetoleransietoetse met abnormaliteite van vastende en 2 uur postprandiale suiker is al waargeneem en gevalle van presipitasie van diabetes mellitus is al aangemeld.
v) **Defulide 40** kan die serumkalsiumvlakke verlaag en gevalle van tetanie is al aangemeld.
vi) Oormatige diurese kan dehidrasie en vermindering van bloedvolume tot gevolg hê, met daaropvolgende sirkulatoriese kollaps en die moontlikheid van vaskulêre trombose en embolisme, veral by bejaarde pasiënte. Die oormatige verlies van kalium by pasiënte wat hartglikosiede ontvang kan digitalistoksisiteit bespoedig. Wees ook versigtig met pasiënte wat kaliumuitputtende steroïde ontvang.
vii) Elektrolietversteurings. Hipokalemie kan egter verminder word met 'n kaliumryke dieët. Indien dit reeds bestaan voor die aanvang van die behandeling - wat veral moontlik is in gevalle van sirrose - moet die serumkalium eers na normaal herstel word met kaliumaanvullings en, indien nodig, met die toediening van natrium en chloried. Vanweë die kragtige natriuretiese werking van **Defulide 40**, kan dit 'n daling van die natriumvlak teweegbring, veral wanneer die edeem vinnig opgeklaar word. Elektroliet uitputting word geopenbaar deur swakheid, duiseligheid, letargie, krampe in die bene, verlies van aptyt, braking en/of geestesverwarring.

Hepatiese disfunksie, cholestatiese geelsug en parastesie is al aangemeld. Tinnitus en doofheid kan voorkom veral gedurende vinnige hoë-dosis parenterale behandeling met furosemied. Doofheid kan permanent wees indien furosemied aan pasiënte toegedien is wat ototoksiese middels neem. **Defulide 40** verhoog die urinerê uitskeiding van kalsium. Niersteenvorming is al aangemeld waar furosemied gebruik is om premature babas le behandel. Dit moet met sorg gebruik word by pasiënte met prostaathipertrofie of belemmerde mikturisie **Defulide 40** kan die nefrotoksisiteit van kefalosporienarrlbiotika soos kefalotien en van aminoglikosied antibiolika verhoog. Dit kan ook die ototoksisiteit van aminoglikosied-anlibiotika verhoog. Gelyktydige toediening van fenitoïn of indometasien kan die kliniese effekte van **Defulide 40** verlaag. **Defulide 40** moet met sorg gebruik word by pasiënte met ontoereikende lewerfunksie, aangesien dit die risiko van hepatiese enkefalopatie kan verhoog. Dit moet met sorg gebruik word by pasiënte met nierontoereikendheid. **Defulide 40** kan die toksisiteit van digitalis glikosiede verhoog deur die uitputting van serumkaliumkonsentrasies. Dit kan die neuromuskulere blokkerende werking van kompeterende spierverslappers, soos tubokurarien, verhoog. Dit kan die effek van antihipertensiewe middels verhoog. Die kaliumuitputtingseffek van **Defulide 40** kan verhoog word deur kortikosteroïede, kortikotropien, of karbenoksoloon. Gelyktydige toediening van **Defulide 40** en litium word gewoonlik nie aanbeveel nie, aangesien die assosiasie kan lei tot toksiese bloedvlakke van litium. Bloedglukosekonsentrasies moet gemonitor word by pasiënte wat anti-diabetiese middels neem, aangesien behoeftes kan verander.

BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VAN DIE BEHANDELING DAARVAN: Sien "**NEWE-EFFEKTE**" hierbo. Behandeling is ondersteunend en simptomaties.

IDENTIFIKASIE:
Wit tot naaswit, ronde, plat gehalveerde tablette met skuinskante.

AANBIEDING:
Securitainers met 28, 30, 100, 250 of 500 tablette. PVC/PVDC/Aluminium stolpverpakkings met strokies van 28 of 30 tablette elk in 'n eenheid karton.

BERGINGSINSTRUKSIES:
Berg benede 25 °C.
Beskerm teen lig.
HOU BUITE BEREIK VAN KINDERS.

REGISTRASIENOMMER:
Y/18.1/135

NAAM EN BESIGHEIDSADRES VAN DIE HOUER VAN DIE SERTIFIKAAT VAN REGISTRASIE:
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