PROFESSIONAL INFORMATION

SCHEDULING STATUS

S2

1 NAME OF THE MEDICINE
FLULEZ EFFERVESCENT TABLETS.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each effervescent tablet contains: 2 mg Chlorphenamine maleate, 500 mg Paracetamol and Sodium ascorbate equivalent to 250 mg Vitamin C.
FLULEZ contains aspartame and sorbitol.

3 PHARMACEUTICAL FORM
White, to almost white, round, flat effervescent tablets with slight orange flavour.

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
FLULEZ is indicated for symptomatic relief of a sore throat, runny nose, sneezing, headache and generalised aching due to colds and flu.

4.2 Posology and method of administration
Posology
Adults and children over 12 years:
Take one tablet every 8 hours if necessary.

DO NOT EXCEED THE RECOMMENDED DOSE.
Do not use **FLULEZ** continuously for more than 10 days without consulting your doctor.

Paediatric population
FLULEZ is contraindicated in children aged 0 to 12 years (see section 4.3).

Method of administration
Dissolve one tablet in a glass of water and drink the contents immediately once the whole tablet has dissolved.

4.3 Contraindications
FLULEZ is contraindicated in:
Hypersensitivity to the active substances or to any of the excipients (see section 6.1).
Severe liver function impairment.
Epilepsy.
Children under the age of 12 years.
Pregnancy and lactation

4.4 Special warnings and precautions for use
FLULEZ may lead to drowsiness and impaired concentration that may be aggravated by the simultaneous intake of alcohol or other central nervous system depressants.
Patients should be advised, particularly at the initiation of therapy, against taking charge of vehicles or machinery or performing potentially hazardous tasks where loss of concentration could lead to accidents.
Chlorphenamine, as in **FLULEZ** should be used with caution in patients with prostatic hypertrophy, narrow angle glaucoma, emphysema or chronic bronchitis, porphyria. Paradoxical hyperexcitability, nervousness and insomnia may occur in children and in the elderly. Elderly patients are especially susceptible to dizziness, sedation, confusion, hypotension and anticholinergic effects such as dry mouth and urinary retention. Should be used with care in patients with pyloroduodenal obstruction, epilepsy and severe cardiovascular disorders.
Doses of **FLULEZ** in excess of those recommended may cause severe liver damage.
Consult a medical practitioner if pain or fever persist or gets worse at the recommended dosage or if new symptoms occur or if redness and swelling is present, as these could be signs of a more serious condition.

This product contains paracetamol which may be fatal in overdose. In the event of overdosage or suspected overdosage and notwithstanding the fact the person may be asymptomatic, the nearest doctor, hospital or Poison Centre must be contacted immediately.

Store in a safe place out of reach of children.
Patients suffering from hepatitis or alcoholism, or recovering from any form of liver disease, should not take excessive quantities of **FLULEZ**.
Use with caution in renal disease.
Ascorbic acid should be given with caution to patients with G6PD deficiency, as large doses can cause haemolysis. Ascorbic acid should be given with caution to patients with hyperoxaluria. As large doses may result in the formation of renal calcium oxalate calculi.
Aspartame is hydrolysed in the gastrointestinal tract when orally ingested. One of the major hydrolysis products is phenylalanine. Caution is therefore required in patients with phenylketonuria (PKU). Neither non-clinical nor clinical data are available to assess aspartame use in infants below 12 weeks of age.
Patients with the rare hereditary condition of sorbitol intolerance should not take **FLULEZ**.

4.5 Interaction with other medicines and other forms of interaction
No interaction studies have been performed.

Chlorphenamine:
Chlorphenamine maleate may enhance the sedative effect of central nervous system depressants, including alcohol, barbiturates, hypnotics, opioid analgesics, anxiolytic sedatives and antipsychotics.
Concurrent use of MAO inhibitors may prolong and intensify the anticholinergic and CNS depressant effect of chlorphenamine maleate. Concurrent use is not recommended. Care should be observed when tricyclic antidepressants, guanethine, reserpine, methyldopa or atropine are taken concomitantly.
Chlorphenamine maleate given with ototoxic medication may mask the symptoms of ototoxicity such as tinnitus, dizziness or vertigo. Chlorphenamine may increase the risk of phenytoin toxicity.

Paracetamol:
Hepatotoxic medicines – Increased risk of hepatotoxicity.
Enzyme inducing medicines – increased risk of hepatotoxicity.
Possible decrease in therapeutic effects of **FLULEZ**.
Metoclopramide – absorption of **FLULEZ** may be accelerated.
Cholestyramine – absorption of **FLULEZ** is reduced if given within one hour of cholestyramine.
Prolonged concurrent use of **FLULEZ** with salicylates increases the risk of adverse renal effects. Excretion may be affected and plasma concentrations
altered when given with probenecid.

Vitamin C:
Vitamin C should not be given for the first month after starting treatment with desferrioxamine due to increased iron toxicity.
Large doses of Vitamin C may increase serum ethinylestradiol concentrations in women taking oral contraceptives.
Concomitant use of Vitamin C and fluphenazine may result in decreased serum concentrations of fluphenazine. May interact with warfarin.

4.6 Fertility, pregnancy and lactation
Pregnancy
The safety of this medicine in pregnancy has not been established.

Breastfeeding
The safety of this medicine in lactating women has not been established.

Fertility
No fertility data is available.

4.7 Effects on ability to drive and use machines
FLULEZ may affect mental and/or physical abilities to perform or execute tasks or activities requiring mental alertness, judgment and/or sound coordination and vision.
FLULEZ may lead to drowsiness and impaired concentration that may be aggravated by the simultaneous intake of alcohol or other central nervous system depressants. Patients should be advised, particularly at the initiation of therapy, against taking charge of vehicles or machinery or performing potentially hazardous tasks where loss of concentration could lead to accidents.

4.8 Undesirable effects
Tabulated summary of adverse reactions
Chlorphenamine maleate:

MedDRA system organ class	Frequency	Adverse reactions
Immune system disorder	Less frequent	Anaphylaxis including tightness of the chest and hypersensitivity reactions (including bronchospasm, angioedema)
Psychiatric disorders	Frequency unknown	Depression
Nervous system disorders	Frequent	Drowsiness.
	Less frequent	Convulsions or seizures, dizziness, increased sweating, abnormal coordination, tremor, lassitude, euphoria, nervousness, insomnia, headache, sedation.
	Frequency unknown	Confusion, hallucinations, paraesthesias, ataxia
Eye disorders	Less frequent	Blurred vision, diplopia.
Ear and labyrinth disorders	Less frequent	Tinnitus.
Cardiac disorders	Less frequent	Palpitations, dysrhythmia and tachycardia.
	Frequency unknown	Tightness of the chest, tingling, heaviness and weakness of the hands.
Vascular disorders	Less frequent	Hypotension, hypertension
Respiratory, thoracic and mediastinal disorders	Less frequent	Thickening of mucous
	Frequency unknown	Dryness of respiratory passages
Gastrointestinal disorders	Frequent	Dryness of mouth, nose or throat, gastrointestinal upset, loss of appetite, constipation, diarrhoea, nausea, vomiting.
	Frequency unknown	Epigastric pain, gastric reflux
Hepato-biliary disorders	Less frequent	Cholestasis, hepatitis or other hepatic function abnormalities.
Skin and subcutaneous tissue disorders	Less frequent	Exfoliative dermatitis, rashes.
	Frequency unknown	Photosensitivity and skin rash, allergic dermatitis, drug fever, hair loss and sweating
Musculoskeletal, connective tissue and bone disorders	Frequency unknown	Extrapyramidal effects with muscle spasms and dystonia, myalgia
Renal and urinary disorders	Less frequent	Difficult or painful urination, dysuria.
General disorders and administrative site conditions	Less frequent	Oedema, fatigue.

Paracetamol:

MedDRA system organ class	Frequency	Adverse reactions
Blood and the lymphatic system disorders	Less frequent	Agranulocytosis, thrombocytopenia, leucopenia, pancytopenia, neutropenia and anaemia.
Hepato-biliary disorders	Less frequent	Hepatitis.
	Frequency unknown	Pancreatitis
Skin and subcutaneous tissue disorders	Less frequent	Allergic dermatitis.
Renal and urinary disorders	Less frequent	Renal colic, renal failure and sterile pyuria.
General disorders and administrative site conditions	Frequency unknown	Dermatitis, skin rashes and other allergic reactions. The rash is usually erythematous or urticarial but sometimes more serious and accompanied by fever and mucosal lesions.

Sodium Ascorbate (Vitamin C):

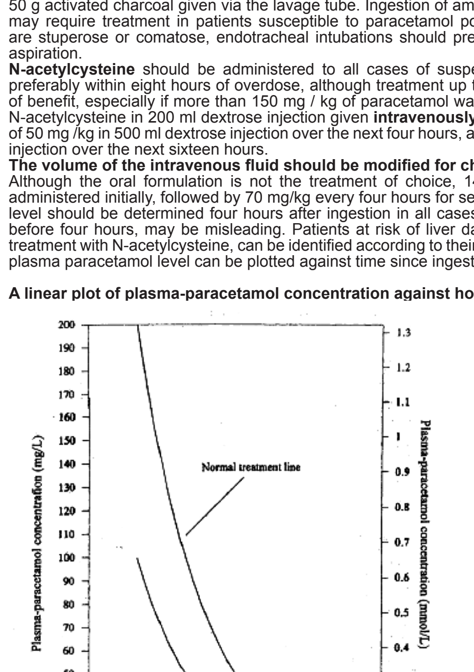
MedDRA system organ class	Frequency	Adverse reactions
Blood and the lymphatic system disorders	Frequency unknown	Ascorbic acid in large doses may also result in haemolysis in patients with glucose – 6 – phosphate dehydrogenase deficiency.
Gastrointestinal disorders	Frequency unknown	Large doses are reported to cause diarrhoea and other gastrointestinal disturbances.
Renal and urinary disorders	Frequency unknown	Large doses may result in hyperoxaluria and the formation of renal calcium oxalate calculi. Tolerance may be included with prolonged use of large doses

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 "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications:
https://www.sahpra.org.za/Publications/Index/8

Overdose
Paracetamol:
Prompt treatment is essential. In the event of an overdosage, consult a doctor immediately, or take the person directly to a hospital. A delay in starting treatment may mean that antidote is given too late to be effective. Evidence of liver damage is often delayed until after the time for effective treatment has lapsed.
Susceptibility to paracetamol toxicity is increased in patients who have taken repeated high doses (greater than 5 -10 g/day) of paracetamol for several days, in chronic alcoholism, chronic liver disease, AIDS, malnutrition, and with the use of medicines that induce liver microsomal oxidation such as barbiturates, isoniazid, rifampicin, phenytoin and carbamazepine.
Symptoms of paracetamol overdosage in the first 24 hours include pallor, nausea, vomiting, anorexia and possibly abdominal pain. Mild symptoms during the first two days of acute poisoning, do not reflect the potential seriousness of the overdosage.
Liver damage may become apparent 12 to 48 hours, or later after ingestion, initially by elevation of the serum transaminase and lactic dehydrogenase activity, increased serum bilirubin concentration and prolongation of the prothrombin time. Liver damage may lead to encephalopathy, coma and death. Acute renal failure with acute tubular necrosis may develop even in the absence of severe liver damage. Abnormalities of glucose metabolism and metabolic acidosis may occur. Cardiac arrhythmias have been reported.

Treatment for paracetamol overdosage
Although evidence is limited, it is recommended that any adult person who has ingested 5 to 10 grams or more of paracetamol (or child who has had more than 140 mg / kg body weight) within the preceding four hours, should have stomach emptied (emesis may be adequate for children) and a single dose of 50 g activated charcoal given via the lavage tube. Ingestion of amounts of paracetamol smaller than this may require treatment in patients susceptible to paracetamol poisoning (see above). In patients who are stuperose or comatose, endotracheal intubations should precede gastric lavage in order to avoid aspiration.
N-acetylcysteine should be administered to all cases of suspected overdose as soon as possible, preferably within eight hours of overdose, although treatment up to 36 hours after ingestion may still be of benefit, especially if more than 150 mg / kg of paracetamol was taken. An initial dose of 150 mg / kg N-acetylcysteine in 200 ml dextrose injection given **intravenously** over 15 minutes, followed by infusion of 50 mg /kg in 500 ml dextrose injection over the next four hours, and then 100 mg/kg in 1000 ml dextrose injection over the next sixteen hours.
The volume of the intravenous fluid should be modified for children.
Although the oral formulation is not the treatment of choice, 140 mg/kg dissolved in water may be administered initially, followed by 70 mg/kg every four hours for seventeen doses. A plasma paracetamol level should be determined four hours after ingestion in all cases of suspected overdose. Levels done before four hours, may be misleading. Patients at risk of liver damage and hence requiring continued treatment with N-acetylcysteine, can be identified according to their 4-hour plasma paracetamol level. The plasma paracetamol level can be plotted against time since ingestion in the nomogram below.

A linear plot of plasma-paracetamol concentration against hours after ingestion:



1. The time coordinates refer to time after ingestion.
2. Plasma-paracetamol concentration drawn before four hours may not represent peak concentrations.
3. The graph should be used only in relation to a single acute ingestion.
4. Patients whose plasma-paracetamol concentrations are above the normal treatment line should be treated.
5. Patients on enzyme-inducing drugs or with malnutrition or a history of alcohol abuse should be treated if the plasma-paracetamol concentrations are above the high-risk treatment line.
6. The value of such charts is uncertain if the patient is first seen 15 hours or more after ingestion or has taken modified release preparations of paracetamol.

Those, whose plasma-paracetamol levels are above the "normal treatment line", should continue N-acetylcysteine treatment with 100 mg/kg IV over sixteen hours repeatedly until recovery. Patients with increased susceptibility to liver damage as identified above, should continue treatment if concentrations are above the "high risk treatment line". Prothrombin index correlates best with survival.

Monitor all patients with significant ingestions for at least ninety six hours.

Chlorphenamine maleate
Central excitatory effects constitute the greatest danger in overdose.
Overdosage with **FLULEZ** may result in anticholinergic effects (paradoxical excitement, hallucinations, ataxia, unsteadiness, severe drowsiness, severe dryness of throat, nose and mouth, redness of face and shortness of breath and athetosis). Convulsions, tachycardia and cardiac arrhythmias may occur. Overdosage may be fatal, especially in infants and children in whom the main symptoms are central nervous system stimulation and antimuscarinic effects. Deepening coma, cardiorespiratory collapse and death may occur within 18 hours. In adults, the usual symptoms are of central nervous system depression with drowsiness, coma and convulsions. Hypotension may occur. Elderly patients are more susceptible to the central nervous system depressant and hypotensive effects even at the therapeutic doses.
Treatment is symptomatic and supportive.

5 PHARMACOLOGICAL PROPERTIES
Pharmacodynamic properties
A.5.8 Preparations for the common cold including nasal decongestants. **FLULEZ** has analgesic, antipyretic and antihistaminic properties.

Pharmacokinetic properties
Chlorphenamine maleate:
Chlorphenamine maleate is absorbed relatively slowly from the gastrointestinal tract. Peak plasma concentrations occurs about 2,5 to 6 hours after oral administration and the effects usually last 4-6 hours. Chlorphenamine appears to undergo considerable first-pass metabolism. Unchanged chlorphenamine and the metabolites are excreted mainly in the urine. Excretion is dependent on the urinary pH and flow rate. About 70% of the chlorphenamine in the circulation is bound to plasma proteins. The half-life in adults is 20 ± 5 hours but elimination is much more rapid in children.
Chlorphenamine is widely distributed in the body and enters the CNS.

Paracetamol:
Pharmacokinetics:
Paracetamol is well absorbed after oral administration. Peak plasma concentrations are reached 0,5 to 1,0 hours after administration. The plasma half life is about 2 hours.
Plasma protein binding varies. Paracetamol is relatively uniformly distributed
throughout most body fluids.
Paracetamol is metabolised in the liver primarily by conjugation with glucuronic acid (about 60%); sulphuric acid (about 35%) and cysteine (about 3%). Paracetamol is mainly excreted renally as conjugated metabolites. Some 90 % to 100 % of the substance may be recovered in the urine within the first day at therapeutic dosing. Children have less capacity for glucuronidation of the substance than do adults.

Sodium ascorbate:
Pharmacokinetics:
Sodium ascorbate is readily absorbed from the gastrointestinal tract and is widely distributed in the body tissue.
The plasma concentrations of ascorbic acid rise as the dose ingested are increased until a plateau is reached with doses of about 90 to 150 mg daily. Excess of the body's needs is rapidly eliminated in the urine. Ascorbic acid crosses the placenta and is distributed into breast milk.

6 PHARMACEUTICAL PARTICULARS
List of excipients
Aspartame
Citric acid anhydrous
Lemon flavour
Orange flavour
Povidone K30
Simethicone emulsion
Sodium carbonate anhydrous
Sorbitol

Incompatibilities
In the absence of compatibility studies, this medicine must not be mixed with other medicines.

Shelf life
36 months

Special precautions for storage
Store at or below 25 ºC in a dry place.
Protect from light.
Keep the tube tightly closed.
KEEP OUT OF REACH OF CHILDREN

Nature and contents of container
10, 12, 20 Effervescent tablets packed in a Polypropropylene tube with polyethylene stoppers filled with silica gel.
Not all pack sizes may be marketed.

Special precautions for disposal and other handling
No special requirements

7 HOLDER OF CERTIFICATE OF REGISTRATION
Trinity Pharma
106 16th Road
Midrand
1686

8 REGISTRATION NUMBER(S)
49/5.8/0941

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
21 June 2022

10 DATE OF REVISION OF THE TEXT
N.A

TRINITY PHARMA

Tel: 010 594 5610. Email: PV@kahmagroup.co.za

PROFESSIONELE INLIGTING

SKEDULERINGSTATUS

S2

1 NAAM VAN DIE MEDISYNE
FLULEZ BRUISTABLETTE.

2 KWALITATIEWE EN KWANTITATIEWE SAMESTELLING
Elke bruistablet bevat: 2 mg Chloorfenamienmaleaat, 500 mg Parasetamol en Natriumaskorbaat gelykstaande aan 250 mg Vitamien C.
FLULEZ bevat aspartaam en sorbitol.

3 FARMASEUTIESE VORM
Wit, tot naaswit, ronde, plat bruistablette met ligte lemoengeur.

4 KLINIESE BESONDERHEDE
Terapeutiese indikasies
FLULEZ word aangedui vir simptomatiese verligting van 'n seer keel, loopneus, nies, hoofpyn en algemene pyne as gevolg van verkoue en griep.

4.2 Posologie en metode van toediening
Posologie
Volwassenes en kinders oor 12 jaar:
Neem een tablet elke 8 uur indien nodig.

MOET NIE DIE AANBEVOLE DOSIS OORSKRY NIE.
Moet nie **FLULEZ** aaneenlopend gebruik vir meer as 10 dae sonder om u dokter te konsulteer nie.

Pediatriese populasie
FLULEZ is gekontraïndikeerd by kinders van 0 tot 12 jarige ouderdom (sien afdeling 4.3).

Metode van toediening
Los een tablet in 'n glas water op en drink die inhoud onmiddellik sodra die hele tablet opgelos het.

4.3 Kontraïndikasies
FLULEZ is gekontraïndikeerd by:
Hipersensitiwiteit vir die aktiewe bestanddele of vir enige van die hulpstowwe (sien afdeling 6.1).
Ernstige lewerfunksie inkorting.
Epilepsie.
Kinders onder die ouderdom van 12 jaar.
Swangerskap en laktasie.

4.4 Spesiale waarskuwings en voorsorgmaatreëls vir gebruik
FLULEZ kan lei tot lomerigheid en verswakte konsentrasie wat vererger kan word deur die gelyktydige inname van alkohol of ander sentrale senuweestelsel depressante.
Pasiënte moet veral, met die aanvang van terapie, gewaarsku word teen die gebruik van voertuie of masjinerie of die uitvoering van potensieel gevaarlike take waar konsentrasieverlies tot ongelukke kan lei.
Chloorfenamien, soos in **FLULEZ**, moet met omsigtigheid gebruik word by pasiënte met prostaat hipertrofie, nouhoek gloukoom, emfiseem of chroniese brongitis, porfirie. Paradoksale hipereksitabiliteit, senuweeagtigheid en slapeloosheid kan by kinders en bejaardes voorkom. Bejaarde pasiënte is veral vatbaar vir duiseligheid, sedasie, verwarring, hipotensie en anticholinergiese effekte soos droë mond en urinêre retensie. Moet met sorg gebruik word by pasiënte met piloroduodenale obstruksie, epilepsie en ernstige kardiovaskulêre versteurings.
Dosisse van **FLULEZ** bo die aanbevole kan ernstige lewerskade veroorsaak.
Raadpleeg 'n mediese praktisyn indien pyn of koors voortduur of erger word by die aanbevole dosis of indien nuwe simptome voorkom of as rooiheid en swelling teenwoordig is, aangesien dit tekens van 'n ernstiger toestand kan wees.

Die produk bevat parasetamol wat noodlottig kan wees met oordosering. In geval van oordosering of vermoedelike oordosering, en ondanks die feit dat die persoon asimptomaties kan wees, moet die naaste dokter, hospitaal of Gifsentrum onmiddellik gekontak word.

Berg in 'n veilige plek, buite bereik van kinders.
Pasiënte wat aan hepatitis of alkoholisme ly, óf wat herstel van enige vorm van lewersiekte, moet nie oormatige hoeveelhede van **FLULEZ** neem nie.
Gebruik met sorg by renale siekte.
Askorbiensuur moet met sorg vir pasiënte met G6PD tekort gegee word, aangesien hoë dosisse hemolise kan veroorsaak. Askorbiensuur moet met sorg gegee word aan pasiënte met hiperoksalurie, aangesien hoë dosisse kan lei tot die vorming van kalsiumoksalaat nierstene.
Aspartaam word in die gastroïntestinale kanaal gehidroliseer wanneer dit mondelings ingeneem word. Een van die belangrikste hidrolise-produkte is fenielalanien. Dus, sorg word aanbeveel by pasiënte met fenielketonurie (FKU). Geen nie-kliniese of kliniese data is beskikbaar om die gebruik van aspartaam by babas onder die ouderdom van 12 weke te assesseer nie.
Pasiënte met die seldsame oorerflike probleme van sorbitol onverdraagsaamheid moet nie **FLULEZ** neem nie.

4.5 Interaksie met ander medisyne en ander vorme van interaksie
Geen interaksiestudies is uitgevoer nie.

Chloorfenamien:
Chloorfenamienmaleaat kan die kalmerende effek van sentrale senuweestelsel depressante verhoog, insluitend alkohol, barbiturate, hipnotika, opioïed analgetika, angsiolitiese kalmeermiddels en antipsigotika.
Gelyktydige gebruik van MAO-inhibeerders kan die anticholinergiese en SSS-depressante effek van chloorfenamienmaleaat verleng en versterk. Gelyktydige gebruik word nie aanbeveel nie. Sorg moet geneem word wanneer trisikliese antidepressante, guanetidien, reserpien, metieldopa of atropien gelyktydig geneem word.
Chloorfenamienmaleaat gegee met ototoksiese medikasie kan die simptome van ototoksisiteit soos tinnitus, duiseligheid of vertigo verberg. Chloorfenamien kan die risiko van fenitoïentoksisiteit verhoog.

Parasetamol:
Hepatotoksiese medisyne - verhoogde risiko vir hepatotoksisiteit.
Ensieme-induserende medisyne - verhoogde risiko vir hepatotoksisiteit.
Moontlike afname in terapeutiese effekte van **FLULEZ.**
Metoklopramied - absorpsie van **FLULEZ** kan versnel word.
Cholestiramien - absorpsie van **FLULEZ** word verminder indien dit binne een uur na cholestiramien gegee word.
Verlengde gesamentlike gebruik van **FLULEZ** met salisilate verhoog die risiko van nadelige renale effekte. Uitskeiding kan beïnvloed word en plasmakonsentrasies verander wanneer dit met probenesied gegee word.

Vitamien C:
Vitamien C moet nie gegee word vir die eerste maand nadat die behandeling met desferrioksamien begin is nie as gevolg van verhoogde ystertoksisiteit.
Hoë dosisse Vitamien C kan die serumkonsentrasies van etinielestradiol, by vroue wat orale kontrasepsie neem, verhoog.
Gelyktydige gebruik van Vitamien C en flufenasien kan lei tot 'n verminderde serumkonsentrasies van flufenasien.
Mag interaksie met warfarien hê.

4.6 Vrugbaarheid, swangerskap en laktasie
Swangerskap
Die veiligheid van hierdie medisyne tydens swangerskap is nie vasgestel nie.

Borsvoeding
Die veiligheid van hierdie medisyne by lakterende vroue is nie vasgestel nie.

Vrugbaarheid
Geen vrugbaarheidsdata is beskikbaar nie.

4.7 Uitwerking op die vermoë om te bestuur en masjiene te gebruik
FLULEZ kan verstandelike en/of fisiese vermoëns beïnvloed om take of aktiwiteite uit te voer wat verstandelike waaksaamheid, oordeel en/of gesonde koördinasie en visie vereis.
FLULEZ kan lei tot lomerigheid en verswakte konsentrasie wat vererger kan word deur die gelyktydige inname van alkohol of ander sentrale senuweestelsel depressante. Pasiënte moet gewaarsku word, veral by die aanvang van terapie, teen die gebruik van voertuie of masjinerie of die uitvoering van potensieel gevaarlike take waar konsentrasieverlies tot ongelukke kan lei.

4.8 Newe-effekte
Getabuleerde opsomming van newe-effekte
Chloorfenamienmaleaat:

MedDRA sisteem-orgaanklas	Frekwensie	Ongewenste effekte
Immuunstelselversteurings:	Minder gereeld	Anafilakse insluitend benoude bors en hipersensitiwiteitsreaksies (insluitend brongospasma, angio-edeem)
Psigiatriese versteurings	Frekwensie onbekend	Depressie.
Senusisteemversteurings	Gereeld	Lomerigheid.
	Minder gereeld	Konvulsies of stuiptrekkings, duiseligheid, verhoogde sweet, abnormale koördinasie, bewerigheid, lusteloosheid, euforie, senuweeagtigheid, slapeloosheid, hoofpyn, sedasie.
	Frekwensie onbekend	Verwarring, hallusinasies, paraestesie, ataksie
Oogversteurings	Minder gereeld	Dowwe visie, diplopie.
Oor- en doolhofversteurings	Minder gereeld	Tinnitus.
Hartversteurings	Minder gereeld	Palpitasies, disritmie en tagikardie.
	Frekwensie onbekend	Benoudheid in die bors, tinteling, swaarheid en swakheid van die hande.
Vaskulêre versteurings	Minder gereeld	Hipotensie, hipertensie.
Respiratoriese, torakale- en mediastinale versteurings	Minder gereeld	Verdikking van mukus.
	Frekwensie onbekend	Droogheid van nasale weë.
Gastroïntestinale versteurings	Gereeld	Droogheid van mond, neus of keel, gastroïntestinale omgekraptheid, verlies aan eetlus, konstipasie, diarree, naarheid, braking.
	Frekwensie onbekend	Epigastriese pyn, gastriese refluks.
Hepato-biliêre versteurings	Minder gereeld	Cholestase, hepatitis of ander hepatiese abnormaliteite.
Vel- en Onderhuidse weefselversteurings	Minder gereeld	Eksfoliatiewe dermatitis, uitslae.
	Frekwensie onbekend	Fotosensitiwiteit en veluitslag, allergiese dermatitis, medisyne-koors, haarverlies en sweet
Muskuloskeletale, bindweefsel-, en beenversteurings	Frekwensie onbekend	Ekstrapiramidale effekte met spierspasmas en distonie, mialgie.
Renale en urinêre versteurings	Minder gereeld	Moeilike of pynlike urinering, disurie.
Algemene versteurings en toedieningsarea toestande	Minder gereeld	Edeem, moegheid.

Parasetamol:

MedDRA sisteem-orgaanklas	Frekwensie	Ongewenste effekte
Bloed- en Limfatiese Sisteemversteurings	Minder gereeld	Agranulositose, trombositopenie, leukopenie, pansitopenie, neutropenie en anemie.
Hepato-biliêre versteurings	Minder gereeld	Hepatitis.
	Frekwensie onbekend	Pankreatitis.
Vel- en Onderhuidse weefselversteurings	Minder gereeld	Allergiese dermatitis.
Renale en urinêre versteurings	Minder gereeld	Renale koliek, renale versaking en steriele piurie.
Algemene versteurings en toedieningsarea toestande	Frekwensie onbekend	Dermatitis, veluitslag en ander allergiese reaksies. Die uitslag is gewoonlik eritemateus of urtikaries, maar soms ernstiger en gepaard met koors en mukosale letsels.

Natriumaskorbaat (Vitamien C):

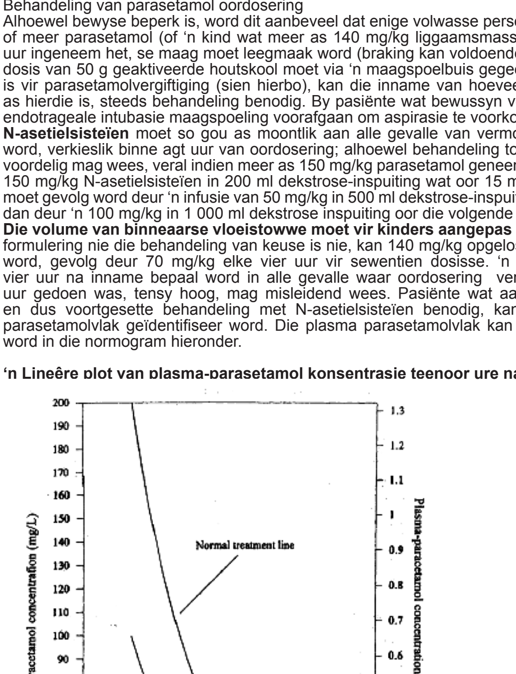
MedDRA sisteem-orgaanklas	Frekwensie	Ongewenste effekte
Bloed- en Limfatiese Sisteemversteurings	Frekwensie onbekend	Askorbiensuur in hoë dosisse kan ook lei tot hemolise by pasiënte met glukose-6-fosfaat- dehidrogenase gebrek.
Gastroïntestinale versteurings	Frekwensie onbekend	Daar word berig dat hoë dosisse diarree en ander gastroïntestinale versteurings oorsaak.
Renale en urinêre versteurings	Frekwensie onbekend	Hoë dosisse kan lei tot hiperoksalurie en die vorming van renale kalsiumoksalaat stene. Verdraagsaamheid kan ingesluit word met langdurige gebruik van hoë dosisse

Rapportering van vermoedelike newe-effekte
Dit is belangrik om vermoedelike newe-effekte wat waargeneem word nadat die medisyne goedgekeur is, te rapporteer. Dit laat volgehoue observering van die voordeel/risiko-balans van die medisyne toe. Gesondheidsorgverskaffers word versoek om enige vermoedelike newe-effekte aan SAHPRA te rapporteer via die "**6.04 Adverse Drug Reactions Reporting Form**", wat aanlyn by SAHPRA se publikasies gevind kan word: https://www.sahpra.org.za/Publications/Index/8

Oordosering
Parasetamol:
Onmiddellike behandeling is noodsaaklik. In die geval van 'n oordosering moet 'n dokter onmiddellik geraadpleeg word, of die persoon direk na 'n hospitaal geneem word. Indien behandeling vertraag word, kan die teenmiddel te laat toegedien word om doeltreffend te werk. Bewyse van lewerskade word dikwels vertraag tot nadat die tyd vir doeltreffende behandeling verby is.
Vatbaarheid vir parasetamoltoksisiteit word verhoog by pasiënte wat herhaaldelik hoë dosisse (meer as 5-10 g/dag) parasetamol gebruik het vir verskeie dae, in geval van chroniese alkoholisme, chroniese lewersiekte, VIGS, wanvoeding en indien middels wat mikrosomale oksidasie van die lewer induseer, soos barbiturate, isoniasied, rifampisien, fenitoïen en karbamasepien gebruik word.
Simptome van parasetamol oordosering in die eerste 24 uur sluit, bleekheid, naarheid, braking, anoreksie en moontlik abdominale pyn in. Ligte simptome gedurende die eerste twee dae na akute vergiftiging dui nie op die moontlike erns van die oordosering nie.
Lewerskade kan eers 12 tot 48 uur of later na inname sigbaar word, aanvanklik met die verhoging van die serumtransaminase en laktiese dehidrogenase aktiwiteit, verhoogde serumbilirubienkonsentrasie en verlenging van die protrombientyd. Lewerskade kan lei tot enkefalopatie, koma en dood. Akute renale versaking met akute buisnekrose kan ontwikkel, selfs in die afwesigheid van ernstige lewerskade. Abnormaliteite van glukosemetabolisme en metaboliese asidose kan voorkom. Hartaritmieë is aangemeld.

Behandeling van parasetamol oordosering
Alhoewel bewyse beperk is, word dit aanbeveel dat enige volwasse persoon wat ongeveer 5 tot 10 gram of meer parasetamol (of 'n kind wat meer as 140 mg/kg liggaamsmassa) binne die voorafgaande vier uur ingeneem het, se maag moet leeggmaak word (braking kan voldoende wees vir kinders) en 'n enkele dosis van 50 g geaktiveerde houtskool moet via 'n maagspoelbuis gegee word. In pasiënte wat vatbaar is vir parasetamolvergiftiging (sien hierbo), kan die inname van hoeveelhede parasetamol wat kleiner as hierdie is, steeds behandeling benodig. By pasiënte wat bewussyn verloor het of komatose is, moet endotrageale intubasie maagspoeling voorafgaan om aspirasie te voorkom.
N-asetielsisteïen moet so gou as moontlik aan alle gevalle van vermoedelike oordosering toegedien word, verkieslik binne agt uur van oordosering; alhoewel behandeling tot 36 uur na inname nog steeds voordelig mag wees, veral indien meer as 150 mg/kg parasetamol geneem was. 'n Aanvanklike dosis van 150 mg/kg N-asetielsisteïen in 200 ml dekstrose-inspuiting wat oor 15 minute intraveneus toegedien is, moet gevolg word deur 'n infusie van 50 mg/kg in 500 ml dekstrose-inspuiting oor die volgende vier uur en dan deur 'n 100 mg/kg in 1 000 ml dekstrose inspuiting oor die volgende sestien uur.
Die volume van binneaarse vloeistowwe moet vir kinders aangepas word. Alhoewel die mondelinge formulering nie die behandeling van keuse is nie, kan 140 mg/kg opgelos in water aanvanklik toegedien word, gevolg deur 70 mg/kg elke vier uur vir sewentien dosisse. 'n Plasma parasetamolvlak moet vier uur na inname bepaal word in alle gevalle waar oordosering vermoed is. Vlakke wat voor vier uur gedoen was, tensy hoog, mag misleidend wees. Pasiënte wat aan die risiko van lewerskade ly en dus voortgesette behandeling met N-asetielsisteïen benodig, kan volgens hul vier-uur plasma parasetamolvlak geïdentifiseer word. Die plasma parasetamolvlak kan teen tyd sedert inname geplot word in die normogram hieronder.

'n Lineêre plot van plasma-parasetamol konsentrasie teenoor ure na inname:



1. Die tydkoördinate verwys na tyd na inname.
2. Plasma-parasetamol konsentrasie wat voor vier uur getrek is, verteenwoordig moontlik nie die piekkonsentrasies nie.
3. Die grafiek moet slegs gebruik word met betrekking tot 'n enkele akute inname.
4. Pasiënte wie se plasma-parasetamol konsentrasies bo die normale behandelingslyn is, moet behandel word.
5. Pasiënte op ensiem-induserende middels of met wanvoeding of 'n geskiedenis van alkohol misbruik het, moet behandel word indien die plasma-parasetamol konsentrasies bo die hoërisiko-behandelingslyn is.
6. Die waarde van sulke grafieke is onduidelik indien die pasiënt eers 15 uur of langer na inname gesien word of gemodifiseerde vrystelling preparate van parasetamol geneem het.

Diegene wie se plasmaparasetamolvlakke bokant die "normale behandelingslyn" is, moet N-asetielsisteïen behandeling met 100 mg/ kg IV oor sestien ure herhaaldelik ondergaan totdat hulle herstel. Pasiënte met verhoogde vatbaarheid vir lewerskade soos hierbo geïdentifiseer, moet voortgaan met behandeling indien die konsentrasies bo die "hoërisiko behandelingslyn" val. Protrombien indeks korreleer die beste met oorlewing.

Monitor alle pasiënte wat 'n beduidende hoeveelheid ingeneem het vir minstens ses-en-negentig uur

Chloorfenamienmaleaat
Sentrale eksitatoriese effekte is die grootste gevaar tydens oordosering.
Oordosering met **FLULEZ** kan lei tot anticholinergiese effekte (paradoksiese opgewondenheid, hallusinasies, ataksie, wankelrigheid, ernstige lomerigheid, ernstige droogheid van die keel, neus en mond, rooiheid van gesig en aamborstigheid en atetose). Konvulsies, tagikardie en kardiale aritmieë kan voorkom. Oordosering kan fataal wees, veral by babas en kinders in wie die hoof simptome sentrale senuweestelsel stimulasie en antimuskariene effekte is. Verdieping van koma, kardiorespiratoriese ineenstorting en dood kan binne 18 uur voorkom. By volwassenes is die algemene simptome dié van sentrale senuweestelsel depressie met lomerigheid, koma en stuiptrekkings. Hipotensie kan voorkom. Bejaarde pasiënte is meer vatbaar vir sentrale senuweestelsel depressie en hipotensiewe effekte, selfs by die terapeutiese dosisse.
Behandeling is simptomaties en ondersteunend.

5 FARMAKOLOGIESE EIENSKAPPE
Farmakodinamiese eienskappe
A.5.8 Preparate vir verkoue, insluitend nasale dekongestante.
FLULEZ het analgetiese, antipiretiese en antihistamieniese eienskappe.

Farmakokinetiese eienskappe
Chloorfenamienmaleaat:
Chloorfenamienmaleaat word relatief stadig van die gastroïntestinale kanaal geabsorbeer. Piek plasmakonsentrasies word ongeveer 2,5 tot 6 uur na orale toediening bereik, en die effekte duur gewoonlik 4-6 ure.
Dit blyk asof chloorfenamien aansienlike eerstedeurgangsmetabolisme ondergaan. Onveranderde chloorfenamien en die metaboliete word hoofsaaklik in die urine uitgeskei. Uitskeiding is afhanklik van die urinêre pH en vloeitempo. Ongeveer 70 % van die chloorfenamien in die sirkulasie is aan plasmaproteïene gebind. Die halfleeftyd in volwassenes is 20 ± 5 uur, maar die eliminasie is baie vinniger by kinders.
Chloorfenamien word wyd in die liggaam versprei en betree die SSS.

Parasetamol:
Farmakokinetika:
Parasetamol word goed geabsorbeer na orale toediening. Piek plasmakonsentrasies word 0,5 tot 1,0 uur na toediening bereik. Die plasma halfleeftyd is ongeveer 2 uur.
Plasmaproteïenbinding varieer. Parasetamol is relatief uniform versprei oor meeste van die liggaamsvloeistowwe.
Parasetamol word hoofsaaklik in die lewer gemetaboliseer deur konjugasie met glukuroniese suur (ongeveer 60 %); swaelsuur (ongeveer 35 %) en sisteien (ongeveer 3 %). Parasetamol word hoofsaaklik renaal uitgeskei as gekonjugeerde metaboliete. Sowat 90 % tot 100 % van die substans kan binne die eerste dag by terapeutiese dosering in die urine herwin word. Kinders het minder kapasiteit vir glukuronidasie van die substans as volwassenes.

Natriumaskorbaat:
Farmakokinetika:
Natriumaskorbaat word geredelik uit die gastroïntestinale kanaal opgeneem en is wyd versprei in die liggaamsweefsel.
Die plasmakonsentrasies van askorbiensuur styg soos die ingenome dosis verhoog word totdat 'n plato bereik word met daagliks dosisse van ongeveer 90 tot 150 mg. Die oormaat, ten opsigte wat die liggaam benodig, word vinnig in die urine uitgeskei. Askorbiensuur kruis die plasenta en word in borsmelk versprei.

6 FARMSEUTIESE BESONDERHEDE
Lys van hulpstowwe
Aspartaam
Anhidriese sitroensuur
Suurlemoen geurmiddel
Lemoen geurmiddel
Povidoon K30
Simetikoon emulsie
Anhedriese natriumkarbonaat
Sorbitol

Onverenigbaarheid
In die afwesigheid van verenigbaarheidstudies, moet hierdie medisyne nie met ander medisyne gemeng word nie.

Rakleeftyd
36 maande

Spesiale voorsorgmaatreëls tydens berging
Stoor teen of benede 25 ºC in 'n droë plek.
Beskerm teen lig.
Hou die buis dig geseël.
HOU BUITE BEREIK VAN KINDERS

Aard en inhoud van die houer
10, 12, 20 Bruistablette verpak in 'n Polipropileen buis met poliëtileenstopper gevul met silikagel.
Nie alle verpakkingsgroottes mag moontlik bemark word nie.

Spesiale voorsorgmaatreëls vir die wegdoen en ander hantering
Geen spesiale vereistes.

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8 REGISTRASIENOMMER(S)
49/5.8/0941

9 DATUM VAN EERSTE MAGTIGING / HERNUWING VAN DIE MAGTIGING
21 Junie 2022

10 DATUM VAN HERSIENING VAN DIE TEKS
N.V.T