



PC.NO.: 8475

SCHEDULING STATUS: S2
PROPRIETARY NAME (AND DOSAGE FORM):
COGESIC (Tablets)

COMPOSITION:

Each tablet contains:
 Codeine phosphate 8 mg
 Paracetamol 500 mg
Preservative:
 Sodium metabisulphite 0.081 % m/m
 Contains sugar (sucrose) 20 mg
Other ingredients: gelatin, Indigo carmine lake E 132 IH (CI 73015:1), povidone, magnesium stearate, maize starch, modified starch and powdered sucrose.

PHARMACOLOGICAL CLASSIFICATION:

A 2.8 Analgesic Combinations

PHARMACOLOGICAL ACTION:

COGESIC tablets have analgesic and antipyretic action.

INDICATIONS

COGESIC tablets are indicated for the relief of mild to moderate pain and for the reduction of temperature in febrile conditions.

CONTRAINDICATIONS

Hypersensitivity to any of the ingredients.
 Codeine is contraindicated in respiratory depression, especially in the presence of cyanosis and excessive bronchial secretion and after operations on the biliary tract, in the presence of acute alcoholism, head injuries and conditions in which intracranial pressure is raised, during an attack of bronchial asthma or in heart failure secondary to lung disease.

WARNINGS AND SPECIAL PRECAUTIONS:

Paracetamol:

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

- Do not use continuously for more than 5 days without consulting your doctor.
- Dosages in excess of those recommended may cause severe liver damage.
- Consult your doctor if no relief is obtained with the recommended dosage.
- Patients suffering from liver or kidney disease should take paracetamol under medical supervision.

Codeine:

COGESIC contains codeine and exceeding the prescribed dose, together with prolonged and continuous use of this medication, may lead to dependency and addiction.

Codeine should be given with extreme caution in patients taking monoamine oxidase inhibitors or within 14 days of stopping such treatment.

Codeine should be given with caution to patients with:

- hypothyroidism,
- adrenocortical insufficiency,
- myasthenia gravis,
- impaired renal function,
- impaired liver function,
- prostatic hypertrophy
- shock or
- inflammatory or obstructive bowel disorders.

The dosage should be reduced in elderly and debilitated patients.
 The administration of codeine during labour may cause respiratory depression in the newborn infant (see "HUMAN REPRODUCTION").

COGESIC contains sucrose which may have an effect on the glycaemic control of patients with diabetes mellitus. Patients with rare hereditary conditions such as fructose intolerance, glucose-galactose mal-absorption or sucrase- isomaltase insufficiency should not take COGESIC.

Effects on ability to drive and use machines

COGESIC may cause drowsiness.
 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.

INTERACTIONS

Codeine should be given with extreme caution in patients taking monoamine oxidase inhibitors or within 14 days of stopping such treatment (see "WARNINGS AND SPECIAL PRECAUTIONS").

The depressant effects of codeine are enhanced by depressants of the central nervous system such as:

- alcohol,
- anaesthetics,
- hypnotics and sedatives,
- phenothiazines and tricyclic antidepressants

HUMAN REPRODUCTION

The administration of codeine during labour may cause respiratory depression in the newborn infant (see "WARNINGS AND SPECIAL PRECAUTIONS").

DOSAGE AND DIRECTIONS FOR USE

DO NOT EXCEED THE RECOMMENDED DOSE.
Adults: One or two tablets every four to six hours.
 Do not exceed an adult dose of 8 tablets per day.
Children over 12 years: One tablet every four to six hours.
Children 6 to 12 years: Half to one tablet every six hours.
 Do not use continuously for longer than five (5) days without consulting your doctor (see "WARNINGS AND SPECIAL PRECAUTIONS").

SIDE EFFECTS:

Paracetamol:
 Sensitivity reactions resulting in reversible rash or blood disorders may occur.

Codeine:
 Codeine may cause nausea, vomiting, constipation, drowsiness, confusion, dry mouth, sweating, facial flushing, vertigo, bradycardia, palpitations, orthostatic hypotension, hypothermia, restlessness, changes of mood and miosis, circulatory failure, hypotension, deepening coma, muscle rigidity. Micturition may be difficult and there may be ureteric or biliary spasm.
 Raised intracranial pressure may occur. Reactions such as urticaria and pruritus may occur. Codeine may have an antidiuretic effect.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

Paracetamol:
Prompt treatment is essential. In the event of an overdose, consult a doctor immediately, or take the person to a hospital directly. A delay in starting treatment may mean that the 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 include liver microsomal oxidation such as barbiturates, isoniazid, rifampicin, phenytoin

and carbamazepine.
 Symptoms of paracetamol overdose 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 overdose.
 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 prothrombin time. The 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.

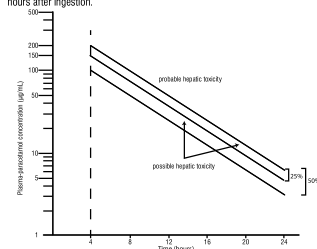
Treatment for paracetamol overdose:
 Although evidence is limited it is recommended that any adult person who has ingested about 5 - 10 grams or more of paracetamol (or a child who has had more than 140 mg/kg) within the preceding four hours should have the stomach emptied by lavage (emesis may be adequate 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 stuporose or comatose, endotracheal intubation 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 8 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 an infusion of 50 mg/kg in 500 ml dextrose injection over the next 4 hours, and then 100 mg/kg in 1 000 ml dextrose injection over the next 16 hours. The volume of intravenous fluids 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 4 hours for 17 doses. A plasma paracetamol level should be determined 4 hours after ingestion in all cases of suspected overdose. Levels done before 4 hours, unless high, may be misleading. Patients at risk of liver damage, and hence requiring continued treatment with N-acetylcysteine, can be identified according to their plasma paracetamol level. The plasma paracetamol level can be plotted against time since ingestion in the nomogram below. The nomogram should be used only in relation to a single acute ingestion. Those whose plasma paracetamol levels are above the "normal treatment line", should continue N-acetylcysteine treatment with 100 mg/kg IV over 16 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 ingestion for at least ninety six hours.

Figure 1. A semi-logarithmic plot of plasma-paracetamol concentration against hours after ingestion.



Sweetman, S ed. (2002) 'Martindale The Complete Drug Reference' Great Britain, The Bath Press (pg 72)

The latest information regarding the treatment of overdose can be obtained from the nearest poison information centre.

Codeine:
 Symptoms include restlessness, excitement, respiratory depression and hypotension with circulatory failure and coma. In children convulsions may occur. The specific antagonist, naloxone hydrochloride is used to counteract the severe respiratory depression.
 In the event of overdose, consult a doctor or take the patient to the nearest hospital immediately.
 Treatment is supportive and symptomatic.

IDENTIFICATION:
 Flat blue tablet, scored on the one side.

PRESENTATION:
 Cartons containing 2 x 10 tablets in push through blister packs.
 White plastic (LDPE) Ziploc bag (Patient Ready Pack) containing 56 tablets.
 Amber plastic (PVC) bottles containing 100, 500, and 1 000 tablets.
 White plastic (HDPE) bottles containing 1 000 tablets.
 Blue / green plastic buckets containing 5 000 tablets.

STORAGE INSTRUCTIONS:
 Store at or below 25 °C and protect from strong light in a well-closed container. Protect from moisture. Exposure to air should be minimal.
 KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER:
 X/2.8/109

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:
Oethman Biosims (PTY) Ltd
 Office 207A, Sherwood House
 Greenacres Office Park
 c/o Victory and Rustenburg Roads
 Victory Park, Johannesburg
 2195

DATE OF PUBLICATION OF THE PACKAGE INSERT:
 Date of registration: 23 August 1989

1224443





PC.NO.: 8475

SKEDULERINGSSTATUS: S2
EIENDOMSNAAM (EN DOSEERVORM):
COGESIC (tablette)

SAMESTELLING:

Eke tablet bevat:
Kodeïenfosfaat 8 mg
Parasetamol 500 mg
Freseerwagmiddel:
Natriumbisulfit 0,081 % n/m
Bevat suiker (sukrose) 20 mg
Ander bestanddele: gelatien, Indigo carmine lake E132 IH (CI 73015:1), povidoon, magnesiumstearaat, mellesylsel, veranderde stysel, gepoeierde suiker.

FARMAKOLOGIESE KLASSEFIKASIE:
A2.3 Analgetiese Samestellings

FARMAKOLOGIESE WERKING:
COGESIC se werking is pynverliggend en koorsverend.

INDIKASIES:

COGESIC tablette word aangedui vir die verligting van ligte tot matige pyn en vir die verligting van koors in koors toestande.

KONTRA-INDIKASIES:

Hipersensiwiteit vir enige van die bestanddele
Kodeïen word teenaangewys in respiratoriese onderdrukking veral in die teenwoordigheid van sianose en oormatige broniale sekresie en na galweg chirurgie, in die teenwoordigheid van akute alkoholisme, hoofbeserings en toestande waar intrakraniale druk verhoog is, gedurende 'n aanval van broniale asma of in hartversaking sekondêr tot longsekte.

WAARSKUWINGS EN SPESIALE VOORSORGMATREËLS:

Parasetamol

COGESIC bevat parasetamol wat doodlik kan wees indien dit in oordosis geneem word. In geval van oordosering of vermoedlike oordosering, selfs wanneer die persoon asptomaties is, moet die naaste dokter, hospitaal of gifsentrum onmiddellik gekontak word.

- Moet nie langer as 5 dae aanneem gebruik sonder om 'n geneesheer te raadpleeg nie.
- Groter dosisse as dié wat aanbeveel is kan ernstige lewerskade veroorsaak.
- Raadpleeg u geneesheer indien geen verligting met die aanbevole dosis verkry word nie.
- Pasiënte wat aan die lewer of niërsiekte ly, moet parasetamol onder mediese toësig neem.

Kodeïen

• **COGESIC** bevat kodeïen en die oorskrywing van die voorgeskrewe dosis, tesame met langdurige en aanhoudende gebruik van hierdie medikasie, kan tot **afhanklikheid en verslawing** lei.

• Kodeïen moet uiters versigtig gebruik word in pasiënte wat mono- amienoksidase - inhiëbers gebruik of binne 14 dae nadat sulke toediening gestaak is.

- Kodeïen moet versigtig toegedien word aan pasiënte met:
 - hipotensie
 - adrenergetiese oortoeriktheid
 - miastenie gravis
 - ingekorte nierfunksie
 - ingekorte lewerfunksie
 - prostaat hipertrie
 - skok
 - inflamatoriese of obstruktiel dermsiektes

Die dosering moet verminder word by bejaarde en verswakte pasiënte. Die toediening van kodeïen gedurende kraam kan respiratoriese onderdrukking by die pasgebore baba veroorsaak (Sien **HENSLIKE VOORTPLANTING**).

COGESIC bevat suikrose wat 'n uitwerking op die glukemiese beheer van pasiënte met diabetes mellitus kan hê. Pasiënte met seldsame oorerlike toestande soos fruktose-intoleransie, glukose-galaktose-malabsorpsie of sucrase-isomaltase- oortoeriktheid het, moet nie **COGESIC** gebruik nie.

Effekte op die vermoë om masjien te bestuur en te gebruik

COGESIC mag slaperigheid veroorsaak. Pasiënte moet aangepas word, teen die bestuur van voertuie of masjinerie, of om nie moontlike gevaarlike take te verrig waar verlies aan konsentrasie tot ongelukke kan lei, veral tydens die aanvang van terapie.

INTERAKSIES:

- Kodeïene moet met uiters versigtigheid toegedien word by pasiënte wat mononamien oksidas- inhiëbers gebruik of binne 14 dae na die staking van sodanige behandeling (Sien **WAARSKUWINGS EN SPESIALE VOORSORGMATREËLS**).
- Die depressiewe effekte van kodeïen word versterk deur depressante wat die sentrale senuweestelsel soos:
 - alkohol,
 - narkose,
 - hipnotika en kalmeer middels
 - fenotasiene en triskliese antidepressante

HENSLIKE VOORTPLANTING

Die toediening van kodeïen gedurende kraam kan respiratoriese onderdrukking by die pasgebore baba veroorsaak (Sien **WAARSKUWINGS EN SPESIALE VOORSORGMATREËLS**).

DOSIS EN GEBRUIKSAANWYSINGS:

MOET NIE DIE VOORGESKREWE DOSIS OORSKRY NIE

Volwassenes: Een of twee tablette elke vier tot ses uur.
Meer as 8 tablette in 24 uur neem nie.
Kinders 6 tot 12 jaar: Een tablet elke vier tot ses uur.
Kinders 6 tot 12 jaar: 'n Halwe tot een tablet elke ses uur.
Moet nie langer as vyf (5) dae aanneem gebruik sonder om u geneesheer te raadpleeg nie (Sien **WAARSKUWINGS EN SPESIALE VOORSORGMATREËLS**).

NEWE-EFFEKTE:

Parasetamol:
Sensitiwiteitsreaksies wat omkeerbare veluitslag of bloedaafwykings tot gevolg het, kan voorkom.

Kodeïen:

Kodeïen kan naarheid, braking, hardtygheid, slaperigheid, verwarwing, droë mond, sweet, bloes, vertigo, bradikardie, hartkloppings, ortostasiese hipotensie, hipotermie, rusteloosheid, buie veranderings, mirose, bloedsomloopversaking, hipotensie, verdiepende koma, en spierstyfheid veroorsaak. Moelike mikturisie, ureter- en gaspasme kan voorkom.
Verhoogde intrakraniale druk kan voorkom. Urtikarie en pruritus kan voorkom. Kodeïen kan 'n antidiuretiese werking hê.

BEKENDTE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VAN DIE BEHANDLING DAARVAN:

Parasetamol:

Spoeidige behandeling is noodsaaklik. In die geval van oordosering, raadpleeg onmiddellik 'n dokter of neem die persoon direk na 'n hospitaal. 'n Vertraging in die aanvang van behandeling kan beteken dat dit te laat sal wees vir die toediening van doeltreffend te wees. Bewyse van lewerskade is dikwels vertraag tot na die tydperk vir effektiewe behandeling verval het.
Gevoelheid vir parasetamol toksisiteit word verhoog in pasiënte wat vir 'n paar dae herhaalde hoë dosisse (meer as 5 - 10 g/dag) parasetamol geneem het. In chroniese alkoholisme, chroniese lewersiekte, vigs, wanvoeding en met die gebruik van medisyne

wat mikrosomale oksidasie deur die lewer insluit soos barbiturate, isoniasied, rifampisien, fenitoin en karbamasepin.

Simptome van parasetamol-oordosering in die eerste 24 uur sluit in bleekheid, naarheid, braking, anoreksie en moontlik buikpyn. Ligte simptome gedurende die eerste twee dae van akute vergiftiging wees op nie die potensiale ernst van die oordosering nie.
Lewerskade kan 12 tot 48 uur, of later, na inname, duidelik word, aanvanklik deur die verhoging van die serumtransaminase - en laktiese dehidrogenase-aktiwiteit, verhoogde serum bilirubinkonsentrasie en verlenging van die protrombientyd. Die lewerskade kan lei tot enkefalopatie, koma en dood.

Akute nierversaking met akute tubulêre nekrose kan selfs ontwikkel in die afwesigheid van ernstige lewerskade. Abnormalliteite van glukosemetabolisme en metaboliese asidose kan voorkom. Hartaritmieë is al aangemeld.

Behandeling vir parasetamol oordosering:

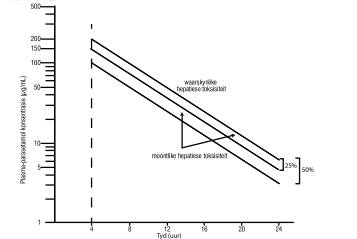
Alhoewel bewyse beperk is, word dit aanbeveel dat enige volwasse persoon wat ongeveer 5 - 10 g of meer parasetamol (of 'n kind wat meer as 140 mg/kg) binne die voorgaande vier uur ingeneem het, so magtig moet besgemaak word (braking kan voldoende wees vir kinders) en 'n enkele dosis van 50 g geaktiverde houtskool moet via 'n maagspoelbus 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. In pasiënte wat bewussyn verloor het of komatose is, moet endotragiese intubasie maagspoeling voorafgaan om aspirasie te voorkom.

N-asetielsteien moet so gou as moontlik aan alle gevalle van vermoedlike oordosering toegedien word, verkieslik binne 8 uur van oordosering; alhoewel behandeling tot 36 uur na inname nog steeds voordelig mag wees, veral as meer as 150 mg/kg parasetamol geneem was. 'n Aanvanklike dosis van 150 mg/kg N-asetielsteien in 200 ml dekstrose-inspuiting wat oor 15 minute intravenus toegedien is, moet gevolg word deur 'n infusie van 50 mg/kg in 500 ml dekstrose-inspuiting oor die volgende 4 uur en dan deur 'n 100 mg/kg in 1 000 ml dekstrose inspuiting oor die volgende 16 uur. **Die volume van binnearese vloeistowwe moet vir kinders aangepas word.**

Alhoewel die mondige formulering nie die behandeling van kouse is nie, kan 140 mg/kg oppelols in water aanvanklik toegedien word, gevolg deur 70 mg/kg elke 4 uur vir 17 dosisse.

'n Plasma parasetamolvlak moet 4 uur na inname bepaal word in alle gevalle waar oordosering vermoed is. Vlakke wat voor 4 uur getoon was, tensy hoog, mag misleidend wees. Pasiënte wat aan die risiko van lewerskade ly en dus voortgesette behandeling met N-asetielsteien benodig, kan volgens hul plasma parasetamolvlak geïdentifiseer word. Die plasma parasetamolvlak kan teen tyd sedert inname geplot word in die nomogram hieronder. Die nomogram moet slegs gebruik word in verband met 'n enkele akute inname.
Diene wat plasmaparasetamolvlakke bokant die "normale behandelingslyn" is, moet N-asetielsteien behandeling met 100 mg/kg IV oor 16 ure herhaaldelik ondergaan totdat hulle herstel. Pasiënte met verhoogde vatbaarheid vir lewerskade soos hierbo geïdentifiseer, moet behandeling ondergaan as konsentrasies bo die "hoë-risiko behandelingslyn" val. Protrombin indeks korreler die beste met oerlewing. Monitor alle pasiënte wat 'n beduidende hoefheid ingeneem het vir minstens ses-en-negentig uur.

Figuur 1. 'n Semi-logaritmesiese plot van plasma-parasetamol konsentrasie teenoor ure na inname.



Sweetman, S ed. (2002) 'Martindale The Complete Drug Reference' Great Britain, The Bath Press (bladsy 72)

Die nuutste inligting oor die behandeling van oordosering kan by u naaste gif sentrum verkry word.

Kodeïen:

Simptome sluit in rusteloosheid, opegewondenheid, respiratoriese onderdrukking en hipotensie met sirkulatoriese versaking en koma.
Konwulsies kan by kinders voorkom.
Die spesifieke antagonis, naloxoon/diandrochloried word gebruik om erge respiratoriese onderdrukking teen te werk.
In geval van oordosering, raadpleeg 'n geneesheer of neem die pasiënt onmiddellik na die naaste hospitaal.
Behandeling is simptomaties en ondersteunend.

IDENTIFIKASIE:

Plat, blou tablet, gekoop aan die een kant.

AANBIEDING:

Buiterkante vorme met 2 x 10 tablette in stulpverpakking.
Wit plastiese (LDPE) n-luit sakke (Pasiënt Gereed Pak) met 56 tablette.
Bruin plastiekbottels (PVC) met 100, 500 en 1 000 tablette.
Wit plastiekbottels (HDPE) met 1000 tablette.
Blou/groen plastiekemmers met 5 000 tablette.

BERGINGSANWYSINGS:

Berg teen of benede 25 °C, beskerm teen skerp lig in 'n digeslote houër. Beskerm teen voç.
Bloeistofping van lug moet minimaal wees.
HOU BUITE BEREIK VAN KINDERS.

REGISTRASIONOMMER:

X/2.8/109

NAAM EN BESIGHEIDSAADRES VAN DIE APPLIKANT:

Oethman Biosims (EDMS) Bpk
Kantoor 207A, Sherwood House
Greenacres Besigheidspark
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Victory Park, Johannesburg
2195

DATUM VAN PUBLIKASIE VAN HERDIE VOUBLIJF:

Datum van registrasie: 23 Augustus 1989

