SCHEDULING STATUS: S0 Pack sizes smaller than 25 tablets
S1 Pack sizes equal to and larger than 25 tablets

PROPRIETARY NAME: (AND DOSAGE FORM) **PANADO® TABLETS (TABLET)**

COMPOSITION: Each tablet contains 500 mg paracetamol and 0,12 % m/m potassium sorbate as preservative. Sugar free
PHARMACOLOGICAL CLASSIFICATION: A 2.7 Antipyretics or antipyretic and anti-inflammatory analgesics
PHARMACOLOGICAL ACTION: Paracetamol has analgesic and antipyretic properties. It acts predominantly by inhibiting prostaglandin synthesis.
Pharmacokinetics: Following oral administration, paracetamol is well absorbed, with peak plasma concentrations obtained after 0,5 to 1 hour. The plasma half-life is about 2 hours. Plasma protein binding is variable.
Paracetamol is metabolised in the liver primarily by conjugation with glucuronic acid (about 60 %), sulphuric acid (about 35 %) and cysteine (about 3 %). Paracetamol is renally excreted primarily as conjugated metabolites.

INDICATIONS: PANADO TABLETS is indicated for the symptomatic treatment of mild to moderate pain and fever.

CONTRAINDICATIONS: Hypersensitivity to any of the ingredients of **PANADO TABLETS**. Severe liver function impairment.

WARNINGS: Dosages of **PANADO TABLETS** in excess of those recommended may cause severe liver damage. Consult a medical practitioner if pain or fever persists or gets worse at the recommended dosage, if new symptoms occur or if redness and swelling is present, as these could be signs of a more serious condition. Do not use this product continuously without consulting a medical practitioner:
for pain – for more than seven days in adults (5 days for children);
for fever – for more than 3 days.

In the event of overdosage or suspected overdose and notwithstanding the fact that 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 **PANADO TABLETS**. Use with caution in renal disease.

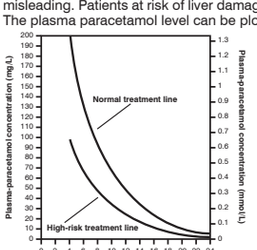
INTERACTIONS: Hepatotoxic medicines – Increased risk of hepatotoxicity.
Enzyme inducing medicines – Increased risk of hepatotoxicity. Possible decrease in therapeutic effects of **PANADO TABLETS**.
Metoclopramide – Absorption of **PANADO TABLETS** may be accelerated.
Cholestyramine – Absorption of **PANADO TABLETS** is reduced if given within one hour of cholestyramine.
Prolonged concurrent use of **PANADO TABLETS** with salicylates increases the risk of adverse renal effects.

PREGNANCY AND LACTATION: Safety and efficacy in pregnancy and lactation have not been established.

DOSAGE AND DIRECTIONS FOR USE: DO NOT EXCEED THE RECOMMENDED DOSE.
Adults: One tablet every 3 hours or one to two tablets every 4 to 6 hours while symptoms persist. Do not exceed 4 grams in 24 hours.
Children 6 to 12 years: Half to one tablet while symptoms persist, to be repeated every 4 hours if needed to a maximum of 4 doses per 24 hours for not longer than 5 days.
Children under 6 years: Not recommended. Paracetamol syrup should rather be considered for use if such a medicine is necessary.

SIDE EFFECTS AND SPECIAL PRECAUTIONS:
Side effects:
Blood and lymphatic system disorders:
Less frequent: Agranulocytosis, thrombocytopenia, leucopenia, pancytopenia, neutropenia, anaemia.
Renal and urinary disorders: *Less frequent:* Renal colic, renal failure and sterile pyuria.
Hepatobiliary disorders: *Less frequent:* Hepatitis.
Gastrointestinal disorders: *Less frequent:* Pancreatitis.
Skin and subcutaneous tissue disorders:
Less frequent: 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.
Special precautions: (See '**WARNINGS**')

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:
Prompt treatment is essential. In the event of an overdosage, consult a doctor immediately, or take the person to a hospital directly. 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 to 10 g/day) of paracetamol for several days, in chronic alcoholism, chronic liver disease, AIDS, malnutrition, and with the use of drugs 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 progress 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 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 stuperose 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 eight hours of overdosage, 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 four hours, and then 100 mg/kg in 1 000 ml dextrose injection over the next sixteen 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 a 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 overdosage. 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.



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.

IDENTIFICATION: Round, white, biconvex tablets, 13 mm in diameter and 5 mm in thickness. Name "PANADO" impressed on face. Reverse side is scored and carries a dot in the centre of the top hemisphere and a 1 mm indentation in the centre of the periphery of the lower hemisphere.

PRESENTATION: Polypaper strips of 2 tablets
PVC/Aluminium foil blister packs of 12 and 24 tablets
White, polypropylene tracer packs of 24, 50 and 100 tablets
White, polypropylene securitainers of 10, 20 and 500 tablets
White, HDPE "Spartan" containers of 24, 50 and 100 tablets
White, round HDPE buckets of 5 000 tablets
White, square HDPE cans of 5 000 tablets

STORAGE INSTRUCTIONS: Store below 25 °C in a well-closed container protected from light. Exposure to air should be kept to a minimum. KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER: B/2.8/858

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:
Adcock Ingram Limited
1 New Road
Erand Gardens, Midrand, 1685
Private Bag X69, Bryanston, 2021
www.adcock.com

DATE OF PUBLICATION OF THE PACKAGE INSERT: 27 June 2005

ADCOCK INGRAM LIMITED			
CUSTOMER: **Adcock Ingram Limited, South Africa**		COMPONENT: **Panado Tablets - D/L - PIL**	
ITEM CODE: **1208513 (WOA)**		DIMENSION: **160 x 240 mm (Open size)**	ARTWORK SCALE: **90%**
REASON FOR CHANGE: **Change in dimension to suit auto-cartanator**		COLOUR SCHEME: **Single - Black**	
SUPERSEDED ITEM CODE: **A03.049.10.01/EAf**		SPECIFICATION: **Printed on 56 - 60 GSM, Maplitho paper.**	
PDC Prepared by: Date:	**Head - TT/PDC** Checked by: Date:	**Head - Tech. Services /Production** Approved by: Date:	**Head CQA/QA** Authorized by: Date:

SKEDULERINGSTATUS: S0 Verpakking kleiner as 25 tablette
S1 Verpakking gelyk aan en groter as 25 tablette

EIENDOMSNAAM: **PANADO® TABLETS**
(EN DOSEERVORM) **(TABLET)**

SAMESTELLING: Elke tablet bevat 500 mg parasetamol en 0,12 % m/m kaliumsorbaat as preserveermiddel. Suikervry

FARMAKOLOGIESE KLASSIFIKASIE: A 2.7 Antipiretiese of antipiretiese en antiïnflammatoriese analgetika

FARMAKOLOGIESE WERKING: Parasetamol het pynstillende en koorswerende eienskappe. Dit werk hoofsaaklik deur die remming van prostaglandiensintese.
Farmakokinetika: Na mondelike toediening word parasetamol goed geabsorbeer, met piek-plasmakonsentrasies wat na 0,5 tot 1 uur bereik word. Die plasma-halfleeftyd is ongeveer 2 uur. Plasma-proteïenbinding is wisselend.
Parasetamol word in die lewer gemetaboliseer, hoofsaaklik deur konjugasie met glukuroonsuur (ongeveer 60 %), swaelsuur (ongeveer 35 %) en sisteïen (ongeveer 3 %). Parasetamol word deur die niere uitgeskei, hoofsaaklik as gekonjugeerde metaboliete.

INDIKASIES: PANADO TABLETS word aangedui vir die simptomatiese behandeling van ligte tot matige pyn en koors.

KONTRA-INDIKASIES: Oorgevoeligheid vir enige van die bestanddele van **PANADO TABLETS**. Ernstige lewerfunksiebelemmering.

WAARSKUWINGS: Dosisse van **PANADO TABLETS** hoër as dié wat aanbeveel word, kan ernstige lewerskade veroorsaak. Raadpleeg 'n mediese praktisyn as pyn en koors aanhou of erger word teen die aanbevole dosering, as nuwe simptome te voorskyn tree of as rooiheid en swelling teenwoordig is, aangesien hierdie tekens van 'n meer ernstige toestand kan wees.
Moet nie hierdie produk aaneenlopend gebruik sonder om 'n geneesheer te raadpleeg nie:
vir pyn – vir langer as sewe dae by volwassenes (5 dae by kinders);
vir koors – vir langer as 3 dae.

In die geval van oordosering of vermoedelike oordosering en ondanks die feit dat die persoon dalk asimptomaties is, moet die naaste geneesheer, hospitaal of Giftnulpsentrum onmiddellik geraadpleeg word.

Bêre in 'n veilige plek buite bereik van kinders. Pasiënte wat aan hepatitis of alkoholisme ly, of wat besig is om van enige vorm van lewersiekte te herstel, behoort nie oormatige hoeveelhede van **PANADO TABLETS** te neem nie. Gebruik met sorg by nieraantasting.

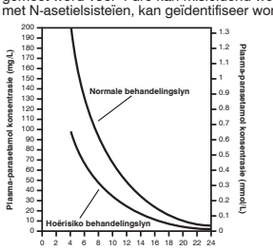
INTERAKSIES: Hepatotoksiese geneesmiddels – Verhoogde risiko van hepatotoksisiteit.
Ensiemopwekkende geneesmiddels - Verhoogde risiko van hepatotoksisiteit. Moontlike verlaging in terapeutiese uitwerking van **PANADO TABLETS**.
Metoklopramied – Absorpsie van **PANADO TABLETS** kan vesnel word.
Cholestiramien - Absorpsie van **PANADO TABLETS** word verlaag wanneer dit binne een uur na cholestiramien toegedien word.
Verlengde gelyktydige gebruik van **PANADO TABLETS** saam met salisilate verhoog die risiko van ongunstige renale uitwerkings.

SWANGERSKAP EN LAKTASIE: Veiligheid en doeltreffendheid in swangerskap en laktasie is nog nie vasgestel nie.

DOSIS EN GEBRUIKSAANWYSINGS: MOET NIE DIE AANBEVOLE DOSIS OORSKRY NIE.
Volwassenes: Een tablet elke 3 uur of een tot twee tablette elke 4 tot 6 uur vir solank as simptome aanhou. Moenie 4 gram in 24 uur oorskry nie.
Kinders 6 tot 12 jaar: Halwe tot een tablet vir solank as simptome aanhou, herhaal elke 4 uur indien nodig tot 'n maksimum van 4 dosisse per 24 uur vir nie langer as 5 dae nie.
Kinders onder 6 jaar: Nie aanbeveel nie. Parasetamolstroop behoort eerder vir toediening oorweeg te word indien so 'n middel nodig is.

NEWE-EFFEKTE EN SPESIALE VOORSORGMAATREËLS:
Newe-effekte
Bloed- en limfvaatstelselaandoenings: *Minder dikwels:* Agranulositose, trombositopenie, leukopenie, pansitopenie, neutropenie, anemie.
Nier- en urienwegaandoenings: *Minder dikwels:* Nierkoliek, nierversaking en steriele etterurien.
Hepatobiliêre aandoenings: *Minder dikwels:* Hepatitis.
Gastroïntestinale aandoenings: *Minder dikwels:* Pankreatitis.
Vel en subkutane weefselaandoenings: *Minder dikwels:* Dermatitis, veluitslag en ander hipersensitiwiteitsreaksies. Die uitslag is gewoonlik eritemateus of urtikaries van aard maar somtyds is dit erger en kan gepaard gaan met geneesmiddelkoors en mukosale letsels.
Spesiale voorsorgmaatreëls: (sien '**WAARSKUWINGS**')

BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VAN DIE BEHANDELING DAARVAN:
Onmiddellike behandeling is noodsaaklik. In die geval van 'n oordosis, raadpleeg onmiddellik 'n dokter, of neem die persoon direk na 'n hospitaal. 'n Vertraging in die aanvang van behandeling kan beteken dat die teenmiddel te laat gegee word om effektief te wees. Tekens van lewerskade is dikwels vertraag en wanneer hulle sigbaar word, is die tyd vir effektiewe behandeling reeds verby. Vatbaarheid vir parasetamol-toksisiteit is verhoog by pasiënte wat herhaaldelike hoë dosisse (meer as 5 tot 10 g/dag) parasetamol vir verskeie dae geneem het, by chroniese alkoholisme, chroniese lewersiekte, VIGS, wanvoeding, en met die gebruik van middels wat lewermikrosomale oksidasie aanbring soos barbiturate, isoniasied, rifampisien, fenitoïen en karbamasepien. Simptome van parasetamoloordosis in die eerste 24 uur sluit in bleekheid, naarheid, braking, anoreksie en moontlike abdominale pyn. Matige simptome gedurende die eerste twee dae van akute vergiftiging reflekteer nie die potensiële ernstigheid van die oordosis nie. Lewerbeskadiging kan manifesteer 12 tot 48 uur of later, na inname, aanvanklik deur verhoging in serumtransaminase en laktaatdehidrogenase-aktiwiteit, verhoogde serumbilirubien-konsentrasie en verlenging van die protrombientyd. Die lewerskade mag vorder tot enkefalopatie, koma en die dood. Akute niersversaking met akute tubulêre nekrose mag ontwikkel, selfs in die afwesigheid van ernstige lewerskade. Abnormaliteite in glukosemetabolisme en metaboliese asidose kan voorkom. Hartaritmieë is aangemeld.
Behandeling van parasetamoloordosering: Alhoewel bewyse daarvan beperk is, word dit aanbeveel dat enige volwasse persoon wat 5 tot 10 gram of meer parasetamol ingeneem het, (of 'n kind wat meer as 140 mg/kg ingeneem het) binne die voorafgaande vier ure, se maag geledig moet word deur 'n maagspoeling (emese mag voldoende wees by kinders) en 'n enkeldosis van 50 g geaktiveerde koolstof via die lavagebuis gegee word. Pasiënte wat vatbaar is vir parasetamolvergiftiging (sien hierbo), mag behandeling benodig indien kleiner hoeveelhede van parasetamol as dié, ingeneem is. By pasiënte wat bedwelmd is of in 'n koma is, moet endotrageale intubasie voor gastriese lavage gedoen word, om sodoende aspirasie te voorkom.
N-asetielsisteïen moet so gou as moontlik toegedien word by alle gevalle van 'n vermoedelike oordosis, verkieslik binne agt ure na die oordosis, alhoewel behandeling tot en met 36 uur na inname steeds voordelig kan wees, veral indien meer as 150 mg/kg parasetamol ingeneem is. 'n Aanvangsdosis van 150 mg/kg N-asetielsisteïen in 'n 200 ml dekstrose-inspuiting, binneaars toegedien oor 'n 15 minute tydperk, gevolg deur 'n **intraveneuse** infusie van 50 mg/kg in 500 ml dekstrose-inspuiting, oor die volgende vier ure en dan 100 mg/kg in 1 000 ml dekstrose-inspuiting oor die volgende sestien ure. **Die volume van die intraveneuse vloeistowwe moet aangepas word vir kinders.** Alhoewel die orale formulering nie die behandeling van keuse is nie, kan 140 mg/kg opgelos in water aanvanklik toegedien word, gevolg deur 'n 70 mg/kg oplossing elke vier ure vir sewentien doserings. 'n Parasetamol-plasmavlak moet bepaal word, vier ure na inname in alle gevalle van 'n vermoedelike oordosis. Vlakke wat gemeet word voor 4 ure kan misleidend wees, tensy die vlakke hoog is. Pasiënte wat die risiko loop van lewerskade, en daarom ook voortgaande behandeling benodig met N-asetielsisteïen, kan geïdentifiseer word volgens hulle parasetamol-plasmavlakke. Die parasetamol-plasmavlakke kan teen tyd vanaf inname grafies voorgestel word.



Pasiënte wie se parasetamol-plasmavlakke bo die "normale behandelingslyn" is, moet voortgaan met N-asetielsisteïenbehandeling van 100 mg/kg IV oor sestien uur, wat herhaal moet word tot herstel. Pasiënte met 'n verhoogde vatbaarheid vir lewerskade soos hierbo geïdentifiseer, moet met die behandeling voortgaan indien konsentrasies bo die "hoërisiko behandelingslyn" voorkom. Protrombien-indeks korreleer die beste met oorlewing. Moniteer alle pasiënte wat 'n beduidende hoeveelheid ingeneem het vir ten minste ses-en-negentig uur.

IDENTIFIKASIE: Ronde, wit, bikonvekse tablette, 13 mm in deursnee en 5 mm dik. Die naam "PANADO" is op die voorkant ingedruk. Die agterkant is ingekeep met 'n kolletjie in die middel van boonste halfrond en 'n 1 mm indentasie in die middel van die rand van die onderste halfrond.

AANBIEDING: Polipapierstrokies van 2 tablette
PVC/Aluminiumfoelie stulppakke van 12 en 24 tablette
Wit, polipropileen "tracer packs" van 24, 50 en 100 tablette
Wit, polipropileen securitainers van 10, 20 en 500 tablette
Wit, HDPE "Spartan" houers van 24, 50 en 100 tablete
Wit, ronde HDPE emmers van 5 000 tablette
Wit, viekantige HDPE kanne van 5 000 tablette.

BERGINGSAANWYSINGS: Bêre benede 25 °C in 'n diggeslote houer en beskerm teen lig. Blootstelling aan lug moet tot 'n minimum beperk word.
HOU BUITE BEREIK VAN KINDERS.

REGISTRASIENOMMER: B/2.8/858

NAAM EN BESIGHEIDSADRES VAN DIE HOUER VAN DIE REGISTRASIESERTIFIKAAT:
Adcock Ingram Limited
New Road 1, Erand Gardens, Midrand, 1685
Privaatsak X69, Bryanston, 2021
www.adcock.com

DATUM VAN PUBLIKASIE VAN HIERDIE VOUBILJET: 27 Junie 2005

02/2011 1208513 A03.049.10.01/EAf

ADCOCK INGRAM LIMITED			
CUSTOMER: **Adcock Ingram Limited, South Africa**		COMPONENT: **Panado Tablets - D/L - PIL**	
ITEM CODE: **1208513 (WOA)**		DIMENSION: **160 x 240 mm (Open size)**	ARTWORK SCALE: **90%**
REASON FOR CHANGE: **Change in dimension to suit auto-cartanator**		COLOUR SCHEME: **Single - Black**	
SUPERSEDED ITEM CODE: **A03.049.10.01/EAf**		SPECIFICATION: **Printed on 56 - 60 GSM, Maplitho paper.**	
PDC	**Head - TT/PDC**	**Head - Tech. Services /Production**	**Head CQA/QA**
Prepared by: Date:	Checked by: Date:	Approved by: Date:	Authorized by: Date: