SCHEDULING STATUS:
S3

PROPRIETARY NAME AND DOSAGE FORM:
PARACETAMOL BIOTECH IV (solution for infusion)

COMPOSITION:
PARACETAMOL BIOTECH IV contains 10 mg per ml paracetamol as active ingredient.
The following inactive ingredients are also included:
Citric acid monohydrate, disodium hydrogen phosphate dihydrate, nitrogen gas, propylene glycol, sodium metabisulphite, water for injection.

PHARMACOLOGICAL CLASSIFICATION:
A2. 7 Antipyretics or antipyretic and anti-inflammatory analgesics.

PHARMACOLOGICAL ACTION:
Pharmacodynamic Properties
The mechanism of analgesic and antipyretic actions of paracetamol has not been fully determined. It may involve central and peripheral actions.
Pharmacokinetic Properties
Absorption:
Paracetamol pharmacokinetics is linear up to 2 g after a single administration and after repeated administration during 24 hours. The maximal plasma concentration (C_{max}) of 30 µg/ml paracetamol is observed after 15 minutes of an intravenous infusion of 1 g of paracetamol.
Distribution:
Paracetamol is relatively uniformly distributed throughout most body fluids. Binding of paracetamol to plasma proteins is variable. The volume of distribution is about 1ℓ/kg. Significant concentrations of paracetamol of about 1,5 µg/ml were observed in the cerebrospinal fluid after about 20 minutes of a 1 g paracetamol intravenous infusion.
Metabolism:
Paracetamol is metabolised in the liver by conjugation with glucuronic acid (60 %), sulphuric acid (35 %), and cysteine (± 3 %). A minor hydroxylated metabolite (N-acetyl-p-benzoquinone imine) is usually produced in very small amounts by cytochrome P450 isoenzymes (mainly CYP2E1 and CYP3A4) in the liver and kidneys. It is usually detoxified by conjugation with glutathione but may accumulate after paracetamol overdosage and cause tissue damage. Neonates, infants and children up to 10 years excrete significantly more sulphate and less glucuronide conjugates than adults.
Elimination:
Paracetamol and its metabolites are mainly excreted in the urine.
Less than 5 % of the dose is excreted as unchanged paracetamol. Some 90 % to 100 % of the dose may be recovered in the urine as metabolites within the first 24 hours of administration. The plasma half-life of paracetamol is 2,7 hours for adults, 1,5 to 2 hours for infants and children and 3,5 hours in neonates. Total body clearance is 18 ℓ/h at all ages.
Special Populations
Renal insufficiency:
In cases of severe renal impairment (creatinine clearance < 30 mℓ/min), the elimination of paracetamol is delayed, the elimination half-life ranging from 2 to 5,3 hours. For the glucuronide and the sulphate conjugates, the elimination rate is 3 times slower in subjects with severe renal impairment than in healthy subjects. Therefore, it is recommended to leave an interval of at least 6 hours between administrations in patients with severe renal impairment (creatinine clearance ≤ 30 mℓ/min) (see DOSAGE AND DIRECTIONS FOR USE).
Elderly subjects:
The pharmacokinetics and the metabolism of paracetamol are not modified in elderly subjects.
No dose adjustment is required in this population.

INDICATIONS:
PARACETAMOL BIOTECH IV is indicated for:
The short-term treatment (not exceeding 24 hours) of mild to moderate pain e.g. after dental procedures and minor orthopaedic procedures, and the short-term treatment of fever, when the oral route is unsuitable.

CONTRAINDICATIONS:
PARACETAMOL BIOTECH IV is contraindicated in:
Situations where there is a hypersensitivity to paracetamol or to paracetamol hydrochloride (prodrug of paracetamol) or to any of the excipients of PARACETAMOL BIOTECH IV.
Cases of severe hepatocellular insufficiency or active liver disease including alcoholic hepatitis.
Children weighing less than 33 kg (approximately 11 years old) as safety and efficacy have not been established.

WARNINGS:
It is recommended to use suitable oral analgesic treatment as soon as this administration route is possible.
Dosages of PARACETAMOL BIOTECH IV in excess of those recommended may cause severe liver damage.
Clinical symptoms and signs of liver damage are usually seen first after two days with a maximum usually after 4 – 6 days. Treatment with an antidote should be given as soon as possible as PARACETAMOL BIOTECH IV overdose may be fatal (see KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT).
In order to avoid the risk of overdose, ensure that the other medicines administered do not contain paracetamol.
PARACETAMOL BIOTECH IV contains paracetamol which may be fatal in overdose. 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.
Salicylates in prolonged treatments together with PARACETAMOL BIOTECH IV significantly increased the risk of analgesic nephropathy, renal papillary necrosis, end-stage renal diseases, and cancer of the urinary bladder. Do not exceed the recommended individual dosages for salicylates and PARACETAMOL BIOTECH IV (see INTERACTIONS).
The anticoagulant effect could be increased when high doses of PARACETAMOL BIOTECH IV are used together with anticoagulants, such as warfarin (see INTERACTIONS). The risk of PARACETAMOL BIOTECH IV toxicity may be increased in patients receiving potentially hepatotoxic medicines or medicines that induce liver microsomal enzymes (see INTERACTIONS). Patients suffering from alcoholism, liver disease or malnutrition are at special risk of hepatic damage and caution is advised.
PARACETAMOL BIOTECH IV should be used with caution in patients suffering from renal disease, as prolonged excessive use of paracetamol can produce nephropathy. Paracetamol-induced renal function impairment may be sufficiently severe and could result in uraemia, especially with prolonged use of high doses. In patients with renal impairment with a creatinine clearance of 30 ml/minute or less the elimination of paracetamol is delayed, therefore a 6 hourly dose interval is recommended (see DOSAGE AND DIRECTIONS FOR USE).

INTERACTIONS:
Probenecid could increase the plasma concentrations of PARACETAMOL BIOTECH IV by almost a 2-fold reduction in clearance of paracetamol. A decrease in PARACETAMOL BIOTECH IV dose may be considered with concomitant use.
The absorption of paracetamol may be accelerated when used together with metoclopramide.
Salicylamide may prolong the elimination half-life of paracetamol as contained in PARACETAMOL BIOTECH IV.
Salicylates in prolonged treatments together with paracetamol significantly increased the risk of analgesic nephropathy, renal papillary necrosis, end-stage renal diseases, and cancer of the urinary bladder. The recommended individual doses for PARACETAMOL BIOTECH IV and the salicylates should not be exceeded.
Medicines that induce liver microsomal enzymes such as barbiturates or primidone could decrease the therapeutic effect of PARACETAMOL BIOTECH IV.
Concomitant use of PARACETAMOL BIOTECH IV and hepatic enzyme inducers should be used with caution as these medicines increase the risk of paracetamol induced hepatotoxicity. These substances include, but are not limited to barbiturates, isoniazid, rifampicin, carbamazepine, phenytoin, anticoagulants, zidovudine, amoxicillin, clavulanic acid, ethanol or hepatotoxic medicines.
The anticoagulant effects may increase when high doses of PARACETAMOL BIOTECH IV are used together with anticoagulants, coumarin (e.g. warfarin) and/or indadione derivates. Increased monitoring of INR values should be conducted during the period of concomitant use, as well as 1 week after discontinuation of PARACETAMOL BIOTECH IV.

PREGNANCY AND LACTATION:
Pregnancy:
Clinical experience of intravenous administration of paracetamol in pregnant women is limited. Epidemiological data from the use of oral therapeutic doses of paracetamol did not result in any unwanted effects in pregnant women or on the health of the foetus/new-born infant.
Nevertheless, PARACETAMOL BIOTECH IV should only be used during pregnancy after careful benefit/risk assessment, and the recommended dosage and duration must be strictly observed.
Lactation:
Paracetamol is excreted in breast milk in small quantities. No unwanted side effects have been reported in breastfed infants. However, caution should be used when administering PARACETAMOL BIOTECH IV to women who are breastfeeding their babies.

DOSAGE AND DIRECTIONS FOR USE:
Do not exceed the recommended dose
The maximum daily dose takes in account all the medicines containing paracetamol.
The prescribed dose must be based on the patient's non-oedematous weight.
Unintentional overdose can lead to serious liver damage and death.
Healthcare providers are reminded that it is essential to follow both the weight-related dose recommendations and to consider individual patient risk factors for hepatotoxicity including hepatocellular insufficiency, chronic alcoholism, chronic malnutrition (low reserves of hepatic glutathione) and dehydration (see WARNINGS, SPECIAL PRECAUTIONS, DOSAGE AND DIRECTIONS FOR USE (Recommended dosage in patients with hepatic impairment) and KNOWN SYMPTOMS OF OVERDOSE AND PARTICULARS OF ITS TREATMENT).
Adults and adolescents weighing more than 50 kg:
PARACETAMOL BIOTECH IV 1 g per administration, i.e. one 100 ml vial, up to four times a day. The minimum interval between each administration must be 4 hours. The maximum daily dose must not exceed 4 g in 24 hours.
Adolescents and adults weighing less than 50 kg and children weighing more than 33 kg (approximately 11 years old):
PARACETAMOL BIOTECH IV: 15 mg/kg per administration, i.e. 1,5 ml solution per kg. The minimum interval between each administration must be 4 hours. The maximum daily dose must not exceed 60 mg/kg (without exceeding 3 g in 24 hours).
Severe renal insufficiency:
It is recommended to leave a minimum interval of 6 hours between each administration in patients with severe renal impairment (creatinine clearance ≤ 30 ml/min) (see WARNINGS).
Hepatic impairment:
In patients with chronic or active hepatic disease, especially those with hepato-cellular insufficiency, chronic alcoholism, chronic malnutrition (low reserves of hepatic glutathione) and dehydration, the dose should not exceed 3 g/day.
Method of administration:
General:
PARACETAMOL BIOTECH IV should be administered as a 15-minutes intravenous infusion. Before administration, the product should be visually inspected for any particulate matter and discolouration, e.g. yellowing. It is intended for single-use only. Once opened, the vial should be used immediately.
Careful monitoring to avoid air embolism is needed, notably at the end of the infusion, especially if a central venous catheter is used for the infusion.
Any unused solution should be discarded.
PARACETAMOL BIOTECH IV should not be mixed with other medicinal products.

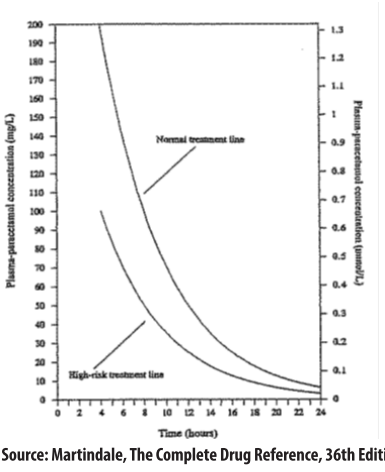
SIDE EFFECTS AND SPECIAL PRECAUTIONS:
Side Effects
Blood and the lymphatic system disorders
Less frequent: Thrombocytopenia, agranulocytosis, leucopenia, pancytopenia, neutropenia, anaemia
Immune system disorders
Frequency unknown: Hypersensitivity reactions such as anaphylaxis, angioedema.
Endocrine disorders
Less frequent: Pancreatitis.
Cardiac disorders
Less frequent: Tachycardia.
Vascular disorders
Less frequent: Hypotension.
Hepato-biliary disorders
Less frequent: Hepatitis, increased levels of hepatic transaminases.
Frequency unknown: Hepatic necrosis, hepatic failure.
Renal and urinary disorders
Less frequent: Renal colic, renal failure, sterile pyuria.
Skin and subcutaneous tissue disorders
Less frequent: Dermatitis, skin rash or urticaria, erythema, flushing, pruritus.
Gastrointestinal disorders
Frequency unknown: Nausea and vomiting.
General disorders and administration site conditions
Less frequent: Malaise.
Frequency unknown: Administration site reaction.

SPECIAL PRECAUTIONS:
PARACETAMOL BIOTECH IV should be used with caution in cases of:
- Hepatocellular insufficiency (see WARNINGS, CONTRAINDICATIONS, DOSAGE AND DIRECTIONS FOR USE).
- Severe renal insufficiency (creatinine clearance ≤ 30 ml/min) (see WARNINGS, DOSAGE AND DIRECTIONS FOR USE, PHARMACOKINETIC PROPERTIES).
- Chronic alcoholism, excessive alcohol intake (3 or more alcoholic drinks every day) (see CONTRAINDICATIONS).
- Anorexia, bulimia or cachexia, chronic malnutrition (low reserves of hepatic glutathione).
- Dehydration, hypovolaemia.
- Glucose 6 Phosphate Dehydrogenase (G6PD) deficiency (may lead to haemolytic anaemia).

Effects on ability to drive and use machines:
PARACETAMOL BIOTECH IV should have no influence on the ability to drive and the use of machines. No unwanted effects which could influence the ability to drive and to operate machinery have been reported by patients using PARACETAMOL BIOTECH IV.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:
Prompt treatment is essential in the event of an overdosage.
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. There is a risk of poisoning, particularly in chronic alcoholism, chronic liver disease, AIDS, malnutrition, and with the use of medicine 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 administration of PARACETAMOL BIOTECH IV, initially by elevation of the serum transaminase and lactic dehydrogenase activity, increased serum bilirubin concentration and prolongation of the prothrombin or increased INR time. Clinical symptoms of liver damage are usually evident initially only after 2 days and reach a maximum after 4 to 6 days. 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 dysrhythmias have been reported.
Treatment of paracetamol overdosage following IV administration of PARACETAMOL BIOTECH IV:
As soon as possible after the suspected overdose, and before starting treatment, draw blood for a paracetamol plasma assay.
N-acetylcysteine (NAC) 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 the overdose may still be of benefit, especially if more than 150 mg/kg of paracetamol was administered. An initial dose of 150 mg/kg N-acetylcysteine in 200 ml dextrose 5 % w/v injection given **intravenously** over 15 minutes, followed by an infusion of 50 mg/kg in 500 ml dextrose 5 % w/v injection over the next four hours, and then 100 mg/kg in 1000 ml dextrose 5 % w/v injection over the next sixteen hours. Sodium chloride 0,9 % w/v may be used where glucose 5 % w/v is unsuitable. **The volume of 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.

Paracetamol overdose with IV Infusions:



Source: Martindale, The Complete Drug Reference, 36th Edition, page 109

After an overdosage with an intravenous infusion, the standard nomogram used for determining treatment from paracetamol plasma concentrations following oral ingestion of an overdose of paracetamol, may not be appropriate. Paracetamol plasma concentrations more than 4 hours after intravenous injection may be lower than those predicted for the same oral dose at the same time point after 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 overdose for at least ninety six hours.
Treatment is symptomatic and supportive.

IDENTIFICATION:
The solution for infusion is a clear, colourless solution.

PRESENTATION:
PARACETAMOL BIOTECH IV is available in: 100 ml sterile, clear colourless Type I glass vial with brown bromobutyl rubber stopper and purple aluminium seal and flip-off cap. 100 ml transparent white LDPE bottle wrapped with a transparent clear polypropylent wrapper.

STORAGE INSTRUCTIONS:
Store at or below 30 °C. Protect from light.
Do not refrigerate or freeze.
Do not administer if visible particles are present.
Use immediately after opening. Discard remaining portion.
Keep out of reach of children.

REGISTRATION NUMBER:
45/2.7/0443

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:
Biotech Laboratories (Pty) Ltd.
Ground Floor, Block K West, Central Park
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SKEDULERINGSTATUS:
S3

EIENDOMSNAAM (EN DOSEERVORM):
PARACETAMOL BIOTECH IV (oplossing vir infusie)

SAMESTELLING:
PARACETAMOL BIOTECH IV bevat 10 mg per mℓ parasetamol as aktiewe bestandeel.
Die volgende onaktiewe bestandele is ook ingesluit:
Sitroensuurmonohidraat, dinatrium-waterstoffosfaatdihidraat, stikstof gas, propileenglikool, natrium metabisulfiet, water vir inspuiting.

FARMAKOLOGIESE KLASSIFIKASIE:
A2. 7 Koorswerende of koorswerende en anti-inflammatoriese pynstillers.

FARMAKOLOGIESE WERKING:
Farmakodinamiese eienskappe
Die meganisme van pynstillende en koorswerende effekte van parasetamol is nog nie ten volle vasgestel nie. Dit kan sentrale en perifere werking insluit.
Farmakokinetiese eienskappe
Absorpsie:
Parasetamol se farmakokinetika is liniêer tot by 2 g na 'n enkele toediening en na herhaaldelike toedienings oor 24 uur. Die maksimum plasmakonsentrasie (C_{max}) van 30 µg/mℓ parasetamol word waargeneem na 15 minute van 'n intraveneuse infusie van 1 g parasetamol.
Verspreiding:
Parasetamol word relatief uniform versprei deur die meeste liggaamsvloeistowwe. Die binding van parasetamol aan plasmaproteïene is veranderlik. Die volume van verspreiding is ongeveer 1 ℓ/kg. Merkwaardige konsentrasies van parasetamol van ongeveer 1,5 µg/mℓ is waargeneem in die serebrospinale vloeistof na omtrent 20 minute van 'n 1 g parasetamol intraveneuse infusie.
Metabolisme:
Parasetamol word gemetaboliseer in die lewer deur konjugasie met glukuronsuur (60 %), swaelsuur (35 %), en sisteïen (± 3 %). 'n Mindere gehidroksileerde metaboliet (N-asetiel-p-bensoquinimien) word geproduseer in baie klein hoeveelhede deur sitochroom P450 isoënsieme (hoofsaaklik CYP2E1 en CYP3A4) in die lewer en niere. Dit word gewoonlik ontgiftig deur konjugasie met glutatioon maar kan opgaar na parasetamol oordosering wat dan weefselskade kan veroorsaak.
Pasgeborenes, babas en kinders tot by 10 jaar skei aansienlik meer sulfate en minder glukuroniedkonjugate uit as volwassenes.
Eliminasie:
Parasetamol en sy metaboliete word hoofsaaklik uitgeskei in die urine. Minder as 5 % van die dosis word uitgeskei as onveranderde parasetamol. Ongeveer 90 % tot 100 % van die dosis kan herwin word in die urine as metaboliete binne 24 uur na toediening. Die plasma halfleeftyd van parasetamol is 2,7 uur vir volwassenes, 1,5 tot 2 uur vir babas en kinders en 3,5 uur in pasgeborenes. Die totale liggaamsopruiming is 18 ℓ/h in alle ouderdomsgroepe.
Spesiale Populasies
Nier ontoereikendheid:
In gevalle van erge nierontoereikendheid (kreatinien opruiming < 30 mℓ/min), word die eliminasie van parasetamol vertraag, die eliminasie halfleeftyd wissel tussen 2 tot 5,3 ure. Die eliminasietempo van glukuronied- en sulfaatkonjugate is 3 keer stadiger in pasiënte met erge nierontoereikendheid as in gesonde pasiënte. Dus word 'n doseringsinterval van ten minste 6 ure tussen toedienings in pasiënte met erge nierontoereikendheid (kreatinienopruiming ≤ 30 mℓ/min) aanbeveel (sien DOSIS EN GEBRUIKSAANWYSINGS).
Bejaarde pasiënte:
Die farmakokinetika en metabolisme van parasetamol is onveranderd in bejaarde pasiënte.
Geen dosisaanpassings is nodig in hierdie populasie nie.

INDIKASIES:
PARACETAMOL BIOTECH IV is aangedui vir:
Die korttermyn behandeling (nie langer as 24 uur nie) van ligte tot matige pyn bv. na tandheelkundige prosedures en klein ortopediese prosedures, en die korttermyn behandeling van koors wanneer orale toediening nie moontlik is nie.

KONTRA-INDIKASIES:
PARACETAMOL BIOTECH IV is teenaangedui in:
Gevalle van hipersensitiwiteit vir parasetamol of parasetamolhidrochloried (voorlopergeneesmiddel van parasetamol) of enige bestandeel van PARACETAMOL BIOTECH IV.
Gevalle van erge hepatosellulêre ontoereikendheid of aktiewe lewersiekte insluitende alkoholiese hepatitis.
Kinders wat minder as 33 kg weeg (ongeveer 11 jarige ouderdom) aangesien veiligheid en effektiwiteit nog nie vasgestel is nie.

WAARSKUWINGS:
Dit word aanbeveel dat 'n orale pynstiller gebruik word sodra orale toediening moontlik is.
Dosering van PARACETAMOL BIOTECH IV in hoeveelhede meer as wat aanbeveel word kan erge lewerskade veroorsaak.
Kliniese simptome en tekens van lewerskade word gewoonlik eers na twee dae waargeneem met die maksimum effekte eers na 4 – 6 dae. Behandeling met 'n teenmiddel moet so gou moontlik toegedien word aangesien PARACETAMOL BIOTECH IV oordosering tot die dood kan lei (sien BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VIR DIE BEHANDELING DAARVAN).
Om die risiko van oordosering te vermy, verseker dat ander geneesmiddels wat toegedien word nie parasetamol bevat nie.
PARACETAMOL BIOTECH IV bevat parasetamol wat tot die dood kan lei met oordosering. In die geval van oordosering of vermoede oordosering, al is die pasiënt asimptomaties, moet die naaste doktor, hospitaal of Vergiftigingssentrum onmiddelik gekontak word.
Salisilate in verlengde vrystellings produkte tesame met PARACETAMOL BIOTECH IV verhoog die risiko vir pynstillende nefropatie, nierpapilêre nekrose, finale fase niersiekte en kanker van die blaas aansienlik. Moenie die voorgestelde individuele doseering van salisilate en PARACETAMOL BIOTECH IV oorskry nie (sien INTERAKSIES).
Die bloedstollings effekte kan verhoog word indien hoë dosisse van PARACETAMOL BIOTECH IV tesame met antikoagulante, soos warfarin toegedien word (sien INTERAKSIES).
Die risiko van PARACETAMOL BIOTECH IV toksisiteit kan hoër wees in pasiënte wat potensiële lewertoksiese geneesmiddels of geneesmiddels wat lewer mikrosomale-ensieme induseer gebruik (sien INTERAKSIES).
Pasiënte wat aan alkoholisme ly, lewersiekte het of ondervoed is, het verhoogde risiko van lewerskade en moet met sorg behandel word.
PARACETAMOL BIOTECH IV moet met sorg gebruik word in pasiënte wat niersiektes het, aangesien verlengde oormatige gebruik van parasetamol kan aaleiding gee tot nefropatie.
Parasetamol geïnduseerde nierfunksie ontoereikendheid kan erg genoeg wees en kan uremie veroorsaak, veral in verlengde gebruik van hoë dosisse. In pasiënte met nierontoereikendheid met 'n kreatinien opruiming van 30 mℓ/minuut of minder, word die eliminasie van parasetamol vertraag, daarom word 'n doseringsinterval van 6 ure aanbeveel (sien DOSIS EN GEBRUIKSAANWYSINGS).

INTERAKSIES:
Probenesied kan die plasmakonsentrasie van PARACETAMOL BIOTECH IV verhoog met 'n amper 2-voud verlaging in die opruiming van parasetamol. 'n Vermindering in PARACETAMOL BIOTECH IV dosis kan oorweeg word met gesamentlike gebruik.
Die absorpsie van parasetamol kan versnel word indien dit saam met metoklopramied gebruik word.
Salisielamied kan die eliminasie halfleeftyd van parasetamol, wat voorkom in PARACETAMOL BIOTECH IV, verleng.
Salisilate in verlengde vrystellings produkte tesame met PARACETAMOL BIOTECH IV verhoog die risiko vir pynstillende nefropatie, nierpapilêre nekrose, finale fase niersiekte en kanker van die blaas aansienlik. Moenie die voorgestelde individuele doseering van salisilate en PARACETAMOL BIOTECH IV oorskry nie.
Geneesmiddels wat lewer mikrosomale-ensieme induseer, soos barbituraat of primidoon, kan die terapeutiese effekte van PARACETAMOL BIOTECH IV verminder.
Gelyktydige gebruik van PARACETAMOL BIOTECH IV en lewerensiem-induseerende middels moet met sorg gebruik word aangesien hierdie geneesmiddels die risiko van parasetamol geïnduseerde lewertoksisiteit verhoog. Hierdie geneesmiddels sluit in, maar is nie beperk tot barbituraat, isoniasied, rifampisien, karbamasepien, fenitoïen, antikoagulante, zidovudien, amoksisillien, klavulaansuur, etanol of lewertoksiese geneesmiddels, nie.
Die antikoagulant effekte kan verhoog indien hoë dosisse van PARACETAMOL BIOTECH IV gelyktydig saam met antikoagulante, koumarien (bv. warfarin) en/of indadioonderivate toegedien word. Verhoogde monitering van INR waardes moet tydens hierdie periode van gelyktydige toediening, asook 1 week na staking van PARACETAMOL BIOTECH IV, geskied.

SWANGERSKAP EN BORSVOEDING:
Swangerskap:
Kliniese ondervinding van intraveneuse toediening van parasetamol in swanger vroue is beperk. Epidemiologiese data van die orale terapeutiese dosisse van parasetamol het nie gelei to enige newe-effekte in swanger vroue of in die gesondheid van die fetus/pasgebore baba nie.
Nieteenstaande, PARACETAMOL BIOTECH IV moet slegs tydens swangerskap gebruik word na deeglike voordeel/risiko assesering, en die voorgestelde dosis en tydsduur moet streng waargeneem word.
Borsvoeding:
Parasetamol word in klein hoeveelhede uitgeskei in borsmelk. Geen newe-effekte is gerapporteer in borsvoed babas nie. Alhoewel, sorg moet toegepas word indien PARACETAMOL BIOTECH IV toegedien word aan vroue wat hulle babas borsvoed.

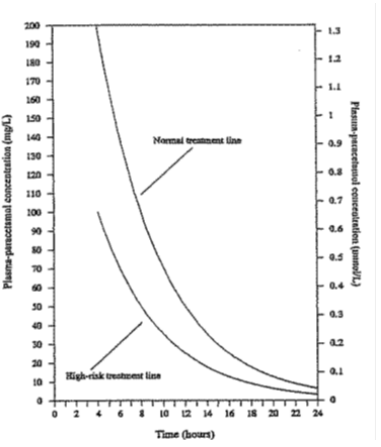
DOSIS EN GEBRUIKSAANWYSINGS:
Moenie die voorgestelde dosis oorskry nie.
Die maksimum daaglikse dosis neem alle geneesmiddels wat parasetamol bevat in ag. Die voorgeskrewe dosis moet gebaseer wees op die pasiënt se nie-oedemateuse gewig.
Onopsetlike oordosering kan lei tot erge lewerskade en dood.
Gesondheidsorgwerkers word daaraan herinner dat dit noodsaaklik is om beide die gewigsverwante doserings voorstelle en die individuele pasiënt risikofaktore vir lewertoksisiteit, insluitende hepatosellulêre ontoereikendheid, kroniese alkoholisme, kroniese ondervoeding (lae reserwes van hepatiese glutatioon) en dehidrasie, in ag te neem (sien WAARSKUWINGS, SPESIALE VOORSORGMAATREËLS, DOSIS EN GEBRUIKSAANWYSINGS (Voorgestelde dosering in pasiënte met lewer ontoereikendheid) en BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VIR DIE BEHANDELING DAARVAN).
Volwassenes en adolessente wat meer as 50 kg weeg:
PARACETAMOL BIOTECH IV 1 g per toediening, dit is een 100 mℓ flessie, tot vierkeer per dag. Die minimum interval tussen elke toediening moet 4 ure wees. The maksimum daaglikse dosis moet nie 4 g in 24 uur oorskrei nie.
Adolessente en volwassenes wat minder as 50 kg weeg en kinders wat meer as 33 kg (omtrent 11 jarige ouderdom) weeg:
PARACETAMOL BIOTECH IV: 15 mg/kg per toediening, dit is 1,5 mℓ oplossing per kg. Die minimum interval tussen elke toediening moet 4 ure wees.
Die maksimum daaglikse dosis moet nie 60 mg/kg oorskrei nie (sonder om 3 g in 24 uur te oorskrei).
Erge nierontoereikendheid:
'n Minimum interval van 6 ure tussen elke toediening in pasiënte met erge nierontoereikendheid word voorgestel (kreatinien opruiming ≤ 30 mℓ/min) (sien WAARSKUWINGS).
Lewerontoereikendheid:
In pasiënte met kroniese of aktiewe lewersiekte, veral pasiënte met hepatosellulêre ontoereikendheid, kroniese alkoholisme, kroniese ondervoeding (lae reserwes van hepatiese glutatioon) en dehidrasie, moet die dosis nie 3 g/dag oorskrei nie. Metode van toediening.
Algemeen:
PARACETAMOL BIOTECH IV moet toegedien word as 15 minuut intraveneuse infusies. Voor toediening moet die produk visueel geinspekteer word vir enige deeltjies en verkleuring bv. geel oplossing. Dit is slegs 'n enkeldosering en indien die flessie oopgemaak is, moet dit onmiddelik gebruik word.
Sorg moet toegepas word om lug embolisme te vermy, in besonder aan die einde van die infusie veral as 'n sentraleveneuse kateter gebruik word vir infusie. Enige ongebruikte oplossing moet weggegooi word.
PARACETAMOL BIOTECH IV mag nie met ander medisinale produkte gemeng word nie.

NEWE-EFFEKTE EN SPESIALE VOORSORGMAATREËLS:
Newe-effekte
Versteurings van die bloed en limfvatstelsel
Minder gereeld: Trombositopenie, agranulositose, leukopenie, neutropenie, anemie.
Immuunsisteem versteurings
Frekwensie onbekend: Hipersensitiwiteitsreaksies soos anafilakse, angioedeem.
Endokriene versteurings
Minder gereeld: Pankreatitis.
Kardiale versteurings
Minder gereeld: Tagikardie.
Vaskulêre versteurings
Minder gereeld: Hipotensie.
Versteurings van die lewer en gal
Minder gereeld: Hepatitis, verhoogde vlakke van lewertransaminases.
Frekwensie onbekend: Lewernekrose, lewerversaking.
Nier- en urienwegversteurings
Minder gereeld: Nierkoliek, nierversaking, steriele piurie.
Versteurings van die vel- en onderhuidseweefsel
Minder gereeld: Dermatitis, veluitslag of netelroos, eriteem, blosing, pruritus.
Gastro-intestinale versteurings
Frekwensie onbekend: Naarheid en braking.
Algemene en plek van toediening versteurings
Minder gereeld: Ongesteldheid.
Frekwensie onbekend: Toedingingsplek reaksie.
Spesiale voorsorgmaatreëls
PARACETAMOL BIOTECH IV moet met sorg gebruik word in gevalle van:
- Hepatosellulêre ontoereikendheid (sien WAARSKUWINGS, KONTRA-INDIKASIES, DOSIS EN GEBRUIKSAANWYSINGS).
- Erge nierontoereikendheid (kreatinien opruiming ≤ 30 mℓ/min) (sien WAARSKUWINGS, DOSIS EN GEBRUIKSAANWYSINGS, FARMAKOKINETIESE EIENSKAPPE).
- Kroniese alkoholisme, oormatige alkohol inname (3 or meer alkoholiese drankies elke dag) (sien KONTRA-INDIKASIES).
- Anoreksie, bulemie of kageksie, kroniese ondervoeding (lae reserwes van hepatiese glutatioon).
- Dehidrasie, hipovolemie.
- Glukose 6 fosfaat dehidrogenase (G6FD) tekort (kan lei tot hemolitiese anemie).

Effekte op die vermoë om te bestuur en masjinerie te gebruik:
PARACETAMOL BIOTECH IV behoort geen invloed te hê op die vermoë om te bestuur of om met masjinerie te werk nie. Geen newe-effekte wat die vermoë om te bestuur of met masjinerie te werk beïnvloed, is aangemeld deur pasiënte wat PARACETAMOL BIOTECH IV gebruik nie.

BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VIR DIE BEHANDELING DAARVAN:
Onmiddelike behandeling is noodsaaklik in die geval van oordosering.
'n Vertraging in die aanvang van behandeling mag beteken dat die teenmiddel te laat toegedien word om effektief te kan werk. Aanduiding van lewerskade is meestal vertraag tot nadat die tyd vir effektiewe behandeling verby is.
Vatbaarheid vir parasetamol toksisiteit is verhoog in pasiënte wat herhaalde verhoogde dosisse (groter as 5 – 10 g/dag) parasetamol geneem het vir 'n paar dae. Daar is 'n risiko vir vergiftiging, veral in kroniese alkoholisme, kroniese lewersiekte, VIGS, ondervoeding, en met die gebruik van geneesmiddels wat lewer mikrosomale oksidasie induseer soos barbituraat, isoniasied, rifampisien, fenitoïn en karbamasepien. Simptome van parasetamol oordosering binne 24 uur sluit in bleekheid, naarheid, braking, anoreksia en moontlike abdominale pyn. Die matigheid van die simptome binne die eerste twee dae na akute oordosering reflekteer nie die potensiële erns van die oordosering nie. Lewerskade kan opgemerk word binne 12 tot 48 uur, of later na die toediening van PARACETAMOL BIOTECH IV, aanvanklik deur verhoging in serumtransaminase en laktaat dehidrogenase aktiwiteit, verhoogde serum bilirubienkonsentrasies en verlenging van die protrombien of verhoogde INR tyd. Kliniese simptome van lewerskade is gewoonlik eers sigbaar na 2 dae and bereik 'n maksimum na 4 tot 6 dae. Lewerskade kan lei tot ensefalopatie, koma en dood.
Akute nierversaking met akute tubulêre nekrose kan ontwikkel selfs in die afwesigheid van erge lewerskade.
Abnormaliteite van glukose metabolisme en metaboliese asidose kan voorkom.
Hartdisritmieë is aangemeld.
Behandeling van parasetamol oordosering na intraveneuse toediening van PARACETAMOL BIOTECH IV:
So gou as moontlik na oordosering vermoed word, en voor die behandeling begin word, trek bloed vir 'n parasetamol plasma analise.
N-asetielsisteïen (NAS) moet toegedien word in alle gevalle van vermoede oordosering so gou as moontlik verkieslik binne agt ure na die oordosering, alhoewel behandeling tot en met 36 ure na oordosering steeds voordeel mag inhou, veral as meer as 150 mg/kg parasetamol toegedien was. 'n Aanvangsdosis van 150 mg/kg N-asetielsisteïen in 200 mℓ dekstrose 5 % m/v inspuiting **intraveneus** toegedien oor 15 minuut, gevolg deur 'n infusie van 50 mg/kg in 500 mℓ dekstrose 5 % m/v inspuiting oor die volgende vier ure, en dan 100 mg/kg in 1000 mℓ dekstrose 5 % m/v inspuiting oor die volgende sestien ure.
Natriumchloried 0,9 % m/v kan gebruik word waar glukose 5 % onvanpas is.
Die volume intraveneuse vloeistof moet aangepas word vir kinders.
Alhoewel die orale formulering nie die voorkeur behandeling is nie, kan 140 mg/kg opgelos in water aanvanklik toegedien word, gevolg deur 70 mg/kg elke vier ure vir sewentien dosisse.

Parasetamol oordosering met IV Infusies:



Bron: Martindale, The Complete Drug Reference, 36ste Uitgawe, bladsy 109

Na oordosering met 'n intraveneuse infusie, kan die standaard nomogram vir die bepaling van behandeling vanaf die plasma parasetamol konsentrasies na 'n orale inname van 'n oordosering van parasetamol, nie van toepassing wees nie. Parasetamol plasma konsentrasies meer as 4 ure na intraveneuse inspuiting kan laer wees as wat verwag word vir dieselfde orale dosis by dieselfde tydspunt na inname. Pasiënte wie se plasma parasetamolvlakke bokant die "normale behandelingslyn" is, moet voortgaan met N-asetielsisteïen behandeling 100 mg/kg IV oor 16 ure herhaaldelik tot by herstel. Pasiënte met 'n verhoogde vatbaarheid vir lewerskade soos hierbo uiteengesit, moet voortgaan met behandeling as die konsentrasies bokant die "hoë risiko behandelingslyn" is. Protrombien indeks korreleer die beste met oorlewing. Monitor alle pasiënte met beduidende oordosering vir ten minste ses en negentig ure. Behandeling is simptomaties en ondersteunend.

IDENTIFIKASIE:
Die oplossing vir infusie is 'n deursigtige, kleurlose oplossing.

AANBIEDING:
PARACETAMOL IV BIOTECH is beskikbaar in: 100ml steriele, helder kleurlose Tipe I glas fles met bruin bromobutiel rubber stopper, en pers aluminium seël met oplig flap. 'n 100 ml deurskynende wit LDPE bottel verpak in 'n deurskynende helder polipropileen omhulsel.

BERGINGSINSTRUKSIES:
Bewaar by of benede 30 °C. Beskerm teen lig. Moenie in die yskas berg of vries nie. Moenie toedien indien sigbare partikels teenwoordig is nie. Gebruik onmiddelik na oopmaak. Gooi enige ongebruikte oplossing weg. Hou buite bereik van kinders.

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