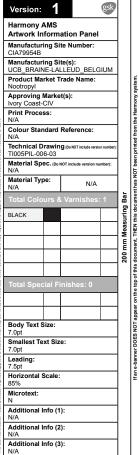
e-Banner	Project: CO-0006085	Document: PPC-4300315	Version: 2
	Site Code: CIA79954B	Operator: ST352674	Date/Time Created: 08.Jun.2018 10:30 GMT+1

Hepatic impairment No dose adjustment is needed in patients with solely hepatic impairment. In patients with hepatic impairment and renal impairment, adjustment of dose is recommended (see dose adjustment in Renal Impairment above). Nootropyl gsk NAME OF THE MEDICINAL PRODUCT Contraindications Piracetam is contraindicated in: • hypersensitivity to piracetam, other pyrrolidone derivatives or any of the QUALITATIVE AND QUANTITATIVE COMPOSITION hyperaterativity to priorderum, other pyrtolidone derivatives or any of the excipient, o server enrol impairment (lendo creatinine clearance of less than 20 ml per minute), cerebrah (haromortinge), particular suffering from Hantington's Chorea.
Warrings and Processions Effects on platelet aggregation but is the effect of procession and platelet aggregation, caution is recommended in partient with server horemorthage, patients at risk of bleading durch suggering duer, patients with underlying durations of haromotasa, patients with a history of horemorthage. CNL, patients and endographic Hargerin kindling durity duration and analysis of the analysis of the contrast and the server of the horemorthage. CNL, patients and regions mole suggery including durits of addition analysis (including) and analysis including durits of duration analysis. Excipients Macrogol 6000, calloidal anhydrous silica, magnesium stearate, Indum concormellase, hydraxypropylmethylcellulase, titanium dioxyde (E171), PHARMACEUTICAL FORM ated tablet, with a bisect line, marked N/N on one side and Vinite, odding, limit-calea lader, with a baser lime, marked VVIN on one sale and point on the affairs side. CINICAL INFORMATION Indicators Adults Procetam is indicated for: • symptomatic treatment of the psycho-organic syndrome whose features, improved by treatment, are memory loss, attention disorders and lack of drive, • treatment of cartical mycdorus, alone or in combination, • treatment of variago and saccided disorder of balance, with the exception of disztress of vacomotor or psychic origin, • pophydrasis and emission of sickle cell vaco-acclusive crises. Children Procetam is indicated for: • treatment of dyslexia, in combination with appropriate measures such as speech theory. rights Renal insufficiency Piracetam is eliminated via the kidneys and care should thus be taken in cases of Enderly Elderly nuerry or long-term treatment in the elderly, regular evaluation of the creatinine clearance is equired to allow dosage adaptation if needed (see Section Dosage and Administrat escription the breach herapy, = prophysics and remission of sickle cell vasc-occlusive crises. Dosage and Administration Firaceism may be taken with ar without food. The film coated tablets should be suellowed with liquid. It is recommended to take the daily dose in two to four therapy, Route of Administration For oral use. Adults Symptomatic treate Advis Symptomatic treatment of psycho-organic syndromes The recommended daily dose ranges from 2.4 g up to 4.8 g, in two or three GSK for widing a service to Acenocoumard In a publiked single-bill dudy on patients with severe recurrent venous thrambasis, pracetare 96 g/d ad at an modify the does of generocumenal necessary to reach INP 25 to 35 star compared with the effects of generocumanal and the Phonomopabulan leasare, level as this program and any of the does Minimum Ace With WV. RCa) and whole blood and planar vecasity. With WV, RCa) and whole blood and planar vecasity. All suppliers pr Anteplaptic drugs A 20 g daily dass of procetam over 4 weeks did not modify the serum levels of anteplaptic drugs (carbamazerine, phenybain, phenobahitone valproate) in pelipetic patients who were receiving stable doses. Alcohol Group of C ompanies. All out a licence constitutes an unplex to declare that they atment of vertigo e recommended daily dose ranges from 2.4 g to 4.8 g, in two or three divided , initant administration of alcohol had no effect on piracetam serum levels and levels were not modified by a 1.6 g oral dose of piracetam. The recommended and remission of sickle cell vaso-acclusive crises Pophylaxis and remission of sickle cell vaso-acclusive crises The recommended daily dose for prophylaxis is 160 mg/kg, orally, in four divided cohol levels copyright is the property of the GSK bution and use of fonts / software witho Pregnancy and Lactation The recommended daily dose for remission is 300 mg/kg introvenously, in four The recommended daily dose for remission is 300 mg/kg introvenously, in four divided doses. Focilia cell anomen the pophlyactic dosage must be permanen A dose lower than 160 mg/kg/day or imegular intake may result in relapse of crise Fertility rtility ere are no relevant data available. There are to reserve and a do aduations. **Progenory** Procession should not be used during pregnancy unless clearly necessary, when beamlet secade the task and the clinical condition of the pregnant mother requires teatment with procession. Subdisk of not flactation theory and the secade to the pregnant women. Annual subdisk of the procession that the secade to the pregnant women. Annual subdisk of not flactation theory of indication than the flacts with respect to pregnancy, enbryond/ facial development, portunition or post-tacial development. Procession cases the placeral barrier. Drug levels in the newborn are approximately 70% to 90% of maternal levels. Bindled dottels, for socie dei diversito trie programpia. Socie en pressure A dose lover than 150 mg/dg/dg/or trienguin intele may real in relapes of crises. **Children** Dysketo in combination with appropriate measures such as speech theory. The recommended douge to school age children from 8 years adj and addecents it 32 get pd/s, that measures 8 ml of 20% solution twice per doy or 2 bbles of 800 mg in the maning and in the evening, usually during the whole period of the school year. PhopMixes and emission of datle cell successful charges in 160 mg/dg/get day divided into 4 divided doses. In case of emission ad one of 300 mg/dg/get day divided into 4 divided doses. In case of emission ad one of 300 mg/dg/get day divided into 4 divided doses. In case of emission ad one of 300 mg/dg/get administeed Theoremound, divided into 4 divided doses. It has prophylactic cell concerns in indication in ecommended doby doses. In case of emission ad one of 300 mg/dg/get definition in school of the children in the opermant. Administeed Theoremound, divided to children with indiced may cause an ellopter of the lines. Theorem in administeed theoremount indication in ecommended doby doses. In case of emission ad one of 300 mg/dg/get definitioned in the day of the cell children in the age range of 13 years. **Eddry** Artwork of The distribution of the GSK 7/26 to VLB of maternal week. Location Pracelism should not be used using breacheding or breacheding should be discontinued, while sectioning treatment with placesam. A decision must be made where the breached of breacheding of the child and the benefit of theory to bit example to the breached of breacheding by the child and the benefit of theory for the common . am is excreted in human breast milk A contrast is exclusion in round Dietan mix. A childry to perform tasks that exquire judgement, motor or cognitive skills In view of the undesirable side effects, which were observed other the administrati the prepartion, here is the possibility of influence on the ability to drive and to op machinery and this should be taken into consideration. coministeed only to a limited number of children in the age range of 1-3 years. Eterly Adjustment of the dare is recommended in elderly patients with componied renal function (see Section Warning and Precations; Renal Impairment below), for long term treatment in the elderly, regular evaluation of the creatinien clearance is required to allow dooge adaptation if needed. Renal impairment Procedam is contrandicated in severe mail impairment (renal creatinine clearance of less than 20 ml per minute) (see Sections; Contraindications; Warnings and Permutinent) Adverse Reactions Clinical Trial and Post Marketing Data Consult mar una ross marxening Data Double-biland proberbo-controlled clinical or phormaco-clinical trials, of which spannfield safety data are available, included more than 3000 subjects seceiving siracetam, regardless of indication, dosage form, daily dosage or population thrapetristics. reas non zU m per minutel [see Sections: Contraindications; Warnings and Percentrions]. The day does must be individualised according to senal function. Refer to the following table and adjust the dose as indicated. To use this dosing table, on asimate of the pointer's creating educatores (CIch a m/m in s needed. The CIr in m/min may be estimated the one serum creatinine (mg/dl) determination using the following famula: Adverse drug reactions (ADRs) are listed below by MedDRA system organ class and y frequency. by requency. reauencies are defined as: tricquences are defined as: Very common ≥1/10 Common ≥1/100 to <1/10 Uncommon ≥1/100 to <1/100 Rare ≥1/10000 to <1/1000 Very rare <1/10000 Not known (cannot be estimated from the available data).  $Clcr = \frac{[140 - age (years)] \times weight (kg)}{(x \ 0.85 \text{ for women})}$ 72 x serum creatinine(*mg/dl*) Naf known (cannot be estimated from the available data Blood and kympholitic system diaordae Nat known: haemorrhagic diaordae Immune system diaordae Nat known: anghylachol traction, hypersensitivity Rychatric diaordae Common: reinourness Uncommon: depression Naf known: agitation, analyt, confusion, hallucination Nervus aystem lacardae Common: hyperkinesia Uncommon: genonleanea Uncommon: somnolence Not known: ataxia, balance disorder, epilepsy aggravated, headache, insomnia



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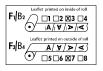
GSK SDC is responsible for site technical requirements and pre-press suitability.

GSK Market is responsible to advise SDC when changes required impact the following: Formulation

Tablet embossing

Storage conditions Shelf Life





Group	Creatinine Clearance (ml/min)	Posology and frequency
Normal	>80	usual daily dose, 2 to 4 divided doses
Mild	50-79	2/3 usual daily dose, 2 or 3 divided doses
Moderate	30-49	1/3 usual daily dose, 2 divided doses
Severe	20-29	1/6 usual daily dose, 1 single intake
	<20	contre-indiqué
End-stage renal disease	-	contraindicated

<b>Ö</b> a	Project: CO-0006085	Document: PPC-4300315	Version: 2
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Ear and labyrinth disorders Nat known: vertigo Vascular disorders Rare: thrombophlebitis (only for injectable form), hypotension (only for injectable form) mg/ nectory to part region of the second management of the second Gastrointestinal disorders Not known: abdominal pain, abdominal pain upper, diarrhoea, nausea, von Skin and subcutaneous tissue disorders Not known: angioneurotic oedema, dermatitis, pruritus, urticaria General disorders and administration site conditions Linearity The pharmocolonatics of piracetam are linear over the dose range of 0.8 to 12 g. Pharmocoknetic variables like half-life and clearance are not changed with respect to the dose and the duration of treatment. Special potient populations Children No termal pharmocokinetic study has been conducted in children. Linearity Rare: pyrexia (only for injectable form), injection site pain (only for injectable form) Investigations on: weight increased Overdosage Symptoms and signs No additional adverse events specifically related to overdose have been reported No formal pharmacosinemic source and the increase is related to the Elderly. In the elderly, the half-life of piracetom is increased and the increase is related to the decrease in renal function in this population (see Section Dosage and Administration). with piracetam. The highest reported overdose with piracetam was oral intake of 75 g wherein bloady diarrhoea with abdominal pain, was most probably related to the extreme high dose of sorbital contained in the used formulation. In the electry, the foll-file of procedam is increased and the increase is reliabed to the decrease in real function in this population (see Section Dozage and Administration **Real important**). Final state of the section boards and administration **Real important**. The section boards and administration in proteins with real important (see Section Dozage and Administration) in antic End Stage Rend Disease subjects, the holf-file of pirocetam is increased up to Schoor. The foreignment (see Section Dozage and Administration) in antic End Stage Rend Disease subjects, the holf-file of pirocetam is increased up to Schoor. The foreignment (see Section Dozage and Administration) in antic Hopatic important line (important electronic music Sto). Ook during a typical Advant didys session. These involved. Biocrass 80 to 100% of the dose is secreted in the une as unchanged durg, heaptic important electronic uside not be expected to have a significant effect on pirocetam island. high acce of social contracts in the Used formulation. **Teachment** There is no specific antidote for overdose with piracetom. Treatment for an overdose should be symptomical and may induce hermodaloyiss. The extraction efficiency of the dialoyer is 30 to 60% for piracetam. Further management should be as chically indicated or as recommended by the national poicons centre, where available. Clinical Pharmacology Pharmacodynamics Pharmacotherapeutic group Psychostimulants, agents used for ADHD and nootropics ATC Code Arc core NG2B003 Mechanism of Action Available data suggest that pracetam basic mechanism of action is natifier call nor organizabec(Le, Princetam binds physically) in a dose-dependent manual the membrane isamiliar instructions characterised by the formation of mobile data physically to truthous characterised by the formation of mobile abability, allowing the membrane and transmissione provide to maintain or recover the fine-dimensional structure or Isaling essential to exert their function. Pracetam has neuronal and avacular effects. Race Clinical Studies Phorecocylonatic ettects Neuroand ettects At the neuroand level, pincetam exerts its membrane activity in various ways. In animals, pincetam enhances a variety of types of neurotransmission, primaly through postsynaptic modulation of receptor density and activity. In both animals man, the functions involved in cognitive processes such as a termina, memory, attention and consciouress were enhanced, in the normal subject ary well as in declicency states, whole the development of sectative or pychostimuland reflexts. Princetam protect and restores cognitive abilities in animals and man after various extendor linuits and shyposic, inclusions and effectionsulsive filterapy. It protects against hyposic-induced changes in borin function and performance as sussessed by electomerephilograph (EEG) and psychametric evolutions. Various and effects ic/s NON-CLINICAL INFORMATION assessed by electioencepholograph (EG) and psychometric evolutions. Youclan affect: Pracetan applies its beamonhagic effect to thomobacytes, enythocytes and the work of the block vestels by increasing the defamability of enythocytes, reducing the aggregability of thobacytes, reduces the adhesion of enythrocytes to the walls of vestels and reduces capitary vacanasm. Effects on notices capitary vacanasm, pracetam improves the defamability of the enythocyte membrane, decrease blocd viscusity, and prevents novieux formation. Effects on polies of pracetam up to 12 was associated with a dase-dependent reduction in platelet functions compared with pre-teamment values less da aggregion induced by APC, collage, enjemphiren and B To release, whout significant change in platelet count. In these studies, pricetam prioring bleeding time. PHARMACEUTICAL INFORMATION Shelf-Life 48 months Storage Store below 30°C Nature and Contents of Container film-coated tablet in PVC Blister . Box of 45. Incompatibilities None known Use and Handling There are no special requirements for use or handling of this product. Ihere are no spec Manufacturer: UCB Pharma SA Chemin du Foriest 1420 Braine-l'Allie aggregation induces by PLD, sowgen, several interaction prolonged bleeding significant change in platelie court. If these studies, picotechan prolonged bleeding time. If the plate interaction is the studies, picotechan plate interaction or available plate plate interaction. If the studies, plate is the plate interaction of the plate plate interaction is the studies. The studies of the plate plate is the studies of the plate is the studies in backly volumes, picotechan reduced the adhesion of BBCs to vascular endohalium and possess do to a divert stimular affect on postocycline synthesis in healthy volumes, picotechan who have heatment volues, picotechan up to 9.6 g reduced planna levels of hitmogen and von Willeband's backs (MLC, VIII E VIC, V Marketing authorization holder: GSK Export Limited 980 Great West Road Brentford Middlesex TW8 9GS – United Kingdom Version number: 03 Version date: 25 January 2017 Trade marks are owned by or licensed to the GSK group of companies ©2018 GSK group of companies or its licensor. Absorption

## Absorption Pincetima is regulidy and extensively absorbed following and administration. In fasted subjects, the peak plasma concentrations are achieved 1 hour after douing. The adouble bioandiability of pincation and formations is achieved 1. Thour after douing. The adouble to another the setter of absorption of pincetamb bit if decreases $\Gamma_{\rm cm}$ by 178 and in 15 µprime 10 s hours. The Aconcentrations are hytically 84 µprime and 15 µprime 10 s hours. The Aconcentrations are hytically 84 µprime and 15 µprime 10 s hours. The Aconcentrations are hytically 84 µprime and 15 µprime and the advantage of 3.2 g and repeat doue of 3.2 g twice therefore the advantage of the a

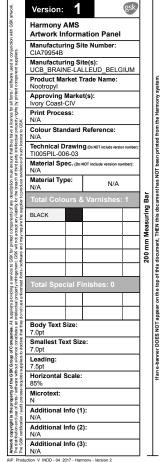
daily, respectivey. Distribution Pracetom is not bound to plasma probeins and its volume of distribution is approximately (0.6 / Vg. Pracetom crosses the blood brain brainer as it has been measured in cerebrospinal fluid blouwing introvenous administration. In cerebrospi Willi, de Tu<sub>w</sub>, and socilised dood 15 hous produkes and the bolffle was about 8.5 hours. In animals, procesam highest concentrations in the bolffle was about 8.5 hours. In animals, procesam highest concentrations in the bolffle was about 8.5 hours. In animals, procesam highest concentrations in the bolffle was about 8.5 hours. In animals, procesam highest concentrations in the bolffle was about 8.5 hours. In animals, procesam highest concentrations in the bolffle was about the bound genglia. Pracetom diffuses to all issues except adopore issues, crosses placental barrier, and penetrates the membranes of isolated ied blood cells.

Metabolism Pracetam is not known to be metabolized in the human body. This lack of metabolism is supported by the lengthy plasma half-life in anuric patients and the high recovery of parent compound in urine.

GenderIn a bioequivalence study comparing formulations at a dose of 2.4 g,  $C_{\rm max}$  and AUC were approximately 30% higher in women (N=6) compared to men (N=6). However, clearances adjusted for body weight were comparable.

Race formal pharmacokinetic studies of the effects of race have not been conducted. Cross study comparisons involving Caucasians and Asians, however, show that pharmacoknetic: a forocaten were comparable batware the two races. Because procedum is primarily rendly excited and there are no important tracial differences in centionic elacance, pharmacokinetic differences due to race and respected.

NON-CLINICAL INFORMATION The preclinical data indicate that priorestem has a low toxicity potential. Single does studies showed no inversible toxicity after and doess of 10 g/m, the most, nata and dogs. No target arguing has taken to a software in prepeted does, character autorises in mice lays to 4.8 g/m/g/day) and in the lays to 2.4 g/m/g/day). Mild autorisestinal fields [lenses], charget in soft a constantion, interacted and/how consumption] were observed in dogs when pinactation was administrated and/how for lay to 1.2 g/m/g/day for 4.5 weeks in nata and dogs and to pravise providently. In with and in vivo studies have shown no potential for genetoxicity and corritogenicity.



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Code

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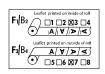
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Shelf Life

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