APPROVED PACKAGE INSERT

SCHEDULING STATUS

Schedule 6

PROPRIETARY NAME AND DOSAGE FORM

NEUCON® 18 mg (extended-release tablets).

NEUCON® 27 mg (extended-release tablets).

NEUCON® 36 mg (extended-release tablets).

NEUCON® 54 mg (extended-release tablets).

COMPOSITION

Extended-release tablets containing 18 mg, 27 mg, 36 mg or 54 mg of methylphenidate hydrochloride.

Contains sugar (lactose monohydrate)

Each NEUCON 18 mg tablet contains 6,49 mg lactose monohydrate

Each NEUCON 27 mg tablet contains 4,94 mg lactose monohydrate

Each NEUCON 36 mg tablet contains 14,44 mg lactose monohydrate

Each NEUCON 54 mg tablet contains 7,6 mg lactose monohydrate

Excipients:

Butylated hydroxytoluene, carnauba wax, cellulose acetate, hypromellose, lactose, poloxamer, polyethylene glycol, polyethylene oxides, povidone, propylene glycol, sodium chloride, stearic acid, succinic acid, synthetic iron oxides, titanium dioxide and triacetin.

PHARMACOLOGICAL CLASSIFICATION

A 1.2 Psychoanaleptics (antidepressants).

PHARMACOLOGICAL ACTION

Pharmacodynamic properties

Methylphenidate HCl is a central nervous system (CNS) stimulant. The mode of therapeutic action in attention deficit hyperactivity disorder (ADHD) is not known. Methylphenidate is thought to block the reuptake of norepinephrine and dopamine into the presynaptic neuron and increase the release of these monoamines into the extraneuronal space. Methylphenidate is a racemic mixture comprised of the d- and l-isomers. The d-isomer is more pharmacologically active than the l-isomer.

Pharmacokinetic properties

Absorption: Following oral administration of extended release methylphenidate to adults, plasma methylphenidate concentrations increase rapidly reaching an initial maximum at about 1 to 2 hours, then increase gradually over the next several hours. Peak plasma concentrations are achieved at about 6 to 8 hours after which a gradual decrease in plasma levels of methylphenidate begins.

The mean pharmacokinetic parameters in 36 adults following the administration of extended release methylphenidate 18 mg once daily are summarised in Table 1.

Table 1.

Mean ± SD Pharmacokinetic Parameters

PARAMETERS	Extended release methylphenidate (18 mg once daily) (n=36)
C_{max} (ng/mL)	3,7 ± 1,0
T_{max} (h)	6,8 ± 1,8
AUC_{inf} (ng·h/mL)	41,8 ± 13,9
$t_{1/2}$ (h)	3,5 ± 0,4

No differences in the pharmacokinetics of extended release methylphenidate were noted following single and repeated once daily dosing indicating no significant accumulation. The AUC and t½ following repeated once daily dosing are similar to those following the first dose of extended release methylphenidate.

Dose proportionality*:* Following administration of extended release methylphenidate in single doses of 18, 36, and 54 mg/day to healthy adults, C_{max} and $AUC_{(0\text{-}inf)}$ of d-methylphenidate were proportional to dose, whereas l-methylphenidate C_{max} and $AUC_{(0\text{-}inf)}$ increased disproportionately with respect to dose. Following administration of extended release methylphenidate, plasma concentrations of the l-isomer were approximately 1/40th the plasma concentrations of the d-isomer.

In healthy adults, single and multiple dosing of once daily extended release methylphenidate doses from 54 to 144 mg/day resulted in linear and dose proportional increases in C_{max} and AUC_{inf} for total methylphenidate (MPH) and its major metabolite, (alpha)-phenyl-piperidine acetic acid (PPAA). The single dose and steady state (Day 4) clearance and half-life parameters were similar, indicating that there was no time dependency in the

pharmacokinetics of methylphenidate. The ratio of metabolite (PPAA) to parent drug (MPH) was constant across doses from 54 to 144 mg/day, both after single dose and upon multiple dosing.

In a multiple dose study in adolescents ADHD patients aged 13 –16 administered a dose of 18 to 72 mg/day of extended release methylphenidate, mean C_{max} and AUC_{TAU} of methylphenidate increased proportionally with respect to the dose.

Distribution: Plasma methylphenidate concentrations in adults decline bi-exponentially following oral administration. The half-life of both d- and l-isomers of methylphenidate in adults following oral administration of extended release methylphenidate was approximately 3,5 h.

Metabolism and excretion: In humans, methylphenidate is metabolised primarily by de-esterification to (alpha)-phenyl-piperidine acetic acid (PPAA) which has little or no pharmacologic activity.

After oral dosing of radio labelled methylphenidate in humans, about 90 % of the radioactivity was recovered in urine. The main urinary metabolite was (PPAA), accounting for approximately 80 % of the dose.

Food effects: There were no differences in either the pharmacokinetics or the pharmacodynamic performance of extended release methylphenidate when administered after a high fat breakfast in patients. There is no evidence of dose dumping in the presence or absence of food.

Special Populations:

Age: The pharmacokinetics of extended release methylphenidate has not been studied in children less than 6 years of age.

Renal insufficiency: There is no experience with the use of extended release methylphenidate in patients with renal insufficiency. Since renal clearance is not an important route of methylphenidate clearance, renal insufficiency is expected to have little effect on the pharmacokinetics of extended release methylphenidate.

Hepatic insufficiency: There is no experience with the use of extended release methylphenidate in patients with hepatic insufficiency.

INDICATIONS

NEUCON is indicated for the treatment of attention deficit hyperactivity disorder (ADHD) in children and adolescents aged 6 - 17 and adults aged 18 to 65 who meet DSM-IV criteria for ADHD.

CONTRAINDICATIONS

NEUCON is contraindicated:

- in patients with marked anxiety, tension, and agitation, since NEUCON may aggravate these symptoms;
- in patients known to be hypersensitive to methylphenidate or other components of NEUCON;
- in patients with glaucoma;
- in patients with a family history or diagnosis of Tourette's syndrome;

- during treatment with monoamine oxidase inhibitors, and also within a minimum of 14 days following discontinuation of a monoamine oxidase inhibitor (as hypertensive crises may result);
- in patients with hyperthyroidism, cardiac dysrhythmias, ischaemic heart disease, uncontrolled hypertension;
- in pregnancy and lactation. (See Pregnancy and Lactation).

WARNINGS AND SPECIAL PRECAUTIONS

NEUCON increases heart rate, systolic and diastolic blood pressure, therefore caution is advised when NEUCON is prescribed for ADHD patients whose underlying medical conditions might be compromised by increases in heart rate and/or blood pressure e.g. heart failure and hypertension. Blood pressure should be monitored in patients treated with NEUCON especially those with hypertension (see Contraindications).

Structural cardiac abnormalities

Cases of sudden death have been reported in ADHD patients with structural cardiac abnormalities treated with NEUCON used, at usual doses. Although the data are inconclusive regarding causal relationship between treatment with NEUCON and sudden death, caution is advised when NEUCON is prescribed for ADHD patients with structural cardiac abnormalities.

Patients under 6 years old

NEUCON should not be used in patients under six years old. Sufficient data on the safety of long-term use of NEUCON is not yet available.

Motor and verbal tics

NEUCON has been associated with the onset or exacerbation of motor and verbal tics. Therefore, clinical evaluation for tics in patients should precede use of NEUCON. Family history should be assessed.

Long-term use

Although a causal relationship has not been established, suppression of growth (i.e. weight gain, and/or height) has been reported with the long-term use of NEUCON in children. Therefore, patients requiring long-term therapy should be carefully monitored. Patients who are not growing or gaining weight as expected should have their treatment interrupted.

Dose administration

NEUCON must be swallowed whole with the aid of liquids. Tablets should not be chewed, divided or crushed. Methylphenidate is contained within a non-absorbable shell designed to release the medicine at an extended rate. The tablet shell, along with insoluble core components, is eliminated from the body; patients should not be concerned if they occasionally notice in their stools something that looks like a tablet.

Because the NEUCON tablet is non-deformable and does not appreciably change in shape in the GI tract, NEUCON should not be administered to patients with pre-existing severe gastrointestinal narrowing (pathologic or iatrogenic) or in patients with dysphagia or significant difficulty in swallowing tablets. There have been reports of obstructive symptoms in patients with known strictures. Due to the extended release design of the tablet, NEUCON should only be used in patients who are able to swallow the tablet whole.

Use in other indications

NEUCON should not be used to treat depression and/or for the prevention of treatment of normal fatigue states.

Psychotic or manic symptoms

Psychotic (e.g., hallucinations) or manic symptoms have been reported in patients without a prior history of psychotic illness or mania during treatment with NEUCON at usual doses. If such symptoms occur, consideration should be given to a possible causal role of NEUCON and discontinuation of treatment may be appropriate.

Aggressive behaviour

Patients beginning treatment with NEUCON should be monitored for the appearance or worsening of aggressive behaviour. Aggression is frequently associated with ADHD; however, emergence or worsening of aggression has been reported during treatment with NEUCON.

Conditions requiring caution

NEUCON should be given with caution in the following conditions:

- ***Psychotic patients:*** Administration of NEUCON may exacerbate symptoms of behaviour disturbances and thought disorder in psychotic patients.
- ***Underlying medical conditions that may be compromised by increases in blood pressure or heart rate:*** In clinical trials in children, NEUCON increased resting pulse by an average of 2-6 bpm and produced average increases of systolic and diastolic blood pressure of roughly 1-4 mm Hg during the day, relative to placebo. In placebo-controlled studies in adults, mean increases in resting pulse rate of approximately 4 to 6 bpm were observed with NEUCON at endpoint vs. a mean change of roughly -2 to 3 bpm with placebo. Mean changes in blood pressure at endpoint ranged from about –1

to 1 mm Hg (systolic) and 0 to 1 mm Hg (diastolic) for NEUCON and from –1 to 1 mm Hg (systolic) and –2 to 0 mm Hg (diastolic) for placebo.

Therefore, caution is indicated in treating patients whose underlying medical conditions might be compromised by increases in blood pressure or heart rate. (see Warnings)

- ***History of drug dependence or alcoholism:*** NEUCON should be given cautiously to patients with a history of drug dependence or alcoholism. Chronic abusive use can lead to marked tolerance and psychological dependence with varying degrees of abnormal behaviour. Frank psychotic episodes can occur, especially with parenteral abuse. Careful supervision is required during withdrawal from abusive use since severe depression may occur. Withdrawal following chronic therapeutic use may unmask symptoms of the underlying disorder that may require follow-up.
- ***History of seizures or prior abnormalities:*** There is evidence that NEUCON may lower the convulsive threshold in patients with prior history of seizures, in patients with prior EEG abnormalities in absence of seizures, and in absence of history of seizures and no prior EEG evidence of seizures. In the presence of seizures, NEUCON should be discontinued.

Visual disturbances

Symptoms of visual disturbances have been reported. Difficulties with accommodation and blurring of vision have been reported.

Haematologic monitoring

Periodic haematologic monitoring (Complete blood count, differential, and platelet counts) is advised during prolonged therapy.

Lactose warning statement

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency of glucose-galactose malabsorption should not take NEUCON.

Effects on ability to drive and use machines:

NEUCON may impair the ability of the patient to operate potentially hazardous machinery or vehicles. Patients should be cautioned accordingly until they are reasonably certain that NEUCON does not adversely affect their ability to engage in such activities.

INTERACTIONS

Because of the effects on blood pressure, NEUCON should be used cautiously with pressor agents.

Human pharmacological studies have shown that methylphenidate may inhibit the metabolism of warfarin anticoagulants, anticonvulsants (e.g. phenobarbital, phenytoin, primidone), and some antidepressants (tricyclics and selective serotonin reuptake inhibitors). Downward dose adjustment of these medicines may be required when given concomitantly with NEUCON. It may be necessary to adjust the dosage and monitor plasma medicines concentrations (or, in the case of coumarin, coagulation times), when initiating or discontinuing concomitant use of NEUCON.

Serious adverse events have been reported in concomitant use with clonidine, although no causality for the combination has been established. The safety of using NEUCON in combination with clonidine or other centrally acting alpha-2 agonists has not been systematically evaluated.

Alcohol may exacerbate the adverse CNS effects of NEUCON. It is therefore desirable for patients to abstain from alcohol during treatment.

PREGNANCY AND LACTATION

NEUCON should not be used in pregnancy and lactation as safety has not been established. Teratogenicity has been shown in laboratory animals.

DOSAGE AND DIRECTIONS FOR USE

NEUCON should not be used in patients under six years old.

NEUCON is administered orally once daily. As the effect has been shown to be present 12 hours after dosing, the product should be taken in the morning.

NEUCON must be swallowed whole with adequate amounts of liquids, and must not be chewed, divided, or crushed.

NEUCON may be administered with or without food.

Dosage should be individualised according to the need and response of each individual patient.

Patients New to NEUCON:

The recommended starting dose of NEUCON for patients who are not currently taking methylphenidate, or for patients who are on stimulants other than methylphenidate, is 18 mg once daily for children and adolescents and 18 or 36 mg once daily for adults.

Patients currently using NEUCON:

The recommended dose of NEUCON for patients who are currently taking methylphenidate three times daily at doses of 15 to 60 mg/day is provided in Table 2. Dosing recommendations are based on current dose regimen and clinical judgement.

Table 2. Recommended Dose Conversion from Other Methylphenidate Regimens to NEUCON

Previous Methylphenidate Daily Dose	Recommended NEUCON Dose
5 mg Methylphenidate hydrochloride twice daily or three times daily.	18 mg once daily
10 mg Methylphenidate hydrochloride twice daily or three times daily	36 mg once daily
15 mg Methylphenidate hydrochloride twice daily or three times daily.	54 mg once daily
20 mg Methylphenidate hydrochloride twice daily or three times daily	72 mg once daily

Clinical judgment should be used when selecting the dose for patients currently taking methylphenidate in other regimens.

Dosage may be adjusted in 18 mg increments to a maximum of 54 mg/day for children aged between 6 – 12 years and to a maximum of 72 mg for adolescents aged between 13 – 18 years and 108 mg in adults. In general, dosage adjustment may proceed at approximately weekly intervals.

Daily dosage above 54 mg is not recommended for children aged between 6 – 12 years.

Daily dosage above 72 mg is not recommended for adolescents aged between 13 – 18 years.

Daily dosage above 108 mg is not recommended in adults.

Maintenance/Extended Treatment:

The long-term use of NEUCON has not been systematically evaluated in controlled clinical trials.

The medical practitioner who elects to use NEUCON for extended periods in patients with ADHD should periodically re-evaluate the long-term usefulness of the medicine for the individual patient with trials off medication to assess the patient's functioning without pharmacotherapy.

Dose reduction and Discontinuation:

If paradoxical aggravation of symptoms or other adverse events occur, the dosage should be reduced, or, if necessary, NEUCON should be discontinued.

ELDERLY:

Use of NEUCON in elderly patients over 65 years has not been studied in controlled trials.

SIDE EFFECTS

Clinical Trial Data

The table below shows all the adverse drug reactions (ADRs) observed during clinical trials of children, adolescents and adults with NEUCON and those, which have been reported with other methylphenidate hydrochloride formulations. If the ADRs with NEUCON and the

methylphenidate formulation frequencies were different, the highest frequency of both databases was used.

Frequency estimate:

Very common (≥ 1/10)

Common (≥ 1/100 to < 1/10)

Uncommon (≥ 1/1 000 to < 1/100)

Rare (≥ 1/10 000 to < 1/1 000)

Very rare (< 1/10 000)

Not known (cannot be estimated from the available data)

System Organ Class	**Adverse Drug Reaction**					
	Frequency					
	Very common	Common	Uncommon	Rare	Very rare	Not known
Infections and infestations		Nasopharyngitis, upper respiratory tract infection*, sinusitis *				
Blood and lymphatic system disorders					Anaemia** , Leukopaenia**	
Metabolism and nutritional disorders		Anorexia, decreased appetite**, moderately reduced weight				

		and height gain during prolonged use in children				
Psychiatric disorders	Insomnia, nervousness	Anorexia, affect lability, aggression, agitation, anxiety**, depression*, irritability, abnormal behaviour, mood swings, tics, initial insomnia*, depressed mood*, depression**, decreased libido*, tension *, bruxism*, panic attack*	Psychotic disorders, anger, suicidal ideation, altered mood, restlessness** , tearfulness, worsening of pre-existing tics of Tourette's syndrome, hypervigilance , sleep disorder	Libido disorder , confusional state**	Suicidal attempt (including completed suicide)**, transient depressed mood, abnormal thinking, apathy**, repetitive behaviours, over-focussing	Delusions**, thought disturbances , dependence, cases of abuse and dependence have been described more often with immediate release formulations
Nervous system disorders	Headache	Dizziness, psychomotor hyperactivity, somnolence, paraesthesia*, tension headache*	Sedation, tremor**, lethargy*		Choreo-athetoid movements, reversible ischaemic neurological deficit, neuroleptic	Cerebrovascular disorders** (including vasculitis, cerebral haemorrhages,

					malignant syndrome (NMS; reports were poorly documented and in most cases, patients were also receiving other medicines, so the role of methylphenidate is unclear)	cerebrovascular accidents, cerebral arteritis, cerebral occlusion), migraine**
Eye disorder		Accommodation disorder*	Blurred vision**, dry eye *	Difficulties in visual accommodation		
Ear and labyrinth disorders		Vertigo*				
Cardiac disorders		Dysrhythmia, tachycardia, palpitations	Chest pain		Cardiac arrest, myocardial infarction	
Vascular disorders		Hypertension	Hot flushes*		Cerebral arteritis and/or occlusion, peripheral coldness**	

Respiratory, thoracic and mediastinal disorders		Cough, oropharyngeal pain	Dyspnoea**			
Gastrointestinal disorders		Upper abdominal pain, diarrhoea, nausea**, abdominal discomfort, vomiting, dry mouth **, dyspepsia*	Constipation**			
Hepatobiliary disorders			Hepatic enzyme elevations		Abnormal liver function, including hepatic coma	
Skin and subcutaneous tissue disorders		Pruritis, rash, urticaria	Angioneurotic oedema, bullous conditions, exfoliative conditions	Hyperhidrosis**, Macular rash	Erythema multiforme, exfoliative dermatitis, fixed medicine eruption	
Musculoskeletal and connective tissue disorders		Muscle tightness*, muscle spasms*			Muscle cramps	

Renal and urinary disorders			Haematuria, pollakiura			
Reproductive system and breast disorders		Erectile dysfunction*		Gynaecomastia		
General disorders and administration site conditions		Pyrexia, growth retardation during prolonged use in children, fatigue**, irritability *, feeling jittery*, asthenia*, thirst*			Sudden cardiac death	
Investigations		Changes in blood pressure and heart rate (usually an increase), decreased weight, increased alanine aminotransferase *	Cardiac murmur			

*Frequency derived from adult clinical trials and not on data from trials in children and adolescents; may also be relevant for children and adolescents

**Frequency derived from clinical trials in children and adolescent and reported at a higher frequency in clinical trials in adult patients.

Postmarketing Data

ADRs identified during post-marketing experience with NEUCON are included in Table 4.

Table 4. Adverse Drug Reactions Identified During Postmarketing Experience with NEUCON
Blood and Lymphatic System Disorders Pancytopenia, thrombocytopenia, thrombocytopenic purpura **Immune System Disorders** Hypersensitivity reactions such as angioedema, anaphylactic reactions, auricular swelling, bullous conditions, exfoliative conditions, urticaria, pruritus, rashes, eruptions and exanthemas **Psychiatric Disorders** Disorientation, hallucination, auditory hallucination, visual hallucination, mania, logorrhoea **Nervous System Disorders** Convulsion, grand mal convulsion, dyskinesia **Eye Disorders** Diplopia, mydriasis, visual impairment **Cardiac Disorders** Angina pectoris, bradycardia, extrasystoles, supraventricular tachycardia, ventricular extrasystoles **Vascular Disorders** Raynaud's phenomenon **Skin and Subcutaneous Tissue Disorders** Alopecia, erythema **Musculoskeletal and Connective Tissue Disorders** Arthralgia, myalgia, muscle twitching

General Disorders and Administration Site Conditions

Decreased therapeutic response

Chest pain, chest discomfort, decreased drug effect, hyperpyrexia

Investigations

Increased blood alkaline phosphatase, increased blood bilirubin, increased hepatic enzyme, decreased platelet count, abnormal white blood cell count

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

Signs and symptoms of NEUCON in overdosage, resulting principally from overstimulation of the CNS and excessive sympathomimetic stimulations. They may include the following: vomiting, agitation, tremors, hyperreflexia, muscle twitching, convulsions, coma, grand mal convulsion, euphoria, confusional state, confusion, hallucinations (auditory and/or visual), hyperhidrosis, flushing, headache, pyrexia, tachycardia, palpitations, heart rate increased, sinus dysrhythmias, hypertension, mydriasis, and dry mouth.

Treatment consists of appropriate supportive measures. The patients must be protected against self-injury and against external stimuli that would aggravate overstimulation already present. Gastric contents may be evacuated by gastric lavage as indicated. Before performing gastric lavage, control agitation and seizures if present and protect the airway. Other measures to detoxify the gut include administration of activated charcoal and a cathartic.

Intensive care must be provided to maintain adequate circulation and respiratory exchange; external cooling procedures may be required for pyrexia.

Efficacy of peritoneal dialysis or extracorporeal haemodialysis for NEUCON overdosage has not been established.

The prolonged release of methylphenidate from NEUCON should be considered when treating patients with overdose.

IDENTIFICATION

18 mg: capsule-shaped yellow tablet with “alza 18” printed on one side in black ink.

27 mg: capsule-shaped grey tablet with “alza 27” printed on one side in black ink

36 mg: capsule-shaped white tablet with “alza 36” printed on one side in black ink.

54 mg: capsule-shaped brownish-red tablet with “alza 54” printed on one side in black ink.

PRESENTATION

NEUCON is available in a square, white, opaque high-density polyethylene (HDPE) bottle with a white polypropylene child resistant closure, with induction sealed tamper-evident membrane.

Each HDPE bottle contains one or two desiccants, and will hold 30 tablets. The HDPE bottle is packed into an outer carton until required for use.

STORAGE CONDITIONS

Store at or below 25 °C.

Keep the container tightly closed.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBERS

18 mg: 46/1.2/0380

27 mg: 46/1.2/0381

36 mg: 46/1.2/0382

54 mg: 46/1.2/0383

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

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DATE OF PUBLICATION OF THE PACKAGE INSERT

Date of registration of the medicine: 20 April 2017

SKEDULERINGSTATUS

Skedule 6

EIENDOMSNAAM EN DOSERINGSVORM

NEUCON® 18 mg (verlengde vrystellende tablette).

NEUCON® 27 mg (verlengde vrystellende tablette)

NEUCON® 36 mg (verlengde vrystellende tablette).

NEUCON® 54 mg (verlengde vrystellende tablette).

SAMESTELLING

Verlengde, vrystellende tablette bevattende 18 mg, 27 mg, 36 mg of 54 mg metielfenidaathidrochloried.

Bevat suiker (laktosemonohidraat)

Elke NEUCON 18 mg tablet bevat 6,49 mg laktosemonohidraat

Elke NEUCON 27 mg tablet bevat 4,94 mg laktosemonohidraat

Elke NEUCON 36 mg tablet bevat 14,44 mg laktosemonohidraat

Elke NEUCON 54 mg tablet bevat 7,6 mg laktosemonohidraat

Eksipiënte:

Gebutileerde hidroksitolueen, palmwas, selluloseasetaat, hipromellose, laktose, poloksameer, poliëtileenglikool, poliëtileen oksiede, povidoon, propileenglikool, natriumchloried, steariensuur, suksiensuur, sintetiese ysteroksiede, titaandioksied en triasetien.

FARMAKOLOGIESE KLASSIFIKASIE

A 1.2 Psigo-analeptika (antidepressante).

FARMAKOLOGIESE WERKING

Farmakodinamiese eienskappe

Metielfenidaat HCl is ‘n sentrale senuweestelsel (SSS)-stimulant. Die terapeutiese werkingswyse t.o.v. aandaggebrek-hiperaktiwiteitsindroom (ADHD) is nie bekend nie. Dit word vermoed dat metielfenidaat die heropname van noradrenalien en dopamien in die presinaptiese neuron blokkeer en die vrystelling van hierdie monoamiene in die ekstraneuronale ruimte verhoog. Metielfenidaat is ‘n rasemiese mengsel van die d- en l-isomere. Die d-isomeer is farmakologies meer aktief as die l-isomeer.

Farmakokinetiese eienskappe

Absorpsie: Na mondelike toediening van verlengde vrystellende metielfenidaat aan volwassenes, neem metielfenidaat-plasmakonsentrasies vinnig toe en bereik ‘n aanvanklike maksimum binne 1 tot 2 uur, waarna dit geleidelik oor die volgende aantal uur toeneem. Piek-plasmakonsentrasies word binne 6 tot 8 uur bereik, waarna ‘n geleidelike afname in metielfenidaat-plasmavlakke begin.

Die gemiddelde farmakokinetiese parameters by 36 volwassenes na toediening van 18 mg verlengde vrystellende metielfenidaat een keer per dag, word in Tabel 1 opgesom.

Tabel 1.

Gemiddelde ± SD Farmakokinetiese Parameters

PARAMETERS	**Verlengde vrystellende metielfenidaat** **(18 mg een keer daagliks)** **(n=36)**
C_{maks} (ng/mL)	3,7 ± 1,0
T_{maks} (h)	6,8 ± 1,8
AOK_{inf} (ng·h/mL)	41,8 ± 13,9
$t_{1/2}$ (h)	3,5 ± 0,4

Geen verskil in die farmakokinetika van verlengde vrystellende metielfenidaat na eenmalige of herhaalde een keer daaglikse doserings is waargeneem nie, wat dui op geen betekenisvolle geneesmiddel- akkumulasie nie. Na herhaalde een keer daaglikse doserings is die AOK en $t_{½}$ soortgelyk aan wat by ‘n eerste dosis verlengde vrystellende metielfenidaat aangetref word.

Dosis-verwantskap*:* Na toediening van verlengde vrystellende metielfenidaat as enkeldosisse van 18, 36, en 54 mg/dag aan gesonde volwassenes, was die K_{maks} en $AOK_{(0-inf)}$ van d-metielfenidaat proporsioneel tot die dosis, terwyl by l-metielfenidaat die K_{maks} en $AOK_{(0-inf)}$ oneweredig met betrekking tot die dosis toegeneem het. Na toediening van verlengde vrystellende metielfenidaat was die plasmakonsentrasie van die l-isomeer ongeveer 1/40ste van die plasmakonsentrasie van die d-isomeer.

By gesonde volwassenes het enkel- en meervoudige doserings van een-keer-daaglikse verlengde vrystellende metielfenidaat by dosisse van 54 tot 144 mg/dag gelei tot liniêre en dosis-proporsionele toenames in die K_{maks} en AOK_{inf} vir totale metielfenidaat (MPH) en die

hoofmetaboliet daarvan, (alfa)-feniel-piperidienasynsuur (FPA). Die enkeldosis en bestendige toestand (Dag 4) opklaring en halfleeftyd parameters was dieselfde, wat daarop dui dat die farmakokinetika van metielfenidaat nie afhanklik van tyd is nie. Die verhouding van metaboliet (PPAA) tot moeder-geneesmiddel (MPH) was konstant binne die bestek van doserings van 54 tot 144 mg/dag, ná ’n enkeldosis en ook na veelvuldige doserings.

In ‘n veelvoudige dosis studie by adolosente ADHD pasiënte (ouderdom 13 – 16 jaar) aan wie ‘n dosis van 18 tot 72 mg/dag van verlengde vrystellende metielfenidaat toegedien is, het die gemiddelde C_{maks} en AOK_{TAU} van metielfenidaat eweredig met betrekking tot die dosis toegeneem.

Distribusie: Metielfenidaat-plasmakonsentrasies by volwassenes neem bi-eksponensieël af na mondelike toediening. Die halfleeftyd van beide d- en l- isomere van metielfenidaat by volwassenes na mondelike toediening van verlengde vrystellende metielfenidaat was ongeveer 3,5 h.

Metabolisme en ekskresie: By volwassenes word metielfenidaat hoofsaaklik deur de-esterifikasie na die (alfa)-feniel-piperidienasynsuur (FPA) gemetaboliseer, wat min of geen farmakologiese aktiwiteit toon nie. .

Na mondelike dosering van radio-gemerkte metielfenidaat by mense, is ongeveer 90 % van die radioaktiwiteit in die urine herwin. Die hoof-urinêre metaboliet was FPA, wat ongeveer 80 % van die dosis verteenwoordig.

Voedsel-effekte: Daar was geen verskil onder pasiënte in die farmakokinetika of die farmakodinamiese gedrag van verlengde vrystellende metielfenidaat nie wanneer na ‘n hoëvet ontbyt toegedien. Daar is geen bewys van dosisopeenhoping in die teenwoordigheid of afwesigheid van voedsel nie.

Spesiale populasies:

Ouderdom: Die farmakokinetika van verlengde vrystellende metielfenidaat is nie onder kinders jonger as 6 jaar nagevors nie.

Nier-ontoereikendheid: Daar is geen ondervinding van die gebruik van verlengde vrystellende metielfenidaat by pasiënte met nierinkorting nie. Aangesien nieropklaring nie ‘n belangrike roete vir metielfenidaatopklaring is nie, word dit verwag dat nierinkorting min effek op die farmakokinetika van verlengde vrystellende metielfenidaat sal hê.

Lewer-ontoereikendheid: Daar is geen ondervinding met die gebruik van verlengde vrystellende metielfenidaat by pasiënte met lewerinkorting nie.

INDIKASIES

NEUCON word aangedui vir die behandeling van aandaggebrek-hiperaktiwiteitsindroom (ADHD) by kinders en adolessente (6-17 jaar) en volwassenes (18-65 jaar) wat aan DSM-IV kriteria vir ADHD voldoen.

KONTRA-INDIKASIES

NEUCON word teenaangedui:

- by pasiënte met merkbare angs, spanning en onrustigheid, aangesien NEUCON hierdie simptome kan vererger;
- by pasiënte met bekende hipersensitiwiteit vir metielfenidaat of ander komponente van NEUCON;
- by pasiënte met gloukoom;
- by pasiënte met ‘n familiegeskiedenis of diagnose van Tourette-sindroom;
- gedurende behandeling met monoamienoksidase-remmers, en binne ‘n minimum van 14 dae nadat ‘n monoamienoksidase-remmer gestaak is (aangesien hipertensiewe krisis kan ontstaan);
- by pasiënte met hipertiroïedisme, hart-disritmee, isgemiese hartsiekte, ongekontroleerde hipertensie;
- by swangerskap en laktasie (kyk Swangerskap en Laktasie).

WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS

NEUCON verhoog die harttempo, sistoliese en diastoliese bloeddruk; gevolglik word versigtigheid aangeraai wanneer NEUCON vir ADHD voorgeskryf word vir pasiënte by wie onderliggende mediese toestande aangetas kan word deur toename in harttempo en /of bloeddruk bv. hartversaking en hipertensie. Bloeddruk moet gemoniteer word by pasiënte wat met NEUCON behandel word, veral by dié met hipertensie (kyk Kontra-indikasies).

Strukturele hartabnormaliteite

Gevalle van skielike sterfte is by ADHD pasiënte met strukturele hartabnormaliteite wat met NEUCON, behandel word by normale dossisse, aangemeld. Alhoewel daar nie afdoende data bestaan oor die oorsaaklike verwantskap tussen die behandeling met NEUCON en

skielike sterfte nie, word versigtigheid aangeraai wanneer NEUCON, aan ADHD pasiënte met strukturele hartabnormaliteite voorgeskryf word.

Pasiënte jonger as 6 jaar

NEUCON moet nie by pasiënte jonger as ses jaar gebruik word nie. Voldoende data oor die veiligheid van langtermyngebruik van NEUCON is nog nie beskikbaar nie.

Motoriese en verbale senuweetrekkings

NEUCON is met die aanvang of verergering van motoriese senuweetrekkings of verbale senuwee-uitings geassosieer. Die kliniese evaluering van senuweetrekkings by pasiënte moet dus die gebruik van stimulant-medikasie voorafgaan. Die familiegeskiedenis moet nagegaan word.

Langtermyn gebruik

Alhoewel ‘n oorsaaklike verwantskap nie vasgestel is nie, is onderdrukking van groei (m.b.t. gewigstoename, en/of hoogte), met die langtermyn gebruik van NEUCON by kinders aangemeld. Pasiënte wat langtermynbehandeling nodig het, moet dus versigtig gemoniteer word. Pasiënte wat nie groei of gewig na verwagting optel nie, moet hulle behandeling laat onderbreek.

Dosis gebruiksaanwysings

NEUCON moet heel gesluk word met behulp van vloeistowwe. Tablette moet nie gekou, verdeel of fyn gedruk word nie. Metielfenidaat word in ‘n nie-absorbeerbare dop, wat ontwerp is om die geneesmiddel teen ‘n beheerde tempo vry te stel, bevat. Die tabletdoppie, saam met onoplosbare kernkomponente, word uit die liggaam

gewerp; pasiënte moet nie bekommerd wees as hulle soms iets soos ‘n tablet in hul stoelgang waarneem nie.

As gevolg van die feit dat die NEUCON-tablet nie vervormbaar is en nie waarneembaar in die spysverteringskanaal van vorm verander nie, moet NEUCON nie aan pasiënte met bestaande gastroïntestinale vernouing (patologies of iatrogeen) of aan pasiënte met disfagie of betekenisvolle probleme met die sluk van tablette, toegedien word nie. Daar is berigte van obstruktiewe simptome by pasïente met bekende vernouing. As gevolg van die verlengde vrystellingsontwerp van die tablet, moet NEUCON slegs by pasiënte, wat in staat is om die tablet heel in te sluk, gebruik word.

Gebruik in ander indikasies

NEUCON moet nie gebruik word om depressie te behandel en/of normale moegheidstoestande te voorkom of te behandel nie.

Psigotiese of maniese simptome

Psigotiese (bv. hallusinasies) of maniese simptome is tydens behandeling met NEUCON teen gewone dosisse by pasiënte sonder 'n vorige geskiedenis van psigotiese siekte of manie, aangemeld. Indien sulke simptome voorkom, moet dit oorweeg word om NEUCON as moontlike oorsaak te beskou en staking van behandeling kan toepaslik wees.

Aggressiewe gedrag

Pasiënte wat behandeling met NEUCON begin, moet gemoniteer word vir die voorkoms of agteruitgang van aggressiewe gedrag. Aggressie word dikwels geassosieer met ADHD; die ontstaan of verergering van aggressie is egter tydens behandeling met NEUCON aangemeld.

Omstandighede wat versigtigheid vereis

NEUCON moet met versigtigheid onder die volgende omstandighede toegedien word:

- ***Psigotiese pasiënte:*** Die toediening van NEUCON kan die simptome van gedrags- of denkversteurings vererger by psigotiese pasiënte.
- ***Onderliggende mediese toestande wat moontlik benadeel word deur verhogings in bloeddruk of harttempo:*** Volgens die kliniese proewe onder kinders, verhoog NEUCON, die rustende polsvlak gemiddeld met 2-6 ppm en die sistoliese en diastoliese bloeddruk met ongeveer 1 tot 4 mm Hg gedurende die dag, relatief tot die plasebo. In plasebo-beheerde navorsingstudies is daar met NEUCON by volwassenes mediane toenames van ongeveer 4 tot 6 ppm in rustende polsslag by die eindpunt waargeneem, teenoor ’n mediane verandering van rofweg -2 tot 3 ppm met plasebo Mediane veranderings in bloeddruk by eindpunt het gereik van omtrent –1 tot 1 mm Hg (sistolies) en 0 tot 1 mm Hg (diastolies) vir NEUCON en van -1 tot 1 mm Hg (sistolies) en –2 tot 0 mm Hg (diastolies) vir plasebo.

  Versigtigheid moet dus uitgeoefen word tydens die behandeling van pasiënte wie se mediese toestand deur verhoging in bloeddruk of harttempo benadeel kan word. (Kyk Waarskuwings)
- ***Geskiedenis van geneesmiddelafhanklikheid of alkoholisme:*** NEUCON moet met versigtigheid aan pasiënte met ‘n geskiedenis van geneesmiddelafhanklikheid of alkoholisme gegee word. Chroniese misbruik kan tot merkbare toleransie en sielkundige afhanklikheid met wisselende grade van abnormale gedrag lei. Volskaalse psigotiese voorvalle kan, veral met parenterale misbruik, voorkom. Deeglike toesighouding word benodig gedurende onttrekking na misbruik, aangesien erge depressie kan voorkom. Onttrekking na chroniese terapeutiese gebruik kan simptome ontmasker van die onderliggende siekte, wat opvolging kan benodig.

- ***Geskiedenis van stuipe of vorige abnormaliteite:*** Daar is getuienis dat NEUCON die konvulsiedrumpel by pasiënte met 'n vorige geskiedenis van stuipe, by pasiënte met EEG-abnormaliteite sonder stuipe, in die afwesigheid van 'n geskiedenis van stuipe en geen vorige EEG getuienis van stuipe, kan verlaag. In die teenwoordigheid van stuipe, moet NEUCON onttrek word.

Visuele versteurings: Simptome van gesigsversteurings is aangemeld. Probleme met akkommodasie en dowwe visie is aangemeld.

Hematologiese monitering

Periodieke hematologiese monitering (Volbloedtelling, differensieel, en bloedplaatjietellings) word gedurende langdurige behandeling aanbeveel.

Laktose waarskuwing

Pasiënte met seldsame oorerflikheidsprobleme van galaktose intoleransie, die Lapp laktase tekort van glukose-galaktose wanabsorpsie behoort nie NEUCON te neem nie.

Effek op bestuursvermoë en om masjinerie te gebruik:

NEUCON kan die vermoë van die pasiënt om moontlik-gevaarlike masjinerie of voertuie te hanteer, aantas. Pasiënte moet dus ingelig word om versigtig te wees totdat hulle redelik seker is dat NEUCON nie hulle vermoë om aan sodanige aktiwiteite deel te neem nadelig beïnvloed nie.

INTERAKSIES

As gevolg van die effek op bloeddruk, moet NEUCON versigtig met pressormiddels gebruik word.

Menslike farmakologiese navorsingstudies het getoon dat metielfenidaat die metabolisme van warfarin-teenstolmiddels, stuipweermiddels (bv. fenobarbitoon, fenitoïen, primidoon) en sommige antidepressante (trisikliese en selektiewe serotonien-heropname remmers) kan rem. Afwaartse dosisaanpassing van hierdie geneesmiddels kan benodig word wanneer saam met NEUCON toegedien. Dit kan nodig word om die dosis aan te pas en geneesmiddel- plasmakonsentrasies te moniteer (of, in die geval van kumarien, stollingstye), wanneer NEUCON begin of gestaak word.

Ernstige newe-effekte is aangemeld met gelyktydige gebruik van klonidien, hoewel geen oorsaaklikheid vir die kombinasie bepaal is nie. Die veiligheid van die gebruik van NEUCON in kombinasie met klonidien of ander sentraalwerkende alfa-2 agoniste is nie stelselmatig ondersoek nie.

Die gebruik van alkohol mag die SSS newe effekte van NEUCON vererger. Die gebruik van alkohol tydens behandeling moet dus vermy word.

SWANGERSKAP EN LAKTASIE

NEUCON moet nie gebruik word tydens swangerskap en laktasie nie aangesien veiligheid nie vasgestel is nie. Teratogenisiteit is by laboratoriumdiere aangetoon.

DOSIS EN GEBRUIKSAANWYSINGS

NEUCON moet nie by pasiënte onder ses jaar oud gebruik word nie.

NEUCON word mondelik toegedien, een keer daagliks. Aangesien dit aangetoon is dat die effek 12 uur na dosering teenwoordig is, moet die produk in die oggend geneem word.

NEUCON moet heel gesluk word met voldoende hoeveelhede vloeistowwe, en moet nie gekou, verdeel of fyn gedruk word nie.

NEUCON kan met of sonder voedsel toegedien word.

Die dosis moet individueel, volgens die behoefte en respons van elke individuele pasiënt aangepas word.

Pasiënte wat nuut op NEUCON is:

Die aanbevole aanvangsdosis van NEUCON by pasiënte wat nie tans metielfenidaat neem nie, of by pasiënte wie op ander stimulante as metielfenidaat is, is 18 mg een keer per dag vir kinders en adolessente en 18 of 36 mg een keer per dag vir volwassenes.

Pasiënte wat tans NEUCON neem:

Die aanbevole dosis NEUCON vir pasiënte wat tans metielfenidaat drie keer per dag, by dosisse van 15 tot 60 mg/dag neem, word in Tabel 2 weergegee. Dosisaanbevelings word baseer op die huidige dosisregimen en kliniese oordeel.

Tabel 2. Aanbevole dosisomrekening van ‘n ander metielfenidaatregimen tot NEUCON

Vorige Daaglikse Metielfenidaatdosis	***Aanbevole NEUCON-dosis***
5 mg Metielfenidaathidrochloried twee keer of drie keer per dag.	18 mg een keer per dag

10 mg Metielfenidaathidrochloried twee keer of drie keer per dag.	36 mg een keer per dag
15 mg Metielfenidaathidrochloried twee keer of drie keer per dag.	54 mg een keer per dag
20 mg Metielfenidaathidrochloried twee keer of drie keer per dag.	72 mg een keer per dag

Kliniese oordeel moet gebruik word wanneer ‘n dosis vir ‘n pasiënt wat tans op ‘n ander metielfenidaatregimen is, bepaal moet word.

Dosisse kan met 18 mg inkremente aangepas word, tot ‘n maksimum van 54 mg/dag vir kinders met ouderdomme van tussen 6-12 jaar en tot a maksimum van 72 mg vir adolessente met ouderdomme tussen 13 – 18 jaar en tot a maksimum van 108 mg vir volwassenes. Oor die algemeen kan dosisaanpassings met ongeveer weeklikse intervalle ingestel word.

‘n Daaglikse dosis wat 54 mg oorskry, word nie aanbeveel by kinders tussen die ouderdom van 6 – 12 jaar nie. ‘n Daaglikse dosis wat 72 mg oorskry, word nie aanbeveel by adolessente tussen die ouderdom van 13 – 18 jaar nie.
Daaglikse dossis wat 108 mg oorskry word nie aanbeveel by volwassenes nie.

Onderhoudsdosis/Langdurige Behandeling:
Die langtermyn gebruik van NEUCON is nie sistematies tydens beheerde kliniese proewe bepaal nie.
‘n Geneesheer wie die gebruik van NEUCON vir verlengde periodes by pasiënte met ADHD verkies, moet gereeld the langtermyn nuttigheid van die geneesmiddel vir die individuele

pasiënt herevalueer met proeftydperke sonder medikasie om die pasiënt se funksionering sonder farmakoterapie te bepaal.

Dosisvermindering en - Staking:

Indien paradoksale opflikkering van simptome, of ander newe-effekte, voorkom, moet die dosis verminder word, of, indien nodig, moet NEUCON gestaak word.

BEJAARDES:

Die gebruik van NEUCON is nie tydens beheerde kliniese proewe onder bejaardes (ouer as 65 jaar) bestudeer nie.

NEWE-EFFEKTE

Kliniese proewe data

Die tabel hieronder toon al die ongunstige geneesmiddelreaksies (OGRs) wat tydens kliniese toetse met NEUCON by kinders, adolessente en volwassenes waargeneem is, asook die wat met ander metielfenidaathidrochloried-formulerings aangemeld is. Waar die OGRs van NEUCON en ‘n metielfenidaat-formulering se frekwensies verskil het, is die hoogste frekwensie van beide databasisse gebruik.

<u>Frekwensieskatting:</u>

Baie algemeen (≥ 1/10)

Algemeen (≥ 1/100 tot < 1/10)

Ongewoon (≥ 1/1 000 tot < 1/100)

Seldsaam (≥ 1/10 000 tot < 1/1 000)

Baie seldsaam (< 1/10 000)

Onbekend (kan nie uit die beskikbare gegewens geskat word nie)

Sisteem/ orgaan klas	**Ongunstige geneesmiddelreaksie**					
	Frekwensie					
	Baie algemeen	Algemeen	Ongewoon	Seldsaam	Baie seldsaam	Onbekend
Infeksies en infestasies		Nasofaringitis, boonste lugweginfeksie*, sinusitis*				
Bloed en limfstelsel afwykings					Anemie**, Leukopenie**	
Metabolisme en voeding afwykings:		Anoreksie, afname in eetlus**, matige vermindering in gewig en lengtegroei met langdurige gebruik by kinders				
Psigiatriese afwykings	Slaaploosheid, senuweeagtigheid	Anoreksie, onstabiele emosies, aggressie, onrustigheid,	Geestesversteurings, woede, gedagtes aan selfmoord, verandering in	Libido afwyking, verwarde toestand**	Poging tot selfmoord (insluitend voltooide selfmoord)**,	Delusies**, gedagte versteurings, afhanklikheid, gevalle van

		angs**, depressie*, prikkelbaarheid, abnormale gedrag, veranderlike luim, senutrekkings, aanvanklike slaaploosheid*, bedrukte gemoed*, depressie**, libido verminder*, spanning*, bruksisme*, paniekaanval*	luim, rusteloosheid**, tranerigheid, verergering van reeds bestaande senutrekkings van Tourette-sindroom, hiper-waaksaamheid, slaapversteuring.		verbygaande depressiewe gemoed, abnormale denke, apatie**, herhalende gedrag, oor -fokussering	misbruik en afhanklikheid is meer dikwels met die onmiddellike-vrystelling formulerings beskryf
Senuweestelsel afwykings:	Hoofpyn	Duiseligheid, psigomotoriese hiperaktiwiteit, slaperigheid, parestesie*, spanningshoof-pyn*	Sedasie, tremor**, letargie*		Choreo-atetoïede bewegings, omkeerbare iskemiese neurologiese gebrek, neuroleptiese maligne sindroom (NMS;	Serebrovasku lêre siektes** (insluitend vaskulitis, serebrale bloedings, serebrovasku-lêre voorvalle, serebrale arteritis,

					verslae is swak gedokumenteer en in die meeste gevalle het pasiënte ook ander medisyne ontvang, sodat die rol van metielfenidaat nie duidelik is nie)	serebrale afsluiting), migraine **
Oog afwyking		Akkommodasie versteuring*	Dowwe visie**, droë oog*	Probleme met visuele akkommodasie		
Oor en doolhof afwykings		Vertigo*				
Hart afwykings		Disritmie, tagikardie, hartkloppings	Borspyn		Hartarres, miokardiale infarksie	
Bloedvat afwykings		Hipertensie	Warmgloede*		Serebrale arteritis en/of afsluiting, perifere koudheid**	

Respiratoriese, bors en mediastinale afwykings		Hoes, orofaringeale pyn	Dispnee**			
Gastroïntestinale afwykings		Bobuik pyn, diarree, naarheid**, buikongemak, braking, droë mond**, dispepsie*	Hardlywigheid**			
Hepatobiliêre afwykings			Lewerensieme verhoog		Abnormale lewerfunksie, insluitend lewerkoma	
Vel en onderhuidse weefsel afwykings		Pruritis, uitslag, urtikarie	Angioneurotiese edeem, bulleuse toestande, eksfoliatiewe toestande	Hiperhidrose**, makulêre uitslag	Veelvuldige eriteem, eksfoliatiewe dermatitis, vaste medisyne-uitbarsting	
Muskuloskeletale en bindweefsel afwykings		Spierstyfheid*, spierspasmas*			Spierkrampe	
Nier- en urienweg afwykings			Hematurie, pollakurie			

Voortplantingstelsel en bors afwykings		Erektiele disfunksie*		Ginekomastie		
Algemene afwykings en toestande by die plek van toediening		Pireksie, groeivertraging met langdurige gebruik by kinders, moegheid**, prikkelbaarheid*, senuweeagtige gevoel*, astenie*, dors*			Skielike hartsterfte	
Ondersoeke		Veranderinge in bloeddruk en tempo van hartklop (gewoonlik 'n toename), afname in gewig, alanienaminotransferase verhoog*	Hartgeruis			

*Frekwensie afgelei van kliniese proewe in volwassenes en nie uit die data van proewe in kinders en adolessente nie; dit kan ook relevant wees vir kinders en adolessente

**Frekwensie afgelei van kliniese toetse in kinders en adolessente en aangemeld teen 'n hoër frekwensie in kliniese proewe in volwasse pasiënte.

Na-bemarkingsdata

Ongunstige reaksies (OGRs) wat gedurende na-bemarking met NEUCON geïdentifiseer is, word by Tabel 4 ingesluit.

Tabel 4. Ongunstige geneesmiddelreaksies tydens na-bemarkingservaring met NEUCON
Bloed- en limfstelsel versteurings Pansitopenie, trombositopenie, trombositopeniese purpura. **Immuunstelsel versteurings** Hipersensitiwiteitsreaksies, soos angioëdeem, anafilaktiese reaksies, ore geswel, blaasagtige toestande, afskilferende toestande, urtikarie, pruritus, uitslag, uitbrake en eksanteem **Psigiatriese versteurings** Disoriëntering, hallusinasie, ouditiewe hallusinasies, visuele hallusinasies, manie, logorrhoea. **Senuweestelsel versteurings** Konvulsie, grand mal konvulsie, diskinesie

Oog versteurings

Diplopie, midriase, visuele belemmering,

Hart versteurings

Angina pectoris, bradikardie, ekstrasistolieë, supraventrikulêre tagikardie, ventrikulêre ekstrasistolieë

Vaskulêre versteurings

Raynaud-siekte

Vel- en onderhuidse weefsel versteurings

Alopesie, eriteem

Skeletspier en bindweefsel versteurings

Artralgie, mialgie, spiertrekkings,

Algemene versteurings en toestande by die plek van toediening

Afname in terapeutiese respons

Borspyn, bors ongemak, geneesmiddel-effek verminder, hiperpireksie

Ondersoeke

Verhoogde bloed alkaliese fosfatase, verhoogde bloed bilirubien, verhoogde lewerensieme, afname in plaatjietelling, abnormale witbloedseltelling.

BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VAN DIE BEHANDELING DAARVAN

Tekens en simptome van NEUCON oordosering , hoofsaaklik as gevolg van oorstimulering van die SSS en oormatige simpatomimetiese stimulasie, kan die volgende insluit: braking, agitasie, bewerigheid, hiperrefleksie, spiertrekkings, konvulsies, koma, grand mal konvulsie, euforie, verwarring, hallusinasies (gehoor en/of visueel), hiperhidrose, warmgloede, hoofpyne, pireksie, tagikardie, palpitasies, hartritme versnel, sinus-disritmieë, hipertensie, midriase en droë mond.

Behandeling geskied d.m.v. toepaslike ondersteunende maatreëls. Die pasiënte moet beskerm word teen selfbesering en teen stimulerende buite-invloede wat reeds teenwoordige oorstimulering kan vererger. Maaginhoud kan geledig word deur maagspoeling, soos aangedui. Voor maagspoeling uitgevoer word, beheer opgewondenheid en stuipe, indien teenwoordig, en beskerm die lugweg. Ander maatreëls om te detoksifiseer sluit in toediening van geaktiveerde houtskool en ‘n purgeermiddel. Intensiewe sorg moet voorsien word om voldoende sirkulasie en respiratoriese gaswisselling te behou; uitwendige verkoelingsmaatreëls kan ingestel word, indien benodig word vir pireksie.

Doeltreffendheid van peritoneale dialise of buiteliggaamlike hemodialise vir NEUCON oordosering is nie vasgestel nie.

Die verlengde duur van vrystelling van metielfenidaat uit NEUCON moet in ag geneem word indien pasiënte na oordoserings behandel word.

IDENTIFIKASIE

18 mg: kapsuulvormige geel tablet met “alza 18” met swart ink aan die een kant bedruk.

27 mg: kapsuulvormige grys tablet met “alza 27” met swart ink aan die een kant bedruk.

36 mg: kapsuulvormige wit tablet met “alza 36” met swart ink aan die een kant bedruk.

54 mg: kapsuulvormige rooibruin tablet met “alza 54” met swart ink aan die een kant bedruk.

AANBIEDING

NEUCON is beskikbaar in ‘n vierkantige, wit hoë-digtheid (HDPE) poliëtileenbottel met ‘n wit polipropileen kinderbestande prop, met ‘n induksiegeseëlde peuterbestande membraan.

Elke HDPE-bottel bevat een of twee desikkante, en bevat 30 tablette. Die HDPE bottel word in ‘n kartonhouer verpak tot voordat dit gebruik word.

BERGINGSAANWYSINGS

Bewaar by of benede 25 °C. Hou die bottel dig gesluit.

HOU BUITE BEREIK VAN KINDERS.

REGISTRASIENOMMERS

18 mg: 46/1.2/0380

27 mg: 46/1.2/0381

36 mg: 46/1.2/0382

54 mg: 46/1.2/0383

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DATUM VAN PUBLIKASIE VAN HIERDIE VOUBILJET

Datum van registrasie van die medisyne: 20 April 2017