SCHEDULING STATUS S3

1. NAME OF MEDICINE
METFORMIN HCl 500 FC KIARA (tablets)
METFORMIN HCl 850 FC KIARA (tablets)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each METFORMIN HCl 500 FC KIARA tablet contains 500 mg metformin hydrochloride.
Each METFORMIN HCl 850 FC KIARA tablet contains 850 mg metformin hydrochloride.
Sugar free.

3. PHARMACEUTICAL FORM
Round, mottled white to off-white, biconvex film-coated tablets.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
METFORMIN HCl KIARA is indicated for Type II diabetes mellitus when the diet has failed and especially if the patient is overweight.
METFORMIN HCl KIARA can be given alone as initial therapy, or can be administered in combination with a sulphonylurea or insulin.

4.2 Posology and method of administration
It is important that METFORMIN HCl KIARA tablets be taken in divided doses with meals.

Adults:
Initially, one 500 mg tablet three times a day, with or after food.
After 10 to 15 days the dose should be adjusted, or increased to 850 mg or 1 000 mg twice daily. A slow increase in dose may improve gastrointestinal tolerability. If control is incomplete a cautious increase in dosage to a maximum of 3 g daily is justified. Once control has been obtained it may be possible to reduce the dosage of METFORMIN HCl KIARA.

Children:
METFORMIN HCl KIARA is not recommended for use in Type 1 diabetes mellitus.

Elderly:
METFORMIN HCl KIARA is indicated in the elderly, but not when renal function is impaired (see Section 4.4 "Special warnings and precautions for use").

Combination therapy:
See Section 4.4 "Special warnings and precautions for use" and Section 4.5 "Interaction with other medicines and other forms of interaction".

4.3 Contraindications
- Hypersensitivity to metformin hydrochloride or any of the excipients (see Section 6.1 "List of excipients").
- Diabetic ketoacidosis, diabetic pre-coma, or a history thereof.
- Impaired renal function.
- Pancreatitis.
- Chronic liver disease.
- History of, or states associated with lactic acidosis such as shock or pulmonary insufficiency.
- Cardiac failure and recent myocardial infarction.
- Conditions associated with hypoxia.
- Hepatic insufficiency, acute alcohol intoxication or alcoholism.
- Safety and efficacy in pregnancy have not been established.
- Safety and efficacy in children have not been established.

4.4 Special warnings and precautions for use
Lactic acidosis:
Lactic acidosis is rare, but serious (high mortality in the absence of prompt treatment) metabolic complications can occur due to METFORMIN HCl KIARA accumulation. Lactic acidosis associated with the use of METFORMIN HCl KIARA in patients with metabolic acidosis and not having evidence of ketoacidosis (ketonuria and ketonaemia), lactic acidosis, should be suspected and METFORMIN HCl KIARA therapy stopped. Reported cases of lactic acidosis in patients on METFORMIN HCl KIARA have occurred primarily in diabetic patients with significant renal failure. The incidence of lactic acidosis can and should be reduced by also assessing other associated risk factors such as poorly controlled diabetics, ketosis, prolonged fasting, excessive alcohol intake, hepatic insufficiency and any condition associated with hypoxia.
Lactic acidosis is a medical emergency, which must be treated in hospital.

Diagnosis:
Lactic acidosis is characterised by acidotic dyspnoea, abdominal pain and hypothermia followed by coma. Diagnostic laboratory findings are decreased blood pH, plasma lactate levels above 5 mmol/ℓ, and an increased anion gap and lactate/pyruvate ratio.

Renal function:
As METFORMIN HCl KIARA is excreted by the kidneys, serum creatinine levels should be determined before initiating treatment and regularly thereafter:
- at least annually in patients with normal renal function.
- at least 2 to 4 times a year in patients with serum creatinine levels at the upper limit of normal and in elderly subjects.

Decreased renal function in elderly subjects is frequent and asymptomatic. Special caution should be exercised in situations where renal function may become impaired, for example when initiating antihypertensive therapy or diuretic therapy and when starting therapy with NSAIDs.
The administration of METFORMIN HCl KIARA may be associated with increased cardiovascular mortality as compared to treatment with diet alone or diet with insulin.

Administration of iodinated contrast agent:
As the intravascular administration of iodinated contrast materials in radiological studies can lead to renal failure, METFORMIN HCl KIARA should be discontinued 2 to 3 days prior to, or at the time of the test and not re-instituted until 48 hours afterwards, and only after renal function has been re-evaluated and found to be normal.

Surgery:
METFORMIN HCl KIARA should be discontinued 48 hours before elective surgery with general anaesthesia and should usually not be resumed earlier than 48 hours afterwards.

Other precautions:
All patients should continue their diet with regular distribution of carbohydrate intake during the day. Overweight patients should continue their energy-restricted diet.
The usual laboratory tests for diabetes monitoring should be performed regularly.
The use of METFORMIN HCl KIARA is not advised in conditions which may cause dehydration, or in patients suffering from serious infections, trauma or on low calorie intake.
Patients on long-term treatment with METFORMIN HCl KIARA should have an annual estimation of vitamin B_{12} levels, since METFORMIN HCl KIARA may cause malabsorption of vitamin B_{12}, which may result in megaloblastic anaemia (see Section 4.5 "Interaction with other medicines and other forms of interaction").
Although METFORMIN HCl KIARA alone never causes hypoglycaemia, caution is advised when it is used in combination with insulin or sulphonylureas. Stabilisation of diabetic patients with METFORMIN HCl KIARA and insulin should be carried out in hospital because of the possibility of hypoglycaemia, until the ratio of the two medicines has been obtained. Contraindications should be carefully observed.

4.5 Interaction with other medicines and other forms of interaction
In-advisable combinations:
Alcohol:
Increased risk of lactic acidosis in acute alcohol intoxication, particularly in case of fasting or malnutrition, and hepatic insufficiency.
Consumption of alcohol and alcohol-containing medications should be avoided.

Iodinated contrast agents:
Intravascular administration of iodinated contrast agents may lead to renal failure, resulting in METFORMIN HCl KIARA accumulation and a risk of lactic acidosis. METFORMIN HCl KIARA should be discontinued prior to, or at time of the test and not re-instituted until 48 hours afterwards, and only after renal function has been re-evaluated and found to be normal (see Section 4.4 "Special warnings and precautions for use").

Glucocorticoids (systemic and local routes), beta-2-agonists, and diuretics:
Have intrinsic hyperglycaemic activity. Inform the patient and perform more frequent blood glucose monitoring, especially at the beginning of treatment. If necessary, adjust the dosage of the antidiabetic medicine during therapy with the other medicine, and upon its discontinuation.

ACE-inhibitors:
May decrease the blood glucose levels. If necessary, adjust the dosage of the antidiabetic medicine during therapy with the other medicine and upon its discontinuation.

Cimetidine:
Reduced renal clearance of METFORMIN HCl KIARA has been reported during cimetidine therapy, so dose reduction should be considered.

Anticoagulants:
METFORMIN HCl KIARA has been reported to diminish the activity of warfarin, and so dose adjustments of warfarin should be considered.

Sulphonylurea:
Concomitant therapy of METFORMIN HCl KIARA with a sulphonylurea may cause hypoglycaemia (see Section 4.4 "Special warnings and precautions for use").

Vitamins:
Long term treatment with METFORMIN HCl KIARA may cause Vitamin B_{12} malabsorption in the gastrointestinal tract, thus a dose reduction of METFORMIN HCl KIARA should be considered.

4.6 Fertility, Pregnancy and Lactation
The use of METFORMIN HCl KIARA during pregnancy is not advised (see Section 4.3 "Contraindications"). There is no information available concerning the safety of use of METFORMIN HCl KIARA during lactation.

4.7 Effects on the ability to drive and use machines
Metformin monotherapy does not cause hypoglycaemia and therefore has no effect on the ability to drive or to use machines.
However, patients should be alerted to the risk of hypoglycaemia when metformin is used in combination with other antidiabetic agents (e.g., sulfonylureas, insulin or meglitinides).

4.8 Undesirable effects
Blood and lymphatic system disorders:
Less frequent: megaloblastic anaemia.

Immune system disorders:
Less frequent: hypersensitivity.

Endocrine disorders:
Less frequent: hypoglycaemia.

Metabolism and nutrition disorders:
Less frequent: ketoacidosis and ketonuria.

Gastrointestinal disorders:
Frequent: anorexia, nausea, vomiting, constipation, diarrhoea, metallic taste.

Hepato-biliary disorders:
Less frequent: severe cholestatic hepatitis.

4.9 Overdose
Symptoms of overdose:
Hypoglycaemia can occur when METFORMIN HCl KIARA is given concomitantly with a sulphonylurea, insulin or alcohol. In excessive dosage, and particularly if there is a possibility of accumulation, lactic acidosis may develop. Intense symptomatic and supportive therapy is recommended which should be particularly directed at correcting fluid loss and correcting blood glucose levels.

Treatment of overdose:
There is no specific antidote for overdose with METFORMIN HCl KIARA. Treatment is supportive and symptomatic and should be directed at correcting fluid loss and metabolic disturbances.
Acute poisoning with metformin calls for intensive symptomatic and supportive therapy.
(See also Section 4.8 "Undesirable effects".)

5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Pharmacological classification:
A 21.2 Oral hypoglycaemics
Metformin is a biguanide oral anti-hyperglycaemic agent. Its mode of action is thought to be increased peripheral glucose utilisation mediated by increased insulin sensitivity and inhibition of increased hepatic and renal gluconeogenesis.

5.2 Pharmacokinetic properties
Absorption:
After an oral dose of metformin, T_{max} is reached in 2,5 hours. Absolute bioavailability of a 500 mg or 850 mg metformin tablet is approximately 50 to 60 % in healthy subjects. After an oral dose, the non-absorbed fraction recovered in faeces was 20 to 30 %.
After oral administration, metformin absorption is saturable and incomplete. It is assumed that the pharmacokinetics of metformin absorption is non-linear.
At the usual metformin doses and dosing schedules, steady state plasma concentrations are reached within 24 to 48 hours and are generally less than 1 µg/mℓ. In controlled clinical trials, maximum metformin plasma levels (C_{max}) did not exceed 4 µg/mℓ, even at maximum doses.
Food decreases the extent and slightly delays the absorption of metformin; following administration of a dose of 850 mg, a 40 % lower plasma peak concentration, a 25 % decrease in AUC (area under the curve) and a 35-minute prolongation of time to peak plasma concentration were observed. The clinical relevance of these decreases is unknown.

Distribution:
Plasma protein binding is negligible. Metformin partitions into erythrocytes. The blood peak is lower than the plasma peak and appears at approximately the same time. The red cells most likely volume of distribution ranged between 63 to 276 ℓ.

Metabolism:
Metformin is excreted unchanged in the urine. No metabolites have been identified in humans.

Elimination:
Renal clearance of metformin is < 400 mℓ/min, indicating that metformin is eliminated by glomerular filtration and tubular secretion. Following an oral dose, the apparent terminal elimination half-life is approximately 6,5 hours.
When renal function is impaired, renal clearance is decreased in proportion to that of creatinine and thus the elimination half-life is prolonged, leading to increased levels of metformin in plasma.

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Colloidal silicon dioxide, croscarmellose sodium, magnesium stearate, opadry white (consists of hydroxypropyl methylcellulose, titanium dioxide, polyethylene glycol), povidone.

6.2 Incompatibilities
Not applicable.

6.3 Shelf-life
Metformin HCl 500 FC Kiara: 48 months.
Metformin HCl 850 FC Kiara: 60 months.

6.4 Special precautions for storage
Keep in well-closed containers at or below 25 °C and protect from light.

6.5 Nature and contents of container
METFORMIN HCl 500 FC KIARA tablets:
56, 84 or 100 tablets packed in securitainers, blisters, sealed aluminium bags or amber glass bottles.
500 tablets packed in securitainers, blisters or amber glass bottles.

METFORMIN HCl 850 FC KIARA tablets:
56, 60 or 84 tablets packed in securitainers, blisters, sealed aluminium bags or amber glass bottles.
300 tablets packed in securitainers, blisters or amber glass bottles.

6.6 Special precautions for disposal
No special requirements.

7. HOLDER OF THE CERTIFICATE OF REGISTRATION
Kiara Health (Pty) Ltd
72 Steel Road
Spartan
Kempton Park
1619
South Africa

8. REGISTRATION NUMBER
METFORMIN HCl 500 FC KIARA: 28/21.2/0046
METFORMIN HCl 850 FC KIARA: 28/21.2/0047

9. DATE OF FIRST AUTHORISATION
25 November 1994

10. DATE OF REVISION OF THE TEXT
8 July 2021

Additional countries registration details:

Country	Product name	Scheduling status (or Category of distribution)	Registration number
Namibia	METFORMIN HCl 500 FC KIARA	NS2	05/21.2/0088
Namibia	METFORMIN HCl 850 FC KIARA	NS2	05/21.2/0089
Mauritius	METFORMIN HCl 500 FC KIARA		R3001/02/14
Mauritius	METFORMIN HCl 850 FC KIARA		R3002/02/14

Name and address of manufacturer:
Kiara Health (Pty) Ltd
72 Steel Road, Spartan,
Kempton Park, 1619
South Africa

SKEDULERINGSTATUS S3

1. NAAM VAN DIE MEDISYNE
METFORMIN HCl 500 FC KIARA (tablette)
METFORMIN HCl 850 FC KIARA (tablette)

2. KWALITATIEWE EN KWANTITATIEWE SAMESTELLING
Elke METFORMIN HCl 500 FC KIARA-tablet bevat 500 mg metformienhidrochloried.
Elke METFORMIN HCl 850 FC KIARA-tablet bevat 850 mg metformienhidrochloried.
Suikervry.

3. FARMASEUTIESE VORM
Ronde, gevlekte, wit tot naaswit, bikonvekse, filmbedekte tablette.

4. KLINIESE BESONDERHEDE
4.1 Terapeutiese indikasies
METFORMIN HCl KIARA is aangedui vir Tipe II diabetes mellitus wanneer die dieet gefaal het en veral indien die pasiënt oorgewig is.
METFORMIN HCl KIARA kan alleen gegee word as inisiële behandeling of dit kan in kombinasie met 'n sulfonielureum of insulien toegedien word.

4.2 Posologie en metode van toediening
Dit is belangrik dat METFORMIN HCl KIARA-tablette in verdeelde dosisse saam met maaltye geneem word.

Volwassenes:
Aanvanklik, een 500 mg-tablet drie keer per dag, met of na voedsel.
Na 10 tot 15 dae moet die dosis aangepas word of tot 850 mg of 1000 mg twee keer daagliks vermeerder word. 'n Stadige vermeerdering van die dosis mag gastro-intestinale toleransie verbeter. Indien kontrole onvoldoende is, is 'n versigtige vermeerdering van die dosis tot 'n maksimum van 3 g daagliks regverdigbaar. Wanneer kontrole verkry is, mag dit moontlik wees om die dosis van METFORMIN HCl KIARA te verminder.

Kinders:
METFORMIN HCl KIARA word nie aanbeveel vir gebruik in Tipe 1 diabetes mellitus nie.

Bejaardes:
METFORMIN HCl KIARA is aangedui in bejaardes, maar nie wanneer renale funksie ingekort is nie (sien Afdeling 4.4 "Spesiale waarskuwings en voorsorgmaatreëls vir gebruik").

Kombinasieterapie:
Sien Afdeling 4.4 "Spesiale waarskuwings en voorsorgmaatreëls vir gebruik" en Afdeling 4.5 "Interaksie met ander medisyne en ander vorms van interaksie".

4.3 Kontra-indikasies
- Hipersensitiwiteit vir metformienhidrochloried of enige van die eksipiënte (sien Afdeling 6.1 "Lys van eksipiënte").
- Diabetiese ketoasidose, diabetiese prekoma of die geskiedenis daarvan.
- Ingekorte renale funksie.
- Pankreatitis.
- Chroniese lewersiekte.
- Geskiedenis van, of toestande geassosieer met, melksuurasidose, soos skok of pulmonale ontoereikendheid.
- Hartversaking en onlangse miokardiale infarksie.
- Toestande geassosieer met hipoksie.
- Lewerontoereikendheid, akute alkoholintoksikasie of alkoholisme.
- Veiligheid en effektiwiteit in swangerskap is nog nie vasgestel nie.
- Veiligheid en effektiwiteit in kinders is nog nie vasgestel nie.

4.4 Spesiale waarskuwings en voorsorgmaatreëls vir gebruik
Melksuurasidose:
Melksuurasidose is raar, maar ernstige (hoë mortaliteit in die afwesigheid van spoedige behandeling) metaboliese komplikasies kan vanweë akkumulasie van METFORMIN HCl KIARA voorkom. In pasiënte met metaboliese asidose en wat nie bewyse van ketoasidose (ketonurie of ketonemie) het nie, moet melksuurasidose vermoed en behandeling met METFORMIN HCl KIARA gestaak word. Aangemelde gevalle van melksuurasidose in pasiënte op METFORMIN HCl KIARA het hoofsaaklik in diabetiese pasiënte met beduidende nierversaking voorgekom. Die insidensie van melksuurasidose kan en moet verminder word deur ook ander geassosieerde risikofaktore te assesseer, soos swak gekontroleerde diabetiese pasiënte, ketose, verlengde vas, oormatige alkoholinname, hepatiese ontoereikendheid en enige toestand geassosieer met hipoksie.
Melksuurasidose is 'n mediese noodgeval wat in die hospitaal behandel moet word.

Diagnose:
Melksuurasidose word gekenmerk deur asidotiese dispnee, abdominale pyn en hipotermie gevolg deur koma. Diagnostiese laboratoriumbevindings is verlaagde bloed-pH, plasmalaktaatvlakke bo 5 mmol/ℓ en 'n verhoogde anioongaping en laktaat/piruvaat-verhouding.

Renale funksie:
Aangesien METFORMIN HCl KIARA deur die niere uitgeskei word, moet serumkreatinienvlakke voor die aanvang van behandeling bepaal word asook gereeld daarna:
- ten minste jaarliks in pasiënte met normale nierfunksie.
- ten minste 2 tot 4 keer 'n jaar in pasiënte met serumkreatinienvlakke bo die boonste limiet van normaal en in bejaardes.

Verlaagde nierfunksie in bejaardes is algemeen en asimptomaties. Spesiale sorg moet uitgeoefen word in situasies waar nierfunksie ingekort mag word, byvoorbeeld met die aanvang van antihipertensiewe of diuretiese terapie en wanneer behandeling met NSAIMs begin word.
Die toediening van METFORMIN HCl KIARA mag met verhoogde kardiovaskulêre mortaliteit, vergeleke met behandeling met dieet alleen of dieet met insulien, geassosieer wees.

Toediening van gejodeerde kontrasmiddels:
Aangesien die intraveneuse toediening van gejodeerde kontrasmiddels in radiologiese studies tot nierversaking kan lei, behoort METFORMIN HCl KIARA 2 tot 3 dae voor die tyd gestaak te word, of ten minste ten tye van die toets en dit moenie weer voor 48 uur daarna begin word nie en dan slegs nadat renale funksie herevalueer is en bevind is om normaal te wees.

Chirurgie:
METFORMIN HCl KIARA behoort 48 uur voor elektiewe chirurgie met algemene narkose gestaak te word en behoort normaalweg nie vroeër as 48 uur daarna hervat te word nie.

Ander voorsorgmaatreëls:
Alle pasiënte behoort met hulle dieet met gereelde verspreiding van koolhidraatinname gedurende die dag voort te gaan. Oorgewig pasiënte behoort met hulle energiebeperkte dieet voort te gaan.
Die gewone laboratoriumtoetse vir diabetes monitering behoort gereeld gedoen te word.
Die gebruik van METFORMIN HCl KIARA word nie aanbeveel in toestande wat dehidrasie mag veroorsaak nie en ook nie in pasiënte met ernstige infeksie, trauma of op 'n laekalorie-inname nie.
Pasiënte wat op langtermynbehandeling met METFORMIN HCl KIARA is, behoort 'n jaarlikse bepaling van vitamien B_{12}-vlakke te hê, aangesien METFORMIN HCl KIARA wanabsorpsie van vitamien B_{12} mag veroorsaak wat megaloblastiese anemie tot gevolg kan hê (sien Afdeling 4.5 "Interaksie met ander medisyne en ander vorms van interaksie").
Alhoewel METFORMIN HCl KIARA alleen nooit hipoglisemie veroorsaak nie, word omsigtigheid aanbeveel wanneer dit in kombinasie met insulien of sulfonielureums gebruik word. Stabilisasie van diabetiese pasiënte met METFORMIN HCl KIARA en insulien behoort in die hospitaal uitgevoer te word totdat die verhouding van die twee geneesmiddels verkry is vanweë die moontlikheid van hipoglisemie.
Kontra-indikasies moet noukeurig nagekom word.

4.5 Interaksie met ander medisyne en ander vorms van interaksie
Onraadsame kombinasies:
Alkohol:
Verhoogde risiko vir melksuurasidose met akute alkoholintoksikasie, veral in geval van vas of wanvoeding en hepatiese ontoereikendheid.
Vermy gebruik van alkohol en alkoholbevattende geneesmiddels.

Gejodeerde *kontrasmiddels:*
Intravaskulêre toediening van gejodeerde kontrasmiddels mag tot nierversaking lei wat akkumulasie van METFORMIN HCl KIARA en 'n risiko vir melksuurasidose tot gevolg mag hê.
METFORMIN HCl KIARA behoort gestaak te word voor, of ten tye van, die toets en nie hervat te word tot 48 uur daarna nie en dan slegs nadat renale funksie herevalueer is en bevind is om normaal te wees (sien Afdeling 4.4 "Spesiale waarskuwings en voorsorgmaatreëls vir gebruik").

Glukokortikoïede (sistemiese en lokale roetes), beta-2-agoniste en diuretika:
Het intrinsieke hiperglisemiese aktiwiteit. Lig die pasiënt in en monitor bloedglukose meer gereeld, veral aan die begin van behandeling. Indien nodig, pas die dosis van die antidiabetiese medisyne gedurende terapie met die ander geneesmiddel en met staking daarvan aan.

Angiotensienomsettingsensiem-inhibeerders:
Mag bloedglukosevlakke verlaag. Indien nodig, pas die dosis van die antidiabetiese medisyne gedurende terapie met die ander geneesmiddel en met die staking daarvan aan.

Simetidien:
Verlaagde renale opruiming van METFORMIN HCl KIARA is tydens terapie met simetidien gerapporteer; derhalwe moet dosisverlaging oorweeg word.

Antistolmiddels:
METFORMIN HCl KIARA is gemeld om die aktiwiteit van warfarien te verlaag en dus behoort aanpassing van die warfariendosis oorweeg te word.

Sulfonielureums:
Gepaardgaande gebruik van METFORMIN HCl KIARA en 'n sulfonielureum mag hipoglisemie veroorsaak (sien Afdeling 4.4 "Spesiale waarskuwings en voorsorgmaatreëls vir gebruik").

Vitamiene:
Langtermynbehandeling met METFORMIN HCl KIARA mag wanabsorpsie van vitamien B_{12} in die gastro-intestinale kanaal veroorsaak en dus behoort 'n dosisverlaging van METFORMIN HCl KIARA oorweeg te word.

4.6 Fertiliteit, swangerskap en laktasie
Die gebruik van METFORMIN HCl KIARA word nie gedurende swangerskap aanbeveel nie (sien Afdeling 4.3 "Kontra-indikasies"). Daar is geen inligting rakende die veiligheid van die gebruik van METFORMIN HCl KIARA gedurende laktasie nie.

4.7 Effekte op die vermoë om te bestuur en masjiene te gebruik
Metformienmonoterapie veroorsaak nie hipoglisemie nie en het derhalwe geen effek op die vermoë om te bestuur of masjiene te gebruik nie. Pasiënte moet egter op die risiko vir hipoglisemie bedag gemaak word wanneer metformien in kombinasie met ander antidiabetiese middels (bv. sulfonielureums, insulien of meglitiniede) gebruik word.

4.8 Ongewenste effekte
Bloed- en limfatiese sisteemsteurings:
Minder dikwels: megaloblastiese anemie.

Immuunsisteemsteurings:
Minder dikwels: hipersensitiwiteit.

Endokriene steurings:
Minder dikwels: hipoglisemie.

Metaboliese en voedingsteurings:
Minder dikwels: ketoasidose en ketonurie.

Gastro-intestinale steurings:
Dikwels: anoreksie, naarheid, braking, hardlywigheid, diarree, metaalagtige smaak.

Hepatobilière steurings:
Minder dikwels: erge cholestatiese hepatitis.

4.9 Oordosis
Simptome van oordosis:
Hipoglisemie kan voorkom wanneer METFORMIN HCl KIARA saam met 'n sulfonielureum, insulien of alkohol geneem word. Met oormatige dosisse, en veral indien daar die moontlikheid van akkumulasie is, mag melksuurasidose ontwikkel. Intensiewe simptomatiese en ondersteunende behandeling word aanbeveel en dit moet veral daarop gemik wees om vloeistofverlies en bloedglukosevlakke te korrigeer.

Behandeling van oordosis:
Daar is geen spesifieke teenmiddel vir oordosis met METFORMIN HCl KIARA nie. Behandeling is ondersteunend en simptomaties en moet daarop gemik wees om vloeistofverliese en metaboliese steurings reg te stel.
Akute vergifting met metformien vra vir intensiewe simptomatiese en ondersteunende behandeling.
(Sien ook Afdeling 4.8 "Ongewenste effekte".)

5. FARMAKOLOGIESE EIENSKAPPE
5.1 Farmakodinamiese eienskappe
Farmakologiese klassifikasie:
A 21.2 Orale hipoglisemiese middels

Metformien is 'n biguanied orale antihiperglisemiese middel. Die werkingswyse word gereken om verhoogde perifere glukoseverbruik gemedieer deur verhoogde insuliensensitiwiteit en inhibisie van verhoogde hepatiese en renale glukoneogenese te wees.

5.2 Farmakokinetiese eienskappe
Absorpsie:
Na 'n orale dosis metformien, word T_{maks} in 2,5 uur bereik. Absolute biobeskikbaarheid van 'n 500 mg- of 850 mg-metformientablet is ongeveer 50 tot 60 % in gesonde persone. Na 'n orale dosis was die nie-geabsorbeerde fraksie wat in die feses herwin was 20 tot 30 %.
Na orale toediening is metformienabsorpsie versadigbaar en onvolledig. Dit word aanvaar dat die farmakokinetika van metformienabsorpsie nie-liniër is.
Teen die gewone metformiendosisse en doseringskedules, word ewewigsplasmakonsentrasies binne 24 tot 48 uur bereik en is dit oor die algemeen minder as 1 µg/mℓ. In gekontroleerde kliniese studies het die maksimum metformienplasmavlakke (C_{maks}) nie 4 µg/mℓ oorskry nie, self nie teen maksimum dosisse nie.
Voedsel verminder die omvang en vertraag effens die absorpsie van metformien; na toediening van 'n dosis van 850 mg, was die piekplasmakonsentrasie 40 % minder; die AOK (area-onder-die-kurwe) 25 % kleiner en was daar 'n 35 minute verlenging in die tyd tot piekplasmakonsentrasie waargeneem. Die kliniese betekenis van hierdie afnames is onbekend.

Distribusie:
Plasmaproteïenbinding is weglaatbaar. Metformien versprei na eritrosiete. Die bloedpiek is laer as die plasmapiek en verskyn ongeveer op dieselfde tyd. Die rooibloedselle se mees waarskynlike volume van verspreiding het tussen 63 tot 276 ℓ gewissel.

Metabolisme:
Metformien word onveranderd in die urien uitgeskei. Geen metaboliete is in mense geïdentifiseer nie.

Eliminasie:
Renale opruiming van metformien is < 400 mℓ/min wat daarop dui dat metformien deur glomerulêre filtrasie en tubulêre sekresie geëlimineer word. Na 'n orale dosis is die oënskynlike terminale eliminasiehalflewe ongeveer 6,5 uur.
Wanneer nierfunksie ingekort is, is renale opruiming in verhouding tot dié van kreatinien verminder en dus is die eliminasiehalflewe verleng wat tot die verhoogde vlakke van metformien in die plasma lei.

6. FARMASEUTIESE BESONDERHEDE
6.1 Lys van eksipiënte
Kolloïdale silikondioksied, natriumkroskarmellose, magnesiumstearaat, opadry-wit (bestaan uit hidroksipropielmetielsellulose, titaandioksied, poliëtileenglikol), povidoon.

6.2 Onverenigbaarhede
Nie van toepassing nie.

6.3 Raklewe
Metformin HCl 500 FC Kiara: 48 maande.
Metformin HCl 850 FC Kiara: 60 maande.

6.4 Spesiale voorsorgmaatreëls vir berging
Bewaar in diggeslote houers teen of onder 25 °C en beskerm teen lig.

6.5 Aard en inhoud van die houer
METFORMIN HCl 500 FC KIARA-tablette:
56, 84 of 100 tablette verpak in sekuriteitsbewaarders, stulpstroke, geseëlde aluminiumsakke of amber glasbottels.
500 tablette verpak in sekuriteitsbewaarders, stulpstroke of amber glasbottels.

METFORMIN HCl 850 FC KIARA-tablette:
56, 60 of 84 tablette verpak in sekuriteitsbewaarders, stulpstroke, geseëlde aluminiumsakke of amber glasbottels.
300 tablette verpak in sekuriteitsbewaarders, stulpstroke of amber glasbottels.

6.6 Spesiale voorsorgmaatreëls vir wegdoening
Geen spesiale vereistes nie.

7. HOUER VAN DIE SERTIFIKAAT VAN REGISTRASIE
Kiara Health (Pty) Ltd
72 Steel Road
Spartan
Kempton Park
1619
South Africa

8. REGISTRASIENOMMERS
METFORMIN HCl 500 FC KIARA: 28/21.2/0046
METFORMIN HCl 850 FC KIARA: 28/21.2/0047

9. DATUM VAN EERSTE MAGTIGING
25 November 1994

10. DATUM VAN HERSIENING VAN DIE TEKS
8 Julie 2021

Bykomende lande se registrasiebesonderhede:

Land	Produknaam	Skeduleringstatus (of Kategorie van verspreiding)	Registrasie-nommer
Namibië	METFORMIN HCl 500 FC KIARA	NS2	05/21.2/0088
Namibië	METFORMIN HCl 850 FC KIARA	NS2	05/21.2/0089
Mauritius	METFORMIN HCl 500 FC KIARA		R3001/02/14
Mauritius	METFORMIN HCl 850 FC KIARA		R3002/02/14

Naam en adres van vervaardiger:
Kiara Health (Pty) Ltd
72 Steel Road, Spartan,
Kempton Park, 1619
South Africa

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