Skeduleringstatus: S3

Eiendomsnaam en doseervorm:

Rautevene™ oplossing vir inspuiting / konsentraat vir oplossing vir infusie

Samestelling:
Elke ampule bevat 100 mg yster as yster-(III)-hidroksiedsukrosekompleks met 20 mg yster per ml.

Hulpstof: Water vir inspuiting.
Osmolariteit: Ongeveer 1250 mOsmol/l.
Bevat geen bewaarmiddels nie.
Bevat ongeveer 30 % sukrose.

Farmakologiese klassifikasie:
A.8.3 Eritropoiëtika (hematinika).

Farmakologiese werking:
Farmakodinamiese eienskappe:
Die meerkernige yster-(III)-hidroksieddeeltjies is losweg omring deur 'n groot aantal nie-kovalentgebonde sukrosemolekules in 'n kompleks met 'n molekulêre massa van ongeveer 43 kD.
Dit is groot genoeg om uitskeiding deur die niere te verhoed.
Die gevormde kompleks is stabiel en onder fisiologiese toestande stel dit nie ioniese yster vry nie.
Die yster in die meerkernige deeltjies is in dieselfde struktuur as in natuurlik voorkomende ferritien gebind.

Farmakokinetika:
Die farmakokinetika van die yster-(III)-hidroksiedsukrosekompleks is na 'n enkele binneaarse inspuiting van 100 mg yster in gesonde vrywilligers bestudeer. Piek konsentrasies van yster in die serum, gemiddeld 538 µmol/l, word 10 minute na die inspuiting bereik.
Die volume van verspreiding van die sentrale kompartement stem ooreen met die serumvolume (ongeveer 3 liter).
Die ingespuite yster word vinnig uit die serum opgeruim. Die halfleeftyd van verspreiding is ongeveer 6 uur.
Die volume van verspreiding by gelykvlakke is ongeveer 8 liter. Dit toon 'n lae verspreiding van yster in die liggaamsvloeistof.
Omdat die yster-(III)-hidroksiedsukrosekompleks minder stabiel as transferrien is, vind mededingende uitruiling van yster na transferrien plaas, wat lei tot ystertransport van ongeveer 31 mg Fe(III) per 24 uur.
Uitskeiding van yster deur die niere, wat in die eerste 4 ure na die inspuiting voorkom, is minder as 5 % van die totale opruiming uit die liggaam (ongeveer 20 ml/minuut).
Na 24 uur neem die serumvlakke van yster af tot konsentrasies soos voor die dosis en ongeveer 75 % van die dosis sukrose is dan uitgeskei.

Indikasies:
Erge ystertekort in volwasse pasiënte wat orale yster nie kan verdra nie of nie daarop reageer nie.
RAUTEVENE word aanbeveel vir gebruik waar die aanduiding duidelik en deur toepaslike ondersoeke bevestig is.

Kontra-indikasies:
Gebruik van RAUTEVENE is onder die volgende omstandighede teenaangedui:
- Bloedarmoede wat nie deur ystertekort veroorsaak word nie (bv. hemolitiese anemie).
- Bekende hipersensitiwiteit teenoor ystermonosakkaried- of disakkariedkomplekse of enige van die bestanddele van RAUTEVENE.
- Ysterbergingsiekte (ysteroorbelading, bv. hematochromatose, hematosiderose).
- Versteurings in die gebruik van yster (bv. talassemie, sideroakrestiese anemie).
- Kliniese of biochemiese getuienis van lewerskade.
- Infektiewe hepatitis.
- Akute of chroniese infeksie.
- 'n Geskiedenis van asma, ekseem, ander allergiese siektes of anafilaktiese reaksies.
- Die veiligheid vir kinders is nie bepaal nie.
- Die veiligheid tydens borsvoeding is nie bepaal nie.
- Eerste trimester van swangerskap.

Waarskuwings:
RAUTEVENE het 'n pH van 11 en moet daarom **slegs intraveneus gegee word**.
Die maksimum daaglikse dosis van 200 mg moet nie oorskry word nie.
RAUTEVENE moet slegs vir die goedgekeurde indikasies gebruik word.

RAUTEVENE moet slegs toegedien word indien ystertekort diagnosties bepaal en met geskikte laboratoriumtoetse bevestig is (bv. ferritienvlakke in die bloed, hemoglobien, hematokrit of rooibloedseltelling), en bereken vanaf die laasgenoemde die gemiddelde korpuskulêre volume (GKV), gemiddelde korpuskulêre hemoglobien (GKH) en gemiddelde korpuskulêre hemoglobienkonsentrasie (GKHK).

Parenteraal toegediende ysterpreparate kan erge allergiese of anafilaktiese reaksies veroorsaak.
Daarom moet fasiliteite vir kardiopulmonêre resussitasie beskikbaar wees.
Ligte allergiese reaksies kan bestuur word deur die toediening van RAUTEVENE te staak en antihistamiene te gee.
In geval van 'n ernstige anafilaktiese of allergiese reaksie moet toediening van RAUTEVENE gestop word.
Binneaarse of binnespierse adrenalien (epinefrien) moet onmiddellik gegee en ander ondersteunende maatreëls volgens gevestigde prosedures vir kardiopulmonêre resussitasie moet ingestel word.
Episodes van hipotensie kan voorkom as die inspuiting te vinnig gegee word.
Pasiënte met 'n lae bindingskapasiteit en/of foliensuurtekort het 'n hoër risiko vir allergiese of anafilaktiese reaksies.
Paraveneuse lekkasie moet vermy word. In geval van onopsetlike paraveneuse lekkasie en terwyl die naald nog in die aar is, moet daar gespoel word met 'n klein hoeveelheid 0,9 % m/v natriumchloriedoplossing.
Ampules moet voor gebruik visueel vir skade geïnspekteer word en slegs dié met 'n oplossing sonder 'n neerslag kan gebruik word.
Uit 'n mikrobiologiese oogpunt moet die produk gebruik word onmiddellik nadat die houer vir eerste keer oopgemaak is of na verdunning met steriele 0,9 % m/v natriumchloriedoplossing.
Oplosmiddel wat oorbly, moet weggegooi word sodra die ampule oopgemaak is.

Interaksies:
RAUTEVENE moet nie saam met orale ysterpreparate gegee word nie omdat die absorpsie van orale yster laer sal wees.

Swangerskap en borsvoeding:
RAUTEVENE moet nie aan borsvoedende vroue gegee word nie (kyk **Kontra-indikasies**).
RAUTEVENE moet slegs na deeglike evaluering van voordele teenoor risiko in die tweede en derde trimesters gebruik word, en slegs in gevalle van ernstige anemie vanweë ystertekort waar voldoende hoeveelhede mondelikse yster nie geabsorbeer of verdra kan word nie.
Die veiligheid tydens borsvoeding is nie bepaal nie.

Dosis en gebruiksaanwysings:

RAUTEVENE moet nie saam met orale ysterpreparate gegee word nie.
RAUTEVENE moet nie vir gelyktydige toediening met ander medisyne gemeng word nie. Die enigste aanbevole verdunningsmiddel vir 'n infusie is 'n 0,9 % natriumchloriedoplossing.

RAUTEVENE is vir eenmalige gebruik alleenlik - gooi die ongebruikte gedeelte asseblief weg.

Toediening:
RAUTEVENE moet toegedien word as 'n stadige binneaarse inspuiting, as 'n binneaarse drupinfusie of, vir pasiënte wat hemodialise ondergaan, in die veneuse been van die dialisemasjien (kyk **Waarskuwings**).
RAUTEVENE is 'n sterk alkaliese oplossing en moet nooit deur die onderhuidse of binnespierse roetes toegedien word nie.
Paraveneuse lekkasie moet vermy word omdat die lekkasie van RAUTEVENE by die inspuitplek tot pyn, inflammasie, weefselnekrose, en bruin verkleuring van die vel kan lei.

RAUTEVENE is nie geskik vir binnespierse gebruik of vir TDI (totale-dosisinfusie) nie.

TOETSDOSIS:
Voor toediening van die eerste terapeutiese dosis van RAUTEVENE, moet 'n toetsdosis van 1 tot 2,5 ml RAUTEVENE (20 tot 50 mg yster) deur die gekose metode van toediening vir alle pasiënte gegee word (kyk hieronder).
Indien geen nadelige reaksies binne 'n wagperiode van 15 minute na toediening voorkom nie, kan die oorblywende deel van die aanvanklike dosis gegee word.

Infusie:
Die inhoud van een ampule moet onmiddellik voor infusie uitsluitlik in 100 ml van 'n steriele 0,9 % m/v natriumchloriedoplossing (d.w.s. 2 ampules in 200 ml steriele 0,9 % m/v NaCl) verdun word.

Die eerste 25 mg yster (d.w.s. 25 ml van die oplossing) moet as 'n toetsdosis oor 'n tyd van 15 minute ingedrup word (kyk TOETSDOSIS hier bo). As geen nadelige reaksie in hierdie tyd voorkom nie, kan die oorblywende deel van die infusie as volg gegee word:
- 100 mg yster (5 ml RAUTEVENE) in ten minste 15 minute
- 200 mg yster (10 ml RAUTEVENE) in ten minste 30 minute

Intraveneuse inspuiting:
As 'n binneaarse inspuiting moet RAUTEVENE stadig teen 'n tempo van 1 ml onverdunde oplossing per minuut toegedien word (d.w.s. 5 minute per ampule), en nie meer as 2 ampules RAUTEVENE (200 mg yster) per inspuiting nie.
Voor toediening van 'n stadige intraveneuse inspuiting, moet 'n toetsdosis van 1 ml (20 mg yster) stadig oor 'n periode van 1 tot 2 minute ingespuit word.
Indien geen nadelige reaksie binne 15 minute na toediening van die toetsdosis voorkom nie, kan die oorblywende deel van die inspuiting gegee word.

Inspuiting in die dialisemasjien:
RAUTEVENE kan tydens 'n hemodialisesessie direk volgens dieselfde prosedure as vir intraveneuse toediening in die veneuse deel van die dialisemasjien toegedien word.

Dosis:
Berekening van die dosis:
Volwassenes en bejaardes:
Die totale kumulatiewe dosis RAUTEVENE word deur die hemoglobienvlak en liggaamsmassa bepaal.
Die dosis en doseerskedule van RAUTEVENE moet individueel vir elke pasiënt op grond van 'n berekening van die totale ystertekort beraam word.

Totale ystertekort [mg] =
liggaamsmassa [kg] x (teiken Hb – werklike Hb) [g/dl] x 2,4* + depotyster [mg].

Massa onder 35 kg: Teiken Hb = 13 g/dl plus depotyster = 15 mg/kg liggaamsmassa
Massa bo 35 kg: Teiken Hb = 15 g/dl plus depotyster = 500 mg/kg liggaamsmassa

* Faktor 2,4 = 0,0034 x 0,07 x 1000 x 10
waar: 0,0034 = Ysterinhoud van hemoglobien = 0,34 %
0,07 = Bloedvolume = 7 % van liggaamsmassa
1000 = faktor vir omskakeling van g na mg
10 = faktor vir omskakeling van g/dl na g/l

TOTALE AANTAL AMPULES RAUTEVENE WAT GEGEE MOET WORD.

Liggaamsmassa kg	Hemoglobien 6 g/dl	Hemoglobien 7,5 g/dl	Hemoglobien 9 g/dl	Hemoglobien 10,5 g/dl
30	9,5	8,5	7,5	6,5
35	12,5	11,5	10,0	9,0
40	13,5	12,0	11,0	9,5
45	15,0	13,0	11,5	10,0
50	16,0	14,0	12,0	10,5
55	17,0	15,0	13,0	11,0
60	18,0	16,0	13,5	11,5
65	19,0	16,5	14,5	12,0
70	20,0	17,5	15,0	12,5
75	21,0	18,5	16,0	13,0
80	22,5	19,5	16,5	13,5
85	23,5	20,5	17,0	14,0
90	24,5	21,5	18,0	14,5

Totale aantal ampules RAUTEVENE wat gegee moet word =
Totale ystertekort (mg)
100 mg

Die totale enkele dosis moet nie meer as 200 mg yster wat drie keer per week gegee word oorskry nie. As die totale benodigde dosis die maksimum toegelate enkele dosis oorskry, moet die toediening opgedeel word.

Kinders:
RAUTEVENE word nie vir kinders aanbeveel nie, omdat die gebruik van RAUTEVENE deur kinders nog nie voldoende bestudeer is nie.

Newe-effekte en spesiale voorsorgmaatreëls:
Newe-effekte:
Hartversteurings:
Minder dikwels: Tagikardie en palpitasies.

Vaskulêre versteurings:
Minder dikwels: Hipotensie en ineenstorting.

Gastro-intestinale versteurings:
Minder dikwels: Naarheid, braking, buikpyn, diarree.

Algemene versteurings en by die plek van toediening:
Minder dikwels: Koors, bewerasie, blosing, borspyn en toe bors.
Versteurings by die plek van inspuiting soos oppervlakkige flebitis, brandgevoel, swelling.
Moegheid, astenie, ongesteldheid.
Hiperhidrose.

Versteurings van immuunstelsel:
Minder dikwels: Anafilaktiese en anafilaktoïede reaksies (waaronder artralgie), perifere edeem, angioedeem.

Versteurings van die senustelsel:
Minder dikwels: Laer vlak van bewussyn, lighoofdigheid verwardheid.

Versteurings van die muskuloskeletale stelsel, bindweefsel en skeletbene:
Minder dikwels: Spierkrampe, mialgie, swelling van gewrigte, rugpyn.

Versteurings van die senustelsel:
Dikwels: Verbygaande smaakversteuring (veral metaalsmaak).
Minder dikwels: Hoofpyn, duiseligheid, parestesie.

Respiratoriese, toragiese en mediastinale versteurings:
Minder dikwels: Brongospasma, dispnee.

Versteurings van die vel en subkutane weefsel:
Minder dikwels: Pruritus, urtikarie, veluitslag, eksanteem, eriteem.

Spesiale voorsorgmaatreëls:
Anafilaktiese reaksies is die mees ernstige nadelige reaksies (kyk **Waarskuwings**).
Porfirie: Die veiligheid is nie bepaal nie.

Effek op die vermoë om motor te bestuur en masjiene te gebruik:
Na toediening van RAUTEVENE kan die pasiënt duiselig, verward of lighoofdig voel. As dit gebeur, moet die pasiënt aangeraai word om nie te bestuur of enige masjinerie te gebruik nie.

Bekende simptome van oordosering en besonderhede vir die behandeling daarvan:
Oordosering kan akute oorbelading met yster veroorsaak wat as hemosiderose kan manifesteer.
Wees besonder versigtig om ysteroorbelading te voorkom waar anemie, wat nie op behandeling reageer nie, foutief as 'n ystertekortanemie gediagnoseer is (kyk **Kontra-indikasies**).
Oordosering moet, indien nodig, met 'n ystercheleermiddel behandel word.

Identifikasie:
Donkerbruin kolloïedale oplossing in helder glasampules van 5 ml.

Aanbieding:
Helder glasampules van 5 ml in pakke met 5 ampules.

Bergingsinstruksies:
Bewaar op of onder 25 °C in die oorspronklike houer totdat dit vir gebruik benodig word.
Moenie verkoel of vries nie.
Oplossing vir inspuiting:
Nadat dit oopgemaak is, moet die ampules onmiddellik gebruik word.
Konsentraat vir oplossing vir infusie:
Nadat dit aangemaak (verdun) is, moet die oplossing vir infusie onmiddellik gebruik word.
HOU BUITE BEREIK VAN KINDERS.

Registrasienommer:
46/8.3/0849

Naam en besigheidsadres van die houer van die registrasiesertifikaat:
Actor Pharma (Edms) Bpk[1]
Eenheid 7, Royal Palm Sake Landgoed
Washingtonstraat 646
Halfway House
Midrand, 1685
Gauteng

Datum van publikasie van hierdie voubiljet:
05 Desember 2013

™ – RAUTEVENE is 'n Handelsmerk van Actor Pharma (Edms) Bpk
[1] Maatskappyregistrasienommer: 2008/008787/0 Pro-Print

PASIËNTINLIGTINGSBLAD

Skeduleringstatus: S3

RAUTEVENE™ 100 mg/5 ml oplossing vir inspuiting / konsentraat vir oplossing vir infusie

Yster

Lees hierdie hele blad noukeurig deur voordat u RAUTEVENE ontvang:
- Hou hierdie blad. Dit mag nodig wees dat u dit weer moet lees.
- As u nog vrae het, moet u u dokter of apteker raadpleeg.
- RAUTEVENE is vir u persoonlik voorgeskryf en u moet nie u medisyne vir ander mense gee nie. Dit kan hulle skaad, selfs al is hulle simptome dieselfde as u s'n.
- As enige van die newe-effekte ernstig raak of as u newe-effekte opmerk wat nie in hierdie blad gelys is nie, moet u u dokter asseblief daarvan sê.

1. Wat RAUTEVENE bevat:
Die aktiewe bestanddeel is ystersukrose gelykstaande aan 100 mg yster per 5 ml ampul.
Die ander bestanddeel is water vir inspuiting.
Bevat geen bewaarmiddels nie.
Bevat ongeveer 30 % sukrose.

2. Waarvoor RAUTEVENE gebruik word:
RAUTEVENE is medisyne wat yster bevat.
Medisyne wat yster bevat, word vir 'n "ystertekort" gebruik, d.w.s. wanneer daar nie genoeg yster in die liggaam is nie.

RAUTEVENE word gegee wanneer:
- u nie yster per mond kan inneem nie - soos wanneer ystertablette u siek laat voel.
- u yster per mond gedrink het, maar dit het nie gewerk nie.

3. Voordat RAUTEVENE aan u gegee / toegedien word:
RAUTEVENE moet nie aan u gegee / toegedien word nie:
- as u hipersensitief (allergies) vir yster of enige van die bestanddele van RAUTEVENE is.
- as u anemie (bloedarmoede) het wat nie deur 'n tekort aan yster veroorsaak word nie.
- as u te veel yster in u liggaam het of 'n probleem met die manier waarop u liggaam yster gebruik.
- as u 'n geskiedenis van asma, ekseem of ander allergieë het.
- as u in die eerste trimester van swangerskap is (d.w.s. eerste drie maande).
- as u 'n infeksie het.
- as u lewerprobleme het.

Sê vir u dokter of gesondheidsorgdeskundige voordat RAUTEVENE aan u gegee word indien enige van die bogenoemde op u van toepassing is.
RAUTEVENE word nie vir gebruik deur kinders aanbeveel nie.
Die veiligheid tydens borsvoeding is nie bepaal nie.

U moet weet dat:
- 'n Bloedtoets moet gedoen word om te verseker dat die behandeling met hierdie medisyne gepas is.
- As u 'n geskiedenis van asma, ekseem of ander allergiese siektes of anafilaktiese reaksies het, u meer vatbaar is om allergiese reaksies teenoor hierdie medisyne te ervaar.
- As u 'n lae bindingskapasiteit en/of foliensuurtekort het, u 'n hoër risiko vir allergiese of anafilaktiese reaksies kan hê.
- Intraveneuse ysterpreparate erge allergiese reaksies kan veroorsaak. Daarom moet hierdie medisyne slegs gegee word as toepaslike mediese geriewe onmiddellik beskikbaar is.
- In geval van 'n ligte allergiese reaksie, moet toediening van RAUTEVENE stop en 'n antihistamien aan u gegee word.
- In geval van 'n ernstige anafilaktiese of allergiese reaksie moet adrenalien onmiddellik toegedien word en ander ondersteunende maatreëls moet ingestel word.
- RAUTEVENE intraveneus (in 'n aar) aan u gegee sal word. In geval van onopsetlike lekkasie in die gebied aangrensend aan die aar sal die gebied met 'n natrium-chloriedoplossing gespoel word terwyl die naald nog steeds in is.
- Ampules met RAUTEVENE voor gebruik visueel vir skade geïnspekteer moet word en slegs dié met 'n oplossing sonder 'n neerslag gebruik kan word.
- Die produk onmiddellik gebruik moet word nadat dit oopgemaak of verdun is.

Sê voordat u RAUTEVENE kry vir u dokter of gesondheidsorgdeskundige as:
- u medisyne drink wat yster bevat. Dit kan dalk nie werk nie as dit gedrink word op dieselfde tyd as wanneer RAUTEVENE aan u gegee word.

Spesiale sorg moet met RAUTEVENE geneem word:
- as u aan porfirie ly ('n seldsame oorerflike siekte waartydens die bloedpigment hemoglobien abnormaal gemetaboliseer word) omdat die veiligheid nog nie bepaal is nie.

Swangerskap en borsvoeding:
RAUTEVENE moet nie in die eerste drie maande van swangerskap gebruik word nie. U dokter sal besluit of RAUTEVENE tydens die vierde tot die negende maande van swangerskap gebruik kan word.
RAUTEVENE moet slegs deur swanger vroue gebruik word waar daar ernstige anemie vanweë ystertekort is.
Die veiligheid tydens borsvoeding is nie bepaal nie.

As u swanger is of u baba borsvoed terwyl hierdie medikasie aan u gegee word, moet u asseblief u dokter, apteker of ander gesondheidsorgdeskundige om advies vra.

Motorbestuur en gebruik van masjinerie:
Nadat RAUTEVENE aan u gegee is, kan u duiselig, verward of lighoofdig voel.
As dit gebeur, moet u nie motor bestuur of enige gereedskap of masjiene gebruik nie. Vra u dokter, apteker of ander gesondheidsorgdeskundige as u onseker is.

Gebruik van ander medisyne saam met RAUTEVENE:

As u ander medisyne op 'n gereelde basis drink of gebruik, waaronder aanvullende of tradisionele medisyne, kan die gebruik van RAUTEVENE saam met hierdie medisyne ongewensde interaksies veroorsaak. Raadpleeg u dokter, apteker of ander gesondheidsorgdeskundige asseblief om raad.

Dit is baie belangrik om u dokter in te lig as u medisyne drink wat yster bevat. Dit kan dalk nie werk nie as dit gedrink word op dieselfde tyd as wanneer RAUTEVENE aan u gegee word.

4. Hoe om RAUTEVENE te kry:
RAUTEVENE kan op drie verskillende maniere aan u gegee word:
- stadige inspuiting in u aar - 1 tot 3 keer per week.
- 'n infusie (drup) in u aar - 1 tot 3 keer per week.
- tydens dialise - dit sal in die veneuse been van die dialisemasjien gegee word.

Dit sal nie van u verwag word om RAUTEVENE aan uself te gee nie. Dit sal aan u gegee word deur 'n persoon wat bevoeg is om dit te doen.
U dokter sal besluit hoeveel RAUTEVENE aan u gegee moet word.
Hy of sy sal ook besluit hoe dikwels en vir hoe lank u dit nodig het.
U dokter sal 'n bloedtoets doen om die dosis te help bereken.

As u nog nooit tevore RAUTEVENE gehad het nie, sal 'n klein hoeveelheid van die medisyne ('n toetsdosis) eers aan u gegee word. Dit is om te verseker dat u nie allergies vir die medisyne is nie.

RAUTEVENE is 'n bruin vloeistof en die inspuiting of infusie sal dus bruin lyk.
RAUTEVENE word nie vir gebruik vir kinders aanbeveel nie.

As u meer RAUTEVENE gekry het as wat u moes:
Omdat 'n gesondheidsorgdeskundige hierdie medisyne sal gee, sal hy/sy die dosis beheer. In geval van oordosering, sal u dokter die oordosering egter bestuur.

5. Moontlike newe-effekte:
RAUTEVENE kan newe-effekte veroorsaak.

Nie al die newe-effekte wat vir RAUTEVENE aangemeld is, is in hierdie blad opgeneem nie. As u algemene gesondheidstoestand versleg terwyl u RAUTEVENE gebruik, as enige newe-effek ernstig raak of as u enige newe-effekte opmerk wat nie in hierdie inligtingsblad genoem word nie, moet u asseblief u dokter, apteker of ander gesondheidsorgdeskundige om advies raadpleeg.

Ernstige reaksies:
Allergiese reaksies:
Tekens van 'n allergiese reaksie kom soms voor en kan die volgende insluit:
- lae bloeddruk (voel duiselig, lighoofdig of flou)
- swelling van die gesig
- probleme met asemhaling

Laat weet asseblief vir u dokter of verpleegkundige as u dink dat u 'n allergiese reaksie ervaar.

Ander newe-effekte is onder meer:
Dikwels:
- veranderings in smaak (metaalsmaak). Dit duur gewoonlik nie baie lank nie.

Minder dikwels:
- vinnige polsslag
- hoofpyn of duiseligheid
- lae bloeddruk en ineenstorting
- kragtige hartklop (hartkloppings)
- maagpyn of diarree
- mislikheid (naarheid) of braking
- dispnee, probleme met asemhaling
- jeuk, galbulte, veluitslag of rooi vel
- spierkrampe of spierpyn
- blosing
- koors of bewerasie
- borspyn en toe bors
- reaksies by die plek van inspuiting soos inflammasie, 'n brandgevoel
- floutes
- verlies van bewussyn
- tinteling of "naalde en spelde"
- 'n brandgevoel
- hoë bloeddruk
- warm gevoel
- swelling
- pyn in die gewrigte
- swelling van die hande en voete
- moegheid, swakheid of algemene siek gevoel
- voel minder wakker, lighoofdig of verward
- swelling van gewrigte, gesig en tong
- meer sweet
- rugpyn

6. Bewaring en wegdoening van RAUTEVENE:
Bewaar op of onder 25 °C in die oorspronklike houer totdat dit vir gebruik benodig word.
Moenie verkoel of vries nie.
Oplossing vir inspuiting:
Nadat dit oopgemaak is, moet die ampules onmiddellik gebruik word.
Konsentraat vir oplossing vir infusie:
Nadat dit aangemaak (verdun) is, moet die oplossing vir infusie onmiddellik gebruik word.
RAUTEVENE sal gewoonlik deur u dokter of die hospitaal vir u gehou word.
Hou alle medikasie buite bereik en sig van kinders.

7. Aanbieding van RAUTEVENE:
Helder glasampules van 5 ml in pakke met 5 ampules.

8. Identifikasie van RAUTEVENE:
Donkerbruin oplossing in helder glasampules van 5 ml.

9. Registrasienommer:
46/8.3/0849

10. Naam en besigheidsadres van die houer van die registrasiesertifikaat:
Actor Pharma (Edms) Bpk[1]
Eenheid 7, Royal Palm Sake Landgoed
Washingtonstraat 646
Halfway House
Midrand, 1685
Gauteng

11. Datum van publikasie:
05 Desember 2013

™ – RAUTEVENE is 'n Handelsmerk van Actor Pharma (Edms) Bpk
[1] Maatskappyregistrasienommer: 2008/008787/0 Pro-Print

Scheduling status: S3

Proprietary name and dosage form:

Rautevene™ solution for injection / concentrate for solution for infusion

Composition:
Each 5 ml ampoule contains 100 mg iron in the form of iron (III)-hydroxide sucrose complex, 20 mg iron per ml.
Excipient: Water for injection.
Osmolarity: Approximately 1250 mOsmol/l.
Contains no preservatives.
Contains approximately 30 % sucrose.

Pharmacological classification:
A.8.3 Erythropoietics (haematinics).

Pharmacological action:
Pharmacodynamic properties:
The polynuclear iron (III)-hydroxide cores are superficially surrounded by a large number of non-covalently bound sucrose molecules resulting in a complex with a molecular weight of approximately 43 kD.
This is sufficiently large to prevent renal elimination.
The resulting complex is stable and does not release ionic iron under physiologic conditions.
The iron in the polynuclear cores is bound in a similar structure to naturally occurring ferritin.

Pharmacokinetics:
The pharmacokinetics of the iron (III)-hydroxide sucrose complex was studied in healthy volunteers following the administration of a single intravenous injection of 100 mg iron. Peak serum iron concentrations, averaging 538 µmol/l were reached 10 minutes after injection.
The volume of distribution of the central compartment corresponds to the serum volume (approximately 3 litres).
The iron injected is quickly cleared from the serum. The distribution half-life is approximately 6 hours.
The volume of distribution at steady state is about 8 litres. This indicates a low iron distribution in the body fluid.
As a result of the lower stability of the iron (III) hydroxide-sucrose complex compared with transferrin, competitive exchange of iron to transferrin was observed, resulting in iron transport of approximately 31 mg Fe (III) per 24 hours.
Renal elimination of iron, occurring in the first 4 hours after injection, corresponds to less than 5 % of the total body clearance (approximately 20 ml/minute).
After 24 hours the serum iron levels decreased to the pre-dose iron concentration and, approximately 75 % of the sucrose dose was excreted.

Indications:
Severe iron deficiency in adult patients not tolerating or responding to oral iron.
RAUTEVENE is recommended for use only where the indication is definite and confirmed by appropriate investigations.

Contra-indications:
The use of RAUTEVENE is contra-indicated in the following conditions:
- Anaemias not caused by iron deficiency (e.g. haemolytic anaemias).
- Known hypersensitivity to iron monosaccharide or disaccharide complexes or any of the ingredients of RAUTEVENE.
- Iron storage disease (iron overload e.g. haemochromatosis, haemosiderosis).
- Disturbances in utilisation of iron (e.g. thalassaemia, sideroachrestic anaemias).
- Clinical or biochemical evidence of liver damage.
- Infectious hepatitis.
- Acute or chronic infection.
- A history of asthma, eczema, other allergic disorders or anaphylactic reactions.
- The safety in children has not been established.
- The safety in lactation has not been established.
- First trimester of pregnancy.

Warnings:
RAUTEVENE has a pH of 11 and must therefore be given **strictly by the intravenous route**.
The maximum daily dose of 200 mg should not be exceeded.
RAUTEVENE should only be used for the approved indications.

RAUTEVENE should only be administered if iron deficiency has been diagnostically established and confirmed by suitable laboratory tests (e.g. blood ferritin levels, haemoglobin, haemocrit or red blood cell count) and, calculated from the latter mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH) and mean corpuscular haemoglobin concentration (MCHC).

Parentally administered iron preparations can cause severe allergic or anaphylactic reactions.
Therefore, cardio-pulmonary resuscitation facilities should be available.
Mild allergic reactions should be managed by stopping the administration of RAUTEVENE and administering antihistamines.
The administration of RAUTEVENE must be stopped in the event of a serious anaphylactic or allergic reaction.
Intravenous or intramuscular epinephrine (adrenaline) should be administered immediately and other supportive measures must be initiated in line with established cardio-pulmonary resuscitation procedures.
Hypotensive episodes may occur if the injection is administered too rapidly.
Patients with low binding capacity and/or folic acid deficiency are at increased risk of allergic or anaphylactic reactions.
Paravenous leakage must be avoided. In cases of inadvertent paravenous leakage, and while the needle is still inserted, rinse with a small amount of 0,9 % m/v sodium chloride solution.

Ampoules should be visually inspected for damage before use and only those with a sediment free solution may be used.
From a microbiological point of view, the product should be used immediately after first opening the container or after dilution with sterile 0,9 % m/v sodium chloride.
Residual solvents must be discarded, once the ampoule has been opened.

Interactions:
RAUTEVENE should not be administered concomitantly with oral iron preparations, since the absorption of oral preparations is reduced.

Pregnancy and Lactation:
RAUTEVENE should not be used in the first trimester of pregnancy (see **Contra-indications**).
In the second and third trimester RAUTEVENE should only be used after careful benefit-risk assessment and only in cases of severe iron deficiency anaemia where there is an inability to absorb or tolerate adequate amounts of oral iron.
Safety during lactation has not been established.

Dosage and Directions for Use:

RAUTEVENE should not be administered in combination with oral iron preparations.
RAUTEVENE must not be mixed with other medicines for simultaneous administration.
The only recommended diluent for an infusion is a 0,9 % m/v sodium chloride solution.

RAUTEVENE is for single use only – Please discard any unused portion.

Administration:
RAUTEVENE must be administered by slow intravenous injection, by an intravenous drip infusion or, in patients receiving haemodialysis, into the venous limb of the dialyser (see **Warnings**).
RAUTEVENE is a strongly alkaline solution and must never be administered by the subcutaneous or intramuscular route.
Paravenous leakage must be avoided because leakage of RAUTEVENE at the injection site may lead to pain, inflammation, tissue necrosis, and brown discolouration of the skin.

RAUTEVENE is not suitable for intramuscular use or for TDI (Total Dose Infusion).

TEST DOSE:
Before administration of the first therapeutic dose of RAUTEVENE in all patients, a test dose of 1 to 2,5 ml RAUTEVENE (20 to 50 mg iron) should be given by the chosen method of administration (see below).
If no adverse reaction occurs within a waiting period of at least 15 minutes after administration, the remaining portion of the initial dose may be given.

Infusion:
The content of one ampoule has to be diluted exclusively in 100 ml of sterile 0,9 % m/v sodium chloride solution, immediately prior to infusion (i.e. 2 ampoules in 200 ml sterile 0,9 % m/v NaCl).
The first 25 mg of iron (i.e. 25 ml of solution) should be infused as a test dose over a period of 15 minutes (see above TEST DOSE). If no adverse reaction occurs during this time then the remaining portion of the infusion should be given as follows:
- 100 mg iron (5 ml RAUTEVENE) in at least 15 minutes
- 200 mg iron (10 ml RAUTEVENE) in at least 30 minutes

Intravenous injection:
As an intravenous injection RAUTEVENE must be administered slowly at a rate of 1 ml undiluted solution per minute (i.e. 5 minutes per ampoule), not exceeding 2 ampoules RAUTEVENE (200 mg iron) per injection.
Before administering a slow intravenous injection, a test dose of 1 ml (20 mg of iron) should be injected slowly over a period of 1 to 2 minutes.

If within 15 minutes of completing the test dose no adverse event occurs, the remaining portion of the injection may be given.

Injection into dialyser:
RAUTEVENE may be administered during a haemodialysis session directly into the venous limb of the dialyser under the same procedures as those outlined for intravenous injection.

Dosage:
Calculation of dosage:
Adults and the elderly:
The total cumulative dose of RAUTEVENE is determined by the haemoglobin level and body weight.
The dose and dosage schedule for RAUTEVENE must be individually estimated for each patient based on a calculation of the total iron deficit.

Total iron deficit [mg] = body weight [kg] **x** (target Hb – actual Hb) [g/dl] **x** 2,4* **+** depot iron [mg].

Below 35 kg weight: Target Hb **=** 13 g/dl resp. depot iron **=** 15 mg/kg body weight
Above 35 kg body weight: Target Hb **=** 15 g/dl resp. depot iron **=** 500 mg

* Factor 2,4 = 0,0034 x 0,07 x 1000 x 10
Where : 0,0034 = Iron content of haemoglobin = 0,34 %
0,07 = Blood volume = 7 % of body weight
1000 = Factor = conversion from g to mg
10 = Factor = conversion from g/dl to g/L

TOTAL NUMBER OF RAUTEVENE AMPOULES TO BE ADMINISTERED.

Body weight kg	Haemoglobin 6 g/dl	Haemoglobin 7,5 g/dl	Haemoglobin 9 g/dl	Haemoglobin 10,5 g/dl
30	9,5	8,5	7,5	6,5
35	12,5	11,5	10,0	9,0
40	13,5	12,0	11,0	9,5
45	15,0	13,0	11,5	10,0
50	16,0	14,0	12,0	10,5
55	17,0	15,0	13,0	11,0
60	18,0	16,0	13,5	11,5
65	19,0	16,5	14,5	12,0
70	20,0	17,5	15,0	12,5
75	21,0	18,5	16,0	13,0
80	22,5	19,5	16,5	13,5
85	23,5	20,5	17,0	14,0
90	24,5	21,5	18,0	14,5

Total ampoules of RAUTEVENE to be administered = $\frac{\text{Total iron deficit (mg)}}{100 \text{ mg}}$

The total single dose must not exceed 200 mg of iron given not more than three times per week. If the total necessary dose exceeds the maximum allowed single dose, then the administration has to be split.

Children:
RAUTEVENE is not recommended for use in children since the use of RAUTEVENE in children has not been adequately studied.

Side-Effects and Special Precautions:
Side-Effects:
Cardiac disorders:
Less frequent: Tachycardia and palpitations.

Vascular disorders:
Less frequent: Hypotension and collapse.

Gastro-intestinal disorders:
Less frequent: Nausea, vomiting, abdominal pain, diarrhoea.

General disorders and administrative site conditions:
Less frequent: Fever, shivering, flushing, chest pain and tightness.
Injection site disorders such as superficial phlebitis, burning, swelling.
Fatigue, asthenia, malaise.
Hyperhidrosis.

Immune system disorders:
Less frequent: Anaphylactic and anaphylactoid reactions (involving arthralgia), peripheral oedema, angiodema.

Nervous system disorders:
Less frequent: Reduced level of consciousness, lightheaded feeling, confusion.

Musculoskeletal, connective tissue and bone disorders:
Less frequent: Muscle cramps, myalgia, swelling of joints, back pain.

Nervous system disorders:
Frequent: Transient taste perversions (in particular metallic taste).
Less frequent: Headache, dizziness, paraesthesia.

Respiratory, thoracic and mediastinal disorders:
Less frequent: Bronchospasm, dyspnoea.

Skin and subcutaneous tissue disorders:
Less frequent: Pruritus, urticaria, rash, exanthema, erythema.

Special precautions:
Anaphylactoid reactions are the most serious adverse reactions (see **Warnings**).
Porphyria: Safety has not been established.

Effects on ability to drive and use machines:
After being given RAUTEVENE, the patient may feel dizzy, confused or light-headed. If this happens, the patient should be advised not to drive or use any machinery.

Known symptoms of over-dosage and particulars of its treatment:
Over-dosage can cause acute iron overloading which may manifest itself as haemosiderosis.
Particular caution should be exercised to avoid iron overload where anaemia, non-response to treatment, has been incorrectly diagnosed as iron deficiency anaemia (see **Contra-indications**).
Over-dosage should be treated, if required, with an iron chelating agent.

Identification:
Dark brown colloidal solution in 5 ml clear glass ampoules.

Presentation:
5 ml clear glass ampoules in packs of 5 ampoules.

Storage instructions:
Store at or below 25 °C, in the original carton until required for use.
Do not refrigerate or freeze.
Solution for injection:
Once the ampoules have been opened they should be used immediately.
Concentrate for solution for infusion:
Once prepared (diluted), the solution for infusion should be used immediately.
KEEP OUT OF REACH OF CHILDREN.

Registration number:
46/8.3/0849

Name and business address of the holder of the certificate of registration:
Actor Pharma (Pty) Ltd[1]
Unit 7, Royal Palm Business Estate
646 Washington Street
Halfway House
Midrand, 1685
Gauteng

Date of publication of this package insert:
05 December 2013

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[1] Company Registration number: 2008/008787/0

Pro-Print

PATIENT INFORMATION LEAFLET

Scheduling status: S3

RAUTEVENE™ 100 mg/5 ml solution for injection / concentrate for solution for infusion

Iron

Read all of this leaflet carefully before you are given RAUTEVENE:
- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or pharmacist.
- RAUTEVENE has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects experienced become serious, or, if you notice any side effects not listed in this leaflet, please inform your doctor.

1. What RAUTEVENE contains:
The active substance is iron sucrose equivalent to 100 mg iron per 5 ml ampoule.
The other ingredient is water for injection.
Contains no preservatives.
Contains approximately 30 % sucrose.

2. What RAUTEVENE is used for:
RAUTEVENE is a medicine that contains iron.
Medicines that contain iron are used for "iron deficiency" i.e. when there is not enough iron in the body.

RAUTEVENE is given when:
- you cannot take iron by mouth – such as when iron tablets make you feel ill.
- you have taken iron by mouth but it has not worked.

3. Before you are given / administered RAUTEVENE:
You should not be given / administered RAUTEVENE:
- if you are hypersensitive (allergic) to iron or any of the ingredients of RAUTEVENE.
- if you have anaemia which is not caused by a shortage of iron.
- if you have too much iron in your body or a problem in the way your body uses iron.
- if you have a history of asthma, eczema or other allergies.
- if you are in the first trimester of pregnancy (i.e. first three months).
- if you have any infections.
- if you have liver problems.

Tell your doctor or healthcare professional before being given RAUTEVENE if any of the above applies to you.
RAUTEVENE is not recommended for use in children.
Safety during breastfeeding has not been established.

You should be aware that:
- A blood test should have been carried out to ensure that treatment with this medicine is appropriate.
- If you have a history of asthma, eczema or other allergic disorders or anaphylactic reactions you are more susceptible to experience allergic reactions to this medicine.
- If you have low binding capacity and/or folic acid deficiency you may be at an increased risk of allergic or anaphylactic reactions.
- Intravenous iron preparations can cause severe allergic reactions. Therefore this medicine should only be given if there are appropriate medical facilities immediately available.
- In the case of a mild allergic reaction the administration of RAUTEVENE should be stopped and antihistamines should be given to you.
- In the event of a serious anaphylactic or allergic reaction adrenaline should be administered immediately to you and other supportive measures initiated.
- RAUTEVENE will be given to you intravenously (within a vein). In the case of an accidental leakage into the area adjacent to the vein the area will be rinsed with a sodium chloride solution whilst the needle is still inserted.
- The ampoules of RAUTEVENE should be visually inspected for damage before use and only ampoules with a sediment free solution may be used.
- The product should be used immediately after opening or dilution.

Tell your doctor or healthcare professional before being given RAUTEVENE if:
- you are taking medicines that contain iron which you take by mouth. These may not work if they are taken at the same time that RAUTEVENE is given to you.

Special care should be taken with RAUTEVENE:
- if you suffer from porphyria (a rare hereditary disease in which the blood pigment haemoglobin is abnormally metabolised) as safety has not been established.

Pregnancy and Breastfeeding:
RAUTEVENE should not be given during the first three months of pregnancy.
Your doctor will decide if RAUTEVENE can be used during the forth to ninth months of pregnancy.
RAUTEVENE should only be used in pregnant women where there is severe iron deficiency anaemia.
Safety during breastfeeding has not been established.

If you are pregnant or breastfeeding your baby while being given this medicine, please consult your doctor, pharmacist or other healthcare professional for advice.

Driving and using machinery:
You may feel dizzy, confused or light headed after being given RAUTEVENE.
If this happens do not drive or use any tools or machines.
Refer to your doctor, pharmacist or other healthcare professional if you are unsure.

Taking other medicines with RAUTEVENE:

If you are taking or using other medicines on a regular basis, including complementary or traditional medicines, the use of RAUTEVENE with these medicines may cause undesirable interactions. Please consult your doctor, pharmacist or other healthcare professional for advice.

It is very important to inform your doctor if you are taking medicines that contain iron which you take by mouth. These may not work if they are taken at the same time that RAUTEVENE is given to you.

4. How to receive RAUTEVENE:
RAUTEVENE can be given to you in three different ways:
- slow injection into your vein – 1 to 3 times per week.
- an infusion (drip) into your vein – 1 to 3 times per week.
- during dialysis – it will be put into the venous limb of the dialyser.

You will not be expected to give yourself RAUTEVENE. It will be given to you by a person who is qualified to do so.
Your doctor will decide how much RAUTEVENE to give you.
He or she will also decide how often you need it and for how long.
Your doctor will carry out a blood test to help work out the dose.

If you have never had RAUTEVENE before, you will be given a small amount of the medicine first (a test dose). This is to ensure that you are not allergic to the medicine.

RAUTEVENE is a brown liquid and so the injection or infusion will look brown.
RAUTEVENE is not recommended for use in children.

If you are given more RAUTEVENE than you should have:
Since a healthcare professional will administer this medicine, he/she will control the dosage. However, in the event of overdosage your doctor will manage the overdosage.

5. Possible side effects:
RAUTEVENE can have side effects.

Not all side effects reported for RAUTEVENE are included in this leaflet. Should your general health worsen while receiving RAUTEVENE, should any of the side effects become serious, or should you notice any side effects not mentioned in this leaflet, please consult your doctor, pharmacist or other healthcare professional for advice.

Serious reactions:
Allergic reactions:
Signs of an allergic reaction are infrequent and may include the following:
- low blood pressure (feeling dizzy, light headed or faint)
- swelling of your face
- difficulty breathing

Please inform your doctor or nurse straight away if you think you are having an allergic reaction.

Other side effects include:
Frequent:
- changes in your taste (metallic taste). This usually does not last very long.

Less frequent:
- increased pulse rate
- headache or feeling dizzy
- low blood pressure and collapse
- pounding heart beat (palpitations)
- stomach pain or diarrhoea
- feeling sick (nausea) or being sick (vomiting)
- wheezing, difficulty in breathing
- itching, hives, rash or skin redness
- muscle cramps or muscle pain
- flushing
- fever or shivering
- chest pain and chest tightness
- reactions around the site of injection such as inflammation, a feeling of burning
- fainting
- loss of consciousness
- tingling or "pins and needles"
- a feeling of burning
- high blood pressure
- feeling hot
- swelling
- pain in your joints
- swelling of hands and feet
- tiredness, weakness or general feeling of illness
- feeling less alert, light headed or confused
- swelling of your joints, face and tongue
- increased sweating
- back pain

6. Storing and disposing of RAUTEVENE:
Store at or below 25 °C, in the original carton, until required for use.
Do not refrigerate or freeze.
Solution for injection:
Once the ampoules have been opened they should be used immediately.
Concentrate for solution for infusion:
Once prepared (diluted), the solution for infusion should be used immediately.
RAUTEVENE will normally be stored for you by your doctor or the hospital.
Keep all medicines out of the reach and sight of children.

7. Presentation of RAUTEVENE:
5 ml clear glass ampoules in packs of 5 ampoules.

8. Identification of RAUTEVENE:
Dark brown solution in 5 ml clear glass ampoules.

9. Registration number:
46/8.3/0849

10. Name and business address of the holder of the certificate of registration:
Actor Pharma (Pty) Ltd[1]
Unit 7, Royal Palm Business Estate
646 Washington Street
Halfway House
Midrand, 1685
Gauteng

11. Date of publication:
05 December 2013

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