**SUMMARYOF PRODUCTCHARACTERISTICS(SmPC)**

## 1. NAME OFTHE MEDICINALPRODUCT

Emzoron Tonic

Hematinic Syrup ofIron,Folic Acid andVitamin $B_{12}$

## 2. QUALITATIVE ANDQUANTITATIVECOMPOSITION

Each 15 ml (onetablespoonful)
contains:FerricAmmonium CitrateB.P.1973…
160 mg(Equivalent to elementalIron 32.8mg)

| | |
|---|---|
| CyanocobalaminB.P. | … 7.5 mcg |
| Folic AcidB.P. | … 0.5 mg |
| Alcohol U.S.P | … 0.87 ml |

Excipients :

| | |
|---|---|
| SucroseB.P. | … |
| 55%w/vSodium MethylHydroxybenzoateB.P.. | |
| 0.150 w/vSodium PropylHydroxybenzoateB.P... | |
| 0.050 w/vSorbitol Solution(70%)B.P. | … |
| 5%w/v(Non- Crystallising) | |
| LiquidGlucoseUSP/NF | … 31.50%w/v |
| Caramel USP/NF | … 2%w/v |
| Erythrosine | … 0.035%w/v |
| Sodium HydroxideB.P. | … 0.0426 |
| w/vOrangeOil Excellent A543 M-II | … |
| 0.50%v/vPurifiedWaterB.P. | … 32.941%v/v |

## 3. PHARMACEUTICALFORM

OralLiquid

A reddishbrown viscoussyrupyliquid, sweet to tastewith orange flavour.

## 4. CLINICALPARTICULARS

### 4.1 TherapeuticindicationsEmzoron Tonic

is indicatedfor

- Iron deficiencyanaemiadueto chronic blood loss, hook-worminfestation,inadequateintake of iron,etc.
- Dimorphicanaemiadueto deficiencyof Iron,Folic Acid and /orVitamin $B_{12}$(Cyanocobalamin).
- Anemia of pregnancyand lactation.

- Tonicin general weakness, lack of appetite, rundown conditions and convalescence.
- Post surgeryand otherdebilitated states.

## 4.2 Posology and method ofadministration

**ForAdults:**(ForTherapeutic use) 1 tablespoonful (15ml) twiceadayaftermeals.
**ForChildren:**As advised bythe Physician.

Method of administrationOral

## 4.3 Contraindications

- Primary(idiopathic) orsecondaryiron storage disease.
- Anaemiaassociatedwithineffectiveerythropoiesis,marrowhypoplasia,sideroblasticchange, uncomplicatedCyanocobalamin or folate deficiency.
- Intestinal disease (oral iron mayaggravatesevereacute inflammatoryintestinal diseaseand is ineffective in patients with extensive small intestinaldisease eg. celiac sprue.)
- Previoushypersensitivityto anyofthe ingredientin the syrup.
- Known idiosyncrasyto commonlyused excipients.
- Porphyriacutanea tardia.
- Uncontrolledparathyroiddisease, sicklecell patients.

## 4.4 Specialwarningsandprecautions foruse

- Ironcompoundsshouldnotbegiventopatientsreceivingrepeatedbloodtransfusionsortopatientswithanemianotproducedbyirondeficiencyunlessirondeficiencyisalsopresent.
- Careshouldbetakeninpatientswithironstorageourironabsorptiondiseasessuchashaemochromatosis,hemoglobinopathiesorexistinggastro-intestinaldiseasessuchasinflammatorybowel disease,intestinalstructuresanddiverticulae.
- Liquidpreparationsofironsaltsshouldbeswallowedthroughastrawtopreventdiscoloration ofthe teeth.

**4.5 Interaction with othermedicinalproducts andotherforms ofinteraction**

- CompoundscontainingCalciumandMagnesiumincludingantacidsandmineralsupplementsandbicarbonates,carbonates,oxalatesorphosphates,mayalsoimpairtheabsorption of iron bytheformation of insoluble complexes.
- Similarlyabsorptionofbothiron&tetracyclinesisdiminishedwhentheyaretakenconcomitantlybymouth.Iftreatmentwithbothdrugsisrequired,atimeintervalofabout 2 to 3 hours should be allowedbetween them.
- Avoid milk and dairyproducts at least for2 hours.
- SomeagentssuchasAscorbicAcid&CitricAcidmayactuallyincreasetheabsorptionof iron.
- Theresponsetoironmaybedelayedinpatientsreceivingconcomitantparenteralchloramphenicoltherapy.
- Ironsaltscandecreasetheabsorptionofbisphosphonates,fluoroquinolones,levodopa,methyldopa,penicillamine andtetracycline.
- Ironsaltsmayreduce theefficacyof thyroxine.

**4.6 <u>Pregnancy andLactation</u>**

Can be used inIron deficiencyanaemiaduringPregnancyandLactationafterconsideringrisk benefitratio.

**4.7 <u>Effects on ability todrive and usemachines</u>**

Emzoron Tonichasno influence on theabilityto driveor use machines.

**4.8 <u>Undesirable effects</u>**

**<u>FerricAmmoniumCitrate:</u>**

Inhighortoxicdosesorpoisoning-
Gastrointestinalirritation,abdominalpainwithnausea,vomitingandeitherdiarrhoeaorconstipation.Cardiovasculardisorderssuchashypotension,tachycardia,metabolicchangesincludingacidosisandhypoglycemia.CNSdepressionranging fromlethargyto coma.

**<u>Folic acid:</u>**

Almostnontoxicinmanandnoadverseeffectshavebeenreportedexceptarareanddoubtful allergicreaction.

**Cyanocobalamin:**
No known side effects even with verylarge doses.

**4.9 Overdose**

Themostsign&SymptomsofoverdosageareGastrointestinalirritation,abdominalpainwithnausea,vomitingandeitherdiarrhoeaorconstipation.Cardiovasculardisorderssuchashypotension,tachycardia,metabolicchangesincludingacidosisandhypoglycemia.CNS depressionranging from lethargyto coma.

Vomitingisinducedimmediatelyfollowedbyparenteralinjectionofdesferroxaminemesylateandthengastriclavage.Inthemeantimegivemilkand/or5%sodiumbicarbonatesolutionbymouth. Fluidreplacementisessential.Othermeasuresincludesymptomatic management and therapyof metabolic andcardiovasculardisorders.

## 5. PHARMACOLOGICALPROPERTIES

**5.1 Pharmacodynamicsproperties**Pharmacotherapeuticsgroup:Hematinic syrup,ATC code:B03AE01

**FerricAmmoniumCitrate:**

FerricAmmoniumCitrateisoneofthebest-toleratedironsupplements.Itrapidlysupplementselementalironsothatirondeficiencyisquickly controlled,thusleadingtofaster correction ofanaemia andreplenishment oftissue ironstores.

Eachtablespoonfulof**Emzoron Tonic**provides160mgofFerricAmmoniumCitratethatisequivalentto32.8mgofelementaliron. Thus,whenanadulttakestherecommendeddosageof1tablespoonfultwiceaday,hegets65.6mgofelementalironwhichissufficientamountofelementalironperdayforanadultpatientsufferingfrommild to moderateirondeficiency.

**Folic Acid:**

Itissocalledbecauseitispresentingreenleaves,whichischemicallypteroylglutamicacid.Itisagrowthpromoter.IthelpsinthesynthesisofDeoxyriboseNucleicAcid(DNA),thebuildingblockoflife.Itisessentialforpropermaturationofredcells.Ithelpsin interconversionand metabolism of amino acids.

**Cyanocobalamin:**

Cyanocobalamin(Vitamin$B_{12}$)isacomplexorgano-metalliccompoundinwhichacobaltatomisplacedwithinacorrinring.Itplaysanimportantroleinsynthesisof DNAandmaturationofredcells.Itactsasaco-enzymeincertainstepsnecessaryforgeneticreplication.

## 5.2 Pharmacokineticproperties

**Iron(Ferric Ammonium Citrate):**

Ironirregularlyandincompletelyabsorbedfromthegastrointestinaltract,themainsitesofabsorption beingtheduodenumandjejunum.Absorptionisaidedbytheacidsectionofthestomachandbysomedietaryacids(suchasascorbicacid)andismorereadilyaffectedwhen theiron is in theferrous stateor is part of thehaem complex(haem-iron). Absorptionisalsoincreasedinconditionsofirondeficiencyorinthefastingstatebutisdecreasedifthebodystoresareoverloaded.Onlyabout5to15%oftheironingestedinfoodisnormallyabsorbed.

Mostabsorbedironisboundtotransferrinandtransportedtothebonemarrowwhereitisincorporatedintohaemoglobin;theremainderiscontainedwithinthestorageforms,ferritinorhaemosiderin,orasmyoglobin,withsmalleramountsoccurringinhaem-containingenzymes orinplasmabound to transferrin.
Onlyverysmallamountsofironareexcretedasthemajorityreleasedafterthedestructionof thehaemoglobin molecule is re-used.

Folic Acid:

Folicacidisrapidlyabsorbedfromthegastro-intestinaltract,mainlyfromtheduodenumandjejunum.Folicacidadministeredtherapeuticallyenterstheportalcirculationlargelyunchangedsince it is a poorsubstratefor reductionbydihydrofolatereductase.It isconvertedtothemetabolicallyactiveform5-methyltetrahydrofolateintheplasmaandliver.
Theprincipal storagesiteof folate is the liver; it is also activelyconcentrated in the CSF.

Folateundergoesenterohepaticcirculation.Folatemetabolitesareeliminatedintheurineandfolateinexcessofbodyrequirementsisexcretedunchangedintheurine.Folateisdistributed into breast milk. Folic acid is removedbyhaemodialysis.

Cyanocobalamin:

Cyanocobalaminbind tointrinsic factor,aglycoproteinsecretedbythegastricmucosa,andarethenactivelyabsorbedfromthegastro-intestinaltract.Absorptionisimpairedinpatientswithanabsenceofintrinsicfactor,withamalabsorptionsyndromeorwithdiseaseorabnormalityofthegut,oraftergastrectomy.Absorptionfromthegastro-intestinaltractcanalso occur bypassivediffusion.

Cyanocobalaminisextensivelyboundtospecificplasmaproteinscalledtranscobalamins;transcobalaminII

appearstobeinvolvedintherapidtransportofthecobalaminstotissues.Cyanocobalaminisstoredintheliver,excretedinthebileandundergoesextensiveenterohepaticrecycling;partofanadministereddoseisexcretedintheurine,mostofitinthefirst8hours;urinaryexcretion,however,accountsforonlyasmallfractionintherereductionoftotalbodystoresacquiredbydietarymeans.Cyanocobalamindiffusesacrossthe placentaandalsoappears in breast milk.

## 5.3 Preclinical safety data

ToxicologyIron

:

Iron is ageneralcellular poison and is directlycorrosiveto

theGImucosa.Cellulartoxicity

Theabsorptionofexcessivequantitiesofingestediron results insystemicirontoxicity.Severeoverdosecausesimpairedoxidativephosphorylationandmitochondrialdysfunction,whichcanresultincellulardeath.Theliverisoneoftheorgansmostaffectedbyirontoxicity,butotherorganssuchastheheart,kidneys,lungs,andthehematologicsystems also maybe impaired.

MILDTOMODERATEPOISONING:Vomitinganddiarrheamayoccurwithin6hoursof ingestion.

SEVEREPOISONING:Severe vomiting anddiarrhea,lethargy,metabolicacidosis,shock,GIhemorrhage, coma, seizures,hepatotoxicity, and late onsetGIstrictures.

Folicacid:

Theriskoftoxicityfromfolicacidislow,becausefolateisawater-solublevitaminandisregularlyremovedfromthebodythroughurine.Onepotentialissueassociatedwithhighdosagesoffolicacidisthatithasamaskingeffectonthediagnosisofperniciousanaemia (vitaminB12deficiency).

Vitamin$B_{12}$:
VitaminB12 isusuallyconsideredanon-toxicsubstance.Eventakingitbyinjectionathighdosesdoes not seemto increase therisk fortoxicity.

Alcohol:
Eventhoughalcohol contributed to severetoxicity, DEXORANGE®Plus Syrupcontainsverylowlevelofalcoholi.e.0.87ml/15mlasdosagerecommendedistwiceadayhence1.7mlperdayatthislowlevelalcoholmaynotleadtotoxicityevenduringpregnancy.AstheNationalInstituteofHealthandClinicalTrialExcellence(NICE)recommendsthatwomenshouldavoidalcoholduringthe1sttrimester,womenwhochosetodrinkalcoholareadvisedtodrinknomorethan1–2UKunitsofalcoholonceortwiceaweek.Theyfurtherstatethat, *"Although there is uncertainty regardinga safe levelof alcoholconsumptioninpregnancy,atthislowlevelthereisnoevidenceofharmtotheunbornbaby"*.

## 6. PHARMACEUTICALPARTICULARS

### 6.1 List of excipients

SucroseB.P., Sodium MethylHydroxybenzoateB.P., Sodium PropylHydroxybenzoateB.P., Sorbitol Solution (70%)B.P. (Non-Crystallising),LiquidGlucoseUSP/NF,CaramelUSP/NF,Erythrosine, Sodium HydroxideB.P.,Orange Oil Excellent, PurifiedWaterB.P.

### 6.2 Incompatibilities

Not applicable.

### 6.3 Shelflife

24 months

### 6.4 Specialprecautions forstorage

Storebelow 30°C.

## 6.5 Nature and contents of container <and specialequipment for use,administration orimplantation>

Primarypackagingmaterials:200mlambercolouredrectangularglassbottleswith28mmPP caps.
Secondarypackaging material: Mono-carton

## 6.6 Specialprecautions fordisposal

No specialrequirements.

## 7. APPLICANT/MANUFACTURER

**APPLICANT :**
Emzor Pharmaceutical Industries Limited

No 10, Kolawole, Shonibare Street,
Ajao Estate, Isolo, Lagos Nigeria.