Abbreviated Prescribing Information for Use in the International Area. Based on full NCDS (V 04) and prepared to meet the requirements of the GSK International Pharmaceutical Promotional and Marketing Policy.

Theragran Hematinic

**Composition:** Each film-coated tablet contains the following active ingredients: vitamin A 1400 IU, Ascorbic acid (vitamin C), 100 mg, Cholecalciferol (vitamin D), 140 IU, Tocopherol (vitamin E), 5 IU, Thiamine mononitrate (vitamin B1), 3.3 mg, Riboflavin (vitamin B2), 3.3 mg, Niacinamide (nicotinamide), 33.3 mg, Pyridoxine hydrochloride (Vitamin B6), 3.3 mg, Cyanocobalamin (vitamin B12), 50 mcg, Calcium pantothenate, 11.7 mg, Folic acid, 0.33 mg, Iron (elemental), 66.7 mg, Magnesium, 41.7 mg, Copper, 0.67 mg. Excipients: Ethyl cellulose, Povidone K 90, Explotab, Magnesium stearate, Lactose, opadry AWB.

**Indications:** This medicinal product is indicated: For supplementation of vitamins and minerals during pregnancy and Lactation, only after consultation with a physician, in Menorrhagia, Individual following a restrictive diet which may be deficient in certain vitamins and minerals, In iron deficiency anaemia.

**Dosage and Administration:** For oral administration. Populations: Adults: UNLESS otherwise prescribed by the doctor, the usual dose is one to two tablets daily. Tablets should be swallowed as a whole with water. Children: There are no relevant data available. Elderly: There are no relevant data available. Renal impairment: Caution should be exercised when applying this medicinal product to patients with renal disorders. Hepatic impairment: Caution should be exercised when applying this medicinal product to patients with hepatic disorders. Contraindications: This medicinal product is contraindicated in hypersensitivity to any of the components of this medicinal product, during treatment with retinoids. Patients with megaloblastic anemia due to vitamin B12 deficiency, Patients with haemosiderosis, haemochromatosis and haemoglobinopathies, Patients with anaemias other than those due to iron deficiency, Patients with inflammatory bowel disease, including regional enteritis and ulcerative colitis, intestinal strictures and diverticulae, concomitant use with parenteral iron, Patients with active peptic ulcer, Patients who require repeated blood transfusion.

**Warnings and Precautions:** Concomitant conditions: Caution should be used in case of the following concomitant conditions: hepatitis or hepatic disorders, kidney disorders, intestinal inflammation, active duodenal or gastric ulcer, diabetes mellitus, gout. Gastrointestinal symptoms: Chronic diarrhoea from long-term use of magnesium containing products may result in electrolyte imbalance. Taking with food may decrease the incidence of diarrhoea. This medicinal may cause severe abdominal pain, hematemesis and black faeces. Megaloblastic anaemias: The dose of folic acid provided is inadequate for the treatment of megaloblastic anaemias. The development of anaemia despite prophylaxis with this medicinal product requires further investigation and appropriate therapy. Cardiac disorders: This medicinal product should be used with caution in the presence of cardiac disease, as it contains vitamin D. Vision disorders: Cyanocobalamin (vitamin B12) should not be used for Leber’s disease or tobacco ambyloplasia since these optic neuropathies may degenerate further. Hypercalcaemia: This medicinal product is not recommended for patients with hypercalcaemia or diseases associated with hypercalcaemia such as sarcoidosis and some malignancies, as it contains vitamin D. It should be given cautiously to these patients. Erythropoietic protoporphyria: Iron preparations should be used with caution in patients with erythropoietic protoporphyria. Children: As this product contains ferrous, prolonged or excessive use in children without medical supervision may lead to toxic accumulation. Investigations: Iron preparations colour the faeces black, which may interfere with tests used for detection of occult blood in the stools. Large doses of riboflavin (vitamin B2) result in a bright yellow discoloration of the urine that may interfere with certain laboratory tests. Ascorbic acid, a strong reducing agent, interferes with laboratory tests involving oxidation and reduction reactions. Falsely-elevated or false-negative test results may be obtained from plasma, faeces, or urine samples depending on such factors as the dose of ascorbic acid and specific method used. Long-term treatment: Long-term use of large doses of pyridoxine (vitamin B6) is associated with the development of severe peripheral neuropathies; the dose at which these occur is not established. The use of excessive amounts of vitamin A substances over long periods can lead to toxicity. Risk of overdosage: Other medicinal product containing vitamin A should not be used while taking this medicinal product as it may cause overdose symptoms.
Overdose symptoms may occur as a result of prolonged (several weeks or months) administration of doses starting from 10 000 IU daily, in patients with liver or kidney impairment, low body weight, hypoproteinemia and alcohol abuse. Other medicinal product containing vitamin E should not be used while taking this product as it may cause overdose symptoms. Treatment preparation and monitoring: This medicinal product should, if possible, not be given to patients with suspected vitamin B12 deficiency without first confirming the diagnosis, as it contains cyanocobalamin. Tolerance: Tolerance may be induced with prolonged use of large doses of vitamin C, resulting in symptoms of deficiency when intake is reduced to normal. Lactose: this product contains Lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

**Interactions:**

**Diuretics:** As this medicinal product contains vitamin D, hypercalcaemia may occur when it is given with thiazide diuretics. Thiazide diuretics decrease urinary excretion of calcium. Plasma-calcium concentrations should be monitored in patients receiving the drugs together.

**Acetohydroxamic acid:** Iron chelates with acetohydroxamic acid reducing the absorption of both. Corticosteroids: Corticosteroids may counteract the effect of vitamin D. Antibiotics: This medicinal product decreases the absorption of some antibiotics including fluoroquinolones, tetracyclines and penicillamine derivatives, therefore doses should be separated by at least 3 hours. Penicillamine and antituberculous drugs (such as isoniazid) may increase the requirements for folic acid and pyridoxine (vitamin B6). The response to iron may be delayed in patients receiving systemic chloramphenicol. Chloramphenicol delays plasma clearance of iron and incorporation of iron into red blood cells by interfering with erythropoiesis. Neomycin used orally may reduce the absorption of vitamin A, vitamin B12, vitamin E and iron. Rifampicin and isoniazid may reduce the effectiveness of vitamin D. Levodopa, carbidopa, entacapone bisphosphonates, thyroid hormones, mycofenolate, cefdinir and zinc. Iron reduces the absorption of levodopa, carbidopa, entacapone, bisphosphonates, thyroid hormones such as levothyroxine (give at least 2 hours apart), mycofenolate, cefdinir and zinc. This medicinal product contains vitamin B6 which reduces the effects of levodopa, but this does not occur if a dopa decarboxylase inhibitor is also given. Methylprednisolone: The hypotensive effect of methylprednisolone is reduced by iron. Antacids and proton pump inhibitors. Absorption of iron may be reduced in the presence of antacids and proton pump inhibitors which reduce stomach acid. Omeprazole has been reported to impair the bioavailability of vitamin B12 and dietary vitamin C. Folic acid antagonists: Folate deficiency states may be produced by folic acid antagonists such as methotrexate, pyrimethamine, triamterene, trimethoprim and sulfonamides such as sulfasalazine. Bisphosphonates: As this medicinal product contain calcium and magnesium salts, it reduces the absorption of bisphosphonates, therefore doses should be separated by at least 3 hours. Statins: Combination of nicotinic acid and statins may increase risk of myopathy or rhabdomyolysis. Insulin, oral hypoglycaemics: Nicotinic acid may increase the requirements for insulin or oral hypoglycaemics. Acetylsalicylic acid: Acetylsalicylic acid may reduce the clearance of nicotinic acid. Cholestyramine, colestipol and mineral oils: In vitro studies suggest that colestipol and cholestyramine may reduce the availability of nicotinic acid, and some licensed product information recommends an interval of at least 4 to 6 hours between giving nicotinic acid and bile-acid binding resins. Cholestyramine, may impair the absorption of iron, vitamin A and vitamin E. Colestipol, mineral oils used orally may reduce the absorption of vitamin A and vitamin E. Retinoids: Combined treatment with retinoids (isotretinoin, etretinate, bexarotene) and vitamin A in doses exceeding 4000–5000 IU daily may induce vitamin A overdose symptoms. The use of this medicinal product is contraindicated during the treatment with retinoids. Oral contraceptives: Oral contraceptives may increase vitamin A plasma concentration. Serum concentration of vitamin B6, vitamin B12 and folic acid may be decreased by use of oral contraceptives. There are reports that vitamin C increases serum ethinylestradiol concentrations in women taking oral contraceptives. Altretamine: This medicinal product contains vitamin B6 which reduces the activity of altretamine. Antiepileptics/ Anticonvulsants: Vitamin B6 and folic acid has been reported to decrease serum concentrations of phenobarbital and phenytoin. Some antiepileptics (e.g. carbamazepine, phenobarbital, phenytoin, and primidone) may increase vitamin D requirements. Serum levels of anticonvulsant drugs may be reduced by the co-administration of folate e.g. folic acid possibly reduces the plasma concentration of phenobarbital, phenytoin and primidone. Replacement therapy with
Folinic acid or folic acid may become necessary during antiepileptic therapy in order to prevent megaloblastic anaemia developing. Hydralazine: Many drugs may increase the requirements for pyridoxine; such drugs include hydralazine. Anticoagulants: As this medicinal product contains vitamin E, caution should be used during concomitant administration of anticoagulants (dicoumarol, warfarin, indanediones) due to the risk of their efficacy reduction, hypoprothrombinaemia and bleeding. During prolonged administration of vitamin E, the prothrombin time should be monitored on a regular basis. Cyclosporine: Vitamin E may increase the absorption of cyclosporine. Fluoride: As this medicinal product contains calcium (as calcium pantothenate), it reduces the absorption of fluoride, and therefore does should be separated by at least 3 hours. Phosphates: As this medicinal product contains vitamin D, there is an increased risk of hypercalcaemia if it is given with phosphate. Plasma-calcium concentrations should be monitored in such situations. Concomitant administration of phosphates may reduce iron absorption. Oral iron preparations should not therefore be taken within 1 hour before or 2 hours after taking such medications. Vitamin C/ or citric acid: As this medicinal product contains vitamin C, it may increase the absorption of iron in iron-deficiency states. Dimercaprol: Concomitant use of iron and dimercaprol should be avoided as toxic complexes may form. Eltrombopag: Iron possibly reduces the absorption of eltrombopag (give at least 4 hours apart). Raltitrexed: Concomitant use of folic acid with raltitrexed should be avoided. Alcohol: Alcohol enhances the toxic effect of vitamin A and may produce folate deficiency states. Calcium, oral magnesium salts and other mineral supplements, zinc and trientine Iron absorption may be reduced with calcium, oral magnesium salts and other mineral supplements, zinc and trientine. If treatment with both iron and trientine is necessary, a suitable interval is advised. Other: Absorption of vitamin B12 from the gastrointestinal tract may be reduced by aminosalicylic acid, histamine H2-antagonists, and colchicine. Concomitant administration of gastric acid neutralising agents, drugs containing: bicarbonates, carbonates or oxalates, may reduce iron absorption. Oral iron preparations should not therefore be taken within 1 hour before or 2 hours after taking the above medications. Magnesium salts may decrease the absorption of fluoride. Iron absorption may also be reduced in the presence of food (e.g. tea, coffee, wholegrain cereals, eggs and milk).

**Pregnancy and Lactation:**

**Fertility:** There are no relevant data available. **Pregnancy:** This medicinal product is indicated in pregnant women for vitamin and mineral supplementation, but should be used only after consultation with a physician. **Lactation:** This medicinal product is indicated in breastfeeding women, but should be used only after consultation with a physician. **Ability to perform tasks that require judgement, motor or cognitive skills:** There are no clinical data proving that this medicinal product may have an influence on the ability to drive or use machines. **Adverse Reactions:** As Theragran H contains iron, it may sometimes produce gastrointestinal irritation and abdominal pain with nausea and vomiting. Adverse effects can be reduced by giving it with or after food (rather than on an empty stomach) or by beginning therapy with a small dose and increasing gradually. Immune system disorders: Not known: hypersensitivity reactions. Metabolism and nutrition disorders: Not known: haemosiderosis may occur as a result of excessive or mistaken therapy. Gastrointestinal disorders: Not known: abdominal pain, nausea, vomiting, diarrhoea, constipation, gastrointestinal disturbances, and black faeces. Psychiatric disorders: Not known: sleep disturbances. Nervous system disorders: Not known: headache. Skin and subcutaneous tissue disorders: Not known: rash. **Overdosage:** Iron overdosage is an acute emergency requiring urgent medical attention. An acute intake of 75mg/kg of elemental iron is considered extremely dangerous in young children. **Symptoms and signs:** Symptoms include: gastrointestinal disturbances (abdominal pain, nausea, vomiting, diarrhoea, constipation, taste disturbances, thirst), cardiac arrhythmias (tachycardia, bradycardia), hypotension, cardiac arrest, renal impairment, polypia, nocturia, muscle weakness, headache, drowsiness, dizziness/vertigo, irritability, sweating, lassitude, somnolence, confusion, shock, coma, thirst. Inter-individual tolerance to this medicinal product varies considerably; infants and children are generally more susceptible to its toxic effects. **Iron:** Initial symptoms of iron overdosage include nausea, vomiting, diarrhoea, abdominal pain, haematemesis, rectal bleeding, lethargy and circulatory collapse. Hyperglycaemia and metabolic acidosis may occur. However, if overdosage is suspected, treatment should be implemented immediately. In severe cases, after a latent phase, relapse may occur after 24-48 hours manifested by hypotension, coma, hypothermia, hepatocellular necrosis, renal failure, pulmonary oedema, diffuse vascular congestion,
coagulopathy and/or convulsions. In many cases, full recovery may be complicated by long-term effects such as hepatic necrosis, toxic encephalitis, CNS damage and pyloric stenosis.

**Treatment:** The treatment consists of its withdrawal and symptomatic treatment, if necessary. The following advises are recommended to minimise or prevent further absorption of the medication. **Children:** Inducing diarrhoea in children may be dangerous and should not be undertaken in young children. Keep the patient under constant surveillance to detect possible aspiration of vomitus – maintain suction apparatus and standby emergency oxygen in case of need.

**Severe poisoning:** In the presence of shock and/or coma with high serum iron levels (serum iron >90μmol/l) immediate supportive measure plus IV infusion of desferrioxamine should be instituted. Desferrioxamine 15mg/kg body weight should be administered every hour by slow IV infusion to a maximum 80mg/kg/24 hour. **Warning:** Hypotension may occur if the infusion rate is too rapid. **Less severe poisoning:** Intramuscular desferrioxamine 1g 4-6-hourly is recommended. Serum iron levels should be monitored throughout. **Adults:** Treatment of iron overdose in pregnancy should be as for the non-pregnant patient and if clinically indicated, treatment with desferrioxamine should not be withheld. Administer an emetic. A drink of mannitol or sorbitol should be given to induce small bowel emptying. In the presence of shock and/or coma with high serum iron levels (>142μmol/l) immediate supportive measures plus IV infusion of desferrioxamine should be instituted. The recommended dose of desferrioxamine is 15mg/kg/h by a slow IV infusion up to a maximum of 80mg/kg/24 hours. **Warning:** Hypotension may occur if the infusion rate is too rapid. **Less severe poisoning:** Intramuscular deferrioxamine 50mg/kg up to a maximum dose of 4g should be given. Serum iron levels should be monitored throughout. Further management should be as clinically indicated or as recommended by the national poisons centre, where available. **Packs:** pack of 2 strips each of 15 tablets. **FULL PRESCRIBING INFORMATION including Summary of Product Characteristics is available upon request. Date of revision: 23 November 2018**