### Indication

1. Prevention of iron-deficiency anaemia in infants at risk of reduced body stores
   - Preterm infants <1800g
   - Infants 1800-2500g
   - Ex-preterm infants not tolerating feeds of 180 mL/kg/day with iron containing fortifier or formula
   - When ceasing iron containing fortifier or formula prior to discharge

2. Treatment of iron deficiency anaemia

**NOTE:** Formulas with 5-9 mg/L of iron are considered adequate in iron content

### Iron content in common Fortifiers and Formulas at various mL/kg/day:

<table>
<thead>
<tr>
<th>Iron content</th>
<th>140 mL/kg/day</th>
<th>160 mL/kg/day</th>
<th>180 mL/kg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preterm EBM</td>
<td>0.04 mg/kg/day</td>
<td>0.05 mg/kg/day</td>
<td>0.054 mg/kg/day</td>
</tr>
<tr>
<td>EBM+S26 HMF</td>
<td>0.04 mg/kg/day</td>
<td>0.05 mg/kg/day</td>
<td>0.054 mg/kg/day</td>
</tr>
<tr>
<td>EBM+FM 85</td>
<td>2.1 mg/kg/day</td>
<td>2.4 mg/kg/day</td>
<td>2.7 mg/kg/day</td>
</tr>
<tr>
<td>EBM+Nutricia BMF</td>
<td>0.04 mg/kg/day</td>
<td>0.05 mg/kg/day</td>
<td>0.054 mg/kg/day</td>
</tr>
<tr>
<td>Neocate Gold</td>
<td>1.4 mg/kg/day</td>
<td>1.6 mg/kg/day</td>
<td>1.8 mg/kg/day</td>
</tr>
<tr>
<td>Pre Nan Gold</td>
<td>2.5 mg/kg/day</td>
<td>2.9 mg/kg/day</td>
<td>3.2 mg/kg/day</td>
</tr>
<tr>
<td>Aptamil Gold + Preterm</td>
<td>2.2 mg/kg/day</td>
<td>2.6 mg/kg/day</td>
<td>2.9 mg/kg/day</td>
</tr>
<tr>
<td>S26LBW</td>
<td>2.0 mg/kg/day</td>
<td>2.2 mg/kg/day</td>
<td>2.5 mg/kg/day</td>
</tr>
<tr>
<td>Elecare/Elecare LCP</td>
<td>1.7 mg/kg/day</td>
<td>1.9 mg/kg/day</td>
<td>2.2 mg/kg/day</td>
</tr>
<tr>
<td>Pepti-Junior</td>
<td>1 mg/kg/day</td>
<td>1.2 mg/kg/day</td>
<td>1.4 mg/kg/day</td>
</tr>
</tbody>
</table>

### Action

Iron is needed for the production of haemoglobin and certain iron-containing enzymes. Ferrous sulphate corrects iron deficiency by re-saturating iron storage organs.

### Drug Type

Iron supplement

### Trade Name

Ferro-Liquid

### Dosage / Interval

**Prophylaxis:** 2 mg/kg of elemental iron daily. To commence at 2-6 weeks of age (2-4 weeks of age in extremely low-birthweight infants)

**Treatment:** 2 mg/kg of elemental iron 12 hourly

### Maximum daily dose

15 mg daily INDEPENDENT OF WEIGHT

**Prophylaxis:** 2-3 mg/kg/day of elemental iron. Commence only when on full feeds in hospital or prior to discharge when fortification is stopped or preterm formula changed to term formula. Delay in infants with multiple transfusions and increased Serum Ferritin levels (>350 microgram/L) or have received a transfusion in last 2 weeks. Prophylaxis dose >5 mg/kg/day should be avoided in preterm infants because of possible risk of retinopathy of prematurity

**Treatment:** Can commence on 3 mg/kg/day of elemental iron and may need to go up to 6 mg/kg/day in iron deficiency anaemia or on erythropoietin. It is suggested to undertake iron studies to titrate the dose.

### Total cumulative dose

Doses >5 mg/kg/day should be avoided in preterm infants because of possible risk of retinopathy of prematurity

### Presentation

Ferrous sulphate liquid: 150 mg ferrous sulphate/5 mL equivalent to 30 mg elemental iron/5 mL=6 mg/mL of elemental iron

### Route

Oral

### Administration

Oral or intragastric tube

### Monitoring

Periodic haemoglobin and reticulocyte count during therapy. Can take 2 weeks for haemoglobin concentrations to rise. Regular serum ferritin if treating iron deficiency anaemia.
### Contraindications

Haemolytic anaemia, haemochromatosis, haemosiderosis

### Precautions

Excessive iron supplementation can lead to increased risk of infection, poor growth and disturbed absorption or metabolism of other minerals.

Being a potent pro oxidant, non-protein bound iron can cause free oxygen radicals and increase risk of retinopathy of prematurity, especially when given in high doses as a component of blood transfusions or as adjunct to erythropoietin therapy.

Risk of iron induced haemolysis in preterm infants with Vitamin E deficiency is more in first 6 weeks.

### Drug interaction

Zinc supplementation does not impede iron absorption. There is no effect of iron supplementation on zinc or selenium absorption. Iron absorption from fortified milk is intact in spite of its high calcium content.

### Adverse Reactions

GI irritation: epigastric pain, diarrhoea, constipation, dark stools (green or black), erosion of gastric mucosa

Increased RBC haemolysis and haemolytic anaemia in premature infants with low vitamin E levels

Rickets - with large doses of iron over a prolonged period of time.

Acute toxicity - more severe GI effects including haematemesis and malaena, lethargy, pallor, cyanosis and shock

### Compatibility

Can be administered with Penta-vite.

### Stability

Solution may be used up to one month after opening (document date of opening on label).

### Storage

Store below 25°C. Protect from light

### Special comments

Infants on erythropoietin or infants with uncompensated blood loss may initially need higher doses and could be receiving iron supplementation in addition to preterm formula or fortified human milk.

### Evidence summary

1. LBW infant supplementation-RCT (Berglund 2010) suggested all babies born less than 2.5 kg will benefit from early supplementation, main outcome being iron deficiency at 6 months

2. Dose - Low vs high-RCT (Friel 2001)-Preterm infants with an average birth weight of 1.46 kg received an iron intake of 5.9 versus 3.0 mg per kg per day at discharge and about 3 versus 2mg per kg per day at 3 to 9 months. There was no difference between the 2 groups in anaemia prevalence or neurodevelopment at 12 months, but the high-iron group had higher glutathione peroxidase concentrations (a marker of oxidative stress), lower plasma zinc and copper levels, and more respiratory tract infections, suggesting possible adverse effects from the higher intake.

3. Early vs late supplementation-3 RCTs (Franz 2000, Stienmarcher 2007, Arnon 2009)

Steinmacher 2007 - showed increased proportion of children with abnormal clinical neurological examination in late iron group (35% vs 17%; p=0.02)

Franz et al randomised 204 infants with an average birth weight of 0.87 kg into an early iron group receiving 2 to 4 mg/kg/day of iron supplements from about 2 weeks and a late iron group that did not receive iron supplements until 2 months of age. There were no differences in serum ferritin and haematocrit at 2 months of age but infants in the late iron group had received more blood transfusions.

Arnon 2009 - large RCT, 2 weeks vs 4 weeks, improved dermatological parameters in early group.

### References

4. Ferro-Liquid: Product Information (MIMSOnline)


