ENDOTHELIN RECEPTOR ANTAGONISTS

Ambrisentan

20-May-2020

- **INDICATIONS AND DOSE**

Pulmonary arterial hypertension (initiated under specialist supervision)

- BY MOUTH
- Adult: 5 mg once daily, increased if necessary to 10 mg once daily

DOSE ADJUSTMENTS DUE TO INTERACTIONS

- Manufacturer advises max. dose 5 mg daily and close monitoring with concurrent use of ciclosporin.

- **CONTRA-INDICATIONS** Idiopathic pulmonary fibrosis
- **CAUTIONS** Not to be initiated in significant anaemia · pulmonary veno-occlusive disease
- **INTERACTIONS** → Appendix 1: ambrisentan
- **SIDE-EFFECTS**
- **Common or very common** Abdominal pain · anaemia · asthenia · constipation · diarrhoea · dizziness · epistaxis · flushing · headaches · hypersensitivity · increased risk of infection · nasal congestion · nausea · palpitations · skin reactions · syncope · tinnitus · vision disorders · vomiting
- **Uncommon** Hepatic disorders · sudden hearing loss
- **CONCEPTION AND CONTRACEPTION** Exclude pregnancy before treatment and ensure effective contraception during treatment. Monthly pregnancy tests advised.
- **PREGNANCY** Avoid (teratogenic in *animal studies*).
- **BREAST FEEDING** Manufacturer advises avoid—no information available.
- **HEPATIC IMPAIRMENT** Manufacturer advises avoid in severe impairment or if baseline serum transaminases exceed 3 times the upper limit of normal.
- **RENAL IMPAIRMENT** Use with caution if eGFR less than 30 mL/minute/1.73 m^2.
- **MONITORING REQUIREMENTS**
- Monitor haemoglobin concentration or haematocrit after 1 month and 3 months of starting treatment, and periodically thereafter (reduce dose or discontinue treatment if significant decrease in haemoglobin concentration or haematocrit observed).
- Monitor liver function before treatment, and monthly thereafter—discontinue if liver enzymes raised significantly or if symptoms of liver impairment develop.
- **PATIENT AND CARER ADVICE**

Alert card A patient alert card should be provided.

- **NATIONAL FUNDING/ACCESS DECISIONS**

Scottish Medicines Consortium (SMC) decisions

SMC No. 511/08

The *Scottish Medicines Consortium* has advised (November 2008) that ambrisentan (*Volibris* ®) is accepted for restricted use within NHS Scotland for the treatment of patients with pulmonary arterial hypertension (PAH) classified as WHO functional class II and III, to improve exercise capacity, when prescribed by specialists in the Scottish Pulmonary Vascular Unit or similar specialists.

- **MEDICINAL FORMS** There can be variation in the licensing of different medicines containing the same drug.

Tablet

- **Volibris** (GlaxoSmithKline UK Ltd)

Ambrisentan 5 mg Volibris 5mg tablets | 30 tablet PoM £1,618.08 DT = £1,618.08

Ambrisentan 10 mg Volibris 10mg tablets | 30 tablet PoM £1,618.08 DT = £1,618.08

Bosentan

05-Feb-2020

- **INDICATIONS AND DOSE**

Pulmonary arterial hypertension (initiated under specialist supervision)

- BY MOUTH
- Adult: Initially 62.5 mg twice daily for 4 weeks, then increased to 125 mg twice daily (max. per dose 250 mg); maximum 500 mg per day

Systemic sclerosis with ongoing digital ulcer disease (to reduce number of new digital ulcers)

- BY MOUTH
- Adult: Initially 62.5 mg twice daily for 4 weeks, then increased to 125 mg twice daily

- **CONTRA-INDICATIONS** Acute porphyrias p. 1120
- **CAUTIONS** Not to be initiated if systemic systolic blood pressure is below 85 mmHg · pulmonary veno-occlusive disease
- **INTERACTIONS** → Appendix 1: bosentan
- **SIDE-EFFECTS**
- **Common or very common** Anaemia · diarrhoea · flushing · gastrooesophageal reflux disease · headache · nasal congestion · palpitations · skin reactions · syncope
- **Uncommon** Hepatic disorders · leucopenia · neutropenia · thrombocytopenia
- **Rare or very rare** Angioedema
- **Frequency not known** Vision blurred
- **CONCEPTION AND CONTRACEPTION** Effective contraception required during administration (hormonal contraception not considered effective). Monthly pregnancy tests advised.
- **PREGNANCY** Avoid (teratogenic in *animal* studies).
- **BREAST FEEDING** Manufacturer advises avoid—no information available.
- **HEPATIC IMPAIRMENT** Manufacturer advises avoid in moderate-to-severe impairment or if baseline serum transaminases exceed 3 times the upper limit of normal.
- **MONITORING REQUIREMENTS**
- Monitor haemoglobin before and during treatment (monthly for first 4 months, then 3-monthly).
- Monitor liver function before treatment, at monthly intervals during treatment, and 2 weeks after dose increase (reduce dose or suspend treatment if liver enzymes raised significantly)—discontinue if symptoms of liver impairment.
- **TREATMENT CESSATION** Avoid abrupt withdrawal—withdraw treatment gradually.

- **MEDICINAL FORMS** There can be variation in the licensing of different medicines containing the same drug.

Tablet

- **Bosentan (Non-proprietary)**

Bosentan (as Bosentan monohydrate) 62.5 mg Bosentan 62.5mg tablets | 56 tablet PoM £112.50 (Hospital only) | 56 tablet PoM £1,359.19–£1,510.21

Bosentan (as Bosentan monohydrate) 125 mg Bosentan 125mg tablets | 56 tablet PoM £112.50 (Hospital only) | 56 tablet PoM £1,359.19–£1,510.21

- **Stayveer** (Advanz Pharma)

Bosentan (as Bosentan monohydrate) 62.5 mg Stayveer 62.5mg tablets | 56 tablet PoM £208.34

Bosentan (as Bosentan monohydrate) 125 mg Stayveer 125mg tablets | 56 tablet PoM £208.34

- **Tracleer** (Actelion Pharmaceuticals UK Ltd)

Bosentan (as Bosentan monohydrate) 62.5 mg Tracleer 62.5mg tablets | 56 tablet PoM £1,510.21

Bosentan (as Bosentan monohydrate) 125 mg Tracleer 125mg tablets | 56 tablet PoM £1,510.21