

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

Tablet

CAUTIONARY AND ADVISORY LABELS 23, 25

- ▶ **Votrient** (Novartis Pharmaceuticals UK Ltd)

Pazopanib (as Pazopanib hydrochloride) 200 mg Votrient 200mg tablets | 30 tablet [PoM](#) £560.50

Pazopanib (as Pazopanib hydrochloride) 400 mg Votrient 400mg tablets | 30 tablet [PoM](#) £1,121.00

Ponatinib

06-Dec-2019

● **INDICATIONS AND DOSE**

Treatment of chronic, accelerated, or blast phase chronic myeloid leukaemia in patients who have the T3151 mutation or who have resistance to or intolerance of dasatinib or nilotinib, and for whom subsequent treatment with imatinib is not clinically appropriate | Treatment of Philadelphia chromosome-positive acute lymphoblastic leukaemia in patients who have the T3151 mutation or who have resistance to or intolerance of dasatinib, and for whom subsequent treatment with imatinib is not clinically appropriate

▶ **BY MOUTH**

- ▶ **Adult:** 45 mg once daily, for dose adjustments due to side-effects or dose reduction due to risk of vascular occlusive events, consult product literature

DOSE ADJUSTMENTS DUE TO INTERACTIONS

- ▶ Manufacturer advises consider a reduced initial dose of 30 mg daily with concurrent use of potent inhibitors of CYP3A4.

IMPORTANT SAFETY INFORMATION

MHRA/CHM ADVICE: PONATINIB: RISK OF VASCULAR OCCLUSIVE EVENTS—UPDATED ADVICE ON POSSIBLE DOSE REDUCTION (UPDATED APRIL 2017)

The benefits and risks of ponatinib were reviewed by the European Medicines Agency's Committee on Medicinal Products for Human Use in 2014, which recommended that strengthened warnings should be added to the product information aimed at minimising the risk of blood clots and blockages in the arteries. Additional long-term follow-up data are now available that supports new advice on dose modification to reduce this risk. The MHRA advise that although the recommended starting dose of ponatinib remains unchanged, prescribers should consider reducing the dose for patients with chronic phase chronic myeloid leukaemia (CP-CML) who have achieved a major cytogenetic response while on treatment. The following factors should be taken into account in the individual patient assessment:

- cardiovascular risk;
- side-effects of ponatinib therapy (including cardiovascular and other dose-related toxicity);
- time to cytogenetic response;
- BCR-ABL transcript levels.

The MHRA recommends close monitoring of response, if dose reduction is undertaken.

MHRA/CHM ADVICE: RISK OF HEPATITIS B VIRUS REACTIVATION WITH BCR-ABL TYROSINE KINASE INHIBITORS (MAY 2016)

An EU wide review has concluded that ponatinib can cause hepatitis B reactivation; the MHRA recommends establishing hepatitis B virus status in all patients before initiation of treatment.

MHRA/CHM ADVICE: PONATINIB (ICLUSIG®): REPORTS OF POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME (OCTOBER 2018)

Post-marketing cases of posterior reversible encephalopathy syndrome (PRES) have been reported in patients receiving ponatinib.

Treatment should be interrupted if PRES is confirmed and resumed only once the event is resolved and if the benefit of continued treatment outweighs the risk.

Patients should be advised to contact their healthcare professional immediately if they develop sudden-onset severe headache, confusion, seizures, or vision changes.

RISKS OF INCORRECT DOSING OF ORAL ANTI-CANCER MEDICINES
See Cytotoxic drugs p. 938.

- **CAUTIONS** Alcohol abuse—increased risk of pancreatitis · current severe hypertriglyceridaemia—increased risk of pancreatitis · discontinue treatment if a complete haematologic response has not occurred within 3 months · hepatitis B infection · history of myocardial infarction—do not use unless potential benefit outweighs potential risk · history of pancreatitis · history of stroke—do not use unless potential benefit outweighs potential risk · hypertension—medically control during treatment and interrupt treatment if uncontrolled

CAUTIONS, FURTHER INFORMATION

- ▶ Cardiovascular status **Assess** cardiovascular status before treatment—manage cardiovascular risk factors before and during treatment.
- ▶ Hepatitis B infection The MHRA advises that patients who are carriers of hepatitis B virus should be closely monitored for signs and symptoms of active infection throughout treatment and for several months after stopping treatment; expert advice should be sought for patients who test positive for hepatitis B virus and in those with active infection.

- **INTERACTIONS** → Appendix 1: ponatinib

● **SIDE-EFFECTS**

- ▶ **Common or very common** Acute coronary syndrome · alopecia · anaemia · appetite decreased · arrhythmias · arthralgia · asthenia · cerebrovascular insufficiency · chills · constipation · cough · diarrhoea · dizziness · dry eye · dry mouth · dysphonia · dyspnoea · electrolyte imbalance · embolism and thrombosis · erectile dysfunction · eye inflammation · febrile neutropenia · fever · fluid imbalance · gastrointestinal discomfort · gastroesophageal reflux disease · haemorrhage · headaches · heart failure · hyperglycaemia · hypertension · hypertriglyceridaemia · hyperuricaemia · hypothyroidism · increased risk of infection · influenza like illness · insomnia · ischaemic heart disease · lethargy · mass · muscle complaints · nausea · oedema · pain · pancreatitis · pancytopenia · pericardial effusion · peripheral neuropathy · peripheral vascular disease · pleural effusion · pulmonary hypertension · sensation abnormal · sepsis · skin reactions · stomatitis · sweat changes · vasodilation · vision disorders · vomiting · weight decreased
- ▶ **Uncommon** Cardiac discomfort · cardiomyopathy ischaemic · coronary vasospasm · hepatic disorders · hepatic failure (including fatal cases) · intracranial haemorrhage · left ventricular dysfunction · posterior reversible encephalopathy syndrome (PRES) · renal artery stenosis · splenic infarction · tumour lysis syndrome
- **CONCEPTION AND CONTRACEPTION** Ensure effective contraception during treatment in men and women; effectiveness of hormonal contraception unknown—alternative or additional methods of contraception should be used.
- **PREGNANCY** Avoid—toxicity in *animal* studies. See also *Pregnancy and reproductive function* in Cytotoxic drugs p. 938.
- **BREAST FEEDING** Manufacturer advises discontinue breastfeeding—no information available.
- **HEPATIC IMPAIRMENT** Manufacturer advises caution.