PRESCRIBING INFORMATION – Ponatinib Incyte (ponatinib) film-coated tablets

15 mg, 30 mg or 45 mg ponatinib (as hydrochloride)

Legal Category: POM. See Summary of Product Characteristics (SmPC) before prescribing.

Indications:
Adult patients with

- Chronic phase (CP), accelerated phase (AP), or blast phase (BP) chronic myeloid leukaemia (CML) who are resistant/intolerant to dasatinib or nilotinib and for whom subsequent treatment with imatinib is not clinically appropriate; or who have the T315I mutation.
- Philadelphia chromosome positive acute lymphoblastic leukaemia (Ph+ ALL) who are resistant/intolerant to dasatinib and for whom subsequent treatment with imatinib is not clinically appropriate; or who have the T315I mutation.

Dosage and administration:
Recommended starting dose 45 mg once daily; swallow tablets whole.

Assess and actively manage cardiovascular (CV) risk factors before starting treatment and continue throughout treatment; consider other treatment options in patients with prior myocardial infarction (MI), revascularisation or stroke (CVA).

The risk of Arterial Occlusive Events is likely to be dose-related.
Consider dose reduction to 15 mg for CP-CML patients who achieve a Major Cytogenetic Response. If patients lose response, dose can be re-escalated; consult the SmPC for full details of risk:benefit and recommended monitoring of response.

Discontinue in case of disease progression or severe adverse reactions (ADRs); also, if Complete Haematological Response does not occur by 3 months.

Dose modifications, or interruptions, should be considered for haematological and non-haematological toxicities; consult the SmPC for full details of all recommended dose modifications.

Contraindications: Hypersensitivity to ponatinib or excipients.

Warnings and precautions: *Important ADRs: refer to SmPC for full details of recommended monitoring and management.*

Myelosuppression: Perform Full Blood Count every 2 weeks for the first 3 months and then monthly as clinically indicated.
Most severe events occurred in first 3 months; overall, events occurred more frequently in AP-CML, BP-CML or Ph+ ALL than CP-CML.

Arterial Occlusion: Interrupt treatment immediately.
Serious reactions including MI, CVA and retinal artery occlusion have occurred in 20% of patients in the PACE Phase 2 trial of Ponatinib Incyte including patients <50 years and without CV risk factors; events occurred more frequently with increasing age and those with history of ischaemia, hypertension, diabetes, or hyperlipidaemia. Serious reactions have occurred in 4.3% of patients in the OPTIC Phase 2 trial (45 mg cohort).

Venous thromboembolism: Interrupt treatment immediately.
Serious reactions have occurred in 5% of patients in the PACE trial including retinal vein occlusion.

Hypertension: Monitor and manage throughout treatment; may increase risk of arterial thrombotic events including renal artery stenosis.
Treatment-emergent events have occurred, including hypertensive crisis.

Aneurysms and artery dissections: This risk should be considered in patients with hypertension or history of aneurysm.
VEGF pathway inhibitors may promote the formation of aneurysms and/or artery dissections.

Congestive Heart Failure: Consider discontinuing treatment if severe.
Fatal events have occurred, some related to prior vascular occlusive events.

Pancreatitis and serum lipase: Check serum lipase fortnightly for 2 months and then periodically.
Frequency of events is greater in the first 2 months. Caution in patients with history of pancreatitis or alcohol abuse.

Hepatotoxicity: Perform liver function tests (LFTs) before and during treatment.
Hepatic failure (including fatal outcome) has been observed, mostly in first year of treatment.

Haemorrhage: Interrupt treatment if serious or severe.
Most severe events, including gastrointestinal haemorrhage and subdural haematoma, occurred more frequently in AP-CML, BP-CML or Ph+ ALL. Caution with use of anti-clotting agents.

Risk of Hepatitis B reactivation: *Test for HBV before treatment.*
Reactivation has occurred following Ponatinib Incyte treatment. Consult with hepatologist if serology is positive.

Severe Cutaneous Adverse Reaction (SCARs).
Severe skin reactions (such as Stevens-Johnson Syndrome) have been reported with some BCR-ABL TKIs.

Posterior Reversible Encephalopathy Syndrome (PRES).
Post-marketing cases of PRES have been reported in Ponatinib Incyte -treated patients.

Effects on ability to drive and use machines.
Lethargy, dizziness and blurred vision have occurred.

QT prolongation.
A clinically significant effect on QT cannot be excluded.
Ponatinib Incyte contains lactose. Avoid treatment with patients having rare hereditary problems of galactose intolerance.

Drug Interactions: See SmPC for details of all interactions.
Avoid treatment with Ponatinib and strong CYP3A4 inducers if possible. Caution when treating with strong CYP3A inhibitors; consider 30 mg starting dose of Ponatinib Incyte.

Pregnancy and breastfeeding: Advise patients not to become pregnant or father a child during treatment; use effective contraception. Studies in animals have shown reproductive toxicity. Breastfeeding should be discontinued.

Undesirable effects: *Most common serious ADRs:* Pneumonia, CVA, coronary artery disease, peripheral arterial occlusive disease, pancreatitis, pyrexia, abdominal pain, anaemia, angina, decreased platelet count, febrile neutropaenia, hypertension, MI, atrial fibrillation, CCF, sepsis, cellulitis, acute kidney injury, UTI, increased lipase. *Other very common ADRs:* Upper respiratory tract infection, decreased neutrophil count, dyspnoea, cough, diarrhoea, decreased appetite, nausea, vomiting, constipation, increased ALT/AST, peripheral oedema, rash, dry skin, pruritis, pain incl. back, bone & extremities, arthralgia, myalgia, muscle spasms, fatigue, headache, dizziness, asthenia. Consult the SmPC for details of all ADRs.

Quantities and Marketing Authorisation numbers:
45 mg dose
30 tablets PLGB 42338/0019
30 mg dose:
30 tablets PLGB 42338/0018
15 mg dose:
30 tablets PLGB 42338/0017
Cost: 45mg x 30 tablets £5050; 30mg x 30 tablets £5050, 15mg x 30 tablets £2525.

Marketing Authorisation Holder:
Incyte Biosciences UK Ltd.,First Floor Q1, The Square, Randalls Way, Leatherhead, KT22 7TW, UK
For further information phone 00-800-0002-7423

Date of preparation: January 2025 UK/PB/P/25/0001

Adverse events should be reported. Reporting forms and information can be found at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Incyte by calling 00-800-0002-7423.