Package leaflet: Information for the patient

Ponatinib Incyte 15 mg film-coated tablets
Ponatinib Incyte 30 mg film-coated tablets
Ponatinib Incyte 45 mg film-coated tablets
ponatinib

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Ponatinib Incyte is and what it is used for
2. What you need to know before you take Ponatinib Incyte
3. How to take Ponatinib Incyte
4. Possible side effects
5. How to store Ponatinib Incyte
6. Contents of the pack and other information

1. What Ponatinib Incyte is and what it is used for

Ponatinib Incyte is **used to treat** adults with the following **leukaemia** types who are no longer benefiting from treatment with other medicines, or have a certain genetic difference known as a T315I mutation:
- chronic myeloid leukaemia (CML): a blood cancer involving too many abnormal white blood cells in the blood and the bone marrow (where blood cells are formed).
- Philadelphia-chromosome positive acute lymphoblastic leukaemia (Ph+ ALL): a type of leukaemia involving too many immature white blood cells in the blood and blood forming bone marrow. In this kind of leukaemia, some of the DNA (genetic material) has become rearranged to form an abnormal chromosome, the Philadelphia chromosome.

Ponatinib Incyte belongs to a group of medicines called tyrosine kinase inhibitors. In patients with CML and Ph+ ALL, changes in the DNA trigger a signal that tells the body to produce abnormal white blood cells. Ponatinib Incyte blocks this signal, thereby stopping the production of these cells.

2. What you need to know before you take Ponatinib Incyte

Do not take Ponatinib Incyte
- if you are **allergic** to ponatinib or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

Talk to your doctor or pharmacist before taking Ponatinib Incyte if you have:
- a liver or pancreas disorder or reduced kidney function. Your doctor may want to take additional precautions.
- a history of alcohol abuse
- had a prior heart attack or stroke

- a history of blood clots in your blood vessels
- a history of renal artery stenosis (narrowing of the blood vessels to one or both kidneys)
- heart problems, including heart failure, irregular heartbeats, and QT prolongation
- high blood pressure
- or have had an aneurysm (enlargement and weakening of a blood vessel wall) or a tear in a blood vessel wall
- a history of bleeding issues
- ever had or might now have a hepatitis B infection. This is because Ponatinib Incyte could cause hepatitis B to become active again, which can be fatal in some cases. Patients will be carefully checked by their doctor for signs of this infection before treatment is started.

Your doctor will perform:
- evaluations of your heart function and the condition of your arteries and veins
- a complete blood count
  This will be repeated every 2 weeks for the first 3 months after starting the therapy. Afterwards it is performed monthly or as indicated by the doctor.
- checks of the serum protein known as lipase
  A serum protein called lipase will be checked every 2 weeks for the first 2 months, then periodically. A break in treatment or a decrease in dose may be required when lipase is increased.
- liver tests
  Liver function tests will be performed periodically, as indicated by your doctor.

A brain condition called posterior reversible encephalopathy syndrome (PRES) has been reported in patients treated with ponatinib. Symptoms may include sudden onset of severe headache, confusion, seizures, and vision changes. Tell your doctor straight away if you experience any of these symptoms during your treatment with ponatinib, because it could be serious.

Children and adolescents

Do not give this medicine to children under 18 years because no data are available in children.

Other medicines and Ponatinib Incyte

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. The following medicines can affect or be affected by Ponatinib Incyte:
- **ketoconazole, itraconazole, voriconazole:** medicines to treat fungal infections.
- **indinavir, nelfinavir, ritonavir, saquinavir:** medicines to treat HIV infection.
- **clarithromycin, telithromycin, troleandomycin:** medicines to treat bacterial infections.
- **nefazodone:** a medicine to treat depression.
- **St. John's wort:** a herbal product used to treat depression.
- **carbamazepine:** a medicine to treat epilepsy, euphoric/depressive stages and certain pain conditions.
- **phenobarbital, phenytoin:** medicines to treat epilepsy.
- **rifabutin, rifampicin:** medicines to treat tuberculosis or certain other infections.
- **digoxin:** a medicine to treat heart weakness.
- **dabigatran:** a medicine to prevent the formation of blood clots.
- **colchicine:** a medicine to treat gout attacks.
- **pravastatin, rosuvastatin:** medicines to lower elevated cholesterol levels.
- **methotrexate:** a medicine to treat severe joint inflammation (rheumatoid arthritis), cancer and the skin disease psoriasis.
- **sulfasalazine:** a medicine to treat severe bowel and rheumatic joint inflammation.

Ponatinib Incyte with food and drink
Avoid grapefruit products such as grapefruit juice.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.
Cases of congenital megacolon, also known as Hirschsprung's disease (a birth defect where nerve cells are missing from part of the baby's large intestine, resulting in bowel blockage) have been reported in children born to women treated with Ponatinib Incyte in early pregnancy.

- **Contraceptive advice for men and women**
  Women of childbearing age being treated with Ponatinib Incyte should avoid becoming pregnant.
  Men receiving treatment with Ponatinib Incyte are advised not to father a child during treatment.
  Effective contraception must be used during treatment.
  Only use Ponatinib Incyte during pregnancy **if your doctor tells you it is absolutely necessary**, as potential risks exist for the unborn child.

- **Breast-feeding**
  Stop breast-feeding during treatment with Ponatinib Incyte. It is not known if Ponatinib Incyte passes into breast milk.

Driving and using machines

You should take special care when driving and using machines as patients taking Ponatinib Incyte may experience visual disturbance, dizziness, sleepiness, and tiredness.

Ponatinib Incyte contains lactose

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

3. How to take Ponatinib Incyte

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Ponatinib Incyte therapy should be prescribed by a doctor experienced in leukaemia treatment.

Ponatinib Incyte is available as:
- a 45 mg film-coated tablet for the recommended dose.
- a 15 mg film-coated tablet and a 30 mg film-coated tablet to allow for dose adjustments.

The recommended starting dose is one 45 mg film-coated tablet once daily.

Your doctor may reduce your dose or tell you to temporarily stop taking Ponatinib Incyte if:
- an appropriate response to the treatment is reached
- the number of white blood cells called neutrophils is reduced.
- the number of blood platelets is reduced.
- a severe side effect occurs, not affecting the blood
  - pancreas inflammation.
  - increased levels of the serum proteins lipase or amylase.
- you develop heart or blood vessel problems.
- you have a liver disorder.

Ponatinib Incyte use may be resumed at the same, or a reduced dose, after the event is resolved or controlled. Your doctor may evaluate your response to the treatment at regular intervals.

Method of use

Swallow the tablets whole, with a glass of water. The tablets can be taken with or without food. Do not crush or dissolve the tablets.

Do not swallow the desiccant canister contained in the bottle.

Duration of use

Make sure you take Ponatinib Incyte daily for as long as it is prescribed. This is a long-term treatment.

If you take more Ponatinib Incyte than you should

Talk to your doctor immediately if this occurs.

If you forget to take Ponatinib Incyte

Do not take a double dose to make up for a forgotten dose. Take your next dose at your regular time.

If you stop taking Ponatinib Incyte

Do not stop taking Ponatinib Incyte without your doctor's permission.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Patients aged 65 and over are more likely to be affected by side effects.

Seek medical attention immediately if you experience any of the **following serious** side effects.

If abnormal results from blood tests are received, a doctor should be contacted immediately.

Serious side effects (may affect up to 1 in 10 people):
- lung infection (may cause breathing difficulty)
- pancreas inflammation. Inform your doctor immediately if pancreas inflammation occurs. Symptoms are severe pain in the stomach and back.
- fever, often with other signs of infection due to decreased number of white blood cells
- heart attack (symptoms include: sudden feeling of increased heart rate, chest pain, breathlessness)
- changes in blood levels:
  - decreased number of red blood cells (symptoms include: weakness, dizziness, fatigue)
  - decreased number of blood platelets (symptoms include: increased tendency to bleed or bruise)
  - decreased number of white blood cells called neutrophilis (symptoms include: increase tendency of infection)
  - increased level of the serum protein known as lipase
- a heart rhythm disorder, abnormal pulse
- heart failure (symptoms include: weakness, fatigue, swollen legs)
- uncomfortable pressure, fullness, squeezing or pain in the centre of the chest (Angina pectoris) and chest pain not in connection with the heart
- high blood pressure
- narrowing of the arteries in the brain, stroke caused by low blood flow to part of the brain
- problems of the blood vessels in the heart muscle

- blood infection
- swollen, or red area of skin that feels hot and tender (cellulitis)
- dehydration
- breathing difficulties
- fluid in the thorax (may cause breathing difficulty)
- diarrhoea
- blood clot in a deep vein, sudden vein obstruction, blood clot in a blood vessel of the lung (symptoms include: hot flush, flushing, redness of the face, breathing difficulty)
- stroke (symptoms include: difficulty to speak or move, sleepiness, migraine, abnormal sensations)
- blood circulation problems (symptoms include: pain in the legs or arms, coldness of the extremities of the limbs)
- blood clot in the main arteries carrying blood to the head or neck (carotid artery)
- constipation
- sodium decrease in the blood
- increased tendency to bleed or bruise

Other possible side effects that may occur with the following frequencies are:

Very common side effects (may affect more than 1 in 10 people):
- upper airway infection (may cause breathing difficulty)
- decreased appetite
- insomnia
- headache, dizziness
- cough
- diarrhoea, vomiting, nausea, constipation, abdominal pain
- increased blood levels of several liver enzymes called:
  - alanine aminotransferase
  - aspartate aminotransferase
- skin rash, dry skin, itching
- pain in bones, joints, pain in muscles, back, arms or legs, muscle spasms
- fatigue, accumulation of fluid in arms and/or legs, fever, pain
- high blood fat values of triglycerides
- increase in cholesterol that would be detected during blood tests

Common side effects (may affect up to 1 in 10 people):
- inflammation of hair follicles, swollen, red area of skin or underneath skin that feels hot and tender
- decreased activity of thyroid gland
- fluid retention
- low calcium, phosphate or potassium levels in the blood
- increased blood sugar or uric acid levels in the blood
- weight loss
- mini stroke
- nerve disorder in the arms and/or legs (often causes numbness and pain in the hands and feet)
- nerve disorder in the face (often causes numbness or weakness on one or both sides of your face)
- lethargy, migraine
- muscle weakness, musculoskeletal stiffness
- increased or reduced sense of touch or sensation, abnormal sensation such as prickling, tingling and itchiness
- blurred vision, dry eye, infection in the eye, visual disturbance, eye pain
- tissue swelling in eyelid or around the eyes, caused by excess fluid
- palpitation
- pain in one or both legs when walking or exercising, which disappears after some minutes of rest
- hot flush, flushing

- nosebleed, difficulty producing voice sounds, hypertension in the lungs
- increased blood levels of liver and pancreatic enzymes:
  - amylase
  - alkaline phosphatase
  - gamma-glutamyltransferase
- increased level of the serum protein known as C-reactive protein that increases when there is inflammation in your body
- heartburn caused by reflux of stomach juices, peptic ulcer
- inflammation in the mouth, pain in the throat or mouth, dry mouth, bleeding gums
- abdominal swelling or discomfort or indigestion
- stomach bleeding (symptoms include: stomach pain, vomiting blood)
- increased blood level of bilirubin - the yellow breakdown substance of the blood pigment (symptoms include: dark amber urine)
- pain in skeletal system or neck
- pain caused by inflammation in the membrane surrounding the tendons usually in the feet or hands
- peeling of the skin, abnormal thickening of the skin, redness, bruising, skin pain, changes in skin colour, flat discolored areas and small raised bumps on your skin, warts, skin disease resembling acne, symmetrical, red, raised skin areas that can appear all over the body, hair loss
- tissue swelling in face caused by excess fluid
- night sweats, increased sweating
- inability to develop or maintain an erection
- chills, flu-like illness
- herpes zoster
- overactive thyroid gland that speeds up the body's metabolism. That can cause many symptoms, such as weight loss, hand tremors, and rapid or irregular heartbeat.
- weight increase
- anxiety
- heart problems, left sided chest pain, dysfunction of the left heart chamber, changes in the way the heart beats, rapid heartbeat, increased level of the serum protein known as brain natriuretic peptide and that may increase when the heart cannot pump the way it should
- narrowing of the blood vessels, poor blood circulation, sudden increase in blood pressure
- obstruction of the blood vessels in the eye
- painful red lumps, skin pain, skin reddening (inflammation of fatty tissue under the skin)
- metabolic disorders caused by the break down products of dying cancer cells

Uncommon side effects (may affect up to 1 in 100 people):
- renal artery stenosis (narrowing of the blood vessels to one or both kidneys)
- circulatory problems in the spleen
- liver damage, jaundice (symptoms include: yellowing of the skin and eyes)
- headache, confusion, seizures, and loss of vision, which may be symptoms of a brain condition known as posterior reversible encephalopathy syndrome (PRES).

Not known (frequency cannot be estimated from the available data):
- recurrence (reactivation) of Hepatitis B infection when you have had hepatitis B in the past (a liver infection).
- troubling skin rashes involving blisters or peeling and spread across the body, and involving tiredness. Inform your doctor immediately if you experience these symptoms.
- an enlargement and weakening of a blood vessel wall or a tear in a blood vessel wall (aneurysms and artery dissections).

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system:

Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Ponatinib Incyte

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the bottle label and carton after EXP. The expiry date refers to the last day of that month.

Store in the original container in order to protect from light.

The bottle contains one sealed plastic canister containing a molecular sieve desiccant. Keep the canister in the bottle. Do not swallow the desiccant canister.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Ponatinib Incyte contains

- The active substance is ponatinib.
  Each 15 mg film-coated tablet contains 15 mg ponatinib (as ponatinib hydrochloride).
  Each 30 mg film-coated tablet contains 30 mg ponatinib (as ponatinib hydrochloride).
  Each 45 mg film-coated tablet contains 45 mg ponatinib (as ponatinib hydrochloride).
- The other ingredients are lactose monohydrate, microcrystalline cellulose, sodium starch glycolate, silica (colloidal anhydrous), magnesium stearate, talc, macrogol 4000, polyvinyl alcohol, titanium dioxide (E171). See section 2 “Ponatinib Incyte contains lactose”.

What Ponatinib Incyte looks like and contents of the pack

Ponatinib Incyte film-coated tablets are white, round and rounded on the upper and lower side.
Ponatinib Incyte 15 mg film-coated tablets are approximately 6 mm in diameter with "A5" on one side.
Ponatinib Incyte 30 mg film-coated tablets are approximately 8 mm in diameter with "C7" on one side.
Ponatinib Incyte 45 mg film-coated tablets are approximately 9 mm in diameter with "AP4" on one side.

Ponatinib Incyte is available in plastic bottles, each containing one canister of a molecular sieve desiccant. Bottles are packed within a cardboard box.
Bottles of Ponatinib Incyte 15 mg contain 30 film-coated tablets
Bottles of Ponatinib Incyte 30 mg contain 30 film-coated tablets
Bottles of Ponatinib Incyte 45 mg contain 30 film-coated tablets.

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Detailed information on this medicine is available on the Medicines and Healthcare products Regulatory Agency (MHRA) website: www.mhra.gov.uk.