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CLINICAL APPROVAL LETTER: POST REGISTRATION APPLICATIONS

Clinical approval date	29-May-2026
Applicant's cover letter date	14-March-2025
Applicant	Ranbaxy Pharmaceuticals (Pty) Ltd
Proprietary name(s) (including duplicates)	DASAMIA 20/50/70/100
API(s)	dasatinib.
Registration number(s)	Dasamia 20: 56/26/0207, Dasamia 50: 56/26/0208 Dasamia 70: 56/26/0209, Dasamia 100: 56/26/0210
Sequence no	0007

Dear Sir/Madam,

Kindly be informed that the Authority has completed the evaluation of the above-mentioned Professional Information (PI) and Patient Information Leaflet (PIL) variation application.

1. The amendments to the PI and PIL are approved.
2. The PI and PIL be accepted as the currently approved PI and PIL
3. The date of revision reflected on this PI and PIL should be**: 29-May-2026**
4. The final dated version of the above PI and PIL must be submitted via docubridge in a closing sequence using the Sequence Type "Closing sequence" and Sequence Description "Approved " updated PI and PIL within 10 working days.
5. The approved PI and PIL must be uploaded into the SAHPRA repository within 10 working days.

Note to applicant: Amendments to any quality aspects of the medicine within the PI and PIL are subject to P&A unit approval and may only be implemented in the PI if approved by the P&A unit.

Yours Faithfully,

L.DHLAMINI

MANAGER: CLINICAL POST-REGISTRATION UNIT

CLEAN PROPOSED PROFESSIONAL INFORMATION

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

DASAMIA 20 (Film coated tablets)

DASAMIA 50 (Film coated tablets)

DASAMIA 70 (Film coated tablets)

DASAMIA 10 (Film coated tablets)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

DASAMIA 20, film coated tablets contain 20 mg dasatinib.

DASAMIA 50, film coated tablets contain 50 mg dasatinib.

DASAMIA 70, film coated tablets contain 70 mg dasatinib.

DASAMIA 100, film coated tablets contain 100 mg dasatinib.

DASAMIA 20, film coated tablets contains 26,760 mg lactose monohydrate.

DASAMIA 50, film coated tablets contains 66,900 mg lactose monohydrate.

DASAMIA 70, film coated tablets contains 93,660 mg lactose monohydrate.

DASAMIA 100, film coated tablets contains 133,800 mg lactose monohydrate.

For full list of excipients, see **section 6.1.**

3. PHARMACEUTICAL FORM

DASAMIA 20 film coated tablets: White to off-white, biconvex, round, film-coated tablet, debossed with “851” on one side and plain on other side.

DASAMIA 50 film coated tablets: White to off-white, biconvex, oval, film-coated tablet, debossed with “852” on one side and plain on other side.

DASAMIA 70 film coated tablets: White to off-white, biconvex, round, film-coated tablet debossed with “853” on one side and plain on other side.

DASAMIA 100 film coated tablets: White to off-white, biconvex, oval, film-coated tablet, debossed with “855” on one side and plain on other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

DASAMIA is indicated for the treatment of adults with newly diagnosed Philadelphia chromosome-positive (Ph+) chronic myeloid leukaemia (CML) in chronic phase.

- **DASAMIA** is indicated for the treatment of adults with chronic, accelerated, or myeloid or lymphoid blast phase chronic myeloid leukaemia (CML) with resistance or intolerance to prior therapy including imatinib.
- **DASAMIA** is also indicated for the treatment of adults with Philadelphia chromosome-positive acute lymphoblastic leukaemia (Ph+ ALL) with resistance or intolerance to prior therapy.

4.2 Posology and method of administration

The recommended starting dosage of **DASAMIA** for chronic phase CML is 100 mg once daily, administered orally. **DASAMIA** can be taken with or without a meal and should be taken consistently either in the morning or in the evening.

The recommended starting dosage of **DASAMIA** for accelerated, myeloid or lymphoid blast phase (advanced phase) CML or Ph+ ALL is 70 mg twice daily, administered orally. **DASAMIA** can be taken with or without a meal and should be taken consistently in the morning and in the evening.

Dose increase or reduction is recommended based on individual patient response and tolerability.

Dose escalation

In clinical trials of CML and Ph+ ALL, dose escalation to a total maximum of 70 mg twice daily (chronic phase CML) or 90 mg twice daily (advanced phase CML or Ph+ ALL) was allowed in patients who did not achieve a haematologic or cytogenetic response at the recommended starting dosage.

Dose adjustment for undesirable effects

Myelosuppression

Myelosuppression was managed by dose interruption, dose reduction, or discontinuation of study therapy. Platelet transfusion and red cell transfusion were used as appropriate. Haematopoietic growth factor has been used in patients with resistant myelosuppression. Guidelines for dose modifications in adults are summarised in table below.

Table 1: Dose adjustments for neutropenia and thrombocytopenia.

Chronic phase CML (starting dose 100 mg once daily)	ANC* < 0,5 x 10^9/L or platelets < 50 x 10^9/L	1) Stop **DASAMIA** until ANC ≥ 1,0 x 10^9/L and platelets ≥ 50 x 10^9/L. 2) Resume treatment with **DASAMIA** at the original starting dose. 3) If platelets < 25 x 10^9/L or recurrence of ANC < 0,5 x 10^9/L for > 7 days, repeat Step 1 and resume **DASAMIA** treatment at a reduced dose of 80 mg once daily for second episode. For third

		episode, further reduce dose to 50 mg once daily (for newly diagnosed patients) or discontinue **DASAMIA** (for patients resistant or intolerant to prior including imatinib).

Accelerated phase CML, Blast phase CML and Ph+ ALL (starting dose 70 mg twice daily	ANC < 0,5 x 10^9/L or platelets < 10 x 10^9/L	**1.** Check if cytopenia is related to leukaemia (marrow aspirate or biopsy). **2.** If cytopenia is unrelated to leukaemia, stop **DASAMIA** until ANC ≥ 1,0 x 10^9/L and platelets ≥ 20 x 10^9/L and resume at the original starting dose. **3.** If recurrence of cytopenia, repeat Step 1 and resume **DASAMIA** at a reduced dose of 50 mg twice daily (second episode) or 40 mg twice daily (third episode).

		4. If cytopenia is related to leukaemia, consider dose escalation to 100 mg twice daily.	* ANC: absolute neutrophil count

Non-haematological adverse reactions

If a severe non-haematological adverse reaction develops with **DASAMIA** use, treatment must be withheld until the event has resolved or improved. Thereafter, treatment can be resumed as appropriate at a reduced dose depending on the severity and recurrence of the event (see **section 4.4**).

Renal Impairment: See **section 5.2**

Hepatic Impairment: See **section 5.2**

Geriatric: No clinically relevant age-related pharmacokinetic differences have been reported. No specific dose recommendation is necessary.

Paediatric Patients: The safety and efficacy of dasatinib in patients < 18 years of age have not been established.

Method of administration

DASAMIA is administered orally. Tablets should not be crushed or cut; they should be swallowed whole.

4.3 Contraindications

- **DASAMIA** is contra-indicated in patients with hypersensitivity to dasatinib or to any other component of **DASAMIA**.
- The concomitant use of H2 antagonists or proton pump inhibitors with **DASAMIA** is not recommended

4.4 Special warnings and precautions for use

Clinically relevant interactions

Dasatinib is a substrate and an inhibitor of cytochrome P450 (CYP) 3A4. Therefore, there is a potential for interaction with other concomitantly administered medicines that are metabolised primarily by or modulate the activity of CYP3A4 (see **section 4.5).**

Concomitant use of dasatinib and medicines or substances that potently inhibit CYP3A4 (e.g. ketoconazole, itraconazole, erythromycin, clarithromycin, ritonavir, telithromycin, grapefruit juice) may increase exposure to dasatinib. Therefore, in patients receiving dasatinib, coadministration of a potent CYP3A4 inhibitor is not recommended (see **section 4.5**).

Concomitant use of dasatinib and medicines that induce CYP3A4 (e.g. dexamethasone, phenytoin, carbamazepine, rifampicin, phenobarbital or herbal preparations containing Hypericum perforatum, also known as St. John's Wort) may substantially reduce exposure to dasatinib, potentially increasing the risk of therapeutic failure. Therefore, in patients receiving dasatinib, coadministration of alternative medicines with less potential for CYP3A4 induction should be selected (see **section 4.5**).

Concomitant use of dasatinib and a CYP3A4 substrate may increase exposure to the CYP3A4 substrate. Therefore, caution is warranted when dasatinib is co-administered with CYP3A4 substrates of narrow therapeutic index, such as astemizole, terfenadine, cisapride, pimozide, quinidine, bepridil or ergot alkaloids (ergotamine, dihydroergotamine) (see **section 4.5**).

The concomitant use of dasatinib and a histamine-2 (H2) antagonist (e.g. famotidine), proton pump inhibitor (e.g. omeprazole), or aluminium hydroxide/magnesium hydroxide may reduce the exposure to dasatinib. Thus, H2 antagonists and proton pump inhibitors are not recommended and aluminium hydroxide/magnesium

hydroxide products should be administered up to 2 hours prior to, or 2 hours following the administration of dasatinib (see **section 4.5**).

Special populations

Based on the findings from a reported single-dose pharmacokinetic study, patients with mild, moderate or severe hepatic impairment may receive the recommended starting dose. Due to the limitations of this reported clinical study, caution is recommended when administering dasatinib to patients with hepatic impairment.

Important adverse reactions

Myelosuppression

Treatment with dasatinib is very commonly associated with thrombocytopenia, neutropenia, anaemia, which occur earlier and more frequently reported in patients with advanced phase CML or Ph+ ALL than in patients with chronic phase CML. In patients with chronic phase CML, complete blood counts (CBCs) should be performed every two weeks for 12 weeks, then every 3 months thereafter, or as clinically indicated. In patients with advanced phase CML or Ph+ ALL, CBCs should be performed weekly for the first 2 months and then monthly thereafter, or as clinically indicated. Myelosuppression is generally reversible and usually managed by withholding dasatinib temporarily or by dose reduction (see **sections 4.2 and 4.8)**.

Bleeding related events

In patients with chronic phase CML, severe haemorrhage reported in few patients receiving dasatinib at the recommended dose. In patients with advanced phase CML or Ph+ ALL, severe central nervous system (CNS) haemorrhage, including fatalities, occurred in 1 % of patients receiving dasatinib at the recommended dose. Severe gastrointestinal haemorrhage, including fatalities, reported in 6 % of patients and generally required treatment interruptions and transfusions. Other cases of severe haemorrhage occurred in 2 % of patients. Most bleeding events in reported clinical studies were associated with severe thrombocytopenia. Additionally,

reported in vitro and in vivo platelet assays suggest that dasatinib treatment reversibly affects platelet activation.

Caution should be exercised if patients are required to take medicines that inhibit platelet function or anticoagulants.

Fluid retention

Dasatinib is associated with fluid retention. After 5 years of follow-up in the reported Phase III newly diagnosed chronic phase CML study, severe fluid retention was reported in 5 % patients receiving dasatinib. In all patients with newly diagnosed or imatinib resistant or intolerant patients with chronic phase CML, severe fluid retention occurred in 6 % patients receiving dasatinib at the recommended dose. In patients with advanced phase CML or Ph+ ALL receiving dasatinib, severe fluid retention was reported in 8 % of patients, including severe pleural and pericardial effusion reported in 7 % and 1 % of patients, respectively. In these patients, severe pulmonary oedema and severe pulmonary hypertension were reported in 1 % of patients.

Patients who develop symptoms suggestive of pleural effusion or other fluid retention, such as new or worsened dyspnoea on exertion or at rest, pleuritic chest pain, or dry cough should be evaluated promptly with chest X-ray or additional diagnostic imaging as appropriate. Fluid retention events were typically managed by supportive care measures that may include diuretics or short courses of steroids. Severe pleural effusion may require thoracentesis. Dose modification should be considered (see **section 4.2**). While the safety profile of dasatinib in the elderly population was reported to be similar to that in the younger population, patients aged 65 years and older are more likely to experience fluid retention events and dyspnoea and should be monitored closely.

Cardiac adverse reactions

Dasatinib was studied in a randomised trial in patients with newly diagnosed CML in chronic phase which included patients with prior cardiac disease. The cardiac adverse reactions of congestive heart failure/cardiac dysfunction, pericardial effusion, dysrhythmias, palpitations, QT prolongation, and myocardial infarction (including fatal) were reported in patients taking dasatinib. Adverse cardiac events were more frequent in patients with risk factors or a previous medical history of cardiac disease. Patients with risk factors (e.g. hypertension, hyperlipidaemia, diabetes) or a history of cardiac disease (e.g. prior percutaneous coronary intervention, documented coronary artery disease) should be monitored carefully for clinical signs or symptoms consistent with cardiac dysfunction such as chest pain, shortness of breath, diaphoresis and should be evaluated and treated appropriately.

If these clinical signs or symptoms develop, medical practitioners are advised to interrupt **DASAMIA** administration and consider the need for alternative CML-specific treatment. After resolution, a functional assessment should be performed prior to resuming treatment with **DASAMIA**. **DASAMIA** may be resumed at the original dose for mild/moderate adverse reactions (≤ grade 2) and resumed at a dose level reduction for severe adverse reactions (≥ grade 3). Patients continuing treatment should be monitored periodically. Patients with uncontrolled or significant cardiovascular disease were not included in the reported clinical studies.

Thrombotic microangiopathy (TMA)

BCR-ABL tyrosine kinase inhibitors have been associated with thrombotic microangiopathy (TMA), including individual case reports for dasatinib. If laboratory or clinical findings associated with TMA occur in a patient receiving **DASAMIA**, treatment with **DASAMIA** should be discontinued and thorough evaluation for TMA, including ADAMTS13 activity and anti-ADAMTS13-antibody determination, should be completed. If anti-ADAMTS13-antibody is elevated in conjunction with low ADAMTS13 activity, treatment with **DASAMIA** should not be resumed.

Cerebrovascular events

Cerebrovascular events such as central nervous system haemorrhage, cerebral haematoma, cerebral haemorrhage, extradural haematoma, intracranial haemorrhage, haemorrhagic stroke, subarachnoid haemorrhage, subdural haematoma and subdural haemorrhage have been associated with the use of tyrosine kinase inhibitors (TKI) (see **section 4.8**)

Pulmonary arterial hypertension

Pulmonary arterial hypertension (PAH), confirmed by right heart catheterisation, has been reported in association with dasatinib treatment in these cases, PAH was reported after initiation of dasatinib therapy, and also after more than one year of treatment.

Patients should be evaluated for signs and symptoms of underlying cardiopulmonary disease prior to initiating dasatinib therapy. Patients who develop dyspnoea and fatigue after initiation of therapy should be evaluated for more common aetiologies including pleural effusion, pulmonary oedema, anaemia, or lung infiltration. During this evaluation, guidelines for non-haematologic adverse reactions should be followed (see **section 4.2**). If the adverse reaction is severe, treatment must be withheld until the event has resolved or improved. If no alternative diagnosis is found, the diagnosis of PAH should be considered. If PAH is confirmed, **DASAMIA** should be permanently discontinued. Follow up should be performed according to standard practice guidelines. Improvements in haemodynamic and clinical parameters have been reported in dasatinib-treated patients with PAH following cessation of dasatinib therapy.

QT prolongation

Reported in vitro data suggest that dasatinib has the potential to prolong cardiac ventricular repolarisation (QT interval). Of the patients with resistance or intolerance to prior imatinib therapy treated with dasatinib in reported clinical studies, 1 % had QT prolongation reported as an adverse reaction. One percent of these patients experienced a QTcF > 500 ms.

DASAMIA should be administered with caution to patients who have or may develop prolongation of QT interval. These include patients with hypokalaemia or hypomagnesemia, patients with congenital long QT syndrome, patients taking anti- dysrhythmic medicines or other medicines that lead to QT prolongation, and cumulative high-dose anthracycline therapy. Hypokalaemia or hypomagnesemia should be corrected prior to **DASAMIA** administration.

Hepatitis B virus reactivation

BCR-ABL TKIs, including dasatinib have been associated with hepatitis B virus (HBV) reactivation including acute hepatic failure or fulminant hepatitis leading to liver transplantation or a fatal outcome. Screening for HBV should be considered in accordance with guidelines before starting therapy with **DASAMIA**. Consultation with a medical practitioner with expertise in the treatment of HBV is recommended for patients who test positive for HBV serology. Patients who are carriers of HBV and require treatment with **DASAMIA** should be closely monitored for clinical and laboratory signs of active HBV infection throughout therapy and for several months following termination of therapy. In patients who develop reactivation of HBV while receiving **DASAMIA**, prompt consultation with a medical practitioner with expertise in the treatment of HBV is recommended.

Severe dermatologic reactions

Cases of severe mucocutaneous dermatologic reactions, including Stevens-Johnson syndrome, toxic epidermal necrolysis and erythema multiforme have been reported with the use of dasatinib. **DASAMIA** should be permanently discontinued in patients who experience a severe mucocutaneous reaction during treatment if no other etiology can be identified.

Elderly use

Patients aged 65 years and older are more likely to experience the commonly reported adverse reactions of fatigue, pleural effusion, dyspnoea, cough, lower gastrointestinal haemorrhage, and appetite disturbance, and

are more likely to experience the less frequently reported events of abdominal distention, dizziness, pericardial effusion, congestive heart failure, and weight decrease, and should be monitored closely.

Excipients

Lactose

DASAMIA contains lactose. Patients with rare hereditary conditions of galactose intolerance e.g. total lactase deficiency, or glucose-galactose malabsorption should not take **DASAMIA**.

4.5 Interaction with other medicines and other forms of interaction

Effect of other medicines on DASAMIA.

Medicines that may increase dasatinib plasma concentrations

CYP3A4 Inhibitors: Dasatinib is a CYP3A4 substrate. Concomitant use of dasatinib and medicines that inhibit CYP3A4 (e.g. ketoconazole, itraconazole, erythromycin, clarithromycin, ritonavir, atazanavir, indinavir, nelfinavir, saquinavir, telithromycin, grapefruit juice) may increase exposure to **DASAMIA** and should be avoided. Selection of an alternate concomitant medication with no or minimal CYP3A4 inhibition potential is recommended. If systemic administration of a potent CYP3A4 inhibitor cannot be avoided, the patient should be closely monitored for toxicity.

At clinically relevant concentrations, binding of dasatinib to plasma proteins is reported as approximately 96 % on the basis of in vitro experiments. No studies have been performed to evaluate dasatinib interaction with other protein-bound medicines. The potential for displacement and its clinical relevance are unknown.

Medicines that may decrease dasatinib plasma concentrations

CYP3A4 Inducers: Medicines that induce CYP3A4 activity (e.g. dexamethasone, phenytoin, carbamazepine, rifampicin, phenobarbital or St. John's Wort (Hypericum perforatum) may reduce exposure to dasatinib. Concomitant use of potent CYP3A4 inducers with dasatinib is not recommended. In patients for whom CYP3A4 inducers are indicated, alternative medicines with no or minimal CYP3A4 induction potential should be selected. Concomitant use of dexamethasone, a weak CYP3A4 inducer, with dasatinib is allowed; dasatinib AUC is reported to decrease approximately 25 % with concomitant use of dexamethasone, which is not likely to be clinically meaningful.

Rifampicin: Data from a reported study of healthy subjects indicate that when a single morning dose of dasatinib was administered following 8 days of continuous evening administration of 600 mg of rifampicin, a potent CYP3A4 inducer, the mean Cmax, and AUC of dasatinib were decreased by 81 % and 82 %, respectively.

Antacids (aluminium hydroxide/magnesium hydroxide products): Reported non-clinical data demonstrate that the solubility of dasatinib is pH dependent. If antacid therapy is needed, the antacid dose should be administered at least 2 hours prior to or 2 hours after the dose of **DASAMIA**. Simultaneous administration of **DASAMIA** with antacids should be avoided.

H2 antagonists/proton pump inhibitors: Long-term suppression of gastric acid secretion by H2 antagonists or proton pump inhibitors reduces dasatinib exposure by >60 %. The concomitant use of H2 antagonists or proton pump inhibitors with **DASAMIA** is not recommended. The use of antacids should be considered in place of H2 antagonists or proton pump inhibitors in patients receiving **DASAMIA** therapy.

Effect of dasatinib on other medicines

CYP3A4 substrates: Dasatinib is an inhibitor of CYP3A4. Concomitant use of dasatinib and a CYP3A4 substrate may increase exposure to the CYP3A4 substrate. Therefore, CYP3A4 substrates known to have a narrow therapeutic index such as alfentanil, astemizole, terfenadine, cisapride, ciclosporin, fentanyl, pimozide, quinidine, sirolimus, tacrolimus, bepridil or ergot alkaloids (ergotamine, dihydroergotamine) should be administered with caution in patients receiving **DASAMIA**. Reported in vitro data indicate a potential risk for interaction with CYP2C8 substrates, such as glitazones.

Simvastatin: Single dose data from a reported study of healthy subjects indicate that the mean Cmax and AUC of simvastatin, a CYP3A4 substrate, were increased by 37 % and 20 %, respectively, when simvastatin was administered in combination with a single 100 mg dose of dasatinib.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential/contraception in males and females

Women of childbearing

Women of childbearing potential should be advised to avoid becoming pregnant while receiving treatment with **DASAMIA** and after 6 months following completion of treatment with **DASAMIA.** If the patient becomes pregnant while receiving **DASAMIA** the potential hazard to the foetus must be explained. An effective method of contraception should be used during treatment and for 6 months after the last dose of **DASAMIA.**

Males with child-bearing partners

Men should be recommended to use effective contraceptive measures and to not father a child while receiving treatment with **DASAMIA** and for 3 months following completion of treatment.

Based on genetic toxicity findings, male patients with female partners of reproductive potential should use effective contraception during treatment and for 6 months following the last dose of **DASAMIA.**

Pregnancy

Based on reported human experience, DASAMIA suspected to cause congenital malformations including neural tube defects, and harmful pharmacological effects on the foetus when administered during pregnancy. Reported studies in animals have shown reproductive toxicity.

Dasatinib may cause foetal harm when administered to a pregnant woman. There have been post-marketing reports of spontaneous abortion and foetal and infant anomalies from women who have taken dasatinib during pregnancy.

Dasatinib is not recommended for use in women who are pregnant or contemplating pregnancy. If dasatinib is used during pregnancy, or if the patient becomes pregnant while taking dasatinib, the patient should be apprised of the potential hazard to the foetus.

Breastfeeding

There is insufficient/limited information on the excretion of dasatinib in human or animal breast milk. Physico-chemical and available pharmacodynamic/toxicological data on dasatinib point to excretion in breast milk and a risk to the suckling child cannot be excluded. Women who are taking **DASAMIA** should not breastfeed.

Fertility

Medical practitioners and other healthcare providers should counsel male patients of appropriate age about possible effects of **DASAMIA** on fertility, and this counselling may include consideration of semen deposition.

4.7 Effects on ability to drive and use machines

DASAMIA has minor influence on the ability to drive and use machines. Patients should be advised that they may experience adverse reactions such as dizziness or blurred vision during treatment with **DASAMIA**. Therefore, cautions should be recommended when driving a car or operating machines. No studies on the effects on the ability to drive and use machines have been performed.

4.8 Undesirable Effects

Table 2: Tabulated summary of adverse reactions

System	Frequent	Less frequent	Frequency not known

Organ Class			
Infections and infestations	Infection (including bacterial, viral, fungal, non-specified), pneumonia (including bacterial, viral, and fungal), upper respiratory tract infection / inflammation, herpes virus infection (including cytomegalovirus-CMV), enterocolitis infection, sepsis (including uncommon cases with fatal outcomes).	-	Hepatitis B reactivation
Blood and lymphatic system disorders	Myelosuppression (including anaemia, neutropenia, thrombocytopenia), febrile neutropenia	Lymphadenopathy lymphopenia, pure red cell aplasia	-
Immune system	-	Hypersensitivity (including erythema	-

disorders		nodosum), anaphylactic shock	
Endocrine disorders	-	Hypothyroidism, hyperthyroidism, thyroiditis	-
Metabolism and nutrition disorders	Appetite disturbances[a], hyperuricaemia	Tumour lysis syndrome, dehydration, hypoalbuminemia, hypercholesterolemia, diabetes mellitus	-
Psychiatric disorders	Depression, insomnia	Anxiety, confusional state, affect lability, decrease of libido	-
Nervous System disorders	Headache, neuropathy (including, peripheral neuropathy), dizziness, dysgeusia, somnolence,	CNS bleeding[b], syncope, tremor, amnesia, balance disorder, cerebrovascular accident, transient ischaemic attack, convulsion, optic neuritis, VIIth nerve paralysis,	-

		dementia, ataxia.	
Eye disorders	Visual disorder (including visual disturbance, vision, blurred, and visual acuity reduced), dry eye	Visual impairment, conjunctivitis, photophobia, lacrimation increased	-
Ear and labyrinth disorders	Tinnitus	Hearing loss, vertigo	-
Cardiac disorders	Congestive heart failure/cardiac dysfunction [c], pericardial effusion, arrhythmia (including tachycardia), palpitations	Myocardial infarction (including fatal outcome), electrocardiogram QT prolonged, pericarditis, ventricular arrhythmia (including ventricular tachycardia), angina pectoris, cardiomegaly, electrocardiogram T wave abnormal, Troponin increased, Cor pulmonale, myocarditis, acute coronary syndrome, cardiac arrest, electrocardiogram PR	Atrial fibrillation/ atrial flutter

		prolongation, coronary artery disease, pleuro-pericarditis	
Vascular disorders	Haemorrhage[d], hypertension, flushing	Hypotension, thrombophlebitis, thrombosis, deep vein thrombosis, embolism, livedo reticularis.	Thrombotic micro-angiopathy
Respiratory, Thoracic and mediastinal disorders	Pleural effusion, dyspnoea, pulmonary oedema, pulmonary hypertension, lung infiltration, pneumonitis, cough	Pulmonary arterial hypertension, bronchospasm, asthma, dysphonia, acute respiratory distress syndrome, chylothorax	Interstitial lung disease
Gastrointestinal disorders	Diarrhoea, nausea, vomiting, abdominal pain, gastrointestinal bleeding,colitis (including neutropaenic colitis), gastritis, mucosal inflammation (including	Pancreatitis (including Acute pancreatitis) upper gastrointestinal ulcer, oesophagitis, ascites, anal fissure, dysphagia, gastroesophageal reflux disease, Protein-losing gastroenteropathy, ileus, anal fistula	Fatal gastro-intestinal haemorrhage

	mucositis/stomatitis) dyspepsia, abdominal distension, constipation, oral soft tissue disorder		
Hepatobiliary disorders	-	Hepatitis, cholecystitis, cholestasis	-
Skin and Subcutaneous tissue disorders	Skin rash[e], alopecia, dermatitis (including eczema), pruritus, acne, dry skin, urticaria, hyperhidrosis	Neutrophilic dermatosis, photosensitivity, pigmentation disorder, panniculitis, skin ulcer, bullous conditions, nail disorder, palmar-plantar erythrodysesthesiasyndrome, hair disorder, leukocytoclastic vasculitis, skin fibrosis	Stevens-Johnson syndrome[f], toxic necrolysis, erythema multiforme
Musculoskeletal and connective tissue disorders	Musculoskeletal pain, arthralgia, myalgia, Muscular weakness, musculoskeletal stiffness, muscle spasm	Rhabdomyolysis, osteonecrosis, muscle inflammation, tendonitis, arthritis, epiphyses delayed fusion, growth retardation.	-

Renal and urinary disorders	-	Renal failure, urinary frequency, proteinuria, renal impairment.	Nephrotic syndrome
Reproductive system and breast disorders	-	Gynecomastia, menstrual disorder.	Genotoxicity
General disorders and administration site conditions	Peripheral oedema, fatigue, pyrexia, face oedema[g], asthenia, pain, chest pain, generalised oedema[h], chills	Malaise, other superficial oedema[i] gait disturbance	-
Investigations	Decreased weight, increased weight	Increased blood creatinine phosphokinase, increased Gamma- glutamyl-transferase	-
Injury, poisoning, and procedural complications	Confusion	-	-

[a] Includes decreased appetite, early satiety, increased appetite.

[b] Includes central nervous system haemorrhage, cerebral haematoma, cerebral haemorrhage, extradural haematoma, intracranial haemorrhage, haemorrhagic stroke, subarachnoid haemorrhage, subdural haematoma and subdural haemorrhage.

[c] Includes increased brain natriuretic peptide, ventricular dysfunction, left ventricular dysfunction, right ventricular dysfunction, cardiac failure, acute cardiac failure, chronic cardiac failure, congestive cardiac failure, cardiomyopathy congestive cardiomyopathy, diastolic dysfunction, decreased ejection fraction, ventricular failure, left ventricular failure, right ventricular failure, and ventricular hypokinesia.

[d] Excludes gastrointestinal bleeding and CNS bleeding: these ADRs are reported under the gastrointestinal disorders system organ class and the nervous system disorders system organ class, respectively.

[e] Includes drug drug eruption, erythema, erythema multiforme, erythrosis, exfoliative rash, generalised erythema, genital rash, heat rash, milia, miliaria, pustular psoriasis, rash, rash erythematous, rash follicular, rash generalised, rash macular, rash maculo-papular, rash papular, rash pruritic, rash pustular, rash vesicular, skin exfoliation, skin irritation, toxic skin eruption, urticaria vesiculosa, and vasculitic rash.

[f] Includes gravitational oedema, localised oedema, peripheral oedema

[g] Included conjunctival oedema, eye oedema, eye swelling, eyelid oedema, face oedema, lip oedema, macular oedema, mouth oedema, orbital oedema, periorbital oedema, face swelling.

[h] Included fluid overload, fluid retention, gastrointestinal oedema, generalised oedema, peripheral swelling, oedema, oedema due to cardiac disease, perinephric effusion, post procedural oedema, visceral oedema.

[i] Included genital swelling, incision site oedema, oedema genital, penile oedema, penile swelling, scrotal oedema, skin swelling, testicular swelling, vulvovaginal swelling.

Reported post-marketing experience

The following additional adverse reactions have been identified during post approval use of DASAMIA. Because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Special populations

While the safety profile of DASAMIA in elderly was reported to be similar to that in the younger population, patients aged 65 years and older are more likely to experience the commonly reported adverse reactions such as fatigue, pleural effusion, dyspnoea, cough, lower gastrointestinal haemorrhage, and appetite disturbance and more likely to experience less frequently reported adverse reactions such as abdominal distention, dizziness, pericardial effusion, congestive heart failure, and weight decrease and should be monitored closely (see section 4.4).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

4.9 Overdose

Experience with overdose of **DASAMIA** in reported clinical studies is limited to isolated cases. Overdose of 280 mg per day for one week was reported in two patients and both developed a significant decrease in platelet counts. Since **DASAMIA** is associated with severe myelosuppression (see **section 4.4**), patients who ingest more than the recommended dosage should be closely monitored for myelosuppression and appropriate supportive treatment given.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A26 Cytostatic agents

Pharmacotherapeutic group: antineoplastic agents, protein kinase inhibitors, ATC code: L01XE06

Dasatinib inhibits the activity of the BCR-ABL kinase and SRC family kinases (SRC, LCK, YES, FYN), along with a number of other selected oncogenic kinases including c-KIT, ephrin (EPH) receptor kinases, and,

PDGFβ receptor. Dasatinib inhibits the BCR-ABL kinase at a concentration of 0,6-0,8 nM. It binds to both the inactive and active conformations of the BCR-ABL enzyme.

Mechanism of action

In vitro, dasatinib is active in leukemic cell lines representing variants of imatinib sensitive and resistant disease. These reported non-clinical studies show that dasatinib can overcome imatinib resistance resulting from BCR-ABL overexpression, BCR-ABL kinase domain mutations, activation of alternate signalling pathways involving the SRC family kinases (LYN, HCK) and multidrug resistance gene overexpression. Additionally, dasatinib inhibits SRC family kinases at subnanomolar concentrations.

In vivo, in separate experiments using murine models of CML, dasatinib prevented the progression of chronic CML to blast phase and prolonged the survival of mice bearing patient-derived CML cell lines grown at various sites, including the central nervous system.

5.2 Pharmacokinetic properties

Absorption

Dasatinib is rapidly absorbed in patients following oral administration with peak concentrations reported between 0,5 and 6 hours. Following oral administration, the increase in the mean exposure (AUC_T) is approximately proportional to the dose increment across doses ranging from 25 mg to 120 mg twice daily. The overall mean terminal half-life of dasatinib is reported as approximately 5 to 6 hours in patients.

Reported data from healthy subjects administered a single, 100 mg dose of dasatinib 30 minutes following consumption of a high-fat meal indicated a 14 % increase in the mean AUC of dasatinib. Consumption of a low-fat meal 30 minutes prior to dasatinib resulted in a 21 % increase in the mean AUC of dasatinib. The observed food effects were not clinically relevant. Dasatinib exposure variability is reported to be higher under fasted conditions (47 % CV) compared to light-fat meal (39 % CV) and high-fat meal (32 % CV) conditions.

Based on the reported patient population PK analysis, variability in dasatinib exposure was estimated to be mainly due to inter-occasion variability in bioavailability (44 % CV) and, to a lesser extent, due to inter-individual variability in bioavailability and inter- individual variability in clearance (30 % and 32 % CV, respectively). The random inter- occasion variability inexposure is not expected to affect the cumulative exposure and efficacy or safety.

Distribution

In patients, dasatinib has reported a large apparent volume of distribution (2,505 L) suggesting that the medicine is extensively distributed in the extravascular space. At clinically relevant concentrations of dasatinib, binding to plasma proteins in vitro was reported as approximately 96 %.

Biotransformation

Dasatinib is extensively metabolised in humans with multiple enzymes involved in the generation of the metabolites. CYP3A4 is a major enzyme responsible for the metabolism of dasatinib. In healthy subjects administered 100 mg of [14C]-labelled dasatinib, unchanged dasatinib reported 29 % of circulating radioactivity in plasma.

Plasma concentration and measured in vitro activity indicate that metabolites of dasatinib are unlikely to play a major role in the observed pharmacology of the product.

Elimination

The mean terminal half-life of dasatinib is reported as 3 hours to 5 hours. The mean apparent oral clearance is reported as 363.8 L/hr (CV % 81.3 %).

Elimination is predominantly in the faeces, mostly as metabolites. It has been reported that following a single oral dose of [14C]-labelled dasatinib, approximately 89 % of the dose was eliminated within 10 days, with 4 % and 85 % of the radioactivity recovered in the urine and faeces, respectively. Unchanged dasatinib accounted

for 0,1 % and 19 % of the dose in urine and faeces, respectively, with the remainder of the dose as metabolites.

Special populations

Renal impairment: Since the renal clearance of dasatinib and its metabolites is <4 %, a decrease in total body clearance is not expected in patients with renal insufficiency.

Hepatic impairment: Since dasatinib is mainly metabolised through the liver, exposure to dasatinib is expected to increase if liver function is impaired. Dasatinib should be used with caution in patients with hepatic impairment.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose amonohydrate, Calcium hydrogen phosphate anhydrous, Croscarmellose sodium, Hydroxypropyl cellulose, Colloidal anhydrous silica, Magnesium stearate, Opadry White 03K580013 (Hypromellose, Titanium dioxide, Triacetin, Purified water)

6.2 Incompatibilities

Not applicable

6.3 Shelf life

2 years

6.4 Special precautions for storage

Store at or below 25 ºC in original package

6.5 Nature and contents of container

DASAMIA 20, DASAMIA 50 and **DASAMIA 70**

Carton containing 5 blisters of 12 tablets packaged in the Aluminium/Aluminium blister consisting of 242 mm Cold Form Laminate Form Pack with Desiccant 25 OPA/45 AL/HDPE/PE+ Desiccant/HDPE and 240 mm Push Through Lidding Foil 20 micron AL/15 GSM PE for Form Pack Desiccant.

DASAMIA 100

Carton containing 3 blisters of 10 tablets packaged in the Aluminium/Aluminium consisting of 242 mm Cold Form Laminate Form Pack with Desiccant 25 OPA/45 AL/HDPE/PE+Desiccant/HDPE (Expo) and 240 mm Push Through Lidding Foil 20 micron AL/15 GSM PE for Form Pack Desiccant

6.6 Special precautions for disposal and other handling

No special requirements

7. HOLDER OF CERTIFICATE OF REGISTRATION

RANBAXY PHARMACEUTICALS (PTY) LTD

14 Lautre Road, Stormill, Ext.1 Roodepoort, Johannesburg, 1724

8. REGISTRATION NUMBERS

Dasamia 20: 56/26/0207

Dasamia 50: 56/26/0208

Dasamia 70: 56/26/0209

Dasamia 100: 56/26/0210

9. DATE OF FIRST AUTHORISATION

15 August 2023

10. DATE OF REVISION OF THE TEXT

TBC

Reference:

CLEAN PROPOSED PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

S4

DASAMIA (20, 50, 70,100) Film coated tablets

(Dasatinib)

Contains sugar: Lactose monohydrate

Read all of this leaflet carefully before you start taking DASAMIA

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- DASAMIA has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What DASAMIA is and what it is used for

DASAMIA contains the active substance dasatinib. This medicine is used to treat chronic myeloid leukaemia (CML) in adults. Leukaemia is a cancer of white blood cells. These white cells usually help the body to fight infection. In people with CML, white cells called granulocytes start growing out of control. **DASAMIA** inhibits the growth of these leukaemic cells.

DASAMIA is also used to treat Philadelphia chromosome positive (Ph+) acute lymphoblastic leukaemia (ALL) and lymphoid blast CML in adults who are not benefiting from prior therapies. In people with ALL, white cells called lymphocytes multiply too quickly and live too long. DASAMIA inhibits the growth of these leukemic cells.

2. What you need to know before you take DASAMIA

Do not take DASAMIA:

- If you are hypersensitive (allergic) to DASAMIA or any of the other ingredients of this medicine (listed in section 6).
- Using H2 blockers or proton pump inhibitors with DASAMIA is not recommended.

Warnings and precautions

Special care should be taken with **DASAMIA**

- If you are taking medicines to thin the blood or prevent clots (see "**Other medicines and DASAMIA**").
- if you have problems with your immune system
- If you have a liver problem
- If you have a heart problem, including a condition called congenital long QT syndrome.
- If you start having difficulty breathing, chest pain, or a cough when taking **DASAMIA**: this may be a sign of fluid retention in the lungs or chest (which can be more common in patients aged 65 years and older), or due to changes in the blood vessels supplying the lungs.

- If you have ever had or might now have a hepatitis B infection. This is because **DASAMIA** 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.
- If you experience bruising, bleeding, fever, fatigue and confusion when taking **DASAMIA**, contact your doctor. This may be a sign of damage to blood vessels known as thrombotic microangiopathy (TMA).

- If you have a history of skin problems.

Cerebrovascular events (conditions that affect blood flow to your brain) including stroke and brain bleed have been reported with the use of this medicines (see **Possible Side Effects)**.

Your doctor will regularly monitor your condition to check whether **DASAMIA** is having the desired effect. You will also have blood tests regularly while you are taking **DASAMIA**.

Children and adolescents

DASAMIA has not been studied in children.

Other medicines and DASAMIA

Always tell your healthcare professional if you are taking any other medicine (This includes complementary or traditional medicines).

DASAMIA is mainly handled by the liver. Certain medicines may interfere with the effect of **DASAMIA** when taken together.

These medicines are not to be used with **DASAMIA:**

- ketoconazole, itraconazole - these are antifungal medicines
- erythromycin, clarithromycin, telithromycin - these are antibiotics
- ritonavir, atazanavir, indinavir, nelfinavir, saquinqvir - these are antiviral medicines
- dexamethasone – a corticosteroid medicine
- phenytoin, carbamazepine, phenobarbital - these are treatments for epilepsy

- rifampicin - this is a treatment for tuberculosis
- famotidine, omeprazole - these are medicines that block stomach acids
- St. John's wort - a herbal preparation obtained without a prescription, used to treat depression

Do not take medicines that neutralise stomach acids (antacids such as aluminium hydroxide or magnesium hydroxide) in the 2 hours before or 2 hours after taking **DASAMIA.**

Tell your doctor if you are taking medicines to thin the blood or prevent clots.

DASAMIA with food and drink

Do not drink grapefruit juice when you are taking **DASAMIA.**

Pregnancy, breastfeeding and fertility

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, ask your doctor, pharmacist or other health care provider for advice before taking this medicine.

Sexually active men who take **D**, are advised to use a condom to avoid pregnancy in their partner

Women who are pregnant or planning to become pregnant should not take **DASAMIA**. **DASAMIA** may harm the baby when given to a pregnant woman. Women should avoid becoming pregnant while undergoing treatment with **DASAMIA.**

Women of childbearing potential should use effective contraceptive measures while taking **DASAMIA** and for 6 months after you stop taking **DASAMIA.**

If you are a male patient and your female partner could become pregnant, you should use effective contraceptive measure (e,g condom) during treatment with **DASAMIA** and 3 months after taking the last dose of **DASAMIA.**

It is not known if DASAMIA can pass into your breast milk or if it can harm your baby. Do not breastfeed if you are taking **DASAMIA**.

Driving and using machines

No studies on the effects on the ability to drive and use machines when taking **DASAMIA** have been performed. Take special care when driving or using machines in case you experience side effects such as dizziness and blurred vision.

It is not possible to predict to what extent **DASAMIA** may interfere with your activities. You should ensure that you do not engage in the following activities (e.g. driving, riding, sailing, operating machines / equipment) until you are aware of the measure to which **DASAMIA** affects you.

DASAMIA contains lactose

DASAMIA contain lactose monohydrate. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking **DASAMIA.**

3. How to take DASAMIA

Do not share medicines prescribed for you with any other person.

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

The recommended starting dose for **DASAMIA** in patients with chronic phase CML is 100 mg once daily, with or without a meal.

The recommended starting dose for **DASAMIA** in patients with accelerated, myeloid or lymphoid blast phase CML or Ph+ ALL is 70 mg twice daily, with or without a meal. Try to take **DASAMIA** at the same time each day.

Swallow **DASAMIA** tablets whole. Do not break, cut, chew or crush the tablets.

Depending on your response to treatment and any side effects that you may experience, your doctor may adjust your dose of **DASAMIA** upward or downward, or may temporarily discontinue **DASAMIA.**

Your doctor will tell you how long your treatment with **DASAMIA** will last.

You should not change your dose or stop taking **DASAMIA** without first talking with your healthcare provider.

If you take more **DASAMIA** than you should

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre.

If you forget to take **DASAMIA**

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

If you stop taking **DASAMIA**

Do not stop taking your medicine without consulting your doctor.

4. Possible side effects

DASAMIA can have side effects.

Not all side effects reported for **DASAMIA** are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking **DASAMIA** please consult your health care provider for advice.

If any of the following happens, stop taking DASAMIA and tell your doctor immediately or go to the casualty department at your nearest hospital:

- Severe potentially life-threatening allergic reactions symptoms include red-purple swellings on the shins, thighs and, less commonly, the arms. Joint and muscle pains and fever may also occur (anaphylactic shock)
- Rare skin condition with severe blisters and bleeding in the lips, eyes, mouth, nose and genitals (Stevens-Johnson Syndrome)
- Redness, swelling, and pain on the palms of the hands and/or the soles of the feet, sometimes blisters appear (palmar-plantar erythrodysesthesia syndrome)
- Hypersensitivity (allergic) reactions including skin rash with red lumps
- Severe condition of the skin that may affect the mouth and other parts of the body symptoms include red, often itchy spots, similar to the rash of measles, which starts on the limbs and sometimes on the face and the rest of the body. The spots may blister or may progress to form raised, red, pale-centred marks. Those affected may have fever, sore throat, headache and/or diarrhoea (erythema multiforme)
- Unexpected bleeding or bruising without having an injury
- Gastro-intestinal bleeding, blood in your vomit, stools or urine, or have black stools

These are all very serious side effects. If you have them, you may have had a serious reaction to **DASAMIA** You may need urgent medical attention or hospitalization.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

Frequent side effects

- Chest pain, difficulty breathing, shortness of breath, coughing, wheezing and fainting which may be due to swelling of lungs (pneumonitis) or blood clots in the lungs (pulmonary embolism) or accumulation of fluid between the tissues that line the lungs and the chest (pleural effusion, dyspnoea)

- Tiredness, headaches, dizziness, being short of breath when exercising and looking pale, frequent infections such as fever, severe chills, sore throat or mouth ulcers bleeding or bruising more easily than normal which may be due to a disease of the blood with a reduced number of red or white blood cells or platelets (myelosuppression)
- Serious lung infection with fever, chills, cough, phlegm and occasionally blood (pneumonia), herpes virus infection (including cytomegalovirus - CMV), upper respiratory tract infection, serious infection of the blood or tissues (including uncommon cases with fatal outcomes).
- Infection, fever with decrease in the number of a type of white blood cell in the blood (febrile neutropenia)

Less frequent side effects

- Headache, one-sided weakness, vomiting, seizures, decreased level of consciousness, and neck stiffness (CNS bleeding)
- Fatigue, lethargy, and/or abnormal paleness of the skin (pallor) due to anemia, a rare disorder of blood production in which the bone marrow, the spongy tissue in the center of the bones, fails to function in an adequate manner (aplasia pure red cell)

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:

Frequent side effects

Infections

- Including bacterial, viral and fungal

Digestive problems

- Diarrhoea, feeling or being sick (nausea, vomiting)

Pain

- Pain in the muscles (during or after discontinuing treatment), tummy (abdominal) pain

General disorders

- Swelling around the face, hands and feet, headache, feeling tired or weak

Heart and lungs

- Palpitations, irregular heartbeat
- Congestive heart failure
- Weak heart muscle
- High blood pressure
- Increased blood pressure in the lungs

Digestive problems

- Appetite disturbances, high uric acid levels in the blood, which may cause gout (hyperuricaemia)
- Taste disturbance
- Bloated or distended tummy (abdomen)
- Inflammation of the colon
- Constipation, heartburn, mouth ulceration
- Weight increase, weight decrease
- Inflammation or irritation of the lining of the stomach

Skin, hair, eye, general

- Skin tingling
- Allergic reaction including tender, red lumps on the skin (erythema nodosum)

- Itchy rashes(urticaria), dry skin, acne, inflammation of the skin
- Persistent noise in ears
- Hair loss (alopecia), excessive perspiration or sweating (hyperhidrosis)
- Visual disorder (including blurred vision and disturbed vision), dry eye, bruise
- Depression, insomnia, flushing, dizziness, contusion (bruising), anorexia, sleepiness (somnolence), generalised oedema

Pain

- Pain in joints (arthralgia)
- Muscular weakness/pain (myalgia)
- Pain around hands and feet
- Stiffness in muscles and joints, muscle spasm

Tests may show

- Fluid around the heart, gastrointestinal bleeding

Less frequent side effects

Heart and lungs

- Heart attack (including fatal outcome), inflammation of the lining (fibrous sack) surrounding the heart, irregular heartbeat, chest pain due to lack of blood supply to the heart (angina).
- Low blood pressure
- Narrowing of airway that may cause breathing difficulties, asthma
- Increased blood pressure in the arteries (blood vessels) of the lungs
- Enlargement of the right ventricle in the heart, inflammation of the heart muscle, collection of conditions resulting from blockage of blood supply to the heart muscle (acute coronary syndrome), cardiac arrest (stopping of blood flow from the heart), coronary (heart) artery

disease, inflammation of the tissue covering the heart and lungs.

Digestive problems

- Inflammation of the pancreas
- Peptic ulcer, inflammation of the food pipe
- Swollen tummy (abdomen)
- Tear in the skin of the anal canal
- Difficulty in swallowing, inflammation of the gallbladder, blockage of bile ducts, gastro-oesophageal reflux (a condition where acid and other stomach contents come back up into the throat)
- Loss of vital nutrients such as protein from your digestive tract, bowel obstruction, anal fistula (an abnormal opening from the anus to the skin around the anus), impairment of kidney function, diabetes

Psychiatric

- Anxiety, confusion, mood swings, lower sexual drive, fainting, tremor

Skin, hair, eye, general

- Inflammation of the eye which causes redness or pain, discharge with itching of the eyes and crusty eyelids (conjunctivitis)
- A skin disease characterized by tender, red, well-defined blotches with the sudden onset of fever and raised white blood cell count (neutrophilic dermatosis)
- Loss of hearing, sensitivity to light, visual impairment, increased eye tearing, increased sensitivity to light (photophobia) ,disturbance in skin colour
- Dizziness ,spinning sensation (vertigo)
- Inflammation of fatty tissue under the skin, skin ulcer, blistering of the skin, nail disorder, hair disorder , renal failure, urinary frequency
- Breast enlargement in men, menstrual disorder, general weakness and discomfort

- Low thyroid function
- Losing balance while walking
- Convulsion(fits)
- Inflammation of the optic nerve that may cause a complete or partial loss of vision, blue-purple mottling of the skin
- Abnormally high thyroid function, inflammation of the thyroid gland
- Ataxia (a condition associated with lack of muscular coordination),
- Difficulty walking
- Miscarriage
- Inflammation of the skin blood vessels
- Skin fibrosis

Musculoskeletal and connective tissue

- Temporary paralysis or weakness of muscles(rhabdomyolysis)
- Osteonecrosis (a disease of reduced blood flow to the bones, which can cause bone loss and bone death), arthritis, skin swelling anywhere in the body
- Delayed fusion of the rounded ends that form joints (epiphyses)
- Slower or delayed growth

Pain

- Inflammation of vein which can cause redness, tenderness and swelling, inflammation of the tendon

Brain

- Loss of memory
- Stroke (cerebrovascular accident), temporary episode of neurologic dysfunction caused by loss of blood flow, facial nerve paralysis, dementia

Tests may show

- Abnormal blood test results and possibly impaired kidney function caused by the waste products of the dying tumour (tumour lysis syndrome)
- Low levels of albumin in the blood, low levels of lymphocytes (a type of white blood cell) in the blood, high level of cholesterol in the blood, swelling of lymph nodes in response to a bacterial or viral infection (lymphadenopathy).
- Irregularity of the electrical activity of the heart, enlarged heart
- Inflammation of the liver, protein in the urine, raised creatine phosphokinase (an enzyme mainly found in the heart, brain and skeletal muscles), raised troponin (an enzyme mainly found in the heart and skeletal muscles), raised gamma-glutamyltransferase (an enzyme mainly found in the liver)

Frequency not known

- Bleeding in the stomach or bowels that can cause death
- Recurrence (reactivation) of hepatitis B infection when you have had hepatitis B in the past (a liver infection)
- Disease of the kidneys with symptoms including oedema and abnormal laboratory test results such as protein in the urine and low protein level in the blood
- Damage to blood vessels known as thrombotic microangiopathy (TMA), including decreased red blood cell count, decreased platelets, and formation of blood clots

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor or pharmacist. You can also report side effects to SAHPRA

via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications:

https://www.sahpra.org.za/Publications/Index/8

By reporting side effects, you can help provide more information on the safety of **DASAMIA**.

5. How to store DASAMIA

Store at or below 25 ºC in original package

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

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 DASAMIA contains

The active substance is dasatinib

The other ingredients are: Lactose amonohydrate, Calcium hydrogen phosphate anhydrous, Croscarmellose sodium. Hydroxypropyl cellulose, Colloidal anhydrous silica, Magnesium stearate, Opadry White 03K580013 (Hypromellose, Titanium dioxide, Triacetin, Purified water)

What DASAMIA looks like and contents of the pack

DASAMIA 20 film coated tablets: White to off-white, biconvex, round, film-coated tablet, debossed with "851" on one side and plain on other side.

DASAMIA 50 film coated tablets: White to off-white, biconvex, oval, film-coated tablet, debossed with "852" on one side and plain on other side.

DASAMIA 70 film coated tablets: White to off-white, biconvex, round, film-coated tablet debossed with "853" on one side and plain on other side.

DASAMIA 100 film coated tablets: White to off-white, biconvex, oval, film-coated tablet, debossed with “855” on one side and plain on other side.

Contents: 30 and 60 tablets per pack

Holder of Certificate of Registration

RANBAXY PHARMACEUTICALS (PTY) LTD

A Sun Pharma Company

14 Lautre Road, Stormill, Ext.1

Roodepoort, Johannesburg, 1724

This leaflet was last revised in

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