DRUG INFO

UNIT FARMASI
HOSPITAL KOTA MARUDU

ISSUE:04/22

INTRODUCTION

TASIGNA® (nilotinib), is an antineoplastic agent categorized under tyrosine kinase inhibitor. Marketed worldwide by Novartis, it has been listed on the World Health Organization's List of Essential Medicines.

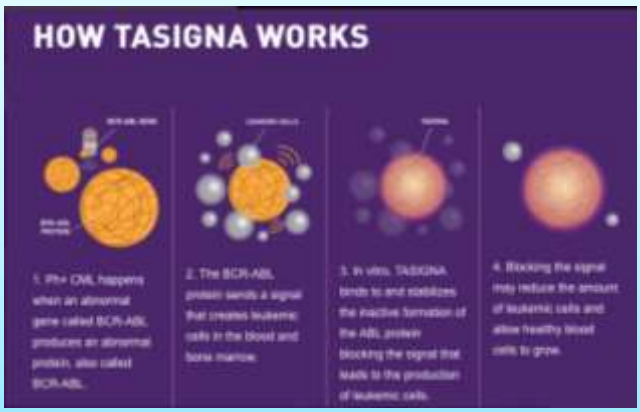
INDICATION

Tasigna is indicated for the treatment of:

- Newly diagnosed Acute lymphoblastic leukemia,Phildelphia chromosome-positive
- Acute lymphoblastic leukemia, Ph+,relapsed/refractory
- Chronic myeloid leukemia,PH+ newlydiagnosed in chronic phase
- Chronic myeloid leukemia, PH+ resistant or intolerant in accelerated phase
- Chronic myeloid leukemia PH+ resistant or intolerant in chronic phase
- Gastrointestinal stromal tumor, refractory

MECHANISM OF ACTION

- Chronic myelogenous leukaemia (CML) is caused by the BCR-ABL oncogene.
- Nilotinib inhibits the tyrosine kinase activity of the BCR-ABL protein.
- Nilotinib fits into the ATP-binding site of the BCR-ABL protein with higher affinity than imatinib, over-riding resistance caused by mutations.
- The ability of nilotinib to inhibit TEL-platelet-derived growth factor receptor-beta (TEL-PDGFRbeta), which causes chronic myelomonocytic leukaemia, and FIP1-like-1-PDGFRalpha, which causes hypereosinophilic syndrome, suggests potential use of nilotinib for myeloproliferative diseases characterised by these kinase fusions.
- Nilotinib also inhibits the c-Kit receptor kinase, including the D816V-mutated variant of KIT, at pharmacologically achievable concentrations, supporting potential utility in the treatment of mastocytosis, and gastrointestinal stromal tumours.



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DOSAGE

- Newly diagnosed Acute lymphoblastic leukemia,Phildelphia chromosome-positive: 400 mg twice daily starting on day 8 of induction chemotherapy in combination with daunorubicin,vincrstine, and prednisolone; continue up to start of stem cell transplant conditioning or until the end of consolidation therapy.
- Acute lymphoblastic leukemia, Ph+,relapsed/refractory :400mg twice daily
- Chronic myeloid leukemia,PH+ newly diagnosed in chronic phase: 300 mg twice daily
- Chronic myeloid leukemia, PH+ resistant or intolerant in accelerated phase: 400mg twice daily
- Chronic myeloid leukemia PH+ resistant or intolerant in chronic phase :400mg twice daily
- Gastrointestinal stromal tumor, refractory :400mg twice daily (off-label use)

DOSE ADJUSTMENTS OR MODIFICATIONS

Tasigna may need to be temporarily withheld and/or dose reduced for haematological toxicities (neutropenia, thrombocytopenia) that are not related to the underlying leukaemia (see Table 2)

Adult patients with newly diagnosed chronic phase CML at 300 mg twice daily	**ANC* <1.0 x 109/l and/or platelet counts <50 x 109/l**	**1. Treatment with nilotinib must be interrupted and blood count monitored.** **2. Treatment must be resumed within 2 weeks at prior dose if ANC >1.0 x 109/l and/or platelets >50 x 109/l.** **3. If blood counts remain low, a dose reduction to 400 mg once daily may be required.**
Paediatric patients with newly diagnosed chronic phase CML at 230 mg/m2 twice daily and imatinib-resistant or intolerant CML in chronic phase at 230 mg/m2 twice daily	ANC* <1.0 x 109/l and/or platelet counts <50 x 109/l	1. Treatment with nilotininb must be interrupted and blood count monitored. 2. Treatment must be resumed within 2 weeks at prior dose if ANC >1.5 x 109/l and/or platelets >75 x 109/l. 3. If blood counts remain low, a dose reduction to 230 mg/m2 once daily may be required. 4. If event occurs after dose reduction, consider discontinuing treatment.

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MONITORING PARAMETERS

- Blood lipids - Tasigna can cause increase in cholesterol levels
- Blood glucose - Tasigna can cause increase in blood glucose levels
- Food effect - The bioavailability of nilotinib is increased by food. Tasigna must not be taken in conjunction with food
- Hepatic impairment
- Serum lipase
- Tumour lysis syndrome

ADVERSE EFFECT

- The most frequent (≥10%) non-haematological adverse reactions were rash, pruritus, headache, nausea, fatigue, alopecia, myalgia and upper abdominal pain.
- Constipation, dry skin, asthenia, muscle spasms, diarrhoea, arthralgia, abdominal pain, vomiting and peripheral oedema were observed less commonly (<10% and ≥5%)
- Treatment-emergent haematological toxicities include myelosuppression: thrombocytopenia (18%), neutropenia (15%) and anaemia (8%).
- Biochemical adverse drug reactions include alanine aminotransferase increased (24%), hyperbilirubinaemia (16%), aspartate aminotransferase increased (12%), lipase increased (11%), blood bilirubin increased (10%), hyperglycaemia (4%), hypercholesterolaemia (3%) and hypertriglyceridaemia (<1%).

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