Tasigna® (nilotinib) – New and expanded indications, new warning

- On March 22, 2018, the FDA approved Novartis' Tasigna (nilotinib) for the treatment of pediatric patients ≥ 1 year of age with newly diagnosed Philadelphia chromosome positive chronic myeloid leukemia in chronic phase (Ph+ CML-CP); and for the treatment of pediatric patients ≥ 1 year of age with Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML) with resistance or intolerance to prior tyrosine-kinase inhibitor (TKI) therapy.
    - Previously Tasigna was only approved for the treatment of adults with newly diagnosed Ph+ CML-CP.
    - Tasigna is also approved for the treatment adults with Ph+ CML-CP and accelerated phase Ph+ CML resistant or intolerant to prior therapy that included Gleevec® (imatinib).
- CML is a type of blood cancer where the body produces malignant white blood cells. Almost all patients with CML have an abnormality known as the "Philadelphia chromosome," which produces a protein that aids the proliferation of malignant white blood cells.
- The approval of the new indications was based on two clinical studies evaluating the efficacy and safety of Tasigna in pediatric patients with Ph+ CML-CP. Sixty-nine patients who were newly diagnosed or who were resistant or intolerant to prior TKI therapy received Tasigna. The median time on treatment with Tasigna was 13.8 months (range: 0.7 to 30.9).
    - In patients with resistant or intolerant CML, the major molecular response (MMR) rate was 40.9% (95% CI: 26.3%, 56.8%) at 12 cycles (28 days per cycle).
    - In patients with newly diagnosed CML, the MMR rate was 60.0% (95% CI: 38.7%, 78.9%) at 12 cycles.
    - In patients with resistant or intolerant CML, the cumulative MMR rate was 47.7% by cycle 12, and the median time to first MMR was 2.8 months (range: 0.0 to 11.3).
    - In patients with newly diagnosed CML, the cumulative MMR rate was 64.0% by cycle 12, and the median time to first MMR was 5.6 months (range: 2.7 to 16.6).
- Tasigna carries a boxed warning for QT prolongation and sudden deaths.
- The *Warnings and Precautions* section was updated with information on effects on growth and development in pediatric patients.
    - Adverse reactions associated with growth and development can occur in pediatric patients receiving BCR-ABL TKIs. The long-term effect of prolonged treatment with BCR-ABL TKIs on growth and development in pediatric patients are unknown.
    - Monitor growth and development in pediatric patients receiving BCR-ABL TKI treatment.
- Information regarding food effects and drug interactions were removed from the *Warnings and Precautions* section.
- The most commonly reported non-hematologic adverse reactions (≥ 20%) with Tasigna use in adult and pediatric patients were nausea, rash, headache, fatigue, pruritus, vomiting, diarrhea, cough, constipation, arthralgia, nasopharyngitis, pyrexia, and night sweats. Hematologic adverse drug reactions include myelosuppression: thrombocytopenia, neutropenia and anemia.
- The recommended pediatric dose of Tasigna for newly diagnosed Ph+ CML-CP or resistant or intolerant Ph+ CML-CP is 230 mg/m^2 orally twice daily, rounded to the nearest 50 mg dose (to a maximum single dose of 400 mg).

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  - If needed, the desired dose may be attained by combining different strengths of Tasigna.
  - Tasigna should be taken twice daily at approximately 12-hour intervals and must be taken on an empty stomach. No food should be consumed for at least 2 hours before the dose is taken and for at least 1 hour after the dose is taken.
  - Treatment should be continued as long as clinical benefit is observed or until unacceptable toxicity occurs.
  - Refer to the Tasigna drug label for dosing recommendations for other indications.

- To support Tasigna's pediatric indications, a new 50 mg capsule strength was approved.