

## IMPORTANT PRESCRIBING INFORMATION

### Subject: Introducing New Recommended Dose for ZYKADIA (ceritinib): Recommended Dose Changed to 450 mg Once Daily with Food from 750 mg Once Daily Fasted

Dear Health Care Provider:

Novartis would like to inform you about important changes to the ZYKADIA (ceritinib) U.S. Prescribing Information (USPI). The recommended ZYKADIA dose has changed to 450 mg once daily with food from 750 mg once daily fasted.

This change is based on the results of ASCEND-8, a dose optimization study, in which ZYKADIA 450 mg daily with food was compared to 750 mg daily under fasted conditions in both previously treated and untreated patients with ALK-positive non-small cell lung cancer (NSCLC).

- There was no clinically meaningful difference in the systemic steady-state exposure of ZYKADIA (AUC and C<sub>Max</sub>) for the 450 mg with food arm compared to the 750 mg fasted arm.
- Initiating treatment with ZYKADIA 450 mg with food decreased the incidence and severity of gastrointestinal (GI) adverse reactions with an overall safety and exposure profile consistent with ZYKADIA 750 mg fasted while achieving comparable steady-state exposure.

#### Section 2 Dosage and Administration has been revised as follows:

The table below summarizes the revisions to ZYKADIA Dosing and Administration

	Previous Dose Level Recommendation	New Dose Level Recommendation
<b>Starting dose</b>	750 mg orally once daily until disease progression or unacceptable toxicity. Take ZYKADIA at least 1 hour before or at least 2 hours after a meal	450 mg orally once daily with food until disease progression or unacceptable toxicity
<b>First dose reduction</b>	600 mg taken orally once daily fasted	300 mg taken orally once daily with food
<b>Second dose reduction</b>	450 mg taken orally once daily fasted	150 mg taken orally once daily with food
<b>Third dose reduction</b>	300 mg taken orally once daily fasted	Not available
<b>Lowest recommended dose</b>	Discontinue ZYKADIA for patients unable to tolerate 300 mg daily.	Discontinue ZYKADIA for patients unable to tolerate 150 mg daily with food

#### Prescriber Action

Doses higher than 450 mg should not be administered with food due to food increasing systemic exposure greater than the 750 mg fasted dose.

Food can range from a small snack to a full meal.

Newly prescribed ZYKADIA patients:

Initiate treatment with ZYKADIA 450 mg once daily with food according to the prescribing information. The dose of 450 mg once daily with food replaces 750 mg once daily fasted as the safe and efficacious recommended dose of ZYKADIA.

Patients currently taking ZYKADIA fasted:

For patients currently taking ZYKADIA once daily fasted who currently have GI adverse reactions or who experience new GI adverse reactions, consider prescribing a dose of ZYKADIA with food based on the dose reduction level corresponding to the patient's current fasted dose reduction level (see Table above). Refer to Table 2 in the prescribing information for additional recommendations for managing GI adverse reactions.

**Other Information**

**Reporting Adverse Events:** Health care providers and patients are encouraged to report adverse events in patients taking ZYKADIA to Novartis at 1-888-669-6682. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit [www.fda.gov/medwatch](http://www.fda.gov/medwatch), or call 1-800-FDA-1088.

**Medical Inquiries:** Please contact the Novartis Medical Information department at 1-844-662-4636 if you have any questions about the information contained in this letter or the safe and effective use of ZYKADIA.

This letter is not intended as a complete description of the benefits and risks related to the use of ZYKADIA. Please refer to the enclosed approved full Prescribing Information and Patient Information.

Sincerely,  
Kris Grzegorzewski  
VP, CDMA, Solid Tumors Franchise  
Novartis Pharmaceuticals Corporation

Enclosure(s): ZYKADIA Full Prescribing Information

