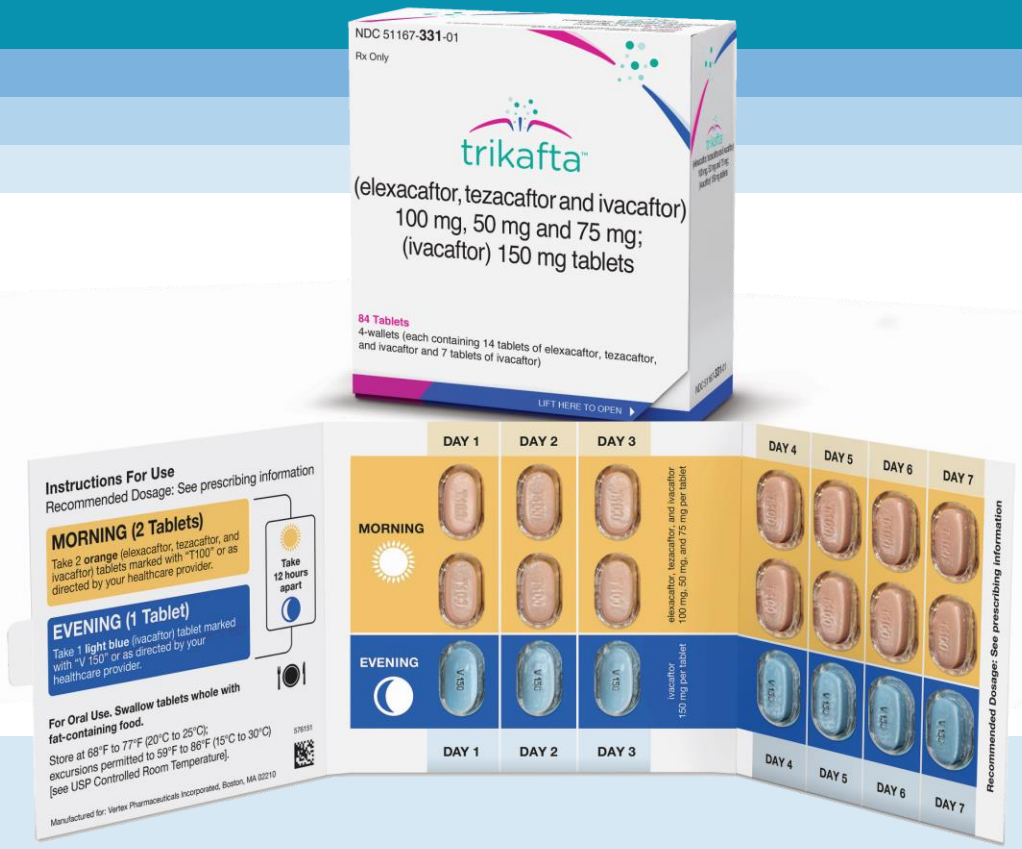
Trikafta (elexacaftor, tezacaftor, ivacaftor tablets; ivacaftor tablets)



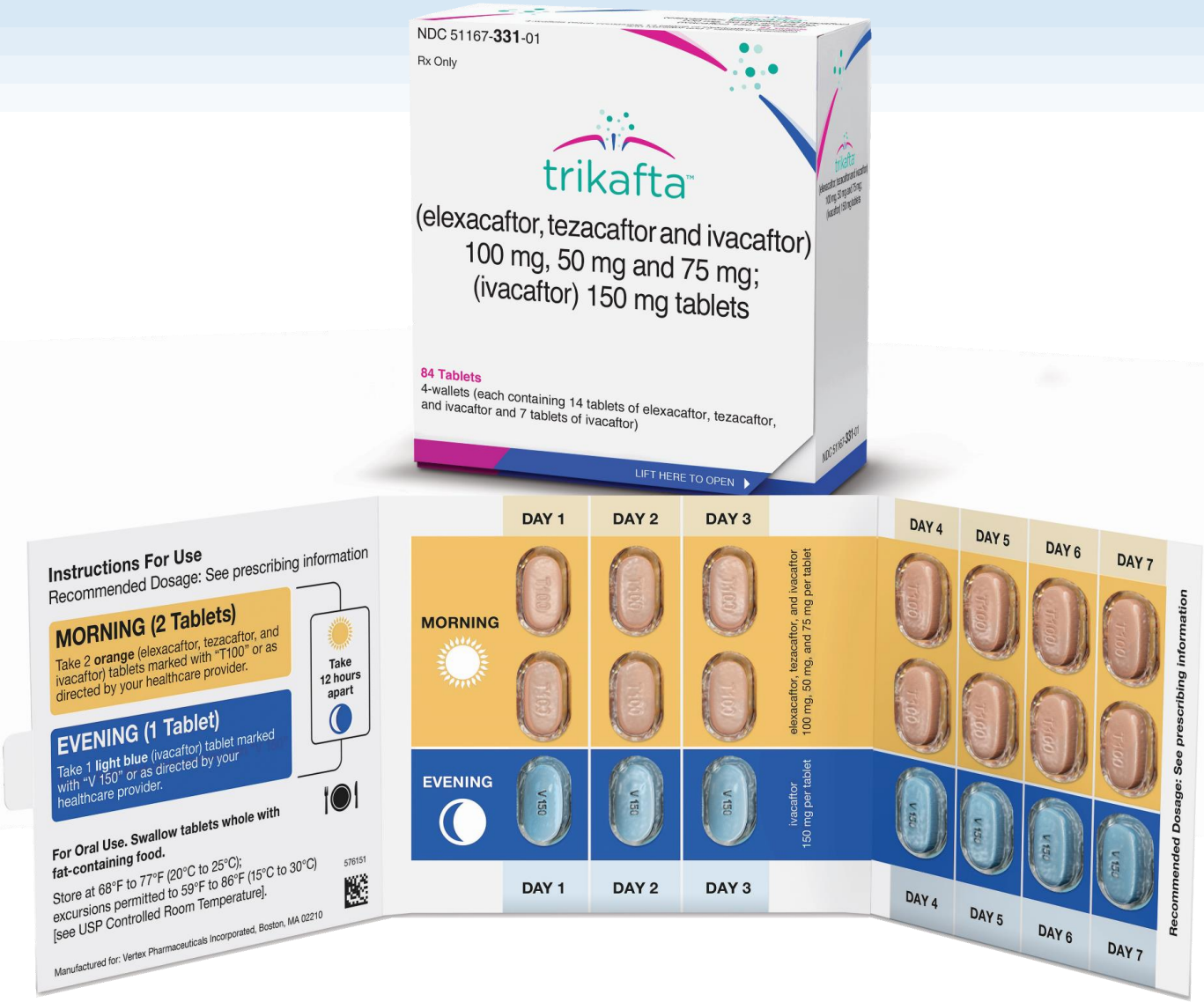
NEW PRODUCT SLIDESHOW

MPR

Introduction

- **Brand name:** Trikafta
- **Generic name:** Elexacaftor, tezacaftor, ivacaftor
- **Pharmacologic class:** Cystic fibrosis transmembrane conductance regulator (CFTR) corrector + CFTR potentiator
- **Strength and Formulation:** 100mg/50mg/75mg; with ivacaftor 150mg; tablets
- **Manufacturer:** Vertex
- **How supplied:** Tablets—84 (4×21)
- **Legal Classification:** Rx

Trikafta


NDC 51167-331-01
Rx Only
trikafta™
(elexacaftor, tezacaftor and ivacaftor)
100 mg, 50 mg and 75 mg;
(ivacaftor) 150 mg tablets
84 Tablets
4-wallets (each containing 14 tablets of elexacaftor, tezacaftor, and ivacaftor and 7 tablets of ivacaftor)
LIFT HERE TO OPEN
Instructions For Use
Recommended Dosage: See prescribing information
MORNING (2 Tablets)
Take 2 orange (elexacaftor, tezacaftor, and ivacaftor) tablets marked with "T100" or as directed by your healthcare provider.
EVENING (1 Tablet)
Take 1 light blue (ivacaftor) tablet marked with "V 150" or as directed by your healthcare provider.
Take 12 hours apart
For Oral Use. Swallow tablets whole with fat-containing food.
Store at 68°F to 77°F (20°C to 25°C); excursions permitted to 59°F to 86°F (15°C to 30°C) [see USP Controlled Room Temperature].
576151
Manufactured for: Vertex Pharmaceuticals Incorporated, Boston, MA 02210
DAY 1
DAY 2
DAY 3
DAY 4
DAY 5
DAY 6
DAY 7
MORNING
EVENING
elexacaftor, tezacaftor, and ivacaftor 100 mg, 50 mg, and 75 mg per tablet
ivacaftor 150 mg per tablet
Recommended Dosage: See prescribing information

Indication

- Treatment of **cystic fibrosis** (CF) in patients aged 12 years and older who have at least one *F508del* mutation in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene

Dosage and Administration

- Swallow whole; take with fat-containing food (eg, eggs, cheeses, nuts, whole milk, meats)

- <12yrs: not established. ≥**12yrs:** 2 tablets (each containing elexacaftor 100mg/tezacaftor 50mg/ivacaftor 75mg) in the AM and 1 ivacaftor tablet (150mg) in the PM, approximately 12 hours apart

- **Moderate hepatic impairment** (not recommended; if needed, use with caution at reduced dose): 2 elexacaftor/tezacaftor/ivacaftor tablets in the AM

Dosage and Administration

- **Concomitant moderate CYP3A inhibitors**:
  - **Day 1:** Two elexacaftor/tezacaftor/ivacaftor tablets in the AM
  - **Day 2:** One ivacaftor tablet (150mg) in the AM
  - **Day 3:** Two elexacaftor/tezacaftor/ivacaftor tablets in the AM
  - **Day 4:** One ivacaftor tablet (150mg) in the AM
  - Continue dosing on **alternate days**
- **Concomitant strong CYP3A inhibitors**: 2 elexacaftor/tezacaftor/ivacaftor tablets twice a week in the AM, approximately 3–4 days apart

Considerations for Special Populations

- **Pregnancy:** limited and incomplete human data from clinical trials
- **Nursing mothers**: consider benefits of breastfeeding along with mother's need for Trikafta and any potential adverse effects
- **Pediatric**: safety and effectiveness in patients younger than 12 years not established
- **Geriatric:** studies did not include any patients ≥65 years
- **Renal impairment:** not studied in patients with severe or end-stage renal disease; use with caution
- **Hepatic impairment:** avoid in patients with severe impairment; use with caution and reduce dose in those with moderate impairment

Warnings/Precautions

- If genotype unknown, use **FDA-cleared CF mutation test** to confirm the presence of at least 1 *F508del* mutation
- **Assess ALT/AST and bilirubin levels** prior to initiating therapy, every 3 months during the first year of treatment, and annually thereafter
- History of **hepatobiliary disease or LFT elevations**; consider more frequent monitoring
- Interrupt dosing and monitor closely if ALT/AST >5×ULN or ALT/AST >3×ULN with bilirubin elevations >2×ULN; after resolution, consider restarting
- Perform baseline and follow-up **eye exams**

Interactions

- **Potentiated by** strong (eg, ketoconazole, itraconazole, posaconazole, voriconazole, telithromycin, and clarithromycin) or moderate (eg, fluconazole, erythromycin) CYP3A inhibitors; adjust dose (see Dosing)
- **Avoid** food or drink containing grapefruit
- **Antagonized by** strong CYP3A inducers (eg, rifampin, rifabutin, phenobarbital, carbamazepine, phenytoin, St. John’s wort): avoid concomitant use

Interactions

- **Caution** with concomitant CYP2C9 substrates (eg, warfarin, glimepiride, glipizide), digoxin or other P-gp substrates with a narrow therapeutic index (eg, cyclosporine, everolimus, sirolimus, tacrolimus), OATP1B1 or OATP1B3 substrates (eg, statins, glyburide, nateglinide, repaglinide): monitor

Adverse Reactions

- **Most common** (occurring in ≥5% of patients and at a frequency higher than placebo by ≥1%): headache, upper respiratory tract infection, abdominal pain, diarrhea, rash, increased alanine aminotransferase, nasal congestion, increased blood creatine phosphokinase, increased aspartate aminotransferase, rhinorrhea, rhinitis, influenza, sinusitis, increased blood bilirubin

Mechanism of Action

- **Elexacaftor** and **tezacaftor** bind to different sites on the CFTR protein and have an additive effect in facilitating the cellular processing and trafficking of *F508del*-CFTR to increase the amount of CFTR protein delivered to the cell surface compared to either molecule alone
- **Ivacaftor** potentiates the channel open probability (or gating) of the CFTR protein at the cell surface
- The combined effect causes an increased quantity and function of *F508del*-CFTR at the cell surface, resulting in increased CFTR activity as measured by CFTR mediated chloride transport

Clinical Trials

- **Trial 1** was a 24-week, randomized, placebo-controlled trial that included 403 patients who had an *F508del* mutation on one allele and a mutation on the second allele that results in either no CFTR protein or a CFTR protein that is not responsive to ivacaftor or tezacaftor/ivacaftor alone
- **Trial 2** was a 4-week, randomized, active-controlled trial that compared Trikafta with tezacaftor/ivacaftor in 107 patients who had 2 identical *F508del* mutations

Clinical Trials

- **Results** from Trials 1 and 2 at Week 4 demonstrated Trikafta significantly improved the mean absolute change from baseline in percent predicted forced expiratory volume in 1 second (ppFEV1) by 13.8 percentage points (95% CI, 12.1-15.4; *P* <.0001) and 10 percentage points (95% CI, 7.4-12.6; *P* <.0001), respectively (primary end point)
- Moreover, Trial 1 showed a mean absolute change from baseline in ppFEV1 at Week 24 of 14.3 percentage points (95% CI, 12.7-15.8; *P* <.0001).

Clinical Trials

- Statistically significant improvements were also observed for key secondary end points (rate of pulmonary exacerbations, absolute change from baseline in BMI [Trial 1], sweat chloride, and Cystic Fibrosis Questionnaire-Revised [CFQ-R] Respiratory Domain score) in both trials

- For more clinical trial data, see full labeling

New Product Monograph

- For more information view the product monograph available at:

  https://www.empr.com/drug/trikafta/