

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**214622Orig1s000**

**LABELING**

## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use TRUSELTIQ safely and effectively. See full prescribing information for TRUSELTIQ.

### TRUSELTIQ (infigratinib) capsules, for oral use

Initial U.S. Approval: 2021

#### INDICATIONS AND USAGE

TRUSELTIQ is a kinase inhibitor indicated for the treatment of adults with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or other rearrangement as detected by an FDA-approved test. (1, 2.1)

This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s). (1)

#### DOSAGE AND ADMINISTRATION

- Confirm the presence of an FGFR2 fusion or rearrangement prior to initiation of treatment with TRUSELTIQ. (2.1)
- Recommended dosage: 125 mg orally once daily for 21 consecutive days followed by 7 days off therapy, in 28-day cycles. (2.2)
- Take on an empty stomach at least 1 hour before or 2 hours after food, at approximately the same time each day. (2.2)
- Swallow capsules whole with a glass of water. Do not crush, chew or dissolve. (2.2)
- Mild and Moderate Renal Impairment: The recommended dosage is 100 mg orally once daily for 21 consecutive days followed by 7 days off therapy, in 28-day cycles. (2.5)
- Mild Hepatic Impairment: The recommended dosage is 100 mg orally once daily for 21 consecutive days followed by 7 days off therapy, in 28-day cycles. (2.6)
- Moderate Hepatic Impairment: The recommended dosage is 75 mg orally once daily for 21 consecutive days followed by 7 days off therapy, in 28-day cycles. (2.6)

#### DOSAGE FORMS AND STRENGTHS

Capsules: 25 mg and 100 mg. (3)

#### CONTRAINDICATIONS

None. (4)

#### WARNINGS AND PRECAUTIONS

- Ocular Toxicity TRUSELTIQ can cause retinal pigment epithelial detachment (RPED). Perform comprehensive ophthalmic

examination including optical coherence tomography (OCT) prior to initiation of TRUSELTIQ and at 1 month, at 3 months, and then every 3 months thereafter during treatment. Withhold as recommended. (2.3, 5.1)

- Hyperphosphatemia and Soft Tissue Mineralization: Increases in phosphate levels can cause hyperphosphatemia leading to soft tissue mineralization, cutaneous calcinosis, non-uremic calciphylaxis, vascular calcification, and myocardial calcification. Withhold, dose reduce, or permanently discontinue as recommended. (2.3, 5.2)
- Embryo-Fetal Toxicity: Can cause fetal harm. Advise patients of reproductive potential of the potential risk to the fetus and to use effective contraception. (5.3, 8.1, 8.3)

#### ADVERSE REACTIONS

- Most common ( $\geq 20\%$ ) adverse reactions were nail toxicity, stomatitis, dry eye, fatigue, alopecia, palmar-plantar erythrodysesthesia syndrome, arthralgia, dysgeusia, constipation, abdominal pain, dry mouth, eyelash changes, diarrhea, dry skin, decreased appetite, vision blurred and vomiting. (6.1)
- Most common laboratory abnormalities ( $\geq 20\%$ ) were increased creatinine, increased phosphate, decreased phosphate, increased alkaline phosphatase, decreased hemoglobin, increased alanine aminotransferase, increased lipase, increased calcium, decreased lymphocytes, decreased sodium, increased triglycerides, increased aspartate aminotransferase, increased urate, decreased platelets, decreased leukocytes, decreased albumin, increased bilirubin and decreased potassium. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact QED Therapeutics, Inc. at 1-844-550-BBIO (2246) or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

#### DRUG INTERACTIONS

- Strong or Moderate CYP3A Inhibitors: Avoid coadministration. (7.1)
- Strong or Moderate CYP3A Inducers: Avoid coadministration. (7.1)
- Gastric Acid Reducing Agents: Avoid coadministration. If coadministration cannot be avoided, stagger administration of TRUSELTIQ from H2-antagonist or locally-acting antacid. (2.4, 7.1)

#### USE IN SPECIFIC POPULATIONS

- Lactation: Advise not to breastfeed. (8.2)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 05/2021

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## FULL PRESCRIBING INFORMATION

### 1. INDICATIONS AND USAGE

TRUSELTIQ is indicated for the treatment of adults with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or other rearrangement as detected by an FDA-approved test [see *Dosage and Administration (2.1)*].

This indication is approved under accelerated approval based on overall response rate and duration of response [see *Clinical Studies (14.1)*]. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

### 2. DOSAGE AND ADMINISTRATION

#### 2.1 Patient Selection

Select patients for the treatment of unresectable locally advanced or metastatic cholangiocarcinoma with TRUSELTIQ based on the presence of an FGFR2 fusion or rearrangement, as detected by an FDA-approved test [see *Clinical Studies (14.1)*].

Information on FDA-approved test(s) for the detection of FGFR2 fusions or rearrangements in cholangiocarcinoma is available at: <http://www.fda.gov/CompanionDiagnostics>.

#### 2.2 Recommended Dosage

The recommended dosage of TRUSELTIQ is 125 mg (one 100 mg capsule and one 25 mg capsule) orally once daily for 21 consecutive days followed by 7 days off therapy, in 28-day cycles. Continue treatment until disease progression or unacceptable toxicity.

Instruct patients to take TRUSELTIQ on an empty stomach at least 1 hour before or 2 hours after food [see *Clinical Pharmacology (12.3)*], at approximately the same time each day. Instruct patients to swallow capsules whole with a glass of water. Advise patients to not crush, chew, or dissolve capsules.

If a dose of TRUSELTIQ is missed by  $\geq 4$  hours or if vomiting occurs, instruct patients to resume the regular daily dose schedule for TRUSELTIQ the next day.

#### 2.3 Dosage Modification for Adverse Reactions

The recommended dose reductions for adverse reactions are listed in Table 1.

**Table 1: Recommended Dose Reduction for TRUSELTIQ for Adverse Reactions**

1 <sup>st</sup> dose reduction	2 <sup>nd</sup> dose reduction	3 <sup>rd</sup> dose reduction
100 mg (one 100 mg capsule)	75 mg (three 25 mg capsules)	50 mg (two 25 mg capsules)

The recommended dosage modifications for adverse reactions are provided in [Table 2](#).

**Table 2: Recommended Dosage Modifications for TRUSELTIQ Adverse Reactions**

<b>Adverse Reaction</b>	<b>Severity<sup>a</sup></b>	<b>TRUSELTIQ Dose Modifications</b>
<b>Retinal Pigment Epithelial Detachment (RPED)</b> [ <i>see Warnings and Precautions (5.1)</i> ]	Not Applicable	Continue TRUSELTIQ at the current dose and continue periodic ophthalmic evaluation: <ul style="list-style-type: none"> <li>• If resolving within 14 days, continue TRUSELTIQ at the current dose.</li> <li>• If not resolving within 14 days, withhold TRUSELTIQ until resolving; then resume TRUSELTIQ at previous or a lower dose.</li> </ul>
<b>Hyperphosphatemia</b> [ <i>see Warnings and Precautions (5.2)</i> ]	Serum phosphate >5.5 – ≤7.5 mg/dL	Continue TRUSELTIQ at the current dose and initiate or dose adjust phosphate binder according to respective label. Monitor serum phosphate weekly. <i>Phosphate binder dosing should be held during the week off TRUSELTIQ therapy each cycle (Days 22-28) and during TRUSELTIQ dose interruptions for non-hyperphosphatemia adverse events.</i>
	Serum phosphate >7.5 mg/dL <b>Or</b> Single serum phosphate >9 mg/dL regardless of duration or dose of phosphate lowering therapy.	Withhold TRUSELTIQ until level returns to serum phosphate ≤5.5 mg/dL. Resume TRUSELTIQ as below, with maximal phosphate binder dosing: <ul style="list-style-type: none"> <li>• If serum phosphate &gt;7.5 mg/dL occurred for less than 7 days: Restart TRUSELTIQ at the same dose.</li> <li>• If serum phosphate &gt;7.5 mg/dL for &gt;7 days or if patient had a one-time serum phosphate of &gt;9 mg/dL: Resume TRUSELTIQ at the next lower dose level.</li> </ul>
	Serum phosphate with life-threatening consequences; urgent intervention indicated (e.g., dialysis)	Permanently discontinue TRUSELTIQ.
<b>Other Adverse Reactions</b>	Grade 3	Withhold dose of TRUSELTIQ until resolved to Grade ≤1, then resume at the next lower dose level of TRUSELTIQ. If not resolved within ≤14 days, permanently discontinue TRUSELTIQ.
	Grade 4	Permanently discontinue TRUSELTIQ.

<sup>a</sup> Severity as defined by National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE version 4.03).

## 2.4 Dosage Modification for Concomitant Use of Gastric Acid Reducing Agents

Avoid coadministration of a proton pump inhibitor (PPI), a histamine-2 (H2) receptor antagonist, or a locally-acting antacid with TRUSELTIQ [*see Drug Interactions (7.1)*]. If coadministration cannot be avoided:

- H2-antagonist: Separate administration of TRUSELTIQ by 2 hours before or 10 hours after.
- Locally-acting antacid: Separate administration of TRUSELTIQ by 2 hours before or after.

## 2.5 Recommended Dosage for Mild and Moderate Renal Impairment

The recommended dosage of TRUSELTIQ for patients with mild to moderate renal impairment (creatinine clearance 30 to 89 mL/min, estimated by Cockcroft-Gault) is 100 mg once daily for 21 consecutive days followed by 7 days off therapy, in 28-day cycles [see *Use in Specific Population (8.6)*, *Clinical Pharmacology (12.3)*].

## 2.6 Recommended Dosage for Mild and Moderate Hepatic Impairment

The recommended dosage of TRUSELTIQ for patients with mild (total bilirubin > upper limit of normal [ULN] to  $1.5 \times$  ULN or AST > ULN) or moderate hepatic impairment (total bilirubin >  $1.5$  to  $3 \times$  ULN with any AST) is as follows [see *Use in Specific Population (8.7)*, *Clinical Pharmacology (12.3)*].

- Mild Hepatic Impairment: 100 mg once daily for 21 consecutive days followed by 7 days off therapy, in 28-day cycles.
- Moderate Hepatic Impairment: 75 mg once daily for 21 consecutive days followed by 7 days off therapy, in 28-day cycles.

## 3. DOSAGE FORMS AND STRENGTHS

Capsules:

- 25 mg: Hard gelatin capsule with a white opaque body and a gray opaque cap - imprinted with black text on the body – INFI 25mg
- 100 mg: Hard gelatin capsule with a white opaque body and a light orange opaque cap - imprinted with black text on the body – INFI 100mg

## 4. CONTRAINDICATIONS

None.

## 5. WARNINGS AND PRECAUTIONS

### 5.1 Ocular Toxicity

#### Retinal Pigment Epithelial Detachment (RPED)

TRUSELTIQ can cause RPED, which may cause symptoms such as blurred vision.

Among 351 patients who received TRUSELTIQ across clinical trials [see *Adverse Reactions (6.1)*] where ophthalmologic monitoring did not routinely include optical coherence tomography (OCT), RPED occurred in 11% of patients, including patients with asymptomatic RPED. The median time to first onset of RPED was 26 days. RPED led to dose interruption/reduction of TRUSELTIQ in 3.4% of patients, and permanent discontinuation in 0.6% of patients.

Perform a comprehensive ophthalmic examination including OCT prior to initiation of TRUSELTIQ, at 1 month, at 3 months, and then every 3 months thereafter during treatment. Refer patients for ophthalmic evaluation urgently for onset of visual symptoms, and follow-up every 3 weeks until resolution or discontinuation of TRUSELTIQ.

Withhold TRUSELTIQ as recommended [see *Dosage and Administration (2.3)*, *Adverse Reactions (6.1)*].

## Dry Eye

Among 351 patients who received TRUSELTIQ across clinical trials [see *Adverse Reactions (6.1)*], dry eye occurred in 29% of patients. Treat patients with ocular demulcents as needed.

## **5.2 Hyperphosphatemia and Soft Tissue Mineralization**

TRUSELTIQ can cause hyperphosphatemia leading to soft tissue mineralization, cutaneous calcinosis, non-uremic calciphylaxis, vascular calcification, and myocardial calcification. Increases in phosphate levels are a pharmacodynamic effect of TRUSELTIQ [see *Clinical Pharmacology (12.2)*]. Among 351 patients who received TRUSELTIQ across clinical trials [see *Adverse Reactions (6.1)*], hyperphosphatemia was reported in 82% of patients based on laboratory values above the upper limit of normal. The median time to onset of hyperphosphatemia was 8 days (range 1-349). Phosphate binders were received by 83% of patients who received TRUSELTIQ.

Monitor for hyperphosphatemia throughout treatment. Initiate phosphate lowering therapy when serum phosphate level is >5.5 mg/dL. For serum phosphate level >7.5 mg/dL, withhold TRUSELTIQ and initiate phosphate lowering therapy. Withhold, dose reduce, or permanently discontinue TRUSELTIQ based on duration and severity of hyperphosphatemia [see *Dosage and Administration (2.3)*].

## **5.3 Embryo-Fetal Toxicity**

Based on findings in animal studies and its mechanism of action, TRUSELTIQ can cause fetal harm when administered to a pregnant woman. Oral administration of infigratinib to pregnant animals during the period of organogenesis caused malformations, fetal growth retardation, and embryo-fetal death at maternal exposures lower than the human exposure based on area under the curve (AUC) at the clinical dose of 125 mg.

Advise pregnant women of the potential risk to the fetus. Advise females of reproductive potential to use effective contraception during treatment with TRUSELTIQ and for 1 month after the final dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with TRUSELTIQ and for 1 month after the final dose [see *Use in Specific Populations (8.1, 8.3)*].

## **6. ADVERSE REACTIONS**

The following adverse reactions are discussed elsewhere in the labeling:

- Ocular Toxicity [see *Warnings and Precautions (5.1)*]
- Hyperphosphatemia and Soft Tissue Mineralization [see *Warnings and Precautions (5.2)*]

### **6.1 Clinical Trials Experience**

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The pooled safety population described in the WARNINGS AND PRECAUTIONS reflect exposure to TRUSELTIQ as a single agent at 125 mg orally once daily for 21 consecutive days followed by 7 days off therapy, in 28-day cycles in 351 patients in Study CBGJ398X2204 and in patients with other advanced solid tumors or hematological malignancies. Among 351 patients who received TRUSELTIQ, 27% were exposed for 6 months or longer and 10% were exposed for greater than one year.

### Previously Treated, Unresectable Locally Advanced or Metastatic Cholangiocarcinoma

The safety of TRUSELTIQ was evaluated in Study CBGJ398X2204, which included 108 patients with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with an FGFR2 fusion or other rearrangement [see *Clinical Studies (14.1)*]. Patients were treated orally with TRUSELTIQ 125 mg once daily for 21 consecutive days followed by 7 days off therapy, in 28-day cycles, until disease progression or unacceptable toxicity. The median duration of treatment was 5.5 months (range: 0.03 to 28.3 months).

The median age of TRUSELTIQ treated patients was 53 years (range 23-81), 62% were females, and 72% were White.

Serious adverse reactions occurred in 32% of patients receiving TRUSELTIQ. Serious adverse reactions in  $\geq 2\%$  of patients who received TRUSELTIQ included infections, anemia, pyrexia, abdominal pain, hypercalcemia, and sepsis. Fatal adverse reactions occurred in 1 (0.9%) patient who received TRUSELTIQ and was due to sepsis.

Permanent discontinuation due to an adverse reaction occurred in 15% of patients who received TRUSELTIQ. Adverse reactions requiring permanent discontinuation in  $\geq 1\%$  of patients were blood creatinine increased, fatigue, subretinal fluid, and calcinosis.

Dosage interruptions due to an adverse reaction occurred in 64% of patients who received TRUSELTIQ. Adverse reactions requiring dosage interruption in  $\geq 5\%$  of patients included hyperphosphatemia, hypercalcemia, palmar-plantar erythrodysesthesia syndrome, stomatitis, diarrhea, and blood creatinine increased.

Dosage reductions due to an adverse reaction occurred in 60% of patients who received TRUSELTIQ. Adverse reactions requiring dosage reductions in  $\geq 2\%$  of patients who received TRUSELTIQ included hyperphosphatemia, stomatitis, palmar-plantar erythrodysesthesia syndrome, increased blood creatinine, increased lipase, hypercalcemia, and onycholysis.

The most common ( $\geq 20\%$ ) adverse reactions were nail toxicity, stomatitis, dry eye, fatigue, alopecia, palmar-plantar erythrodysesthesia syndrome, arthralgia, dysgeusia, constipation, abdominal pain, dry mouth, eyelash changes, diarrhea, dry skin, decreased appetite, vision blurred and vomiting. The most common laboratory abnormalities ( $\geq 20\%$ ) were increased creatinine, increased phosphate, decreased phosphate, increased alkaline phosphatase, decreased hemoglobin, increased alanine aminotransferase, increased lipase, increased calcium, decreased lymphocytes, decreased sodium, increased triglycerides, increased aspartate aminotransferase, increased urate, decreased platelets, decreased leukocytes, decreased albumin, increased bilirubin and decreased potassium.

Table 3 summarizes the adverse reactions in Study CBGJ398X2204. Table 4 summarizes select laboratory abnormalities in Study CBGJ398X2204.

**Table 3: Adverse Reactions ( $\geq 15\%$ ) in Patients Receiving TRUSELTIQ in Study CBGJ398X2204**

Adverse Reaction	TRUSELTIQ N=108	
	All Grades (%)	Grade 3 or 4 <sup>a</sup> (%)
<b>Skin and subcutaneous tissue disorders</b>		
Nail toxicity <sup>b</sup>	57	2*
Alopecia	38	0
Palmar-plantar erythrodysesthesia syndrome	33	7*
Dry skin	23	0

	<b>TRUSELTIQ</b> N=108	
<b>Adverse Reaction</b>	<b>All Grades (%)</b>	<b>Grade 3 or 4 <sup>a</sup> (%)</b>
<b>Gastrointestinal disorders</b>		
Stomatitis <sup>c</sup>	56	15*
Constipation	30	1*
Abdominal pain <sup>d</sup>	26	5*
Dry mouth	25	0
Diarrhea	24	3*
Vomiting	21	1*
Nausea	19	1*
Dyspepsia	17	0
<b>Eye disorders <sup>e</sup></b>		
Dry eye <sup>f</sup>	44	0
Eyelash changes <sup>g</sup>	25	0
Vision blurred	21	0
<b>General disorders and administrative site conditions</b>		
Fatigue <sup>h</sup>	44	4*
Edema <sup>i</sup>	17	1*
Pyrexia	15	1*
<b>Musculoskeletal and connective tissue disorders</b>		
Arthralgia	32	0
Pain in extremity	17	2*
<b>Nervous system disorders</b>		
Dysgeusia	32	0
Headache	17	1*
<b>Metabolism and nutrition disorders</b>		
Decreased appetite	22	1*
<b>Respiratory, thoracic and mediastinal disorders</b>		
Epistaxis	18	0
<b>Investigations</b>		
Weight decreased	15	2*

Graded according to National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE 4.03).

<sup>a</sup> Events of Grade 3 only (no Grade 4 occurred) are marked with an asterisk.

<sup>b</sup> Includes ingrown nail, nail bed bleeding, nail bed disorder, nail bed inflammation, nail bed tenderness, nail discoloration, nail disorder, nail dystrophy, nail hypertrophy, nail infection, nail ridging, onychalgia, onychoclasia, onycholysis, onychomadesis, onychomycosis, and paronychia.

<sup>c</sup> Includes mouth ulceration and stomatitis.

<sup>d</sup> Includes abdominal pain, abdominal pain upper, abdominal discomfort, and abdominal pain lower.

<sup>e</sup> Severity of eye disorders is not represented by CTCAE Grading

<sup>f</sup> Includes dry eye, keratitis, lacrimation increased, pinguecula, and punctate keratitis.

<sup>g</sup> Includes blepharitis, eyelash changes, eyelash discoloration, growth of eyelashes, trichiasis, and trichomegaly.

<sup>h</sup> Includes asthenia and fatigue.

<sup>i</sup> Includes edema peripheral and edema.

Clinically relevant adverse reactions occurring in ≤15% of patients included cataracts (12%) and fractures (1%).



**Table 4: Select Laboratory Abnormalities ( $\geq 10\%$ ) Worsening from Baseline in Patients Receiving TRUSELTIQ in Study CBGJ398X2204**

Laboratory Abnormality	TRUSELTIQ N=108	
	All Grades (%)	Grade 3 or 4 (%)
<b>Hematology</b>		
Decreased hemoglobin	53	5
Decreased lymphocytes	43	9
Decreased platelets	37	4
Decreased leukocytes	26	3
Decreased neutrophils	14	2
<b>Chemistry</b>		
Increased creatinine	93	7
Increased phosphate <sup>a</sup>	90	13
Decreased phosphate	64	31
Increased alkaline phosphatase	54	8
Increased alanine aminotransferase	51	6
Increased lipase	44	7
Increased calcium	43	7
Decreased sodium	41	20
Increased triglycerides	38	3
Increased aspartate aminotransferase	38	4
Increased urate	37	37
Decreased albumin	24	1
Increased bilirubin	24	6
Decreased potassium	21	3
Increased cholesterol	18	1
Increased potassium	17	3
Decreased calcium	10	2

The denominator used to calculate the rate varied from 104 to 107 based on the number of patients with a baseline value and at least one post-treatment value. These laboratory abnormalities are values that reflect worsening from baseline. Graded per NCI CTCAE 4.03.

<sup>a</sup> NCI CTCAE 4.03 does not define grades for increased phosphate. Laboratory value shift table categories were used to assess increased phosphorus levels (Grades  $\geq 3$  defined as  $\geq 9$ mg/dL).

## 7. DRUG INTERACTIONS

### 7.1 Effects of Other Drugs on TRUSELTIQ

#### Strong and Moderate CYP3A Inhibitors

Concomitant use of TRUSELTIQ with a strong or moderate CYP3A inhibitor may increase infgratinib plasma concentrations [see *Clinical Pharmacology (12.3)*], which may increase the risk of adverse reactions. Avoid concomitant use of TRUSELTIQ with strong or moderate CYP3A inhibitors.

## Strong and Moderate CYP3A Inducers

Concomitant use of TRUSELTIQ with a strong or moderate CYP3A inducer may decrease infigratinib plasma concentrations [see *Clinical Pharmacology (12.3)*], which may reduce TRUSELTIQ anti-tumor activity. Avoid concomitant use of TRUSELTIQ with strong or moderate CYP3A inducers.

## Gastric Acid Reducing Agents

The coadministration of TRUSELTIQ with a gastric acid reducing agent may decrease infigratinib plasma concentrations [see *Clinical Pharmacology (12.3)*], which may reduce TRUSELTIQ anti-tumor activity.

Avoid concomitant use of TRUSELTIQ with proton pump inhibitors (PPIs), H<sub>2</sub>-antagonists, and locally-acting antacids. If coadministration of H<sub>2</sub>-antagonists or locally-acting antacids cannot be avoided, stagger administration of TRUSELTIQ [see *Dosage and Administration (2.4)*].

## **8. USE IN SPECIFIC POPULATIONS**

### **8.1 Pregnancy**

#### Risk Summary

Based on findings in animal studies and its mechanism of action TRUSELTIQ can cause fetal harm or loss of pregnancy when administered to a pregnant woman [see *Clinical Pharmacology (13.1)*]. There are no available data on the use of TRUSELTIQ during pregnancy. Oral administration of infigratinib to pregnant animals during the period of organogenesis at maternal exposures below the human exposure at the clinical dose of 125 mg resulted in malformations, fetal growth retardation, and embryo-fetal death (*see Data*). Advise pregnant women of the potential risk to a fetus.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

#### Data

##### *Animal Data*

Once daily oral administration of infigratinib to pregnant rats during organogenesis resulted in an increase in embryo-fetal lethality at 10 mg/kg/day and reductions in fetal body weights at  $\geq 3$  mg/kg/day ( $<0.1$  times the human exposure at the clinical dose of 125 mg). Fetal abnormalities (external, soft tissue, and skeletal) were increased at  $\geq 1$  mg/kg/day ( $<0.1$  times the human exposure at the clinical dose of 125 mg). In the embryo-fetal portion of a rat fertility study, infigratinib decreased the mean number of embryos and increased nonviable embryos and post-implantation loss in females at 3 mg/kg/day.

Once daily oral administration of infigratinib at  $\geq 0.3$  mg/kg/day to pregnant rabbits resulted in maternal toxicity and a corresponding reduction in fetal body weights.

### **8.2 Lactation**

#### Risk Summary

There are no data on the presence of infigratinib or its metabolites in human milk, or their effects on either the breastfed child or on milk production. Because of the potential for serious adverse reactions in breastfed children from TRUSELTIQ, advise women not to breastfeed during treatment and for 1 month after the final dose.

### 8.3 Females and Males of Reproductive Potential

TRUSELTIQ can cause fetal harm when administered to a pregnant woman [*see Use in Specific Populations (8.1)*].

#### Pregnancy Testing

Verify pregnancy status of females of reproductive potential prior to initiating TRUSELTIQ.

#### Contraception

##### *Females*

Advise females of reproductive potential to use effective contraception during treatment with TRUSELTIQ and for 1 month after the final dose.

##### *Males*

Advise males that are partnered with females of reproductive potential to use effective contraception during treatment with TRUSELTIQ and for 1 month after the final dose.

### 8.4 Pediatric Use

The safety and effectiveness of TRUSELTIQ in pediatric patients have not been established.

#### Animal Toxicity Data

In rat and dog repeat-dose toxicity studies  $\geq 13$  weeks in duration, animals displayed toxicities in bones (rats and dogs) and teeth (rats) at exposures lower than the human exposure at the clinical dose of 125 mg. Once daily oral administration of infigratinib in a 13-week rat study resulted in incisor degeneration (degeneration of enamel and loss of ameloblast layer). Once daily oral administration of infigratinib in a 26-week rat study resulted in bone effects (decreased bone strength consistent with decreases in total bone mineral density in lumbar vertebral bodies). Once daily oral administration of infigratinib in a 39-week dog study resulted in increased growth plate thickness and fractures associated with increased physal thickness, focal mixed reaction, and bone loss.

### 8.5 Geriatric Use

Of the 351 patients treated with TRUSELTIQ in clinical studies, 33% were 65 years or older, and 10% were 75 years or older. No overall differences in safety or effectiveness of TRUSELTIQ have been observed between patients 65 years of age and older and younger adult patients.

### 8.6 Patients with Renal Impairment

Reduce the dosage of TRUSELTIQ for patients with mild or moderate renal impairment (creatinine clearance [CL<sub>Cr</sub>] 30 to 89 mL/min estimated by Cockcroft-Gault). The recommended dosage of TRUSELTIQ has not been established for patients with severe renal impairment (CL<sub>Cr</sub> < 30 mL/min) or for patients with end-stage renal disease receiving intermittent hemodialysis [*see Dosage and Administration (2.5) and Clinical Pharmacology (12.3)*].

### 8.7 Patients with Hepatic Impairment

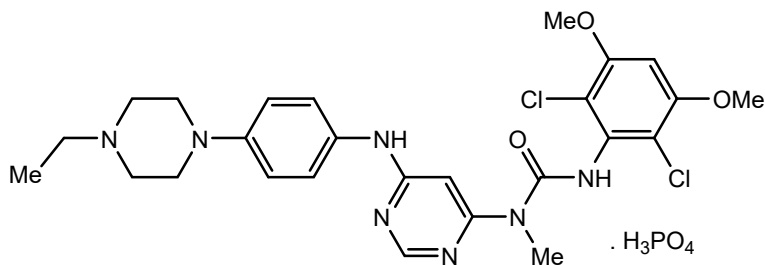
Reduce the dosage of TRUSELTIQ for patients with mild (total bilirubin > upper limit of normal [ULN] to 1.5 × ULN or AST > ULN) or moderate (total bilirubin > 1.5 to 3 × ULN with any AST) hepatic impairment. The

recommended dosage of TRUSELTIQ has not been established in patients with severe (total bilirubin > 3 × ULN with any AST) hepatic impairment [see *Dosage and Administration (2.6), Clinical Pharmacology (12.3)*].

## 11. DESCRIPTION

Infigratinib is a kinase inhibitor. The chemical name is 3-(2,6-dichloro-3,5-dimethoxyphenyl)-1-{6-[4-(4-ethylpiperazin-1-yl)phenylamino]pyrimidin-4-yl}-1-methylurea phosphate (1:1). The molecular formula is C<sub>26</sub>H<sub>31</sub>Cl<sub>2</sub>N<sub>7</sub>O<sub>3</sub>·H<sub>3</sub>PO<sub>4</sub> and the molecular weight is 560.48 g/mol for the free base, 658.47 g/mol for the phosphate salt.

The chemical structure of infigratinib phosphate is as follows:



Infigratinib phosphate is a white to off-white powder. It shows adequate solubility in water and 0.1N HCl. It is practically insoluble in pH 6.8 buffer and poorly soluble in common organic solvents. TRUSELTIQ (infigratinib) is supplied as 25 mg and 100 mg hard gelatin capsules for oral administration. Each capsule contains the following inactive ingredients: colloidal silicon dioxide, crospovidone, hypromellose, lactose monohydrate, magnesium stearate (from vegetable source), and microcrystalline cellulose. The capsule shells contain black iron oxide, gelatin, red iron oxide, titanium dioxide, and yellow iron oxide. The printing ink contains black iron oxide, butyl alcohol, dehydrated alcohol, isopropyl alcohol, potassium hydroxide, propylene glycol, shellac, and strong ammonia solution.

## 12. CLINICAL PHARMACOLOGY

### 12.1 Mechanism of Action

Infigratinib is a small molecule kinase inhibitor of FGFR with IC<sub>50</sub> values of 1.1, 1, 2, and 61 nM for FGFR1, FGFR2, FGFR3, and FGFR4, respectively. The major human metabolites of infigratinib, BHS697 and CQM157, have similar in vitro binding affinities for FGFR1, FGFR2, and FGFR3 compared to infigratinib. Infigratinib inhibited FGFR signaling and decreased cell proliferation in cancer cell lines with activating FGFR amplifications, mutations, or fusions. Constitutive FGFR signaling can support the proliferation and survival of malignant cells. Infigratinib had anti-tumor activity in mouse and rat xenograft models of human tumors with activating FGFR2 or FGFR3 alterations, including two patient-derived xenograft models of cholangiocarcinoma that expressed FGFR2-TTC28 or FGFR2-TRA2B fusions. Infigratinib demonstrated brain-to-plasma concentration ratios (based on AUC<sub>0-inf</sub>) of 0.682 in rats after a single oral dose.

### 12.2 Pharmacodynamics

#### Serum Phosphate

TRUSELTIQ increased serum phosphate levels due to FGFR inhibition. Serum phosphate increased with increasing exposures across the dose range of 20 to 150 mg once daily (0.16 to 1.2 times the approved recommended dosage), with increased risk of hyperphosphatemia with higher exposure to TRUSELTIQ.

## Cardiac Electrophysiology

At the recommended dosing regimen, TRUSELTIQ does not result in a large mean increase (i.e., >20 msec) in the QTc interval. The QT effect of infigratinib at higher exposures associated with CYP3A inhibition has not been studied.

### **12.3 Pharmacokinetics**

The infigratinib pharmacokinetic parameters are presented following administration of the approved recommended dosage in cholangiocarcinoma patients, unless otherwise specified.

The mean (coefficient of variation [%CV]) steady-state maximum plasma concentration ( $C_{max}$ ) and area under the curve over a dosing interval ( $AUC_{0-24h}$ ) of infigratinib and active metabolites, BHS697 and CQM157, are presented in Table 5.

**Table 5. Mean (%CV) Exposure of Infigratinib and Active Metabolites**

	<b>Infigratinib</b>	<b>BHS697</b>	<b>CQM157</b>
$C_{max}$	282.5 ng/mL (54%)	42.1 ng/mL (65%)	15.7 ng/mL (92%)
$AUC_{0-24h}$	3780 ng•h/mL (59%)	717 ng•h/mL (55%)	428 ng•h/mL (72%)

Infigratinib  $C_{max}$  and AUC increased more than proportionally across the dose range of 5 to 150 mg (0.04 to 1.2 times the approved recommended dose). Steady state was achieved within 15 days and the mean accumulation ratio was 8- and 5-fold for  $C_{max}$  and AUC, respectively.

#### Absorption

Median (range) time to achieve peak infigratinib plasma concentration ( $t_{max}$ ) was 6 hours (2 to 7 hours) at steady state.

#### *Effect of Food*

Following administration of TRUSELTIQ with a high-fat and high-calorie meal (800 to 1,000 calories with approximately 50% of total caloric content of the meal from fat) in healthy subjects, the mean  $AUC_{inf}$  of infigratinib increased by 80%-120% and  $C_{max}$  increased by 60%-80%, the median  $T_{max}$  shifted from 4 hours to 6 hours. Following administration of TRUSELTIQ with a low-fat low-calorie meal (approximately 330 calories with 20% of total caloric content of the meal from fat), the mean  $AUC_{inf}$  of infigratinib increased by 70%,  $C_{max}$  increased by 90%, and the median  $T_{max}$  did not change.

#### Distribution

The geometric mean (CV%) apparent volume of distribution of infigratinib was 1600 L (33%) at steady state. The mean infigratinib protein binding was 96.8%, primarily to lipoprotein, and was dependent of drug concentration.

#### Elimination

The geometric mean (CV%) total apparent clearance (CL/F) of infigratinib was 33.1 L/h (59%) at steady state. The geometric mean (CV%) terminal half-life of infigratinib was 33.5 h (39%) at steady state.

#### *Metabolism*

Infigratinib is predominantly metabolized by CYP3A4 (~94%) and to a lesser extent by FMO3 (6%) in vitro. The major drug-related moiety in plasma was unchanged infigratinib (38% of dose) in a human [ $^{14}C$ ] mass

balance study, followed by two active metabolites, BHS697 and CQM157 (each at >10% of dose). BHS697 is mainly metabolized by CYP3A4 and CQM157 is metabolized through both Phase I and Phase II biotransformation pathways.

BHS697 and CQM157 contribute about 16% to 33% and 9% to 12% of overall pharmacologic activity, respectively.

### *Excretion*

After a single oral 125 mg dose of radiolabeled infigratinib in healthy subjects, approximately 77% of the dose was recovered in feces (3.4% as unchanged) and 7.2% in urine (1.9% as unchanged).

### Specific Populations

No clinically significant differences in the systemic exposure of infigratinib were observed based on age (19-86 years), sex, race/ethnicity (White 70.7%, Black 15.4%, and Asian 8%), or body weight (36.4-169 kg).

### *Patients with Renal Impairment*

The relative potency adjusted steady state AUC of infigratinib plus its active metabolites (BHS697, CQM157) in plasma increased by 32% and 37% in patients with mild (creatinine clearance [CLcr] 60 to 89 mL/min estimated by Cockcroft-Gault) and moderate renal impairment (CLcr 30 to 59 mL/min), respectively, relative to patients with normal renal function (CLcr  $\geq$  90 mL/min).

The effect of severe renal impairment (CLcr < 30 mL/min) or renal dialysis in end-stage renal disease on infigratinib exposure is unknown.

### *Patients with Hepatic Impairment*

The relative potency adjusted steady state AUC of infigratinib plus its active metabolites (BHS697, CQM157) in plasma increased by 47%-62% and 99% in patients with mild (total bilirubin > upper limit of normal [ULN] to 1.5  $\times$  ULN or AST > ULN) and moderate hepatic impairment (total bilirubin > 1.5 to 3  $\times$  ULN with any AST), respectively, relative to patients with normal hepatic function (total bilirubin  $\leq$  ULN and AST  $\leq$  ULN).

The effect of severe hepatic impairment (total bilirubin > 3  $\times$  ULN with any AST) on infigratinib exposure is unknown [see *Use in Specific Populations* (8.7)].

### Drug Interaction Studies

#### **Clinical Studies**

*Strong CYP3A Inhibitors:* Coadministration of multiple doses of itraconazole (strong CYP3A inhibitor) increased infigratinib AUC<sub>0-inf</sub> by 622% and C<sub>max</sub> by 164%, increased BHS697 AUC<sub>0-inf</sub> by 174%, and decreased CQM157 C<sub>max</sub> by 69%, respectively [see *Drug Interactions* (7.1)].

*Strong CYP3A Inducers:* Coadministration of multiple doses of rifampin (strong CYP3A inducer) decreased infigratinib AUC<sub>0-inf</sub> by 56% and C<sub>max</sub> by 44%, decreased BHS697 AUC<sub>0-inf</sub> by 65% and C<sub>max</sub> by 27%, and decreased CQM157 AUC<sub>0-inf</sub> by 76% and C<sub>max</sub> by 50%, respectively [see *Drug Interactions* (7.1)].

*Gastric Acid-Lowering Agents:* Coadministration of multiple doses of lansoprazole (proton pump inhibitor) decreased infigratinib AUC<sub>0-inf</sub> by 45% and C<sub>max</sub> by 49%, decreased BHS697 AUC<sub>0-inf</sub> by 32% and C<sub>max</sub> by 44%, and decreased CQM157 AUC<sub>0-inf</sub> by 72% and C<sub>max</sub> by 55%, respectively [see *Drug Interactions* (7.1)].

*CYP3A4 Substrates:* No clinically significant differences in pharmacokinetics of midazolam (sensitive CYP3A4 substrate) were observed when co-administered with TRUSELTIQ [see *Drug Interactions (7.1)*].

## **In Vitro Studies**

*Cytochrome P450 Enzymes:* Infigratinib does not induce CYP1A2, CYP2B6, CYP2C9, or CYP3A4. Infigratinib, BHS697, and CQM157 do not inhibit major CYP450 isozymes at clinically relevant concentrations.

*Transporter Systems:* Infigratinib inhibits MATE1 and BCRP. Infigratinib has a low potential to inhibit P-gp, BSEP, OCT1, OCT2 and MATE-2K at clinically relevant concentrations. Infigratinib is a substrate for P-gp and BCRP. The metabolites BHS697 and CQM157 have a low potential to inhibit OATP1B1, OATP1B3, P-gp, or BCRP at clinically relevant concentrations. The effect of these metabolites to inhibit MATE or OCT at clinically relevant concentrations is unknown.

## **13. NONCLINICAL TOXICOLOGY**

### **13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

Carcinogenicity studies have not been conducted with infigratinib.

Infigratinib was not mutagenic in a bacterial reverse mutation (Ames) assay and was not clastogenic in an in vitro human peripheral blood lymphocyte chromosome aberration assay. Infigratinib did not induce micronuclei in an in vivo rat bone marrow micronucleus assay.

In a rat fertility study, there were no effects on mating or fertility, reproductive organ weights, or sperm motility, density, or morphology in males, and no effect on estrous cycling, mating, or fertility in females administered  $\leq 3$  mg/kg/day infigratinib.

## **14. CLINICAL STUDIES**

### **14.1 Cholangiocarcinoma**

Study CBGJ398X2204 (NCT02150967), a multicenter open-label single-arm trial, evaluated the efficacy of TRUSELTIQ in 108 patients with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with an FGFR2 fusion or rearrangement as determined for enrollment by local (89%) or central testing (11%). Qualifying in-frame fusions and other rearrangements were predicted to have a breakpoint within intron 17/exon 18 of the FGFR2 gene that leaves the FGFR2 kinase domain intact.

Patients received TRUSELTIQ at a dosage of 125 mg orally once daily for 21 consecutive days followed by 7 days off therapy, in 28-day cycles until disease progression or unacceptable toxicity. The major efficacy outcome measures were overall response rate (ORR) and duration of response (DoR), as determined by blinded independent central review (BICR) according to Response Evaluation Criteria in Solid Tumors (RECIST) v1.1.

The median age was 53 years (range: 23 to 81 years), 62% were female, 72% were White, 3.7% were Black or African American, 10% were Asian, and 99% had a baseline Eastern Cooperative Oncology Group (ECOG) performance status of 0 (42%) or 1 (57%). The presence of FGFR2 fusions or other rearrangements was determined in 104 enrolled patients (96%) with Next Generation Sequencing (NGS) testing. Eighty-eight (81%) patients had in-frame FGFR2 fusions, and BICC1 the most commonly reported fusion partner (n=27, 25%). Twenty (19%) patients had other FGFR2 rearrangements that may not be in-frame with the partner gene or the partner gene was not identifiable.

Ninety-nine percent of patients had metastatic (Stage IV) disease at the time of study entry. All patients had received at least 1 prior line of systemic therapy, 32% had 2 prior lines of therapy, and 29% had 3 or more prior



lines of therapy. Ninety-nine percent of patients received prior gemcitabine-based therapy and most (88%) had progressed on their prior gemcitabine-based therapy.

Efficacy results are summarized in Table 6. The median time to response was 3.6 months (range 1.4 – 7.4 months).

**Table 6: Efficacy Results in Study CBGJ398X2204**

Efficacy Parameter	TRUSELTIQ N=108
	BICR Assessment
<b>ORR (95% CI)</b>	23% (16, 32)
Complete Response, n (%)	1 (1%)
Partial Response, n (%)	24 (22%)
<b>Median DoR (months) (95% CI)</b>	5.0 (3.7, 9.3)
Patients with DoR $\geq$ 6 months, n (%)	8 (32%)
Patients with DoR $\geq$ 12 months, n (%)	1 (4%)

Abbreviations: BICR= blinded independent central review; CI=confidence interval; DoR=duration of response; ORR=overall response rate.

Note: Data are according to RECIST v1.1.

## 16. HOW SUPPLIED/STORAGE AND HANDLING

TRUSELTIQ (infigratinib) capsules are available in the strengths and packages listed below:

- 25 mg: Hard gelatin capsule with a white opaque body and a gray opaque cap - imprinted with black text on the body – INFI 25mg
- 100 mg: Hard gelatin capsule with a white opaque body and a light orange opaque cap - imprinted with black text on the body – INFI 100mg

TRUSELTIQ capsules are supplied in 21-day blister pack dose presentations as follows:

- 50 mg daily dose: Each carton contains 1 blister card containing a 21-day supply (42 capsules; 25 mg infigratinib per capsule). [NDC-72730-506-01].
- 75 mg daily dose: Each carton contains 2 blister cards containing a 21-day supply (63 capsules; 25 mg infigratinib per capsule). [NDC-72730-202-01].
- 100 mg daily dose: Each carton contains 1 blister card containing a 21-day supply (21 capsules; 100 mg infigratinib per capsule). [NDC-72730-111-01].
- 125 mg daily dose: Each carton contains 1 blister card containing a 21-day supply (21 capsules, 100 mg infigratinib per capsule and 21 capsules; 25 mg infigratinib per capsule). [NDC-72730-101-01].

Store TRUSELTIQ at 20°C to 25°C (68°F to 77°F), with excursions permitted between 15°C and 30°C (59°F and 86°F).

## 17. PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

### Ocular Toxicity

Advise patients that TRUSELTIQ may cause ocular toxicity including RPED and to immediately inform their healthcare provider if they experience any visual changes. Advise patients to use artificial tear substitutes or



hydrating or lubricating eye gels to prevent or treat dry eyes. Inform patients that their healthcare provider will closely monitor for eye disorders, with ophthalmic examinations performed by an ophthalmologist, and will manage them as clinically indicated [see *Warnings and Precautions (5.1)*].

### Hyperphosphatemia and Soft Tissue Mineralization

Inform patients that TRUSELTIQ may cause hyperphosphatemia and soft tissue mineralization and to immediately inform their healthcare provider of any symptoms related to acute changes in phosphate levels such as muscle cramps, numbness, or tingling around the mouth [see *Warnings and Precautions (5.2)*].

### Nail Disorders

Advise patients that TRUSELTIQ may cause nail disorders [see *Adverse Reactions (6.1)*].

### Embryo-Fetal Toxicity

- Advise females to inform their healthcare provider if they are pregnant or become pregnant. Inform females of the risk to a fetus and potential loss of pregnancy [see *Warnings and Precautions (5.3)* and *Use in Specific Populations (8.1)*].
- Advise females of reproductive potential to use effective contraception while on TRUSELTIQ and for 1 month after the final dose [see *Use in Specific Populations (8.1)* and *(8.3)*].
- Advise males with female partners of reproductive potential or who are pregnant to use effective contraception during treatment and for 1 month after the final dose of TRUSELTIQ [see *Use in Specific Populations (8.3)*].

### Lactation

- Advise patients not to breastfeed during treatment with TRUSELTIQ and for 1 month after the final dose [see *Use in Specific Populations (8.2)*].

### Administration

- Instruct patients to take TRUSELTIQ on an empty stomach at least 1 hour before, or 2 hours after food, at approximately the same time each day.
- Instruct patients to swallow the capsules whole with a glass of water. Advise patients to not crush, chew, or dissolve capsules.
- Instruct patients that if a dose cannot be administered within 4 hours of the regularly scheduled time or if vomiting occurs, the dose should not be made up later that day. Dosing should resume at the usual time on the next day [see *Dose and Administration (2.2)*].

### Drug Interactions

Advise patients to inform their healthcare providers of all concomitant medications, including prescription medicines, over-the-counter drugs, and herbal products. Advise patients to avoid grapefruit products during treatment with TRUSELTIQ [see *Drug Interactions (7.1)*].

Manufactured for:  
QED Therapeutics, Inc.  
Brisbane, CA 94005

TRUSELTIQ is a trademark of QED Therapeutics, Inc  
U.S. Patent Nos. 8,552,002; 9,067,896; 10,278,969  
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**PATIENT INFORMATION**  
**TRUSELTIQ™ (tru sel tik)**  
**(infigratinib) capsules**

**What is TRUSELTIQ?**

TRUSELTIQ is a prescription medicine used to treat adults with bile duct cancer (cholangiocarcinoma) that has spread or cannot be removed by surgery:

- who have already received a previous treatment, **and**
- whose tumor has a certain type of abnormal “FGFR2” gene.

Your healthcare provider will test your cancer for certain FGFR2 gene abnormalities to make sure that TRUSELTIQ is right for you.

It is not known if TRUSELTIQ is safe and effective in children.

**Before taking TRUSELTIQ, tell your healthcare provider about all your medical conditions, including if you:**

- have vision or eye problems
- have kidney problems
- have liver problems
- are pregnant or plan to become pregnant. TRUSELTIQ can harm your unborn baby or cause loss of your pregnancy (miscarriage). You should not become pregnant during treatment with TRUSELTIQ.

**Females who can become pregnant:**

- Your healthcare provider should do a pregnancy test before you start treatment with TRUSELTIQ.
- You should use effective birth control during treatment and for 1 month after your final dose of TRUSELTIQ. Talk to your healthcare provider about birth control methods that may be right for you during this time.
- Tell your healthcare provider right away if you become pregnant or think you may be pregnant during this time.

**Males with female partners who can become pregnant:**

- You should use effective birth control when sexually active during treatment with TRUSELTIQ and for 1 month after your final dose of TRUSELTIQ.
- are breastfeeding or plan to breastfeed. It is not known if TRUSELTIQ passes into your breast milk. Do not breastfeed during treatment and for 1 month after your final dose of TRUSELTIQ.

**Tell your healthcare provider about all the medicines you take**, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Taking TRUSELTIQ with certain other medicines may affect how TRUSELTIQ works.

**Especially tell your healthcare provider** if you take medicines used to decrease stomach acid and treat heartburn, called proton pump inhibitors (PPIs), H2 blockers, or antacids. You should avoid taking these medicines during treatment with TRUSELTIQ. If you cannot avoid taking H2 blockers or antacids, see **“How should I take TRUSELTIQ?”** for more information on how to take TRUSELTIQ with these medicines.

**How should I take TRUSELTIQ?**

- Take TRUSELTIQ exactly as your healthcare provider tells you.
- Take your prescribed dose of TRUSELTIQ 1 time each day for 21 days, followed by 7 days off treatment. This is 1 cycle of treatment (28 days). You will repeat this cycle for as long as your healthcare provider tells you to.
- Take TRUSELTIQ at about the same time each day.
- Take TRUSELTIQ on an empty stomach, at least 1 hour before or 2 hours after food.
- Swallow TRUSELTIQ capsules whole with a glass of water.
- **Do not** crush, chew, or dissolve TRUSELTIQ capsules. Tell your healthcare provider if you have problems swallowing capsules whole.
- If you need to take an acid reducer called H2 blocker, take TRUSELTIQ 2 hours before or 10 hours after taking the acid reducer.
- If you need to take an antacid, take TRUSELTIQ 2 hours before or 2 hours after taking the antacid.
- You should not eat or drink grapefruit products during treatment with TRUSELTIQ.
- Your healthcare provider may change your dose of TRUSELTIQ, temporarily stop, or completely stop treatment if you get certain side effects.
- If you miss a dose of TRUSELTIQ, you can take the missed dose within 4 hours on the same day. If more than 4 hours have passed, do not take the dose. Take your regular dose of TRUSELTIQ the next day at the usual time. Do not take more TRUSELTIQ than prescribed to make up for the missed dose.
- If you vomit after taking TRUSELTIQ, **do not** take an extra dose. Take your regular dose of TRUSELTIQ the

next day at the usual time.

### What are the possible side effects of TRUSELTIQ?

#### TRUSELTIQ may cause serious side effects, including:

- **Eye problems.** Certain eye problems are common with TRUSELTIQ but can also be serious. Eye problems include dry or inflamed eyes, inflamed cornea (front part of the eye), increased tears, and disorders of the retina (an internal part of the eye). You will need to see an eye specialist for a complete eye exam before you begin treatment with TRUSELTIQ, at 1 month, at 3 months, and then every 3 months during treatment with TRUSELTIQ. Your healthcare provider should closely monitor you for eye problems.
  - You should use artificial tear substitutes, hydrating or lubricating eye gels as needed, to help prevent or treat dry eyes.
  - **Tell your healthcare provider right away** if you develop any changes in your vision including blurred vision, during treatment with TRUSELTIQ. You may need to see an eye specialist right away.
- **High phosphate levels in the blood (hyperphosphatemia) and buildup of minerals in different tissues in your body.** Hyperphosphatemia is common with TRUSELTIQ but can also be serious. High levels of phosphate in your blood may lead to buildup of minerals such as calcium in different tissues in your body. Your healthcare provider will check your blood phosphate levels during treatment with TRUSELTIQ.
  - Your healthcare provider may prescribe phosphate lowering therapy or change, interrupt, or stop TRUSELTIQ if needed.
  - Tell your healthcare provider right away if you develop any muscle cramps, numbness, or tingling around your mouth.

#### The most common side effects of TRUSELTIQ include:

- |  |  |   |
|--|--|---|
| • changes in kidney function blood tests                             | • dry eyes   | • constipation                                    |
| • decreased levels of phosphate, sodium, and potassium in the blood  | • feeling tired or weak  | • stomach-area (abdominal) pain or discomfort     |
| • nails separate from the bed or poor formation of the nail          | • increased calcium levels in the blood  | • dry mouth                                       |
| • mouth sores  | • hair loss  | • changes in eyelash                              |
| • changes in liver function blood tests                              | • increased fat levels (triglyceride) in the blood   | • diarrhea  |
| • decreased red blood cell, white blood cell, and platelet counts    | • increased levels of uric acid in the blood   | • decreased protein levels (albumin) in the blood |
| • increased lipase levels (a blood test done to check your pancreas) | • redness, swelling, peeling or tenderness, mainly on the hands or feet ('hand-foot syndrome') | • dry skin  |
|  | • joint pain   | • decreased appetite                              |
|  | • changes in sense of taste  | • blurred vision                                  |
|  |  | • vomiting  |

These are not all possible side effects of TRUSELTIQ. For more information, ask your healthcare provider or pharmacist. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

### How should I store TRUSELTIQ?

- Store TRUSELTIQ at room temperature between 68°F to 77°F (20°C to 25°C).

#### Keep TRUSELTIQ and all medicines out of the reach of children.

### General information about the safe and effective use of TRUSELTIQ.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use TRUSELTIQ for a condition for which it was not prescribed. Do not give TRUSELTIQ to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information that is written for healthcare professionals.

### What are the ingredients in TRUSELTIQ?

**Active ingredient:** infigratinib phosphate

**Inactive ingredients:** colloidal silicon dioxide, crospovidone, hypromellose, lactose monohydrate, magnesium stearate (from vegetable source), and microcrystalline cellulose.

The capsule shells contain: black iron oxide, gelatin, red iron oxide, titanium dioxide, and yellow iron oxide.

The printing ink contains: black iron oxide, butyl alcohol, dehydrated alcohol, isopropyl alcohol, potassium hydroxide, propylene glycol, shellac, and strong ammonia solution.

**Manufactured for:** QED Therapeutics, Inc. Brisbane, CA 94005

TRUSELTIQ is a trademark of QED Therapeutics, Inc; U.S. Patent Nos. 8,552,002; 9,067,896; 10,278,969; © 2021 QED Therapeutics, Inc.

For more information call QED Therapeutics at 1-844-550-BBIO (2246) or go to [www.TRUSELTIQ.com](http://www.TRUSELTIQ.com).

This Patient Information has been approved by the U.S. Food and Drug Administration.

Issued: 05/2021

NDC-72730-506-01  
Rx Only

**TRUSELTIQ**  
(infigratinib) capsules

Oral use

**50 mg daily dose**

Take two 25 mg capsules  
together once daily

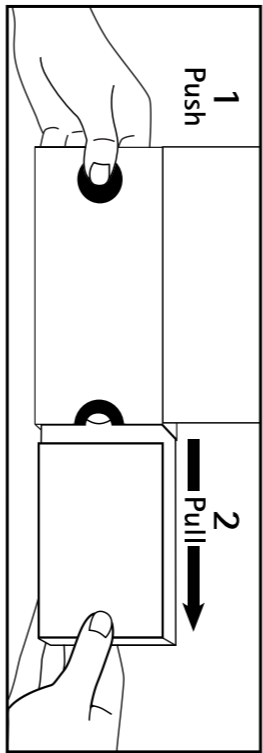
**Blister card contains one treatment cycle**

<b>Days 1-21</b>	<b>Days 22-28</b>
25 mg	Treatment-free days
42 capsules	

LIFT PANEL

**TRUSELTIQ**  
(infigratinib) capsules

**50 mg daily dose**



**TO OPEN**

**1-PUSH AND HOLD**

Use thumb to push the button  
gently, and hold button.

**2-PULL**

While holding the button  
down, pull out card.

**TRUSELTIQ**  
(infigratinib) capsules

**50 mg daily dose**

Distributed by:  
**QED** Therapeutics  
8000 Marina Blvd, #400  
Brisbane, CA 94005



PCR-740-16326

**TRUSELTIQ**  
(infigratinib) capsules

**50 mg daily dose**

**TRUSELTIQ**  
(infigratinib) capsules

**50 mg daily dose**



**Recommended Dosage:** See Prescribing Information.

**Dosing Instructions:** Take TRUSELTIQ for 21 consecutive days, then take a 7-day break. Complete this 28-day treatment cycle before starting the next 28-day treatment cycle.

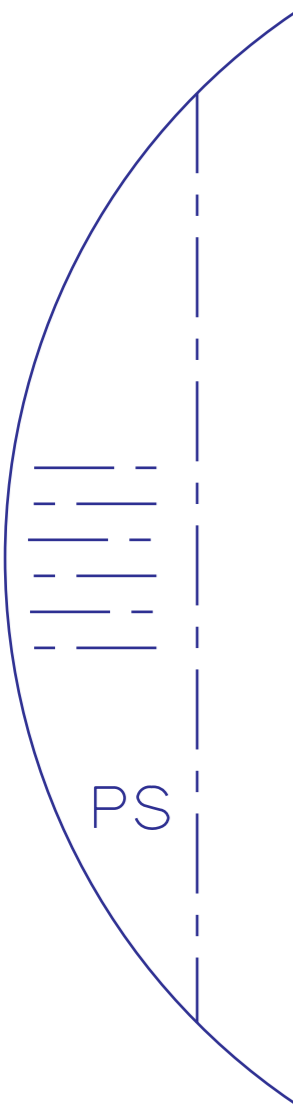
**Days 1-21:** Take two 25 mg capsules once daily on an empty stomach (1 hour before or 2 hours after a meal). Swallow capsules whole with a glass of water. Do not open, crush, chew, or dissolve capsules.

**Days 22-28:** Treatment-free days. Do not take any doses for 7 days.

Store at room temperature between 68°F to 77°F (20°C to 25°C)

CAD File: 19M001923

PS



PCR-740-14350

TRUSELTIQ<sup>®</sup>  
(infirgratinib) capsules

**Days 8-14**

**25 mg per capsule**

Take both capsules at the same time daily

Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14

**Days 1-7**

**25 mg per capsule**

Take both capsules at the same time daily

Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7

Enter start date:

Push to release capsule

**Days 22-28**  
Treatment-free Days

Day 22	Day 23	Day 24	Day 25	Day 26	Day 27	Day 28

Peel here

**Days 15-21**

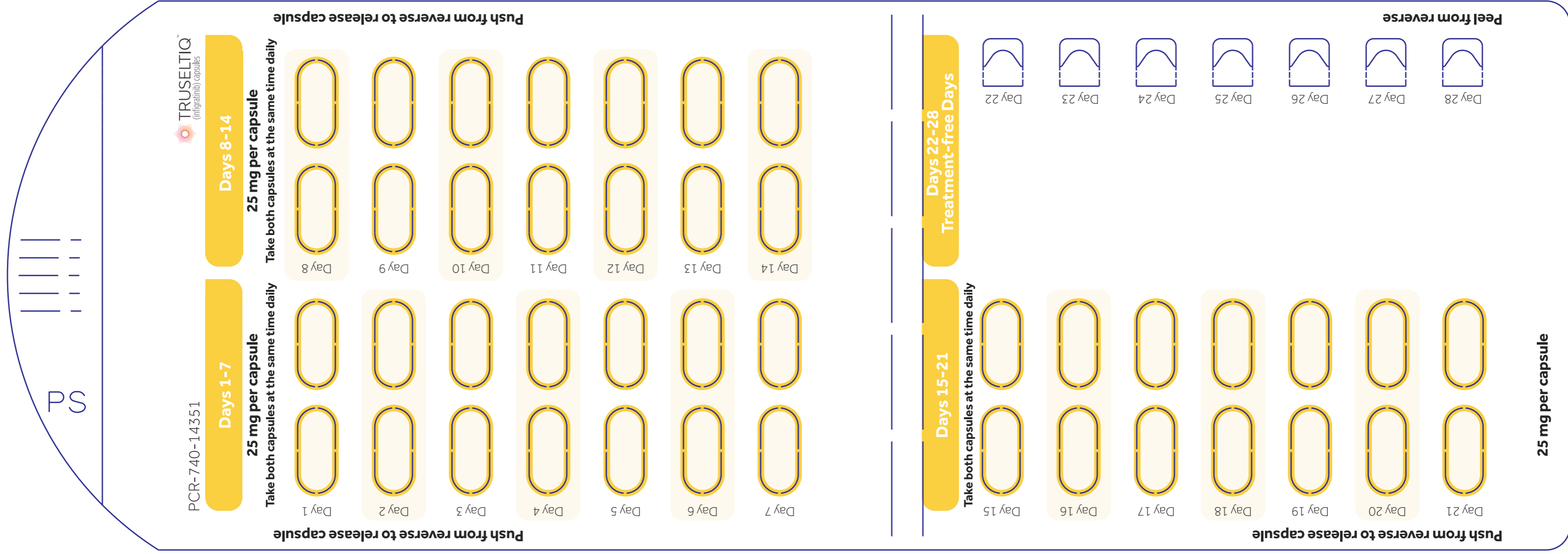
Take both capsules at the same time daily

Day 15	Day 16	Day 17	Day 18	Day 19	Day 20	Day 21

25 mg per capsule

(b) (4)





(b) (4)

142090



Contains two blister cards  
for one treatment cycle  
(63 capsules total)

<b>Days 1-14</b>	<b>Days 15-28</b>
<b>25 mg</b>	<b>25 mg</b>
42 capsules	21 capsules

Days 22-28:  
Treatment-free days

**75 mg daily dose**  
Take three 25 mg capsules  
together once daily

Oral use



**Rx Only**

NDC-72730-202-01

**75 mg daily dose**



**75 mg daily dose**

PS

**75**



**75 mg daily dose**



**Recommended Dosage:** See Prescribing Information.

**Dosing Instructions:**

Take TRUSELTIQ for 21 consecutive days, then take a 7-day break. Complete this 28-day treatment cycle before starting the next 28-day treatment cycle.

**Days 1-21:** Take three 25 mg capsules once daily on an empty stomach (1 hour before or 2 hours after a meal).

Swallow capsules whole with a glass of water. Do not open, crush, chew, or dissolve capsules.

**Days 22-28:** Treatment-free days. Do not take any doses for 7 days.

Store at room temperature between 68°F to 77°F (20°C to 25°C)



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QED Therapeutics  
8000 Marina Blvd., # 400  
Brisbane, CA 94005

**75 mg daily dose**



(b) (4)

CAD File: 20M018701

PCR-740-14333



1421099



NDC-72730-202-01  
Rx Only

TRUSELTIQ<sup>™</sup>  
(infigratinib) capsules

Oral use

**75 mg daily dose**

Take three 25 mg capsules together once daily

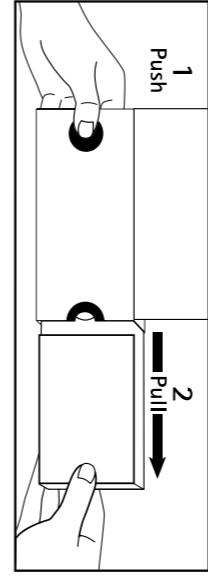
Blister card contains

Days 1-14  
25 mg  
42 capsules

LIFT PANEL

TRUSELTIQ<sup>™</sup>  
(infigratinib) capsules

**75 mg daily dose**



TO OPEN

**1-PUSH AND HOLD**

Use thumb to push the button gently, and hold button.

**2-PULL**

While holding the button down, pull out card.

75 mg daily dose



PCR-740-14332

Distributed by:  
QED Therapeutics  
200 Main Street, Suite #400  
Beverly Hills, CA 90205

TRUSELTIQ<sup>™</sup>  
(infigratinib) capsules

**75 mg daily dose**

TRUSELTIQ<sup>™</sup>  
(infigratinib) capsules

75 mg daily dose



**Recommended Dosage:** See Prescribing Information.

**Dosing Instructions:** Take TRUSELTIQ for 21 consecutive days, then take a 7-day break. To complete this 28-day cycle, continue with the Days 15-28 blister card.

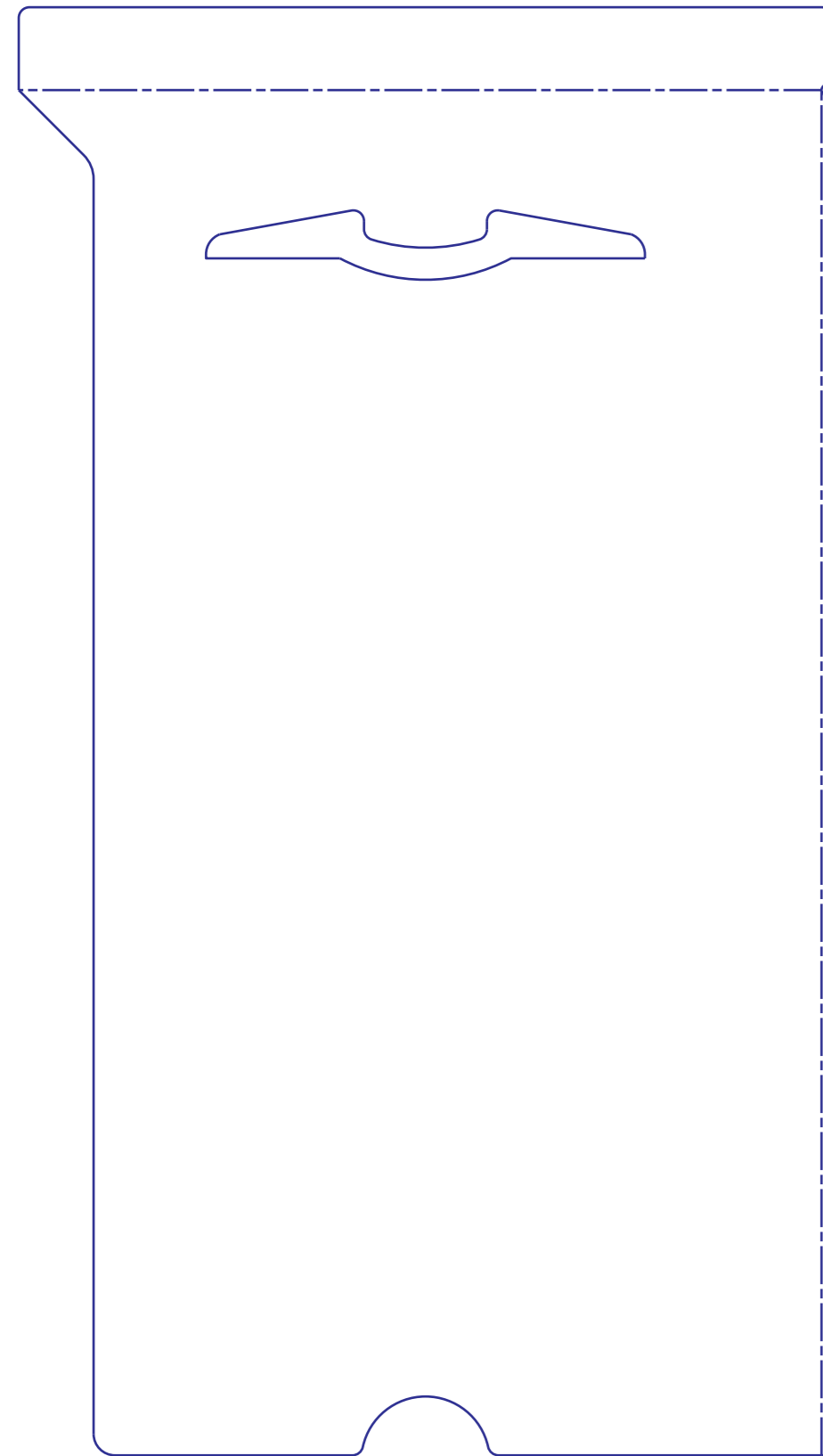
**Days 1-14:** Take three 25 mg capsules once daily on an empty stomach (1 hour before or 2 hours after a meal). Swallow capsules whole with a glass of water. Do not open, crush, chew, or dissolve capsules.

Store at room temperature between 68°F to 77°F (20°C to 25°C)

PS

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1421099



(b) (4)



TRUSELTIQ<sup>™</sup>  
(efgartinib) capsules

PCR-740-14330

**Days 1-7**  
25 mg per capsule  
Take all three capsules at the same time daily

Day 1 Day 2 Day 3 Day 4 Day 5 Day 6 Day 7

**Days 8-14**  
Take all three capsules at the same time daily

Day 8 Day 9 Day 10 Day 11 Day 12 Day 13 Day 14

Enter start date:

Push to release capsule

Push to release capsule

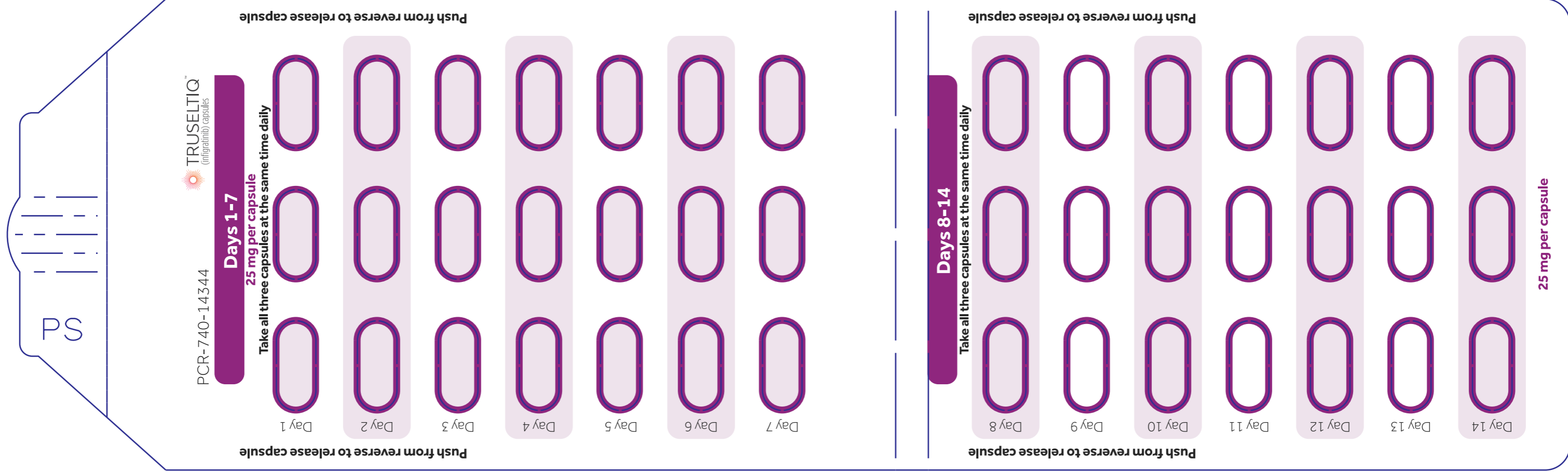
Push to release capsule

25 mg per capsule

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(b) (4)

TS



TRUSELTIQ<sup>™</sup>  
(nifedipine) capsules

**Days 15-21**  
25 mg per capsule  
Take all three capsules at the same time daily

**Enter start date:**

Day 15	Day 16	Day 17	Day 18	Day 19	Day 20	Day 21

Push to release capsule

Push to release capsule

**Days 22-28 Treatment-free Days**



Peel here						
Day 22	Day 23	Day 24	Day 25	Day 26	Day 27	Day 28

(b) (4)

PS

PCR-740-14345

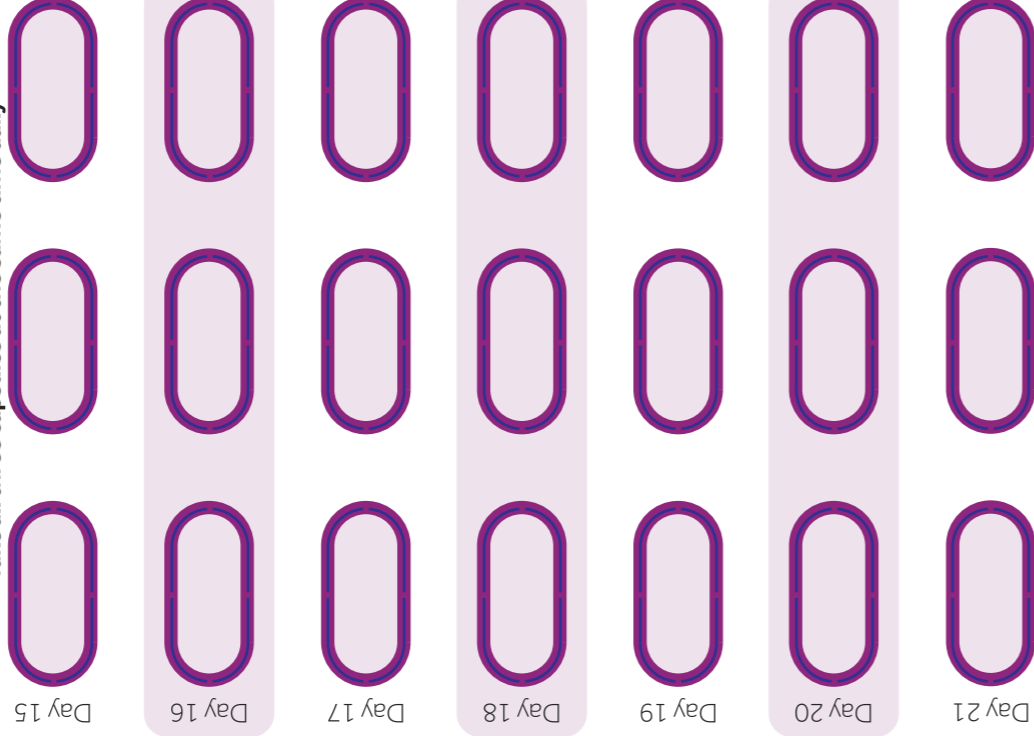
TRUSELTIQ<sup>™</sup>  
(infigratinib) capsules

**Days 15-21**

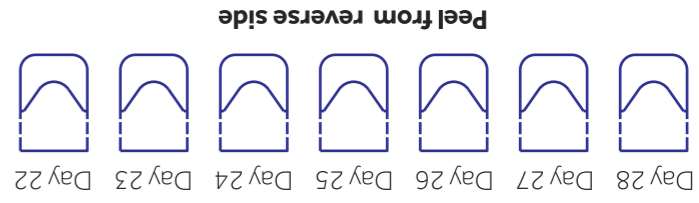
25 mg per capsule

Take all three capsules at the same time daily

Push from reverse to release capsule



**Days 22-28 Treatment-free Days**



(b) (4)

NDC-72730-111-01  
Rx Only

TRUSELTIQ<sup>™</sup>  
(infirgratinib) capsules

Oral use

**100 mg daily dose**

Take one 100 mg capsule once daily

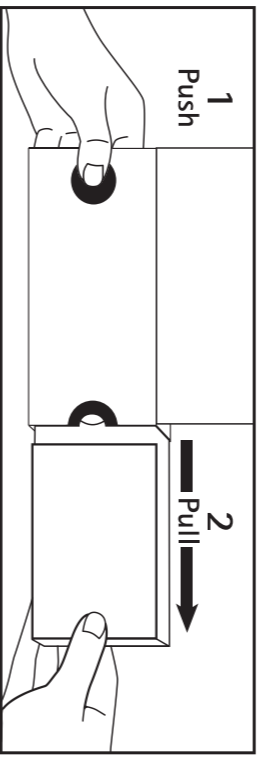
**Blister card contains one treatment cycle**

<b>Days 1-21</b>	<b>Days 22-28</b>
<b>100 mg</b>	Treatment-free days
21 capsules	

LIFT PANEL

TRUSELTIQ<sup>™</sup>  
(infirgratinib) capsules

**100 mg daily dose**



TO OPEN

**1-PUSH AND HOLD**

Use thumb to push the button gently, and hold button.

**2-PULL**

While holding the button down, pull out card.

TRUSELTIQ<sup>™</sup>  
(infirgratinib) capsules

100 mg daily dose

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3000 Central Expressway, Suite 400  
Brisbane, CA 94005



PCR-740-14321

**Days 22-28:** Treatment-free days. Do not take any doses for 7 days.  
Store at room temperature between 68°F to 77°F (20°C to 25°C)

**Days 1-21:** Take one 100 mg capsule once daily on an empty stomach (1 hour before or 2 hours after a meal). Swallow capsules whole with a glass of water. Do not open, crush, chew, or dissolve capsules.

**Recommended Dosage:** See Prescribing Information. **Dosing Instructions:** Take TRUSELTIQ for 21 consecutive days, then take a 7-day break. Complete this 28-day treatment cycle before starting the next 28-day treatment cycle.

**100 mg daily dose**

TRUSELTIQ<sup>™</sup>  
(infirgratinib) capsules

100 mg daily dose

TRUSELTIQ<sup>™</sup>  
(infirgratinib) capsules

TRUSELTIQ<sup>™</sup>  
(infirgratinib) capsules



PS

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**TRUSELTIQ<sup>™</sup>**  
(infirgralimib) capsules

**Days 1-7**  
100 mg per capsule  
Take one capsule at the same time daily

Day 1 Day 2 Day 3 Day 4 Day 5 Day 6 Day 7

**Days 8-14**  
100 mg per capsule  
Take one capsule at the same time daily

Day 8 Day 9 Day 10 Day 11 Day 12 Day 13 Day 14

**Days 15-21**  
100 mg per capsule  
Take one capsule at the same time daily

Day 15 Day 16 Day 17 Day 18 Day 19 Day 20 Day 21

**Days 22-28**  
Treatment-free Days

Day 22 Day 23 Day 24 Day 25 Day 26 Day 27 Day 28

**Enter start date:**

**Push to release capsule**

**Peel here**

PCR-740-14341

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(b) (4)

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PCR-740-14342

**Days 1-7**

**100 mg per capsule**

**Take one capsule at the same time daily**



Day 1



Day 2



Day 3



Day 4



Day 5



Day 6



Day 7

Push from reverse to release capsule

**TRUSELTIQ<sup>™</sup>**  
(infigratinib) capsules

**Days 8-14**

**100 mg per capsule**

**Take one capsule at the same time daily**



Day 8



Day 9



Day 10



Day 11



Day 12



Day 13



Day 14

Push from reverse to release capsule

**Days 15-21**

**Take one capsule at the same time daily**



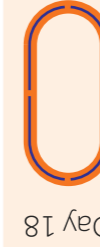
Day 15



Day 16



Day 17



Day 18



Day 19



Day 20



Day 21

Push from reverse to release capsule

**Days 22-28**

**Treatment-free Days**



Day 22



Day 23



Day 24



Day 25



Day 26



Day 27



Day 28

Peel from reverse

**100 mg per capsule**

(b) (4)



NDC-72730-101-01  
Rx Only

**TRUSELTIQ**  
(infirgratinib) capsules

Oral use

**125 mg daily dose**  
Take one 100 mg capsule  
and one 25 mg capsule  
together once daily

**Blister card contains one treatment cycle  
(42 capsules total)**

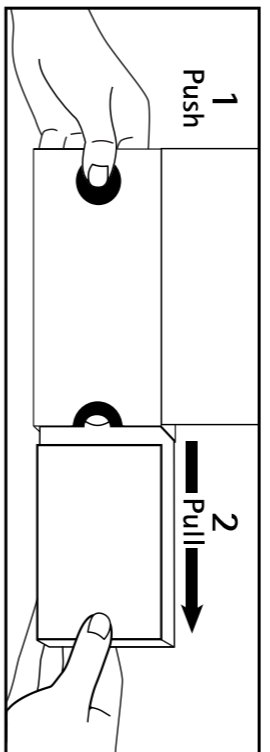
**Days 1-21**  
100 mg 21 capsules | 25 mg 21 capsules

**Days 22-28:** Treatment-free days

LIFT PANEL

**TRUSELTIQ**  
(infirgratinib) capsules

**125 mg daily dose**



**TO OPEN**

**1-PUSH AND HOLD**

Use thumb to push the button  
gently, and hold button.

**2-PULL**

While holding the button  
down, pull out card.

**TRUSELTIQ**  
(infirgratinib) capsules

**125 mg daily dose**

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**QED Therapeutics**  
17000 W. BLOSSOM AVE. | SUITE 100  
8000 Marina Blvd. #400  
Brisbane, CA 94005



PCR-740-14816

**TRUSELTIQ**  
(infirgratinib) capsules

**TRUSELTIQ**  
(infirgratinib) capsules

**125 mg daily dose**

**TRUSELTIQ**  
(infirgratinib) capsules

**125 mg daily dose**

**Recommended Dosage:** See Prescribing Information.  
**Dosing Instructions:** Take TRUSELTIQ for 21 consecutive days, then take a 7-day break. Complete this 28-day treatment cycle before starting the next 28-day treatment cycle.

**Days 1-21:** Take one 100 mg capsule and one 25 mg capsule once daily on an empty stomach (1 hour before or 2 hours after a meal). Swallow capsules whole with a glass of water. Do not open, crush, chew, or dissolve capsules.

**Days 22-28:** Treatment-free days. Do not take any doses for 7 days.

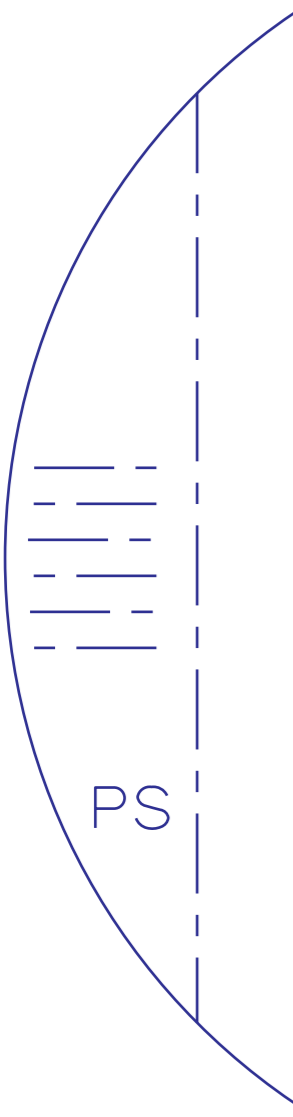
Store at room temperature between 68°F to 77°F (20°C to 25°C)



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PCR-740-14325

TRUSELTIQ<sup>™</sup>  
(infigratinib) capsules

**Days 8-14**

**25 mg per capsule 100 mg per capsule**  
Take both capsules at the same time daily

Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14

**Days 1-7**

**25 mg per capsule 100 mg per capsule**  
Take both capsules at the same time daily

Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7

**Enter start date:**

Push to release capsule

Push to release capsule

**Days 22-28**  
Treatment-free Days

Day 22	Day 23	Day 24	Day 25	Day 26	Day 27	Day 28

**Days 15-21**

Take both capsules at the same time daily

Day 15	Day 16	Day 17	Day 18	Day 19	Day 20	Day 21

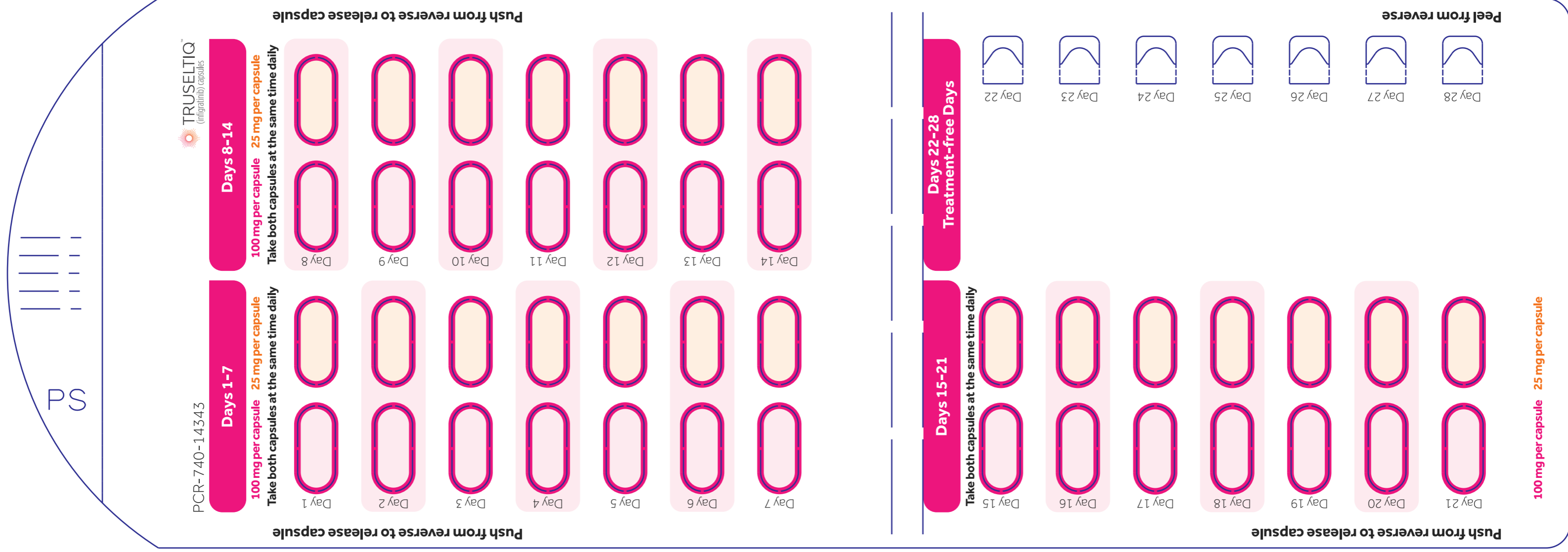
Peel here

**25 mg per capsule 100 mg per capsule**



(b) (4)

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(b) (4)

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/s/  
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PAUL G KLUETZ  
05/28/2021 12:57:35 PM