

HIGHLIGHTS OF PRESCRIBING INFORMATION

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

TAFINLAR (dabrafenib) capsules for oral use

Initial U.S. Approval: 2013

INDICATIONS AND USAGE

TAFINLAR is a kinase inhibitor indicated for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E mutation as detected by an FDA-approved test. (1, 2.1)

Limitation of use: TAFINLAR is not indicated for treatment of patients with wild-type BRAF melanoma. (1, 5.2)

DOSAGE AND ADMINISTRATION

- Confirm the presence of BRAF V600E mutation in tumor specimens prior to initiation of treatment with TAFINLAR. (2.1)
- The recommended dose is 150 mg orally twice daily taken at least 1 hour before or at least 2 hours after a meal. (2.2)

DOSAGE FORMS AND STRENGTHS

Capsules: 50 mg, 75 mg. (3)

CONTRAINDICATIONS

- None. (4)

WARNINGS AND PRECAUTIONS

- New Primary Cutaneous Malignancies: Perform dermatologic evaluations prior to initiation of therapy, every 2 months while on therapy, and for up to 6 months following discontinuation of TAFINLAR. (5.1)
- Tumor Promotion in BRAF Wild-Type Melanoma: Increased cell proliferation can occur with BRAF inhibitors. (5.2)
- Serious Febrile Drug Reactions: Withhold TAFINLAR if fever $\geq 101.3^{\circ}\text{F}$ or complicated fever occurs. (5.3)
- Hyperglycemia: Monitor serum glucose levels in patients with pre-existing diabetes or hyperglycemia. (5.4)
- Uveitis and Iritis: Monitor patients routinely for visual symptoms. (5.5)

- Glucose-6-Phosphate Dehydrogenase Deficiency: Closely monitor for hemolytic anemia. (5.6)
- Embryofetal Toxicity: Can cause fetal harm. Advise females of reproductive potential of potential risk to a fetus. TAFINLAR may render hormonal contraceptives less effective and an alternative method of contraception should be used. (5.7, 8.1)

ADVERSE REACTIONS

Most common adverse reactions ($\geq 20\%$) for TAFINLAR are hyperkeratosis, headache, pyrexia, arthralgia, papilloma, alopecia, and palmar-plantar erythrodysesthesia syndrome. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact GlaxoSmithKline at 1-888-825-5249 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- Concurrent administration of strong inhibitors of CYP3A4 or CYP2C8 is not recommended. (7.1)
- Concurrent administration of strong inducers of CYP3A4 or CYP2C8 is not recommended. (7.1)
- Drugs that increase gastric pH may decrease dabrafenib concentrations. (7.1)
- Concomitant use with agents that are sensitive substrates of CYP3A4, CYP2C8, CYP2C9, CYP2C19, or CYP2B6 may result in loss of efficacy of these agents. (7.2)

USE IN SPECIFIC POPULATIONS

- Nursing Mothers: Discontinue drug or nursing. (8.3)
- Females and Males of Reproductive Potential: Advise female patients to use highly effective contraception during treatment and for 4 weeks following discontinuation of treatment. Advise male patients of potential risk for impaired spermatogenesis. (8.6)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 12/2013

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS AND USAGE

2 DOSAGE AND ADMINISTRATION

- 2.1 Patient Selection
- 2.2 Recommended Dosing
- 2.3 Dose Modifications

3 DOSAGE FORMS AND STRENGTHS

4 CONTRAINDICATIONS

5 WARNINGS AND PRECAUTIONS

- 5.1 New Primary Cutaneous Malignancies
- 5.2 Tumor Promotion in BRAF Wild-Type Melanoma
- 5.3 Serious Febrile Drug Reactions
- 5.4 Hyperglycemia
- 5.5 Uveitis and Iritis
- 5.6 Glucose-6-Phosphate Dehydrogenase Deficiency
- 5.7 Embryofetal Toxicity

6 ADVERSE REACTIONS

- 6.1 Clinical Trials Experience

7 DRUG INTERACTIONS

- 7.1 Effects of Other Drugs on Dabrafenib
- 7.2 Effects of Dabrafenib on Other Drugs

8 USE IN SPECIFIC POPULATIONS

- 8.1 Pregnancy
- 8.3 Nursing Mothers
- 8.4 Pediatric Use
- 8.5 Geriatric Use
- 8.6 Females and Males of Reproductive Potential
- 8.7 Hepatic Impairment
- 8.8 Renal Impairment

10 OVERDOSAGE

11 DESCRIPTION

12 CLINICAL PHARMACOLOGY

- 12.1 Mechanism of Action
- 12.3 Pharmacokinetics

13 NONCLINICAL TOXICOLOGY

- 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
- 13.2 Animal Toxicology and/or Pharmacology

14 CLINICAL STUDIES

16 HOW SUPPLIED/STORAGE AND HANDLING

17 PATIENT COUNSELING INFORMATION

*Sections or subsections omitted from the full prescribing information are not listed.

1 **FULL PRESCRIBING INFORMATION**

2 **1 INDICATIONS AND USAGE**

3 TAFINLAR[®] is indicated for the treatment of patients with unresectable or metastatic melanoma
4 with BRAF V600E mutation as detected by an FDA-approved test.

5 **Limitation of use:** TAFINLAR is not indicated for treatment of patients with wild-type BRAF
6 melanoma [see *Warnings and Precautions (5.2)*].

7 **2 DOSAGE AND ADMINISTRATION**

8 **2.1 Patient Selection**

9 Confirm the presence of BRAF V600E mutation in tumor specimens prior to initiation of
10 treatment with TAFINLAR [see *Warnings and Precautions (5.2)*]. Information on FDA-
11 approved tests for the detection of BRAF V600 mutations in melanoma is available at
12 <http://www.fda.gov/CompanionDiagnostics>.

13 **2.2 Recommended Dosing**

14 The recommended dose for TAFINLAR is 150 mg orally taken twice daily, approximately 12
15 hours apart, until disease progression or unacceptable toxicity occurs. Take either at least 1 hour
16 before or at least 2 hours after a meal [see *Clinical Pharmacology (12.3)*].

17 A missed dose can be taken up to 6 hours prior to the next dose. Do not open, crush, or break
18 TAFINLAR capsule.

19 **2.3 Dose Modifications**

20 For New Primary Cutaneous Malignancies: No dose modifications are recommended.

21

22 **Table 1. Recommended Dose Modifications for TAFINLAR**

Target Organ	Adverse Reactions^a	Dose Modification
Febrile Drug Reaction	<ul style="list-style-type: none"> • Fever of 101.3°F to 104°F 	Withhold TAFINLAR until adverse reaction resolves. Then resume TAFINLAR at same dose or at a reduced dose level (see Table 2).
	<ul style="list-style-type: none"> • Fever higher than 104°F • Fever complicated by rigors, hypotension, dehydration, or renal failure 	Either <ul style="list-style-type: none"> • Permanently discontinue TAFINLAR Or <ul style="list-style-type: none"> • Withhold TAFINLAR until adverse reaction resolves. Then resume TAFINLAR at a reduced dose level (see Table 2).
Other	<ul style="list-style-type: none"> • Intolerable Grade 2 Adverse Reactions • Any Grade 3 Adverse Reactions 	Withhold TAFINLAR until adverse reaction resolves to Grade 1 or less. Then resume TAFINLAR at a reduced dose level (see Table 2).
	<ul style="list-style-type: none"> • First occurrence of Any Grade 4 Adverse Reaction 	Either <ul style="list-style-type: none"> • Permanently discontinue TAFINLAR Or <ul style="list-style-type: none"> • Withhold TAFINLAR until adverse reaction resolves to Grade 1 or less. Then resume TAFINLAR at a reduced dose level (see Table 2).
	<ul style="list-style-type: none"> • Recurrent Grade 4 Adverse Reaction • Intolerable Grade 2 or Any Grade 3 or 4 Adverse Reaction on TAFINLAR 50 mg twice daily 	Permanently discontinue TAFINLAR.

23 ^a Common Terminology Criteria for Adverse Events (CTCAE) version 4.0.

24

25 **Table 2. Recommended Dose Reductions for TAFINLAR**

Dose Reductions	Dose and Schedule
First dose reduction	100 mg orally twice daily
Second dose reduction	75 mg orally twice daily
Third dose reduction	50 mg orally twice daily
If unable to tolerate 50 mg twice daily	Discontinue TAFINLAR

26

27 **3 DOSAGE FORMS AND STRENGTHS**

28 50 mg Capsules: Dark red capsule imprinted with ‘GS TEW’ and ‘50 mg’.

29 75 mg Capsules: Dark pink capsule imprinted with ‘GS LHF’ and ‘75 mg’.

30 **4 CONTRAINDICATIONS**

31 None.

32 **5 WARNINGS AND PRECAUTIONS**

33 **5.1 New Primary Cutaneous Malignancies**

34 TAFINLAR results in an increased incidence of cutaneous squamous cell carcinoma,
35 keratoacanthoma, and melanoma. In Trial 1, cutaneous squamous cell carcinomas and
36 keratoacanthomas (cuSCC) occurred in 7% (14/187) of patients treated with TAFINLAR and in
37 none of the patients treated with dacarbazine. Across clinical trials of TAFINLAR (n = 586), the
38 incidence of cuSCC was 11%. The median time to first cuSCC was 9 weeks (range: 1 to 53
39 weeks). Of those patients who developed a cuSCC, approximately 33% developed one or more
40 cuSCC with continued TAFINLAR. The median time between diagnosis of the first cuSCC and
41 the second cuSCC was 6 weeks.

42 In Trial 1, the incidence of new primary malignant melanomas was 2% (3/187) for patients
43 receiving TAFINLAR while no chemotherapy-treated patient was diagnosed with new primary
44 malignant melanoma.

45 Perform dermatologic evaluations prior to initiation of TAFINLAR, every 2 months while on
46 therapy, and for up to 6 months following discontinuation of TAFINLAR.

47 **5.2 Tumor Promotion in BRAF Wild-Type Melanoma**

48 In vitro experiments have demonstrated paradoxical activation of MAP-kinase signaling and
49 increased cell proliferation in BRAF wild-type cells which are exposed to BRAF inhibitors.
50 Confirm evidence of BRAF V600E mutation status prior to initiation of TAFINLAR [see
51 *Indications and Usage (1) and Dosage and Administration (2.1)*].

52 **5.3 Serious Febrile Drug Reactions**

53 In Trial 1, serious febrile drug reactions, defined as serious cases of fever or fever of any severity
54 accompanied by hypotension, rigors or chills, dehydration, or renal failure in the absence of
55 another identifiable cause (e.g., infection) occurred in 3.7% (7/187) of patients treated with
56 TAFINLAR and in none of the patients treated with dacarbazine. The incidence of fever (serious
57 and non-serious) was 28% in patients treated with TAFINLAR and 10% in patients treated with
58 dacarbazine. In patients treated with TAFINLAR, the median time to initial onset of fever (any
59 severity) was 11 days (range: 1 to 202 days) and the median duration of fever was 3 days (range:
60 1 to 129 days).

61 Withhold TAFINLAR for fever of 101.3°F or greater or for any serious febrile drug reaction and
62 evaluate for signs and symptoms of infection. Refer to Table 1 for recommended dose
63 modifications for adverse reactions [*see Dosage and Administration (2.3)*]. Prophylaxis with
64 antipyretics may be required when resuming TAFINLAR.

65 **5.4 Hyperglycemia**

66 Hyperglycemia requiring an increase in the dose of, or initiation of insulin or oral hypoglycemic
67 agent therapy can occur with TAFINLAR. In Trial 1, five of 12 patients with a history of
68 diabetes required more intensive hypoglycemic therapy while taking TAFINLAR. The incidence
69 of Grade 3 hyperglycemia based on laboratory values was 6% (12/187) in patients treated with
70 TAFINLAR compared to none of the dacarbazine-treated patients.

71 Monitor serum glucose levels as clinically appropriate during treatment with TAFINLAR in
72 patients with pre-existing diabetes or hyperglycemia. Advise patients to report symptoms of
73 severe hyperglycemia such as excessive thirst or any increase in the volume or frequency of
74 urination.

75 **5.5 Uveitis and Iritis**

76 Uveitis (including iritis) occurred in 1% (6/586) of patients treated with TAFINLAR across
77 clinical trials. Symptomatic treatment employed in clinical trials included steroid and mydriatic
78 ophthalmic drops. Monitor patients for visual signs and symptoms of uveitis (e.g., change in
79 vision, photophobia, and eye pain).

80 **5.6 Glucose-6-Phosphate Dehydrogenase Deficiency**

81 TAFINLAR, which contains a sulfonamide moiety, confers a potential risk of hemolytic anemia
82 in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency. Closely observe
83 patients with G6PD deficiency for signs of hemolytic anemia.

84 **5.7 Embryofetal Toxicity**

85 Based on its mechanism of action, TAFINLAR can cause fetal harm when administered to a
86 pregnant woman. Dabrafenib was teratogenic and embryotoxic in rats at doses three times
87 greater than the human exposure at the recommended clinical dose. If this drug is used during

88 pregnancy or if the patient becomes pregnant while taking this drug, the patient should be
89 apprised of the potential hazard to a fetus [see *Use in Specific Populations (8.1)*].

90 Advise female patients of reproductive potential to use a highly effective non-hormonal method
91 of contraception during treatment and for 4 weeks after treatment since TAFINLAR can render
92 hormonal contraceptives ineffective. Advise patients to contact their healthcare provider if they
93 become pregnant, or if pregnancy is suspected, while taking TAFINLAR [see *Drug Interactions*
94 *(7.2)*, *Use in Specific Populations (8.6)*].

95 **6 ADVERSE REACTIONS**

96 The following adverse reactions are discussed in greater detail in another section of the label.

- 97 • New Primary Cutaneous Malignancies [see *Warnings and Precautions (5.1)*]
- 98 • Tumor Promotion in BRAF Wild-Type Melanoma [see *Warnings and Precautions (5.2)*]
- 99 • Serious Febrile Drug Reactions [see *Warnings and Precautions (5.3)*]
- 100 • Hyperglycemia [see *Warnings and Precautions (5.4)*]
- 101 • Uveitis and Iritis [see *Warnings and Precautions (5.5)*]

102 **6.1 Clinical Trials Experience**

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

106 The safety of TAFINLAR was evaluated in 586 patients with BRAF V600 mutation-positive
107 unresectable or metastatic melanoma, previously treated or untreated, who received TAFINLAR
108 150 mg orally twice daily as monotherapy until disease progression or unacceptable toxicity,
109 including 181 patients treated for at least 6 months and 86 additional patients treated for more
110 than 12 months. TAFINLAR was studied in open-label, single-arm trials and in an open-label,
111 randomized, active-controlled trial. The median daily dose of TAFINLAR was 300 mg (range:
112 118 to 300 mg).

113 Table 3 and Table 4 present adverse drug reactions and laboratory abnormalities identified from
114 analyses of Trial 1 [see *Clinical Studies (14)*]. Trial 1, a multi-center, international, open-label,
115 randomized (3:1), controlled trial allocated 250 patients with unresectable or metastatic BRAF
116 V600E mutation-positive melanoma to receive TAFINLAR 150 mg orally twice daily (n = 187)
117 or dacarbazine 1,000 mg/m² intravenously every 3 weeks (n = 63). The trial excluded patients
118 with abnormal left ventricular ejection fraction or cardiac valve morphology (≥Grade 2),
119 corrected QT interval ≥480 milliseconds on electrocardiogram, or a known history of glucose-6-
120 phosphate dehydrogenase deficiency. The median duration on treatment was 4.9 months for
121 patients treated with TAFINLAR and 2.8 months for dacarbazine-treated patients. The

122 population exposed to TAFINLAR was 60% male, 99% white, and had a median age of 53
123 years.

124 The most commonly occurring adverse reactions ($\geq 20\%$) in patients treated with TAFINLAR
125 were, in order of decreasing frequency: hyperkeratosis, headache, pyrexia, arthralgia, papilloma,
126 alopecia, and palmar-plantar erythrodysesthesia syndrome (PPES).

127 The incidence of adverse events resulting in permanent discontinuation of study medication in
128 Trial 1 was 3% for patients treated with TAFINLAR and 3% for patients treated with
129 dacarbazine. The most frequent ($\geq 2\%$) adverse reactions leading to dose reduction of
130 TAFINLAR were pyrexia (9%), PPES (3%), chills (3%), fatigue (2%), and headache (2%).
131

132 **Table 3. Selected Common Adverse Reactions Occurring in ≥10% (All Grades) or ≥2%**
 133 **(Grades 3 or 4) of Patients Treated with TAFINLAR^a**

Primary System Organ Class Preferred Term	TAFINLAR N = 187		Dacarbazine N = 59	
	All Grades (%)	Grades 3 and 4 ^b (%)	All Grades (%)	Grades 3 and 4 (%)
Skin and subcutaneous tissue disorders				
Hyperkeratosis	37	1	0	0
Alopecia	22	NA ^f	2	NA ^f
Palmar-plantar erythrodysesthesia syndrome	20	2	2	0
Rash	17	0	0	0
Nervous system disorders				
Headache	32	0	8	0
General disorders and administration site conditions				
Pyrexia	28	3	10	0
Musculoskeletal and connective tissue disorders				
Arthralgia	27	1	2	0
Back pain	12	3	7	0
Myalgia	11	0	0	0
Neoplasms benign, malignant and unspecified (including cysts and polyps)				
Papilloma ^c	27	0	2	0
cuSCC ^{d, e}	7	4	0	0
Gastrointestinal disorders				
Constipation	11	2	14	0
Respiratory, thoracic, and mediastinal disorders				
Cough	12	0	5	0
Infections and infestations				
Nasopharyngitis	10	0	3	0

134 ^a Adverse drug reactions, reported using MedDRA and graded using CTCAE version 4.0 for
 135 assessment of toxicity.

136 ^b Grade 4 adverse reactions limited to hyperkeratosis (n = 1) and constipation (n = 1).

137 ^c Includes skin papilloma and papilloma.

138 ^d Includes squamous cell carcinoma of the skin and keratoacanthoma.

139 ^e Cases of cutaneous squamous cell carcinoma were required to be reported as Grade 3 per
 140 protocol.

141 ^f NA = not applicable

142

143 **Table 4. Incidence of Laboratory Abnormalities Increased from Baseline Occurring at a**
 144 **Higher Incidence in Patients Treated with TAFINLAR in Trial 1 [Between Arm Difference**
 145 **of $\geq 5\%$ (All Grades) or $\geq 2\%$ (Grades 3 or 4)]**

	Dabrafenib N = 187		DTIC N = 59	
	All Grades (%)	Grades 3 and 4 (%)	All Grades (%)	Grades 3 and 4 (%)
Hyperglycemia	50	6	43	0
Hypophosphatemia	37	6 ^a	14	2
Increased Alkaline phosphatase	19	0	14	2
Hyponatremia	8	2	3	0

146 ^a Grade 4 laboratory abnormality limited to hypophosphatemia (n = 1).
 147

148 Other clinically important adverse reactions observed in <10% of patients (N = 586) treated with
 149 TAFINLAR were:

150 *Gastrointestinal Disorders:* Pancreatitis.

151 *Immune System Disorders:* Hypersensitivity manifesting as bullous rash.

152 *Renal and Urinary Disorders:* Interstitial nephritis.

153 **7 DRUG INTERACTIONS**

154 **7.1 Effects of Other Drugs on Dabrafenib**

155 Drugs that Inhibit or Induce Drug-Metabolizing Enzymes: Dabrafenib is primarily
 156 metabolized by CYP2C8 and CYP3A4. Strong inhibitors or inducers of CYP3A4 or CYP2C8
 157 may increase or decrease, respectively, concentrations of dabrafenib [*see Clinical Pharmacology*
 158 (*12.3*)]. Substitution of strong inhibitors or strong inducers of CYP3A4 or CYP2C8 is
 159 recommended during treatment with TAFINLAR. If concomitant use of strong inhibitors (e.g.,
 160 ketoconazole, nefazodone, clarithromycin, gemfibrozil) or strong inducers (e.g., rifampin,
 161 phenytoin, carbamazepine, phenobarbital, St John's wort) of CYP3A4 or CYP2C8 is
 162 unavoidable, monitor patients closely for adverse reactions when taking strong inhibitors or loss
 163 of efficacy when taking strong inducers.

164 Drugs that Affect Gastric pH: Drugs that alter the pH of the upper GI tract (e.g., proton pump
 165 inhibitors, H₂-receptor antagonists, antacids) may alter the solubility of dabrafenib and reduce its
 166 bioavailability. However, no formal clinical trial has been conducted to evaluate the effect of
 167 gastric pH-altering agents on the systemic exposure of dabrafenib. When TAFINLAR is

168 coadministered with a proton pump inhibitor, H₂-receptor antagonist, or antacid, systemic
169 exposure of dabrafenib may be decreased and the effect on efficacy of TAFINLAR is unknown.

170 **7.2 Effects of Dabrafenib on Other Drugs**

171 Dabrafenib induces CYP3A4 and CYP2C9. Dabrafenib decreased the systemic exposures of
172 midazolam (a CYP3A4 substrate), S-warfarin (a CYP2C9 substrate), and R-warfarin (a
173 CYP3A4/CYP1A2 substrate) [*see Clinical Pharmacology (12.3)*]. Monitor international
174 normalized ratio (INR) levels more frequently in patients receiving warfarin during initiation or
175 discontinuation of dabrafenib. Co-administration of TAFINLAR with other substrates of these
176 enzymes, including dexamethasone or hormonal contraceptives, can result in decreased
177 concentrations and loss of efficacy [*see Use in Specific Populations (8.1, 8.6)*]. Substitute for
178 these medications or monitor patients for loss of efficacy if use of these medications is
179 unavoidable.

180 **8 USE IN SPECIFIC POPULATIONS**

181 **8.1 Pregnancy**

182 Pregnancy Category D

183 Risk Summary: Based on its mechanism of action, TAFINLAR can cause fetal harm when
184 administered to a pregnant woman. Dabrafenib was teratogenic and embryotoxic in rats at doses
185 3 times greater than the human exposure at the recommended clinical dose of 150 mg twice daily
186 based on AUC. If this drug is used during pregnancy or if the patient becomes pregnant while
187 taking this drug, the patient should be apprised of the potential hazard to a fetus [*see Warnings*
188 *and Precautions (5.7)*].

189 Animal Data: In a combined female fertility and embryofetal development study in rats,
190 developmental toxicity consisted of embryo-lethality, ventricular septal defects, and variation in
191 thymic shape at a dabrafenib dose of 300 mg/kg/day (approximately 3 times the human exposure
192 at the recommended dose based on AUC). At doses of 20 mg/kg/day or greater (equivalent to the
193 human exposure at the recommended dose based on AUC), rats demonstrated delays in skeletal
194 development and reduced fetal body weight.

195 **8.3 Nursing Mothers**

196 It is not known whether this drug is present in human milk. Because many drugs are present in
197 human milk and because of the potential for serious adverse reactions from TAFINLAR in
198 nursing infants, a decision should be made whether to discontinue nursing or discontinue the
199 drug, taking into account the importance of the drug to the mother.

200 **8.4 Pediatric Use**

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

202 **8.5 Geriatric Use**

203 One hundred and twenty-six (22%) of 586 patients in clinical trials of TAFINLAR and 40 (21%)
204 of the 187 patients receiving TAFINLAR in Trial 1 were ≥ 65 years of age. No overall
205 differences in the effectiveness or safety of TAFINLAR were observed in the elderly in Trial 1.

206 **8.6 Females and Males of Reproductive Potential**

207 Contraception:

208 Females

209 Advise female patients of reproductive potential to use highly effective contraception during
210 treatment and for 4 weeks after treatment. Counsel patients to use a non-hormonal method of
211 contraception since TAFINLAR can render hormonal contraceptives ineffective. Advise patients
212 to contact their healthcare provider if they become pregnant, or if pregnancy is suspected, while
213 taking TAFINLAR [see *Warnings and Precautions (5.7)*, *Drug Interactions (7.1)*, *Use in*
214 *Specific Populations (8.1)*].

215 Infertility:

216 Males

217 Effects on spermatogenesis have been observed in animals. Advise male patients of the potential
218 risk for impaired spermatogenesis, and to seek counseling on fertility and family planning
219 options prior to starting treatment with TAFINLAR [see *Nonclinical Toxicology (13.1)*].

220 **8.7 Hepatic Impairment**

221 No formal pharmacokinetic trial in patients with hepatic impairment has been conducted. Dose
222 adjustment is not recommended for patients with mild hepatic impairment based on the results of
223 the population pharmacokinetic analysis. As hepatic metabolism and biliary secretion are the
224 primary routes of elimination of dabrafenib and its metabolites, patients with moderate to severe
225 hepatic impairment may have increased exposure. An appropriate dose has not been established
226 for patients with moderate to severe hepatic impairment [see *Clinical Pharmacology (12.3)*].

227 **8.8 Renal Impairment**

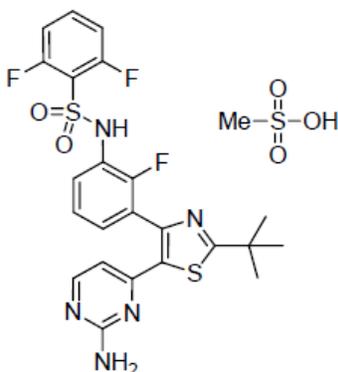
228 No formal pharmacokinetic trial in patients with renal impairment has been conducted. Dose
229 adjustment is not recommended for patients with mild or moderate renal impairment based on
230 the results of the population pharmacokinetic analysis. An appropriate dose has not been
231 established for patients with severe renal impairment [see *Clinical Pharmacology (12.3)*].

232 **10 OVERDOSAGE**

233 There is no information on overdosage of TAFINLAR.

234 **11 DESCRIPTION**

235 Dabrafenib mesylate is a kinase inhibitor. The chemical name for dabrafenib mesylate is N-{3-
236 [5-(2-Amino-4-pyrimidinyl)-2-(1,1-dimethylethyl)-1,3-thiazol-4-yl]-2-fluorophenyl}-2,6-
237 difluorobenzene sulfonamide, methanesulfonate salt. It has the molecular formula
238 $C_{23}H_{20}F_3N_5O_2S_2 \cdot CH_4O_3S$ and a molecular weight of 615.68. Dabrafenib mesylate has the
239 following chemical structure.



240

241

242 Dabrafenib mesylate is a white to slightly colored solid with three pK_a s: 6.6, 2.2, and -1.5. It is
243 very slightly soluble at pH 1 and practically insoluble above pH 4 in aqueous media.

244 TAFINLAR (dabrafenib) capsules are supplied as 50 mg and 75 mg capsules for oral
245 administration. Each 50 mg capsule contains 59.25 mg dabrafenib mesylate equivalent to 50 mg
246 of dabrafenib free base. Each 75 mg capsule contains 88.88 mg dabrafenib mesylate equivalent
247 to 75 mg of dabrafenib free base.

248 The inactive ingredients of TAFINLAR are colloidal silicon dioxide, magnesium stearate, and
249 microcrystalline cellulose. Capsule shells contain hypromellose, red iron oxide (E172), and
250 titanium dioxide (E171).

251 **12 CLINICAL PHARMACOLOGY**

252 **12.1 Mechanism of Action**

253 Dabrafenib is an inhibitor of some mutated forms of BRAF kinases with in vitro IC_{50} values of
254 0.65, 0.5, and 1.84 nM for BRAF V600E, BRAF V600K, and BRAF V600D enzymes,
255 respectively. Dabrafenib also inhibits wild-type BRAF and CRAF kinases with IC_{50} values of 3.2
256 and 5.0 nM, respectively, and other kinases such as SIK1, NEK11, and LIMK1 at higher
257 concentrations. Some mutations in the BRAF gene, including those that result in BRAF V600E,
258 can result in constitutively activated BRAF kinases that may stimulate tumor cell growth [*see*
259 *Indications and Usage (1)*]. Dabrafenib inhibits BRAF V600 mutation-positive melanoma cell
260 growth in vitro and in vivo.

261 **12.3 Pharmacokinetics**

262 **Absorption:** After oral administration, median time to achieve peak plasma concentration (T_{max})
263 is 2 hours. Mean absolute bioavailability of oral dabrafenib is 95%. Following a single dose,
264 dabrafenib exposure (C_{max} and AUC) increased in a dose-proportional manner across the dose
265 range of 12 to 300 mg, but the increase was less than dose-proportional after repeat twice daily
266 dosing. After repeat twice daily dosing of 150 mg, the mean accumulation ratio was 0.73 and the
267 inter-subject variability (CV%) of AUC at steady-state was 38%.

268 Administration of dabrafenib with a high-fat meal decreased C_{max} by 51%, decreased AUC by
269 31%, and delayed median T_{max} by 3.6 hours as compared to the fasted state [*see Dosage and*
270 *Administration (2.2)*].

271 **Distribution:** Dabrafenib is 99.7% bound to human plasma proteins. The apparent volume of
272 distribution (V_d/F) is 70.3 L.

273 **Metabolism:** The metabolism of dabrafenib is primarily mediated by CYP2C8 and CYP3A4 to
274 form hydroxy-dabrafenib. Hydroxy-dabrafenib is further oxidized via CYP3A4 to form carboxy-
275 dabrafenib and subsequently excreted in bile and urine. Carboxy-dabrafenib is decarboxylated to
276 form desmethyl-dabrafenib; desmethyl-dabrafenib may be reabsorbed from the gut. Desmethyl-
277 dabrafenib is further metabolized by CYP3A4 to oxidative metabolites. Hydroxy-dabrafenib
278 terminal half-life (10 hours) parallels that of dabrafenib while the carboxy- and desmethyl-
279 dabrafenib metabolites exhibited longer half-lives (21 to 22 hours). Mean metabolite-to-parent
280 AUC ratios following repeat-dose administration are 0.9, 11, and 0.7 for hydroxy-, carboxy-, and
281 desmethyl-dabrafenib, respectively. Based on systemic exposure, relative potency, and
282 pharmacokinetic properties, both hydroxy- and desmethyl-dabrafenib are likely to contribute to
283 the clinical activity of dabrafenib.

284 **Elimination:** The mean terminal half-life of dabrafenib is 8 hours after oral administration. The
285 apparent clearance of dabrafenib is 17.0 L/h after single dosing and 34.4 L/h after 2 weeks of
286 twice daily dosing.

287 Fecal excretion is the major route of elimination accounting for 71% of radioactive dose while
288 urinary excretion accounted for 23% of total radioactivity as metabolites only.

289 **Specific Populations:**

290 **Age, Body Weight and Gender:** Based on the population pharmacokinetics analysis, age has
291 no effect on dabrafenib pharmacokinetics. Pharmacokinetic differences based on gender and on
292 weight are not clinically relevant.

293 **Pediatric:** Pharmacokinetics of dabrafenib have not been studied in pediatric patients.

294 **Renal:** No formal pharmacokinetic trial in patients with renal impairment has been conducted.
295 The pharmacokinetics of dabrafenib were evaluated using a population analysis in 233 patients
296 with mild renal impairment (GFR 60 to 89 mL/min/1.73 m²) and 30 patients with moderate renal

297 impairment (GFR 30 to 59 mL/min/1.73 m²) enrolled in clinical trials. Mild or moderate renal
298 impairment has no effect on systemic exposure to dabrafenib and its metabolites. No data are
299 available in patients with severe renal impairment.

300 Hepatic: No formal pharmacokinetic trial in patients with hepatic impairment has been
301 conducted. The pharmacokinetics of dabrafenib were evaluated using a population analysis in 65
302 patients with mild hepatic impairment enrolled in clinical trials. Mild hepatic impairment has no
303 effect on systemic exposure to dabrafenib and its metabolites. No data are available in patients
304 with moderate to severe hepatic impairment.

305 Drug Interactions:

306 In vitro studies show that dabrafenib is a substrate of CYP3A4 and CYP2C8 while hydroxy-
307 dabrafenib and desmethyl-dabrafenib are CYP3A4 substrates. Co-administration of dabrafenib
308 75 mg twice daily and ketoconazole 400 mg once daily (a strong CYP3A4 inhibitor) for 4 days
309 increased dabrafenib AUC by 71%, hydroxy-dabrafenib AUC by 82%, and desmethyl-
310 dabrafenib AUC by 68%. Co-administration of dabrafenib 75 mg twice daily and gemfibrozil
311 600 mg twice daily (a strong CYP2C8 inhibitor) for 4 days increased dabrafenib AUC by 47%,
312 with no change in the AUC of dabrafenib metabolites. Dabrafenib is a substrate of human P-
313 glycoprotein (P-gp) and breast cancer resistance protein (BCRP) in vitro.

314 In vitro data demonstrate that dabrafenib is an inducer of CYP3A4 and CYP2B6 via activation of
315 the pregnane X receptor (PXR) and constitutive androstane receptor (CAR) nuclear receptors.
316 Dabrafenib may also induce CYP2C enzymes via the same mechanism. Co-administration of
317 dabrafenib 150 mg twice daily for 15 days and a single dose of midazolam 3 mg (a CYP3A4
318 substrate) decreased midazolam AUC by 74%. Co-administration of dabrafenib 150 mg twice
319 daily for 15 days and a single dose of warfarin 15 mg decreased the AUC of S-warfarin (a
320 CYP2C9 substrate) by 37% and the AUC of R-warfarin (a CYP3A4/CYP1A2 substrate) by 33%
321 [see Drug Interactions (7.2)].

322 Dabrafenib and its metabolites, hydroxy-dabrafenib, carboxy-dabrafenib, and desmethyl-
323 dabrafenib, are inhibitors of human organic anion transporting polypeptide OATP1B1,
324 OATP1B3 and organic anion transporter OAT1 and OAT3 in vitro. Dabrafenib and desmethyl-
325 dabrafenib are inhibitors of BCRP in vitro.

326 **13 NONCLINICAL TOXICOLOGY**

327 **13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

328 Carcinogenicity studies with dabrafenib have not been conducted. TAFINLAR increased the risk
329 of cutaneous squamous cell carcinomas in patients in clinical trials.

330 Dabrafenib was not mutagenic in vitro in the bacterial reverse mutation assay (Ames test) or the
331 mouse lymphoma assay, and was not clastogenic in an in vivo rat bone marrow micronucleus
332 test.

333 In a combined female fertility and embryofetal development study in rats, a reduction in fertility
334 was noted at doses greater than or equal to 20 mg/kg/day (equivalent to the human exposure at
335 the recommended dose based on AUC). A reduction in the number of ovarian corpora lutea was
336 noted in pregnant females at 300 mg/kg/day (which is approximately three times the human
337 exposure at the recommended dose based on AUC).

338 Male fertility studies with dabrafenib have not been conducted; however, in repeat-dose studies,
339 testicular degeneration/depletion was seen in rats and dogs at doses equivalent to and three times
340 the human exposure at the recommended dose based on AUC, respectively.

341 **13.2 Animal Toxicology and/or Pharmacology**

342 Adverse cardiovascular effects were noted in dogs at dabrafenib doses of 50 mg/kg/day
343 (approximately five times the human exposure at the recommended dose based on AUC) or
344 greater, when administered for up to 4 weeks. Adverse effects consisted of coronary arterial
345 degeneration/necrosis and hemorrhage, as well as cardiac atrioventricular valve
346 hypertrophy/hemorrhage.

347 **14 CLINICAL STUDIES**

348 In Trial 1, the safety and efficacy of TAFINLAR were demonstrated in an international, multi-
349 center, randomized (3:1), open-label, active-controlled trial conducted in 250 patients with
350 previously untreated BRAF V600E mutation-positive, unresectable or metastatic melanoma.
351 Patients with any prior use of BRAF inhibitors or MEK inhibitors were excluded. Patients were
352 randomized to receive TAFINLAR 150 mg by mouth twice daily (n = 187) or dacarbazine 1,000
353 mg/m² intravenously every 3 weeks (n = 63). Randomization was stratified by disease stage at
354 baseline [unresectable stage III (regional nodal or in-transit metastases), M1a (distant skin,
355 subcutaneous, or nodal metastases), or M1b (lung metastases) vs. M1c melanoma (all other
356 visceral metastases or elevated serum LDH)]. The main efficacy outcome measure was
357 progression-free survival (PFS) as assessed by the investigator. In addition, an independent
358 radiology review committee (IRRC) assessed the following efficacy outcome measures in pre-
359 specified supportive analyses: PFS, confirmed objective response rate (ORR), and duration of
360 response.

361 The median age of patients in Trial 1 was 52 years. The majority of the trial population was male
362 (60%), white (99%), had an ECOG performance status of 0 (67%), M1c disease (66%), and
363 normal LDH (62%). All patients had tumor tissue with mutations in BRAF V600E as determined
364 by a clinical trial assay at a centralized testing site. Tumor samples from 243 patients (97%) were
365 tested retrospectively, using an FDA-approved companion diagnostic test, THxID™-BRAF
366 assay.

367 The median duration of follow-up prior to initiation of alternative treatment was 5.1 months and
368 3.5 months for TAFINLAR and dacarbazine, respectively. Twenty-eight (44%) patients crossed
369 over from the dacarbazine arm at the time of disease progression to receive TAFINLAR.

370 Trial 1 demonstrated a statistically significant increase in progression-free survival in the patients
 371 treated with TAFINLAR. Table 5 and Figure 1 summarize the PFS results.

372
 373 **Table 5. Investigator-Assessed Progression-Free Survival and Confirmed Objective**
 374 **Response Results**

	TAFINLAR N = 187	Dacarbazine N = 63
Progression-free Survival		
Objective Response Rate	78 (42%)	41 (65%)
(95% CI)	76	41
CR, n (%)	2	0
Median, months (95% CI)	5.1 (4.9, 6.9)	2.7 (1.5, 3.2)
HR ^a (95% CI)	0.33 (0.20, 0.54)	
<i>P</i> -value ^b	<i>P</i> <0.0001	
Confirmed Tumor Responses		
Number of Events (%)	52%	17%
Progressive Disease	(44, 59)	(9, 29)
Death	6 (3%)	0
PR, n (%)	91 (48%)	11 (17%)
Duration of Response		
Median, months (95% CI)	5.6 (5.4, NR)	NR (5.0, NR)

375 ^a Pike estimator, stratified by disease state.

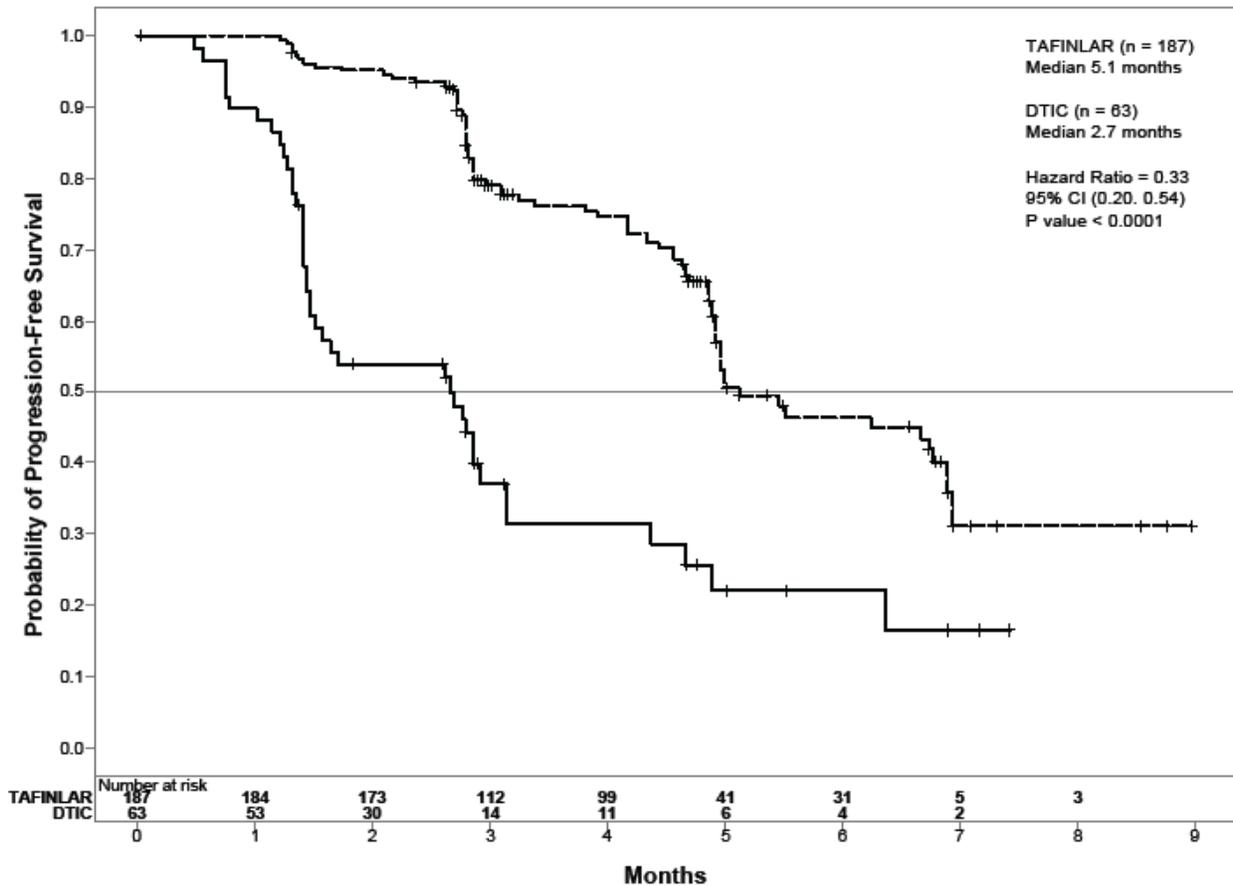
376 ^b Stratified log-rank test.

377 CI = Confidence interval; CR = complete response; HR = hazard ratio; NR = not reached; PR =
 378 partial response

379

380

381 **Figure 1. Kaplan-Meier Curves of Investigator-Assessed Progression-Free Survival**



382
383

384 In supportive analyses based on IRRC assessment and in an exploratory subgroup analysis of
385 patients with retrospectively confirmed V600E mutation-positive melanoma with the THxID™-
386 BRAF assay, the PFS results were consistent with those of the primary efficacy analysis.

387 The activity of TAFINLAR for the treatment of BRAF V600E mutation-positive melanoma,
388 metastatic to the brain was evaluated in a single arm, open-label, two-cohort, multi-center trial
389 (Trial 2). All patients received TAFINLAR 150 mg twice daily. Patients in Cohort A (n = 74)
390 had received no prior local therapy for brain metastases, while patients in Cohort B (n = 65) had
391 received at least one local therapy for brain metastases, including, but not limited to, surgical
392 resection, whole brain radiotherapy, or stereotactic radiosurgery such as gamma knife, linear-
393 accelerated-based radiosurgery, charged particles, or CyberKnife. In addition, patients in Cohort
394 B were required to have evidence of disease progression in a previously treated lesion or an
395 untreated lesion. Additional eligibility criteria were at least one measurable lesion of 0.5 cm or
396 greater in largest diameter on contrast-enhanced MRI, stable or decreasing corticosteroid dose,
397 and no more than two prior systemic regimens for treatment of metastatic disease. The primary
398 outcome measure was estimation of the overall intracranial response rate (OIRR) in each cohort.

399 The median age of patients in Cohort A was 50 years, 72% were male, 100% were white, 59%
 400 had a pre-treatment ECOG performance status of 0, and 57% had an elevated LDH value at
 401 baseline. The median age of patients in Cohort B was 51 years, 63% were male, 98% were white,
 402 66% had a pre-treatment ECOG performance status of 0, and 54% had an elevated LDH value at
 403 baseline. Efficacy results as determined by an independent radiology review committee, masked
 404 to investigator response assessments, are provided in Table 6.

405

406 **Table 6. Efficacy Results in Patients with BRAF V600E Melanoma Brain Metastases (Trial**
 407 **2)**

Endpoint	IRRC Assessed Response	
	Cohort A N = 74	Cohort B N = 65
Overall Intracranial Response Rate (OIRR) % (95% CI)	18 (9.7, 28.2)	18 (9.9, 30.0)
Duration of OIRR Median, months (95% CI)	(N = 13) 4.6 (2.8, NR)	(N = 12) 4.6 (1.9, 4.6)

408 IRRC = Independent radiology review committee; CI = Confidence interval; NR = not reached

409 **16 HOW SUPPLIED/STORAGE AND HANDLING**

410 50 mg Capsules: Dark red capsule imprinted with ‘GS TEW’ and ‘50 mg’ available in bottles of
 411 120 (NDC 0173-0846-08). Each bottle contains a silica gel desiccant.

412 75 mg Capsules: Dark pink capsule imprinted with ‘GS LHF’ and ‘75 mg’ available in bottles of
 413 120 (NDC 0173-0847-08). Each bottle contains a silica gel desiccant.

414 Store at 25°C (77°F); excursions permitted to 15° to 30°C (59° to 86°F) [see USP Controlled
 415 Room Temperature].

416 **17 PATIENT COUNSELING INFORMATION**

417 See FDA-approved patient labeling (Medication Guide).

418 Inform patients of the following:

- 419 • Evidence of BRAF V600E mutation in the tumor specimen is necessary to identify patients
 420 for whom treatment with TAFINLAR is indicated [see *Dosage and Administration (2.1)*].
- 421 • TAFINLAR increases the risk of developing new primary cutaneous malignancies. Advise
 422 patients to contact their doctor immediately for any new lesions or changes to existing lesions
 423 on their skin [see *Warnings and Precautions (5.1)*].

- 424 • TAFINLAR causes pyrexia including serious febrile drug reactions. Instruct patients to
425 contact their doctor if they experience a fever while taking TAFINLAR [*see Warnings and*
426 *Precautions (5.3)*].
- 427 • TAFINLAR can impair glucose control in diabetic patients resulting in the need for more
428 intensive hypoglycemic treatment. Advise patients to contact their doctor to report symptoms
429 of severe hyperglycemia [*see Warnings and Precautions (5.4)*].
- 430 • TAFINLAR may cause hemolytic anemia in patients with glucose-6-phosphate
431 dehydrogenase (G6PD) deficiency. Advise patients with known G6PD deficiency to contact
432 their doctor to report signs or symptoms of anemia or hemolysis [*see Warnings and*
433 *Precautions (5.6)*].
- 434 • TAFINLAR can cause fetal harm if taken during pregnancy. Instruct female patients to use
435 non-hormonal, highly effective contraception during treatment and for 4 weeks after
436 treatment. Advise patients to contact their doctor if they become pregnant, or if pregnancy is
437 suspected, while taking TAFINLAR [*see Use in Specific Populations (8.1)*].
- 438 • Nursing infants may experience serious adverse reactions if the mother is taking TAFINLAR
439 during breastfeeding. Advise breastfeeding mothers to discontinue nursing while taking
440 TAFINLAR [*see Use in Specific Populations (8.3)*].
- 441 • Male patients are at an increased risk for impaired spermatogenesis [*see Use in Specific*
442 *Populations (8.6)*].
- 443 • TAFINLAR should be taken either at least 1 hour before or at least 2 hours after a meal [*see*
444 *Dosage and Administration (2.1)*].

445

446 TAFINLAR is a registered trademark of the GlaxoSmithKline group of companies.

447 THxID is a trademark of bioMérieux.

448

449



450 GlaxoSmithKline

451 Research Triangle Park, NC 27709

452

453 ©Year, GlaxoSmithKline group of companies. All rights reserved.

454 TFR:XPI

455 **MEDICATION GUIDE**
456 **TAFINLAR® (TAFF-in-lar)**
457 **(dabrafenib)**
458 **capsules**

459
460 **What is the most important information I should know about TAFINLAR?**

461 **TAFINLAR may cause serious side effects, including:**

462 **Risk of new cancers. TAFINLAR may cause new cancers, including**
463 **cutaneous squamous cell carcinoma (cuSCC) that can spread to other parts**
464 **of the body. Talk with your healthcare provider about your risk for**
465 **developing skin cancers.**

466 **Check your skin and tell your healthcare provider right away about any**
467 **skin changes including a:**

- 468 • new wart
- 469 • skin sore or reddish bump that bleeds or does not heal
- 470 • change in size or color of a mole

471 Your healthcare provider should check your skin before you start taking TAFINLAR,
472 and every two months while taking TAFINLAR to look for any new skin cancers.

473 Your healthcare provider may continue to check your skin for six months after you
474 stop taking TAFINLAR.

475 See "What are the possible side effects of TAFINLAR?" for more information about
476 side effects.

477
478 **What is TAFINLAR?**

479 TAFINLAR is a prescription medicine used to treat a type of skin cancer called
480 melanoma:

- 481 • that has spread to other parts of the body or cannot be removed by surgery,
482 and
- 483 • that has a certain type of abnormal "BRAF" gene.

484
485 Your healthcare provider will perform a test to make sure that TAFINLAR is right for
486 you.

487 TAFINLAR is not used to treat people with a type of skin cancer called wild-type
488 BRAF melanoma.

489 It is not known if TAFINLAR is safe and effective in children.
490

491 **What should I tell my healthcare provider before taking TAFINLAR?**

492 **Before you start taking TAFINLAR, tell your healthcare provider if you:**

- 493 • have liver or kidney problems
- 494 • have diabetes
- 495 • plan to have surgery, dental, or other medical procedures
- 496 • have a deficiency of the glucose-6-phosphate dehydrogenase (G6PD) enzyme
- 497 • have any other medical conditions
- 498 • are pregnant or plan to become pregnant. TAFINLAR can harm your unborn
499 baby.
 - 500 ○ Females who are able to become pregnant should use birth control during
501 treatment and for 4 weeks after stopping TAFINLAR.
 - 502 ○ Birth control using hormones (such as birth control pills, injections, or
503 patches) may not work as well while you are taking TAFINLAR. You should
504 use another effective method of birth control while taking TAFINLAR. Talk
505 to your healthcare provider about birth control methods that may be right
506 for you.
 - 507 ○ Tell your healthcare provider right away if you become pregnant during
508 treatment with TAFINLAR.
- 509 • are breastfeeding or plan to breastfeed. It is not known if TAFINLAR passes into
510 your breast milk. You and your healthcare provider should decide if you will take
511 TAFINLAR or breastfeed. You should not do both.

512

513 TAFINLAR may cause lower sperm counts in men. This could affect the ability to
514 father a child. Talk to your healthcare provider if this is a concern for you. Talk to
515 your healthcare provider about family planning options that might be right for you.
516

517 **Tell your healthcare provider about all the medicines you take** including
518 prescription and over-the-counter medicines, vitamins, and herbal supplements.
519 TAFINLAR and certain other medicines can affect each other, causing side effects.
520 TAFINLAR may affect the way other medicines work, and other medicines may

521 affect how TAFINLAR works. You can ask your pharmacist for a list of medicines
522 that may interact with TAFINLAR.

523

524 Know the medicines you take. Keep a list of them to show your healthcare provider
525 and pharmacist when you get a new medicine.

526

527 **How should I take TAFINLAR?**

528 • Take TAFINLAR exactly as your healthcare provider tells you. Do not change
529 your dose or stop TAFINLAR unless your healthcare provider tells you.

530 • Take TAFINLAR 2 times a day, about 12 hours apart.

531 • Take TAFINLAR at least 1 hour before or 2 hours after a meal.

532 • Do not open, crush, or break TAFINLAR capsules.

533 • If you miss a dose, take it as soon as you remember. If it is within 6 hours of
534 your next scheduled dose, just take your next dose at your regular time. Do not
535 make up for the missed dose. If you take too much TAFINLAR, call your
536 healthcare provider or go to the nearest hospital emergency room right away.

537

538 **What are the possible side effects of TAFINLAR?**

539 **TAFINLAR may cause serious side effects, including:**

540 • **See “What is the most important information I should know about**
541 **TAFINLAR?”**

542 • **Fever.** TAFINLAR can cause fever, including severe fever. In some cases, too
543 much fluid loss (dehydration), low blood pressure, dizziness, or kidney problems
544 may happen with the fever. Tell your healthcare provider right away if you get a
545 fever while taking TAFINLAR.

546 • **Blood sugar problems.** Some people may develop high blood sugar or
547 worsening diabetes during treatment with TAFINLAR. If you are diabetic, your
548 healthcare provider will check your blood sugar levels before and during
549 treatment with TAFINLAR. Tell your healthcare provider if you have any of the
550 following symptoms of high blood sugar:

551 o increased thirst

552 o urinating more often than normal

553 o your breath smells like fruit

554

555 • **Eye problems.** You should have your eyes examined before and while you are
556 taking TAFINLAR. Tell your healthcare provider right away if you get these
557 symptoms during treatment with TAFINLAR:

558 o eye pain, swelling, or redness

559 o blurred vision or other vision changes during treatment with TAFINLAR

560

561 The most common side effects of TAFINLAR include:

562 • thickening of the outer layers of
563 the skin

564 • headache

565 • joint aches

566 • warts

567 • hair loss

568 • redness, swelling, peeling, or

569 tenderness of hands or feet

570

571 Tell your healthcare provider if you have any side effect that bothers you or that
572 does not go away.

573 These are not all of the possible side effects of TAFINLAR. For more information
574 about side effects, ask your healthcare provider or pharmacist.

575 Call your doctor for medical advice about side effects. You may report side effects
576 to FDA at 1-800-FDA-1088. You may also report side effects to GSK at 1-888-825-
577 5249.

578

579 **How should I store TAFINLAR?**

580 • Store TAFINLAR at room temperature, between 68°F to 77°F (20°C to 25°C).

581 • Ask your healthcare provider or pharmacist how to safely throw away TAFINLAR
582 that is out of date or no longer needed.

583

584 **Keep TAFINLAR and all medicine out of the reach of children.**

585

586 **General information about TAFINLAR**

587 Medicines are sometimes prescribed for purposes other than those listed in a
588 Medication Guide. Do not use TAFINLAR for a condition for which it was not
589 prescribed. Do not give TAFINLAR to other people, even if they have the same
590 symptoms that you have. It may harm them.

591 If you would like more information, talk with your healthcare provider. You can ask
592 your healthcare provider or pharmacist for information about TAFINLAR that is
593 written for health professionals.

594 For more information, call GlaxoSmithKline at 1-888-825-5249 or go to
595 www.TAFINLAR.com.

596

597 **What are the ingredients in TAFINLAR?**

598 Active ingredient: dabrafenib

599 Inactive ingredients: colloidal silicon dioxide, magnesium stearate, microcrystalline
600 cellulose

601 Capsule shells contain: hypromellose, red iron oxide (E172), titanium dioxide
602 (E171).

603

604 This Medication Guide has been approved by the U.S. Food and Drug
605 Administration.

606

607 TAFINLAR is a registered trademark of the GlaxoSmithKline group of companies.

608

609



610 GlaxoSmithKline

611 Research Triangle Park, NC 27709

612

613 ©2013, GlaxoSmithKline group of companies. All rights reserved.

614

615 Issued: 2013

616 TFR:MG