Tasigna®
(nilotinib) 150mg, 200mg capsules

AUTHORIZATION AND APPEALS KIT

TO SUPPORT PATIENTS' ACCESS TO THERAPY

Novartis cannot guarantee insurance coverage or reimbursement. Coverage and reimbursement may vary significantly by payer, plan, patient, and setting of care. It is the sole responsibility of the health care provider to select the proper codes and ensure the accuracy of all statements used in seeking coverage and reimbursement for an individual patient.

Please see Indications and Important Safety Information on pages 18-22.
Please see accompanying full Prescribing Information, including **Boxed WARNING**.

NOVARTIS

INDICATIONS AND IMPORTANT SAFETY INFORMATION FOR TASIGNA® (nilotinib) CAPSULES

INDICATIONS

Adult and Pediatric Patients With Newly Diagnosed Ph+ CML-CP
TASIGNA is indicated for the treatment of adult and pediatric patients greater than or equal to 1 year of age with newly diagnosed Philadelphia chromosome–positive chronic myeloid leukemia (Ph+ CML) in chronic phase (CP).

Adult Patients With Resistant or Intolerant Ph+ CML-CP and CML-AP
TASIGNA is indicated for the treatment of adult patients with CP and accelerated phase (AP) Ph+ CML resistant or intolerant to prior therapy that included imatinib.

Pediatric Patients With Resistant or Intolerant Ph+ CML-CP
TASIGNA is indicated for the treatment of pediatric patients greater than or equal to 1 year of age with Ph+ CML-CP with resistance or intolerance to prior tyrosine kinase inhibitor (TKI) therapy.

IMPORTANT SAFETY INFORMATION

WARNING: QT PROLONGATION AND SUDDEN DEATHS

- **TASIGNA prolongs the QT interval. Prior to TASIGNA administration and periodically, monitor for hypokalemia or hypomagnesemia and correct deficiencies. Obtain ECGs to monitor the QTc at baseline, 7 days after initiation, and periodically thereafter, and following any dose adjustments**
- **Sudden deaths have been reported in patients receiving TASIGNA. Do not administer TASIGNA to patients with hypokalemia, hypomagnesemia, or long QT syndrome**
- **Avoid use of concomitant drugs known to prolong the QT interval and strong CYP3A4 inhibitors**
- **Avoid food 2 hours before and 1 hour after taking the dose**

DOSAGE AND ADMINISTRATION

TASIGNA should be taken twice daily at approximately 12-hour intervals and must be taken on an empty stomach. No food should be consumed for at least 2 hours before the dose is taken and for at least 1 hour after the dose is taken. Advise patients to swallow the capsules whole with water.

For patients who are unable to swallow capsules, the contents of each capsule may be dispersed in 1 teaspoon of applesauce (puréed apple). The mixture should be taken immediately (within 15 minutes) and should not be stored for future use.

TASIGNA may be given in combination with hematopoietic growth factors such as erythropoietin or G-CSF if clinically indicated. TASIGNA may be given with hydroxyurea or anagrelide if clinically indicated.

Dosage in Adults with Newly Diagnosed Ph+ CML-CP
The recommended dose of TASIGNA is 300 mg orally twice daily.

Dosage in Adults with Resistant or Intolerant Ph+ CML-CP and CML-AP
The recommended dose of TASIGNA is 400 mg orally twice daily.

CLINICAL CONSIDERATIONS FOR TASIGNA

RESPONSE RATES FOR ADULTS WITH NEWLY DIAGNOSED Ph+ CML-CP

	TASIGNA 300 mg twice daily (n=282)	Imatinib 400 mg once daily (n=283)
MMR* at 12 months (primary endpoint)	44% (95% CI, 38%-50%) *P*<.0001	22% (95% CI, 18%-28%)
BCR-ABL levels (≤10%) at 3 months†	91% of 258 evaluable patients	67% of 264 evaluable patients

FIVE-YEAR RESPONSE RATES ACCORDING TO SOKAL RISK FOR ADULTS WITH NEWLY DIAGNOSED Ph+ CML-CP[3,4]

	Nilotinib 300 mg twice daily	Imatinib 400 mg once daily
Low Sokal risk, *n*	103	104
MR4.5 by 5 years, *n* (%)	55 (53.4)	38 (36.5)
Intermediate Sokal risk, *n*	101	101
MR4.5 by 5 years, *n* (%)	61 (60.4)	33 (32.7)
High Sokal risk, *n*	78	78
MR4.5 by 5 years, *n* (%)	35 (44.9)	18 (23.1)
Overall		
MR4.5 by 5 years, *n* (%)	151 (53.5)	89 (31.4)

RESPONSE RATES FOR ADULTS WITH RESISTANT OR INTOLERANT Ph+ CML-CP AND CML-AP

Chronic Phase (n=321)	
Cytogenetic Response (CyR) Rate (Unconfirmed)	
Major (efficacy endpoint includes CCyR plus MCyR)	51% (95% CI, 46%-57%)
Complete (CCyR) 0% Ph+ metaphases	37% (95% CI, 32%-42%)
Partial (MCyR) 1% to 35% Ph+ metaphases	15% (95% CI, 11%-19%)
Accelerated Phase (n=137)	
Hematologic response rate (confirmed) (CHR plus NEL)	39% (95% CI, 31%-48%)
Complete hematologic response (CHR) rate	30% (95% CI, 22%-38%)
No evidence of leukemia (NEL)	9% (95% CI, 5%-16%)

SOKAL RISK SCORE CALCULATION

Study	Calculation	Risk Definition by Calculation
Sokal et al. 1984[2]	Exp 0.0116 x (age in years – 43.4) + (spleen – 7.51) + 0.188 x [(platelet count ÷ 700)2 – 0.563] + 0.0887 x (blast cells – 2.10)	Low <0.8 Intermediate 0.8 – 1.2 High >1.2

Calculation of relative risk found at **http://www.icsg.unibo.it/rrcalc.asp**. Age is in years. Spleen is in centimeter below the costal margin (maximum distance). Blast cells, eosinophils, and basophils are in percents of peripheral blood differential. All factors must be collected prior to any treatment.

*MMR=BCR-ABL/ABL ≤0.1% International Scale (IS)

†A post hoc analysis of patients receiving TASIGNA 300 mg bid (n=258) or imatinib 400 mg qd (n=264) in ENESTnd with typical b2a2 and/or b3a2 BCR-ABL transcripts and evaluable RQ-PCR samples at 3 months. Data were grouped based on BCR-ABL transcript levels at 3 months: ≤1%, >1% to ≤10%, and >10%. At 3 months, 24 patients in the TASIGNA arm and 19 patients in the imatinib arm had unevaluable BCR-ABL transcript levels (atypical transcripts at baseline, missing RQ-PCR samples, or discontinued therapy) and were excluded from the analysis.

Please see Indications and Important Safety Information on pages 18-22.
Please see accompanying full Prescribing Information, including **Boxed WARNING**.

Tasigna® (nilotinib) 150mg, 200mg capsules

CLINICAL CONSIDERATIONS FOR TASIGNA (CONT'D)

TREATMENT-FREE REMISSION

Treatment-free remission (TFR) is the ability for eligible adult patients who achieved a sustained MR4.5* to maintain MMR (frontline) *after* discontinuing TASIGNA. These patients no longer take daily oral therapy but continue to be actively managed through frequently scheduled monitoring to identify possible loss of molecular response.

TFR RATES IN PATIENTS RECEIVING TASIGNA FRONTLINE[5]

TFR rate frontline patients, n/N (% [95% CI])	TFR population (*n* = 190)	
	48 weeks	96 weeks
Sokal risk score at diagnosis		
Low	39/62 (62.9 [49.7–74.8])	38/62 (61.3 [48.1–73.4])
Intermediate	25/50 (50.0 [35.5–64.5])	25/50 (50.0 [35.5–64.5])
High	9/28 (32.1 [15.9–52.4])	8/28 (28.6 [13.2–48.7])
Unknown	25/50 (50.0 [35.5–64.5])	22/50 (44.0 [30.0-58.7])
BCR-ABL1 IS level in the consolidation phase		
MR4.5 in all assessments	90/170 (52.9 [45.2–60.6])	86/170 (50.6 [42.8–58.3])
≥ 1 assessment of MR4 but not MR4.5	8/20 (40.0 [19.1–63.9])	7/20 (35.0 [15.4–59.2])

FDA approval of the TFR option is based on the percentage of overall patients that achieved TFR at 96 weeks 49% (n=93/190; 95%CI, 41.6%-56.3%)

ELIGIBILITY CONSIDERATIONS FOR TFR

- Confirmed to express the typical BCR-ABL transcripts (e13a2/b2a2 or e14a2/b3a2)
- No history of AP/BC or prior attempts of TFR discontinuation that resulted in relapse
- An FDA-authorized test with a detection limit up to MR4.5 must be used to determine eligibility for discontinuation

Frontline Patients

- Treated with TASIGNA for at least 3 years
- Maintained at least MR4† for 1 year prior to discontinuation of therapy
- Achieved an MR4.5 for the last assessment taken immediately prior to discontinuation of therapy

BC, blast crisis; CHR, complete hematologic response; CCyr, Complete cytogenetic response; MCyR, major cytogenetic response; MR, molecular response; MMR, major molecular response; NEL, no evidence of leukemia.

*MR4.5=BCR-ABL/ABL ≤0.0032% IS
†MR4=BCR-ABL/ABL ≤0.01% IS

Please see Indications and Important Safety Information on pages 18-22.
Please see accompanying full Prescribing Information, including **Boxed WARNING**.

CLINICAL CONSIDERATIONS FOR TASIGNA® (nilotinib) CAPSULES (CONT'D)

MONITORING DURING TFR

- Monitor BCR-ABL transcript levels in patients eligible for treatment discontinuation using an FDA-authorized test validated to measure MR levels with a sensitivity of at least MR4.5
- Monitor BCR-ABL transcript levels and complete blood count with differential in patients who have discontinued TASIGNA therapy monthly for 1 year, then every 6 weeks for the second year, and every 12 weeks thereafter
- Upon loss of MR4 during TFR, monitor BCR-ABL transcript levels every 2 weeks until BCR-ABL levels remain deeper than MMR for 4 consecutive measurements. The patient can then proceed to the original monitoring schedule
- Advise patients musculoskeletal symptoms (eg, myalgia, pain in extremity, arthralgia, bone pain, spinal pain, or musculoskeletal pain) have been reported in patients during TFR. The rate of new musculoskeletal symptoms (all grades) generally decreased from the first year (34%) to the second year (9%) after treatment discontinuation

REINITIATION OF TREATMENT IN PATIENTS WHO LOSE MR AFTER DISCONTINUATION OF THERAPY WITH TASIGNA

- Frontline patients who lose MMR must re-initiate treatment within 4 weeks at the dose level taken prior to discontinuation of therapy. Monitor monthly BCR-ABL transcript levels until MMR is re-established and every 12 weeks

HOW TO USE THIS INFORMATIONAL KIT

This kit has been created to provide information and sample letters that can be used to help you communicate with health plans about prior authorization (PA) or appeal issues related to TASIGNA® (nilotinib) capsules. Incomplete submissions may delay the appeal process.
This kit includes:

- Examples of information that will usually be required in an appeal letter
- Checklists to help ensure you have provided all needed information

> If an initial appeal is rejected, in addition to a second-level written appeal, you may have the option to engage in a peer-to-peer discussion regarding the appeal.

1 SUGGESTIONS FOR A PRIOR AUTHORIZATION REQUEST LETTER

All PA forms should be completed and submitted to the plan by your office.

Your Novartis Sales Specialist may be able to provide you with PA requirements for specific plans. Benefits verifications performed by the customer service center of the patient's plan and specialty pharmacies can identify PA requirements, step therapies, and form requirements.

A PA letter comes from the patient and/or the physician. Fax the PA request to the health plan. Many specialty pharmacies have the ability to submit a test claim to a payer to confirm coverage of TASIGNA® (nilotinib) capsules.

Many payers will allow up to 3 levels of appeals for PA denials. Refer to tab **2**, the Prior Authorization Appeals letter information.

CHECKLIST

- ❑ **Use the health plan's website to locate their PA form**
- ❑ **Include the patient's information: name, DOB, gender, policy information**
- ❑ **List previous therapies [eg, GLEEVEC® (imatinib mesylate) or other TKI therapies]**
  Explain why each therapy was discontinued and give the duration of therapy for each agent
- ❑ **Document that all PA requirements of the plan have been met, if applicable**
- ❑ **Document patient's Sokal risk score**
- ❑ **Provide rationale and clinical support for your recommendation**
  Information can include:
  - Efficacy and safety trial data vs imatinib [eg, 3-month molecular response)
  - Has contraindication listed for other TKIs
  - Adverse events with other TKIs (ie, intolerability)
  - Resistance to prior therapy including imatinib
  - Potential of TFR after achieving sustained molecular response of MR4.5
  - Applicable therapy guidelines
- ❑ **Review sample letter formats on the next page for additional information**

SAMPLE OUTLINE OF PRIOR AUTHORIZATION REQUEST LETTER FOR TASIGNA

[Date]
[Prior Authorization Dept.]
[Insurance Company]
[Address]
[City, State, ZIP]

Re: [Patient Name]
[Policy Number]
[DOB]
[Gender]

Note: Some plans may require the use of their own letter templates for PA requests.

To Whom It May Concern:

This letter is being submitted for the prior authorization of TASIGNA® (nilotinib) capsules, on behalf of the above referenced patient for the treatment of Ph+ CML [diagnosis code]. The authorization requested is for the current date of [date] through the date of [future date].

(If patient is already taking TASIGNA or has discontinued TASIGNA after achieving treatment free remission, consider including information outlining the severity of Ph+ CML symptoms at the time of TASIGNA prescription. Medical records may need to be pulled from past dates to capture information relevant to TASIGNA treatment.)

If you are addressing a step edit requirement, add a statement about why the required step therapies are not feasible for this patient and why you are requesting the step therapy requirement be eliminated.

This plan currently lists [required step edit therapies] to be attempted prior to treatment with TASIGNA. These step edit therapies are not viable for this patient. We are requesting that the step edit therapy requirement be bypassed.

Document the patient's history, diagnosis, current condition, and symptoms; for example, confirm the patient:

_____ Has been diagnosed with Ph+ CML
_____ Has had an ECG
_____ Has a Sokal risk score
_____ Has a documented CML mutation status
_____ Has received BCR-ABL mutational analysis findings
_____ Does not have hypokalemia, hypomagnesemia, or long QT syndrome
_____ Does not have rare hereditary problems of galactose intolerance, severe lactase deficiency with a severe degree of intolerance to lactose-containing products, or glucose-galactose malabsorption
_____ (If female) is not pregnant or planning to become pregnant
_____ Is currently on TASIGNA and has met the 3-month milestone
_____ Lost MMR after discontinuation of therapy (frontline)

(Attach medical records, such as diagnosis with Ph+ CML and, if available, laboratory work, imaging results, and/or previous therapies (GLEEVEC or other TKI therapies) for Ph+ CML.)

Previous therapies:	**Reason for discontinuation:**	**Duration of therapy:**
_____	_____	_____
_____	_____	_____

(Provide rationale for prescribing TASIGNA. Rationale may include: if the patient is classified as intermediate-to-high-risk; if adverse event occurred with another TKI or should be avoided due to comorbidity; if goal is treatment-free remission.)

(Provide clinical support for your recommendation. This can be clinical trial data from the TASIGNA prescribing information and/or CML guidelines.)

The ordering physician is [physician name, NPI #]. The PA decision may be faxed to [fax #] or mailed to [physician business office address]. Please also send a copy of the coverage determination decision to [patient name].

Sincerely,

_____ _____

[Physician name and signature]
[Name of practice]
[Phone number]

[Patient name and signature]

Encl:

Please see Indications and Important Safety Information on pages 18-22.
Please see accompanying full Prescribing Information, including **Boxed WARNING**.

Tasigna® (nilotinib) 150mg, 200mg capsules

2 SUGGESTIONS FOR A PRIOR AUTHORIZATION APPEALS LETTER

This type of letter can be used when a PA request for TASIGNA® (nilotinib) capsules has been denied. There can be multiple levels of appeal. Please refer to the plan's specific appeal guidelines.

This letter comes from the patient and the physician. It should be submitted along with a copy of the patient's relevant medical records and a Letter of Medical Necessity (see tab 3).

CHECKLIST

- ❑ **Include the patient's information: name, DOB, gender, policy information**
- ❑ **Acknowledge that you are familiar with the company's policy and state the reason for the denial**
- ❑ **Document that all PA requirements of the plan have been met, if applicable**
- ❑ **List previous therapies [eg, GLEEVEC® (imatinib mesylate) or other TKI therapies]**
  Explain why each therapy was discontinued and give the duration of therapy for each agent.
- ❑ **Document patient's Sokal risk score**
- ❑ **If other agents/treatments are not appropriate for this patient, explain why (if they have not already been listed as previous therapies)**
- ❑ **Provide rationale and clinical support for your recommendation**
  Information can include:
  - Efficacy and safety trial data vs imatinib [eg. 3-month molecular response)
  - Adverse events with other TKIs (ie, intolerability)
  - Potential of TFR after achieving sustained molecular response of MR4.5
  - Applicable therapy guidelines
  - Treatment re-initiation due to lost MMR after discontinuation of therapy (frontline)
- ❑ **Attach a Letter of Medical Necessity** (see tab 3)

For second- and third-level appeals, it may be helpful to include

- ❑ **The original letter of denial**
- ❑ **Specific medical notes in response to the denial**

  (A third level of appeal may include review by an independent noninsurance-affiliated external review board or hearing.)

- ❑ **Review sample letter formats on the next page for additional information**

SAMPLE OUTLINE OF PRIOR AUTHORIZATION APPEALS LETTER FOR TASIGNA

[Date]
[Prior Authorization Dept.]
[Insurance Company]
[Address]
[City, State, ZIP]

Re: [Patient Name]
[Policy Number]
[DOB]
[Gender]

To Whom It May Concern:

We have read and acknowledge your policy for the responsible management of drugs in the Ph+ CML category. We are writing to request that you reconsider your denial of coverage of TASIGNA® (nilotinib) capsules.

The reason given for the denial was [state reason from insurer's letter]. A copy of the most recent denial letter is included along with medical notes in response to the denial. After reviewing the denial letter, we continue to feel that TASIGNA [dose, frequency] is the appropriate therapy. The relevant clinical history is summarized below.

(If patient is already taking TASIGNA, consider including information outlining the severity of Ph+ CML symptoms at the time of TASIGNA prescription. Medical records may need to be pulled from past dates to capture the information relevant to TASIGNA treatment.)

Document the patient's history, diagnosis, current condition, and symptoms; for example, confirm the patient:

_____ Has been diagnosed with Ph+ CML

_____ Has had an ECG

_____ Has a Sokal risk score

_____ Has a documented CML mutation status

_____ Has received BCR-ABL mutational analysis findings

_____ Does not have hypokalemia, hypomagnesemia, or long QT syndrome

_____ Does not have rare hereditary problems of galactose intolerance, severe lactase deficiency with a severe degree of intolerance to lactose-containing products, or glucose-galactose malabsorption

_____ (If female) is not pregnant or planning to become pregnant

_____ Is currently on TASIGNA and has met the 3-month milestone

_____ Lost MMR after discontinuation of therapy (frontline)

(Attach medical records, such as diagnosis with Ph+ CML and, if available, laboratory work, imaging results, and/or previous therapies (GLEEVEC or other TKI therapies) for Ph+ CML.)

Previous therapies:	**Reason for discontinuation:**	**Duration of therapy:**
_____	_____	_____
_____	_____	_____

(Provide rationale for prescribing TASIGNA. Rationale may include: if the patient is classified as intermediate-to-high-risk; if adverse event occurred with another TKI or should be avoided due to comorbidity; if goal is treatment-free remission.)

(Provide clinical support for your recommendation. This can be clinical trial data from the TASIGNA prescribing information and/or CML guidelines.)

Please contact me at [office phone number] or [patient name and phone number] for any additional information you may require regarding this appeal. I look forward to your timely approval.

Sincerely,

_____ _____

[Physician name and signature]
[Name of practice]
[Phone number]

[Patient name and signature]

Encl:

Please see Indications and Important Safety Information on pages 18-22.
Please see accompanying full Prescribing Information, including **Boxed WARNING**.

3 SUGGESTIONS FOR A LETTER OF MEDICAL NECESSITY

Some plans require that a Letter of Medical Necessity be submitted along with a PA Appeal (see tab 2) to support the choice of TASIGNA® (nilotinib) capsules over agents that are on formulary. The information provided below and the sample letters inside may be helpful to consider as you prepare that letter.

A Letter of Medical Necessity should also accompany a Formulary Exception Request Letter (see tab 4).

CHECKLIST

- ❑ **Include the patient's information: name, DOB, gender, policy information**
- ❑ **Include specific billing codes where appropriate**
- ❑ **Clearly state the rationale for treatment with TASIGNA and why it is appropriate for your patient**
- ❑ **Document patient's Sokal risk score**
- ❑ **Be sure to include all the listed documents with the letter when you send it to your patient's insurance provider**
- ❑ **List previous therapies [eg, GLEEVEC® (imatinib mesylate) or other TKI therapies]**
  Explain why each therapy was discontinued and give the duration of therapy for each agent.
- ❑ **Explain why formulary-preferred agents are not appropriate if they have not already been listed as previous therapy**
- ❑ **Provide rationale and clinical support for your recommendation**
  Information can include:
  - Efficacy and safety trial data vs imatinib [eg. 3-month molecular response)
  - Adverse events with other TKIs (ie, intolerability)
  - Potential of TFR after achieving sustained molecular response of MR4.5
  - Applicable therapy guidelines
  - Treatment re-initiation due to lost MMR after discontinuation of therapy (frontline)
- ❑ **To close the letter, summarize your recommendation, and provide a phone number should any additional information be required**

SAMPLE OUTLINE OF LETTER OF MEDICAL NECESSITY FOR TASIGNA

[Date]
[Medical Director]
[Insurance Company]
[Address]
[City, State, ZIP]

Re: [Patient Name]
[Policy Number]
[DOB]
[Gender]

To Whom It May Concern:

I am writing this letter on behalf of the above referenced patient to request coverage for TASIGNA® (nilotinib) capsules for the treatment of Ph+ CML. This letter documents the medical necessity for TASIGNA and provides information about the patient's medical history and treatment.

(If patient is already taking TASIGNA, consider including information outlining the severity of Ph+ CML symptoms at the time of TASIGNA prescription. Medical records may need to be pulled from past dates to capture the information relevant to TASIGNA treatment.)

[Patient's name] is a/an [age]-year-old [man/woman] who has been treated for Ph+ CML since [date]. [*Provide a brief medical history emphasizing the most recent events that directly influence your decision to recommend TASIGNA*]. I have included [list enclosed materials] supporting the use of TASIGNA to treat Ph+ CML in [patient's name].

Document the patient's history, diagnosis, current condition, and symptoms; for example, confirm the patient:

_____ Has been diagnosed with Ph+ CML
_____ Has had an ECG
_____ Has a Sokal risk score
_____ Has a documented CML mutation status
_____ Has received BCR-ABL mutational analysis findings
_____ Does not have hypokalemia, hypomagnesemia, or long QT syndrome
_____ Does not have rare hereditary problems of galactose intolerance, severe lactase deficiency with a severe degree of intolerance to lactose-containing products, or glucose-galactose malabsorption
_____ (If female) is not pregnant or planning to become pregnant
_____ Is currently on TASIGNA and has met the 3-month milestone
_____ Lost MMR after discontinuation of therapy (frontline)

(Attach medical records, such as diagnosis with Ph+ CML and, if available, laboratory work, imaging results, and/or previous therapies (GLEEVEC or other TKI therapies) for Ph+ CML.)

Previous therapies:	**Reason for discontinuation:**	**Duration of therapy:**
_____	_____	_____
_____	_____	_____

If you have any questions regarding the material that I have provided, please do not hesitate to contact me. Thank you in advance for your prompt attention to this matter.

Sincerely,

_____ _____

[Physician name and signature]
[Name of practice]
[Phone number]

[Patient name and signature]

Encl:

4 SUGGESTIONS FOR A STEP EDIT APPEALS LETTER IN FRONTLINE LOW RISK

This type of letter can be used when a PA request for TASIGNA® (nilotinib) capsules in the frontline setting has been denied due to step therapy policy for low-risk patients. There can be multiple levels of appeal. Please refer to the plan's specific appeal guidelines.

This letter comes from the patient and the physician. It should be submitted along with a copy of the patient's relevant medical records and a Letter of Medical Necessity (see tab 3).

CHECKLIST

- ❑ **Include the patient's information: name, DOB, gender, policy information**
- ❑ **Acknowledge that you are familiar with the company's policy and state the reason for the denial**
- ❑ **Document that all PA requirements of the plan have been met, if applicable**
- ❑ **Document patient's Sokal risk score**
- ❑ **Provide rationale and clinical support for your recommendation**
  Information can include:
  - Efficacy and safety trial data vs imatinib [eg, 4.5 by Sokal risk group molecular response)
  - Adverse events with other TKIs (ie, intolerability)
  - Potential of TFR after achieving sustained molecular response of MR4.5
  - Applicable therapy guidelines
- ❑ **Attach a Letter of Medical Necessity** (see tab 3)

For second- and third-level appeals, it may be helpful to include

- ❑ **The original letter of denial**
- ❑ **Specific medical notes in response to the denial**
  (A third level of appeal may include review by an independent noninsurance-affiliated external review board or hearing.)
- ❑ **Review sample letter formats on the next page for additional information**

SAMPLE OUTLINE OF STEP EDIT APPEALS LETTER FOR TASIGNA IN FRONTLINE LOW RISK

[Date]
[Prior Authorization Dept.]
[Insurance Company]
[Address]
[City, State, ZIP]

Re: [Patient Name]
[Policy Number]
[DOB]
[Gender]

To Whom It May Concern:

We have read and acknowledge your policy for the responsible management of drugs in the Ph+ CML category. We are writing to request that you reconsider your denial of coverage of TASIGNA® (nilotinib) capsules.

The reason given for the denial was [state reason from insurer's letter]. A copy of the most recent denial letter is included along with medical notes in response to the denial. After reviewing the denial letter, we continue to feel that TASIGNA [dose, frequency] is the appropriate therapy. The relevant clinical history is summarized below.

(If patient is already taking TASIGNA, consider including information outlining the severity of Ph+ CML symptoms at the time of TASIGNA prescription. Medical records may need to be pulled from past dates to capture the information relevant to TASIGNA treatment.)

Document the patient's history, diagnosis, current condition, and symptoms; for example, confirm the patient:

_____ Has been diagnosed with Ph+ CML

_____ Has had an ECG

_____ Has a Sokal risk score

_____ Has a documented CML mutation status

_____ Has received BCR-ABL mutational analysis findings

_____ Does not have hypokalemia, hypomagnesemia, or long QT syndrome

_____ Does not have rare hereditary problems of galactose intolerance, severe lactase deficiency with a severe degree of intolerance to lactose-containing products, or glucose-galactose malabsorption

_____ (If female) is not pregnant or planning to become pregnant

_____ Is currently on TASIGNA and has met the 3-month milestone

(Attach medical records, such as diagnosis with Ph+ CML and, if available, laboratory work and imaging results.

(Provide rationale for prescribing TASIGNA. Rationale may include: if the patient is classified as low risk; if adverse event occurred with another TKI or should be avoided due to comorbidity; if goal is treatment-free remission.)

(Provide clinical support for your recommendation. This can be clinical trial data from the TASIGNA prescribing information and/or CML guidelines.)

Please contact me at [office phone number] or [patient name and phone number] for any additional information you may require regarding this appeal. I look forward to your timely approval.

Sincerely,

_____ _____

[Physician name and signature]
[Name of practice]
[Phone number]

[Patient name and signature]

Encl:

5 SUGGESTIONS FOR A FORMULARY EXCEPTION REQUEST LETTER

This type of letter can be used when TASIGNA® (nilotinib) capsules is not listed on a formulary or if it has an NDC block. While the plan may provide a form on its website that can be used to apply for an exception, you can refer to the sample provided in this kit to see the type of information that is typically required.

This letter is written and sent by the patient, with the help of their physician. The letter should also be signed by the physician. It should be submitted along with a copy of the patient's relevant medical records and a Letter of Medical Necessity (see tab 3).

CHECKLIST

- ❑ **Include the patient's information: name, DOB, gender, policy information**
- ❑ **Document the patient's diagnosis with Ph+ CML**
- ❑ **List of previous therapies [eg, GLEEVEC® (imatinib mesylate) or other TKI therapies]**
- ❑ **Clearly state the main reasons in support of a formulary exemption for TASIGNA for this patient**
- ❑ **Attach the patient's relevant medical records**
- ❑ **If this is a second- or third-level appeal, include the letter of denial and medical notes in response to the denial**
- ❑ **Include a Letter of Medical Necessity** (see example tab 3)

SAMPLE OUTLINE OF FORMULARY EXCEPTION REQUEST LETTER FOR TASIGNA

The following is an example **outline** for information that should be included within the **formulary exception letter**. If your patient is requesting an exception to their formulary in order to fill their prescription for TASIGNA® (nilotinib) capsules ensure they include the following information:

_____ Patient's name, DOB, gender, and policy information at the top of the letter

_____ The patient is a member of [enter name of health plan]. Currently, TASIGNA is not listed on their formulary, and [why it is necessary to use TASIGNA for this patient].

_____ The patient is requesting an exception to your formulary to fill [his/her] prescription for TASIGNA and request that it be available as a preferred drug and that any applicable NDC blocks be removed.

_____ Patient has been diagnosed with Ph+ CML [diagnosis code] and [physician name] has prescribed TASIGNA [dose, frequency].

_____ [Physician name] practices in [medical specialty] at this address: [physician address].

_____ Past treatments include [list previous treatments and drugs]. Enclose medical records and a Letter of Medical Necessity from [physician name] supporting request for the formulary exception approval of TASIGNA. (Note: Medical records should include the records from the date TASIGNA was first prescribed to the patient, and it should include diagnosis severity indicators, if patient is already taking TASIGNA.)

_____ The main reasons for requesting this exception are [main medical necessity points].

_____ [Physician name] can be contacted at [phone number] to answer any additional questions or to participate in a peer-to-peer review discussing the necessity of providing a formulary exception for the use of TASIGNA in this patient.

_____ Include physician and patient signature at the bottom of the letter.

_____ If this is a second- or third level appeal for formulary exception, include level of appeal, letter of denial, and medical notes in response to denial.

INDICATIONS AND IMPORTANT SAFETY INFORMATION FOR TASIGNA® (nilotinib) CAPSULES

INDICATIONS

Adult and Pediatric Patients With Newly Diagnosed Ph+ CML-CP
TASIGNA is indicated for the treatment of adult and pediatric patients greater than or equal to 1 year of age with newly diagnosed Philadelphia chromosome–positive chronic myeloid leukemia (Ph+ CML) in chronic phase (CP).

Adult Patients With Resistant or Intolerant Ph+ CML-CP and CML-AP
TASIGNA is indicated for the treatment of adult patients with CP and accelerated phase (AP) Ph+ CML resistant or intolerant to prior therapy that included imatinib.

Pediatric Patients With Resistant or Intolerant Ph+ CML-CP
TASIGNA is indicated for the treatment of pediatric patients greater than or equal to 1 year of age with Ph+ CML-CP with resistance or intolerance to prior tyrosine kinase inhibitor (TKI) therapy.

IMPORTANT SAFETY INFORMATION

WARNING: QT PROLONGATION AND SUDDEN DEATHS

- **TASIGNA prolongs the QT interval. Prior to TASIGNA administration and periodically, monitor for hypokalemia or hypomagnesemia and correct deficiencies. Obtain ECGs to monitor the QTc at baseline, 7 days after initiation, and periodically thereafter, and following any dose adjustments**
- **Sudden deaths have been reported in patients receiving TASIGNA. Do not administer TASIGNA to patients with hypokalemia, hypomagnesemia, or long QT syndrome**
- **Avoid use of concomitant drugs known to prolong the QT interval and strong CYP3A4 inhibitors**
- **Avoid food 2 hours before and 1 hour after taking the dose**

CONTRAINDICATIONS

Do not use in patients with hypokalemia, hypomagnesemia, or long QT syndrome.

WARNINGS AND PRECAUTIONS

Myelosuppression

Treatment with TASIGNA can cause Grade 3/4 thrombocytopenia, neutropenia, and anemia. Perform complete blood counts every 2 weeks for the first 2 months and then monthly thereafter, or as clinically indicated. Myelosuppression was generally reversible and usually managed by withholding TASIGNA temporarily or dose reduction.

QT Prolongation

TASIGNA prolongs the QT interval. ECGs should be performed at baseline, 7 days after initiation, periodically as clinically indicated, and following dose adjustments. Correct hypokalemia or hypomagnesemia prior to administration and monitor periodically.

Significant prolongation of the QT interval may occur when TASIGNA is inappropriately taken with food and/or strong CYP3A4 inhibitors and/or medicinal products with a known potential to prolong QT. Therefore, co-administration with food must be avoided and concomitant use with strong CYP3A4 inhibitors and/or medicinal products with a known potential to prolong QT should be avoided. The presence of hypokalemia and hypomagnesemia may further enhance this effect.

Sudden Deaths

Sudden deaths have been reported in patients with Ph+ CML treated with TASIGNA. The relatively early occurrence of some of these deaths relative to the initiation of TASIGNA suggests the possibility that ventricular repolarization abnormalities may have contributed to their occurrence.

Cardiac and Arterial Vascular Occlusive Events

Cardiovascular events, including arterial vascular occlusive events, were reported in a randomized, clinical trial in patients with newly diagnosed Ph+ CML and observed in the postmarketing reports of patients receiving TASIGNA therapy. Cases of cardiovascular events included ischemic heart disease-related events, peripheral arterial occlusive disease, and ischemic cerebrovascular events.

If acute signs or symptoms of cardiovascular events occur, advise patients to seek immediate medical attention. The cardiovascular status of patients should be evaluated and cardiovascular risk factors should be monitored and actively managed during TASIGNA therapy according to standard guidelines.

Pancreatitis and Elevated Serum Lipase

TASIGNA can cause increases in serum lipase. Patients with a previous history of pancreatitis may be at greater risk of elevated serum lipase. If lipase elevations are accompanied by abdominal symptoms, interrupt dosing and consider appropriate diagnostics to exclude pancreatitis. Test serum lipase levels monthly or as clinically indicated.

Hepatotoxicity

TASIGNA may result in hepatotoxicity as measured by elevations in bilirubin, AST/ALT, and alkaline phosphatase. Grade 3/4 elevations of bilirubin, AST, and ALT were reported at a higher frequency in pediatric patients than in adults. Monitor hepatic function tests monthly or as clinically indicated.

Please see Indications and Important Safety Information on pages 18-22.
Please see accompanying full Prescribing Information, including **Boxed WARNING**.

Tasigna® (nilotinib) 150mg, 200mg capsules

IMPORTANT SAFETY INFORMATION (cont)

Electrolyte Abnormalities
The use of TASIGNA can cause hypophosphatemia, hypokalemia, hyperkalemia, hypocalcemia, and hyponatremia. Correct electrolyte abnormalities prior to initiating TASIGNA and monitor these electrolytes periodically during therapy.

Tumor Lysis Syndrome
Tumor lysis syndrome cases have been reported in patients taking TASIGNA who have resistant or intolerant Ph+ CML. Malignant disease progression, high white blood cell counts, and/or dehydration were present in most of these cases. Maintain adequate hydration and correct uric acid levels prior to initiating therapy with TASIGNA.

Hemorrhage
Serious hemorrhage, including fatal events, from any site, including the GI tract, was reported in patients with Ph+ CML receiving TASIGNA. Monitor patients for signs and symptoms of bleeding and medically manage as needed.

Total Gastrectomy
Since the exposure of TASIGNA is reduced in patients with total gastrectomy, perform more frequent monitoring of these patients. Consider dose increase or alternative therapy in patients with total gastrectomy.

Lactose
Since the capsules contain lactose, TASIGNA is not recommended for patients with rare hereditary problems of galactose intolerance, severe lactase deficiency with a severe degree of intolerance to lactose-containing products, or of glucose-galactose malabsorption.

Monitoring Laboratory Tests
Complete blood counts should be performed every 2 weeks for the first 2 months and then monthly thereafter. Perform chemistry panels, including electrolytes, calcium, magnesium, liver enzymes, lipid profile, and glucose prior to therapy and periodically. ECGs should be obtained at baseline, 7 days after initiation, and periodically thereafter, as well as following dose adjustments.

Monitor lipid profiles and glucose periodically during the first year of TASIGNA therapy and at least yearly during chronic therapy. Assess glucose levels before initiating treatment with TASIGNA and monitor during treatment as clinically indicated. If test results warrant therapy, physicians should follow their local standards of practice and treatment guidelines.

Fluid Retention
Grade 3/4 fluid retention including pleural effusion, pericardial effusion, ascites, and pulmonary edema have been reported in patients with Ph+ CML receiving TASIGNA. Monitor patients for signs of severe fluid retention (eg, unexpected rapid weight gain or swelling) and for symptoms of respiratory or cardiac compromise (eg, shortness of breath); evaluate etiology and treat patients accordingly.

Effects on Growth and Development in Pediatric Patients

Growth retardation has been reported in pediatric patients with Ph+ CML in chronic phase treated with TASIGNA. Monitor growth and development in pediatric patients receiving TASIGNA treatment.

Embryo-Fetal Toxicity

TASIGNA can cause fetal harm. Advise females to inform their doctor if they are pregnant or become pregnant. Inform female patients of the risk to the fetus and potential for loss of the pregnancy. Advise females of reproductive potential to use effective contraception during treatment and for 14 days after receiving the last dose of TASIGNA. Advise lactating women not to breastfeed during treatment with TASIGNA and for at least 14 days after the last dose.

Monitoring of BCR-ABL Transcript Levels

Monitor BCR-ABL transcript levels in patients eligible for treatment discontinuation using an FDA-authorized test validated to measure molecular response (MR) levels with a sensitivity of at least MR4.5. In patients who discontinue TASIGNA therapy, assess BCR-ABL transcript levels monthly for 1 year, then every 6 weeks for the second year, and every 12 weeks thereafter during treatment discontinuation.

Following a loss of MMR (first line/second line) or confirmed loss of MR4 (2 consecutive measures separated by at least 4 weeks showing loss of MR4 in second line), patients should reinitiate TASIGNA within 4 weeks of when the loss of remission is known to have occurred.

Monitor CBC and BCR-ABL transcripts in patients who reinitiate treatment with TASIGNA due to loss of MR quantitation every 4 weeks until MMR is reestablished and then every 12 weeks.

For patients who fail to achieve MMR after 3 months of treatment reinitiating, BCR-ABL kinase domain mutation testing should be performed.

ADVERSE REACTIONS

The most commonly reported nonhematologic adverse reactions (≥20%) in adult and pediatric patients receiving TASIGNA were nausea, rash, headache, fatigue, pruritus, vomiting, diarrhea, cough, constipation, arthralgia, nasopharyngitis, pyrexia, and night sweats.

Hematologic adverse drug reactions (all grades) include myelosuppression: thrombocytopenia, neutropenia, and anemia.

Musculoskeletal symptoms (eg, myalgia, pain in extremity, arthralgia, bone pain, spinal pain, or musculoskeletal pain) have been reported in eligible patients who discontinued TASIGNA therapy after attaining a sustained MR4.5. The rate of new musculoskeletal symptoms (all grades) generally decreased from the first year (34%-48%) to the second year (9%-15%) after treatment discontinuation.

IMPORTANT SAFETY INFORMATION (cont)

DOSE ADJUSTMENTS OR MODIFICATIONS

TASIGNA may need to be temporarily withheld and/or dose reduced for QT prolongation, hepatic impairment, hematologic toxicities that are not related to underlying leukemia, clinically significant moderate or severe nonhematologic toxicities, laboratory abnormalities (lipase, bilirubin, or hepatic transaminase elevations) or concomitant use of strong CYP3A4 inhibitors.

DRUG INTERACTIONS

Avoid concomitant use of strong CYP3A4 inhibitors with TASIGNA, or reduce TASIGNA dose if co-administration cannot be avoided. Avoid concomitant use of strong CYP3A4 inducers with TASIGNA. Use short-acting antacids or H2 blockers as an alternative to proton pump inhibitors.

Please see accompanying full Prescribing Information, including **Boxed WARNING**.

REFERENCES

1. Tasigna [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corp; 2019.

2. Sokal JE, Cox E, Baccarani M, et al. Prognostic discrimination in "good-risk" chronic granulocytic leukemia. *Blood*. 1984;63(4):789-99.

3. Hochhaus A, Saglio G, Hughes TP, et al. Long-term benefits and risks of frontline nilotinib vs imatinib for chronic myeloid leukemia in chronic phase: 5-year update of the randomized ENESTnd trial. *Leukemia*. 2016;30(5)1044-54. doi:10.1038/leu.2016.5. Accessed February 3, 2016.

4. Larson RA, et al. ENESTnd 5-year (y) update: long-term outcomes of patients (pts) with chronic myeloid leukemia in chronic phase (CML-CP) treated with frontline nilotinib (NIL) versus imatinib (IM). Abstract 7073. Presented at: ASCO Annual Meeting 2014; June 2, 2014; Chicago, IL.

5. Ross DM, Masszi T, Gómez Casares MT, et al. Durable treatment-free remission in patients with chronic myeloid leukemia in chronic phase following frontline nilotinib: 96-week update of the ENEST freedom study. *J Cancer Res Clin Oncol.* 2018;144(5):945-954. doi:10.1007/s00432-018-2604-x. Accessed February 22, 2018.

Tasigna®
(nilotinib) 150mg, 200mg capsules

NOVARTIS

Tasigna®
(nilotinib) 150mg, 200mg capsules

QR CODE FOR INTERNAL USE ONLY.

Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936-1080

Printed in USA 1/20 T-AM7-1224535