**Instructions: *Please complete all required fields. Missing or incomplete information may result in decision delays. Please avoid including any information that could reveal the identity of the patient to AbbVie for privacy reasons.***

|  |  |  |
| --- | --- | --- |
| Treating Physician: | |  |
| Date of Diagnosis (MM/YYYY): |  | |

SECTION 1. Patient Information*:*

|  |
| --- |
| Patient Year of Birth: |
| Gender:  Male  Female |
| Rationale for Request: |
|  |

|  |  |  |
| --- | --- | --- |
| Baseline Information | | |
| 1. Please provide all pertinent medical history of this patient:   \* *Please avoid including any information that could reveal the identity of the patient to AbbVie for privacy reasons.* | | |
| 1. 2. Does the patient have a history of other cancers? 2. If so, please specify: |  |  |

| AML Information | Yes | No |
| --- | --- | --- |
| 1. Does the patient have treatment-related AML? |  |  |
| 1. Did the AML arise from a preceding malignancy (e.g., MDS or MPN)?   If so, describe preceding malignancy: |  |  |
| 1. Did the patient have first line therapy?   If so, please provide:   * Treatment: * Start Date: * End Date: * Best Response (please include BM blast assessment before and after treatment): * Relapse date: |  |  |
| 1. Did the patient have second line or other treatments?   If so, please provide:   * Treatment: * Start Date: * End Date: * Best Response (please include BM blast assessment before and after treatment): * Relapse date:   Additional lines of Treatment(s):   * Start Date: * End Date: * Best Response (please include BM blast assessment before and after treatment): * Relapse date: |  |  |
| 1. Please provide any cytogenetic (chromosomal) and/or mutational information: | | |

| Comorbidities | Yes | No | NA |
| --- | --- | --- | --- |
| 1. Does the patient have any of the below comorbidities? |  |  |  |
| 1. Heart Failure |  |  |  |
| 1. Renal Failure |  |  |  |
| 1. Diabetes |  |  |  |
| 1. Hypertension |  |  |  |
| 1. Other Significant Medical illness(s): |  |  |  |

| Concomitant drugs:  Patients concomitantly treated with either a CYP3A, p-gp, OATP1B1/1B3 or BCRP inhibitor/inducer/substrate (See Appendix A for examples) require dose adjustments of venetoclax (recommendations are given in the provided USPI) | Yes | No | NA |
| --- | --- | --- | --- |
| 1. Will the patient be treated with a CYP3A inhibitor/inducer?   If so, which one:   1. Will the patient be treated with a p-gp inhibitor/substrate?   If so, which one:   1. Will the patient be treated with a BCRP inhibitor/substrate?   If so, which one:   1. Will the patient be treated with a OATP1B1/1B3 inhibitor/substrate?   If so, which one: |  |  |  |

| Patient has been counseled on the following: | Yes | No | NA |
| --- | --- | --- | --- |
| 1. The patient must not consume any of the following within **3 days** prior to the first dose of venetoclax:   grapefruit or grapefruit products  Seville oranges (including marmalade containing Seville oranges)  Star fruit  St John's wort |  |  |  |

SECTION 2. Venetoclax combination information

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| --- |
| Combination with Hypomethylating Agents (azacitidine or decitabine) ***without* concomitant drug use** (see below for concomitant drug use)  ***Decitabine***20 mg/m2: Days 1 – 5  OR  ***Azacitidine*** 75 mg/m2: Days 1 – 7  Venetoclax 400 mg daily final daily dose with initial dose escalation (ramp up) during cycle 1  as per dosing schematic:   * Day 1 -100mg * Day 2 - 200mg * Days 3 to 28 - 400 mg   Venetoclax administered daily at 400 mg during each subsequent 28-day cycle. |
| Combination with Hypomethylating Agents (azacitidine or decitabine) – **concomitant drug use** (please specify type of concomitant drug below):  ***Decitabine***20 mg/m2: Days 1 – 5  OR  ***Azacitidine*** 75 mg/m2: Days 1 – 7  Moderate CYP3A inhibitor:  Venetoclax dose reduction of at least 50%, with an initial dose escalation (ramp up) during cycle 1 (example):   * Day 1 – 50 mg (maximum) * Day 2 – 100 mg (maximum) * Days 3 to 28 – 200 mg (maximum)   Venetoclax administered daily at a maximum of 200 mg during each subsequent 28-day cycle.  Order for the first cycle:   * 50mg pack (7 tablets) * 100mg pack (112 tablets)   Subsequent orders:   * 100mg pack (112 tablets)   Strong CYP3A inhibitor (other than Posaconazole, see below for posaconazole):  Venetoclax dose reduction of at least 75%, with an initial dose escalation (ramp up) during cycle 1 (example):   * Day 1 – 10 mg (maximum) * Day 2 – 20 mg (maximum) * Day 3 – 50 mg (maximum) * Day 4 to 28 – 100 mg (maximum)   Venetoclax administered daily at a maximum of 100 mg during each subsequent 28-day cycle.  Order for the first cycle:   * 10mg pack (14 tablets) * 50mg pack (7 tablets) * 100mg pack (112 tablets)   Subsequent orders:   * 100mg pack (112 tablets)     Posaconazole:   * Day 1 – 10 mg (maximum) * Day 2 – 20 mg (maximum) * Day 3 – 50 mg (maximum) * Day 4 to 28 – 70 mg (maximum)   Order for the first and subsequent cycles:   * 10mg pack (14 tablets) – x4 * 50mg pack (7 tablets) – x4   Venetoclax administered daily at a maximum of 70 mg during each subsequent 28-day cycle. |
| Combination with low dose Cytarabine (LDAC) – ***without* concomitant drug use**  Venetoclax dose ramp up during cycle 1 – 600 mg daily final dose with initial dose escalation as per dosing schematic:   * Day 1 -100mg * Day 2 - 200mg * Day 3 - 400 mg * Days 4 to 28 – 600 mg   ***LDAC*** 20 mg/m2, SC, QD: Days 1 – 10  Venetoclax administered daily at 600 mg during each 28-day cycle. |
| Combination with low dose Cytarabine (LDAC) – **concomitant drug use**  ***LDAC*** 20 mg/m2, SC, QD: Days 1 – 10  Moderate CYP3A inhibitor:  Venetoclax dose reduction of at least 50%, with an initial dose escalation (ramp up) during cycle 1 (example):   * Day 1 – 50 mg (maximum) * Day 2 – 100 mg (maximum) * Day 3 – 200 mg (maximum) * Day 4-28: 300 mg (maximimum)   Venetoclax administered daily at a maximum of 300 mg during each subsequent 28-day cycle.  Order for the first cycle:   * 50mg pack (7 tablets) * 100mg pack (112 tablets)   Subsequent orders:   * 100mg pack (112 tablets)   Strong CYP3A inhibitor (other than Posaconazole, see below for posaconazole):  Venetoclax dose reduction of at least 75%, with an initial dose escalation (ramp up) during cycle 1 (example):   * Day 1 – 10 mg (maximum) * Day 2 – 20 mg (maximum) * Day 3 – 50 mg (maximum) * Day 4 – 100 mg (maximum) * Day 5 to 28 – 150 mg (maximum)   Venetoclax administered daily at a maximum of 100 mg during each subsequent 28-day cycle.  Order for the first cycle:   * 10mg pack (14 tablets) * 50mg pack (7 tablets) – 4 packs * 100mg pack (112 tablets)   Subsequent orders:   * 50 mg pack (7 tablets) – 4 packs * 100mg pack (112 tablets)   Posaconazole:  Venetoclax dose reduction of 75-90%, with an initial dose escalation (ramp up) during cycle 1 (example):   * Day 1 – 10 mg (maximum) * Day 2 – 20 mg (maximum) * Day 3 – 50 mg (maximum) * Day 4 to 28 – 100 mg (maximum)   Order for the first and subsequent cycles:   * 10mg pack (14 tablets) * 100mg pack (112 tablets)   Venetoclax administered daily at a maximum of 100 mg during each subsequent 28-day cycle.  Venetoclax dose ramp up during cycle 1 – 600 mg daily final dose with initial dose escalation as per dosing schematic:   * Day 1 -100mg * Day 2 - 200mg * Day 3 - 400 mg * Days 4 to 28 – 600 mg |
| **Additional Dosing Instructions**:  •  • Venetoclax should be taken thirty minutes (30) after a meal preferably after breakfast |

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| --- | --- | --- | --- | --- | --- | --- | --- |
| **Treating Physician Information:** | | | | | | | |
| HCP Name: |  | | | | | | |
| Institution Name: |  | | | | | | |
| Email Address: |  | | | | | | |
| Phone Number: |  | | | |  | | |
|  | |  | | | |
| **Drug Shipment Contact and Address** | | | | | | | |
| Receiving Contact Person (Pharmacist): | | | |  | | | |
| Contact Email Address: | | | |  | | | |
| Contact Telephone Number: | | | |  | | | |
| **Delivery Address** | | | | | | | |
| Name Hospital /Pharmacy: | | |  | | | | |
| Street Number: | | |  | | | | |
| City: | | |  | | | | |
| State/Province: | | |  | | Postal Code: | | Country: |

**SECTION 3. Physician Declaration**

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| **PHYSICIAN INITIATED**  **Free of charge product declaration**  AbbVie B.V. (“AbbVie”) agrees to provide sufficient quantities of Venetoclax (“Treatment Regimen”) to (“Physician”, “your”, “my” or “I”) for the restricted purpose of the Physician’s treatment of a single patient with a serious or immediately life-threatening disease or condition (“Patient”), effective as of the date this physician initiated free of charge request (the “Declaration”) is fully executed (the “Effective Date”). In consideration of the promises set forth herein, the Physician agrees as follows:   1. Treatment Regimen   I confirm that I accept full responsibility for the use of the Treatment Regimen for the Patient under my care. I will adhere to all written instructions provided by AbbVie.  In my clinical judgment, the Patient does not have any other treatment options for his/her serious or life-threatening disease, has exhausted other treatment options and does not qualify for or is ineligible for, or otherwise unable to participate in clinical trials. I have determined the Patient could benefit from the Treatment Regimen and I am requesting supply of the Treatment Regimen for this patient on a free of charge use basis for the treatment of the indication listed. I have informed the Patient that the Treatment Regimen is provided on a free of charge basis according to local laws. I understand that AbbVie will provide the Treatment Regimen free of charge. I also understand AbbVie will not be responsible for payment of medical care resulting from adverse events experienced by the patient.   1. Processing of Physician Personal Information   I understand and agree that AbbVie will collect certain personal data including Physician’s name, address and place(s) of work, work telephone number and email address and Physician registration/license number to (a) provide the Treatment Regimen and facilitate communication, (b) for participation, activity and safety tracking and reporting; and (c) as otherwise may be required by law or internal business processes. The legal bases for such processing are the performance of a contract, compliance with legal obligations and AbbVie’s legitimate interests in maintaining and improving its internal business processes. For additional information of AbbVie’s privacy practices, including but not limited to a description of the categories of personal data collected, the purposes of processing, data subject rights, and cross-border transfers please see AbbVie’s online privacy policy here <https://www.abbvie.nl/privacy.html>.   1. Patient Data   I confirm that I will comply with all applicable data protection laws and regulations, including the EU General Data Protection Regulation (2016/679) and have provide an adequate privacy notice to my patients and obtained an adequate consent, where needed, to process the patients’ personal data, including their health data.  I confirm that I will not provide any details regarding a patient in this form that will allow AbbVie to identify such patient and I will only provide anonymous data to AbbVie to enable AbbVie to assess whether the Treatment Regimen can be provided to patient.   1. Adverse Event Reporting   I understand that it is my responsibility to report adverse events (“AE”) that occur while the Patient is being treated with the Treatment Regimen to the local Regulatory Authority in line with local regulatory requirements. Simultaneous with the AE report to the local Regulatory Authority, I will send an AE report to AbbVie with the following minimum initial data: patient’s initials or unique identifier, the adverse event, and causality assessment. I will promptly and fully collaborate with AbbVie in case follow-up for AE is requested.   1. **Confidentiality and Proprietary Information**   I will maintain in confidence all of AbbVie’s proprietary information (“AbbVie Information”) disclosed within the context of the free of charge request. I will not disclose AbbVie Information to any third party and will only use AbbVie Information for the purpose of treatment of this patient under this Declaration. AbbVie Information shall include any information provided to Physician by or on behalf of AbbVie, including but not limited to the Treatment Regimen, and all materials and information concerning AbbVie or the Treatment Regimen.  I will not modify, reverse engineer, decompile, disassemble or chemically analyze Treatment Regimen or any of AbbVie’s proprietary information in any way. I shall not conceive, derive, reduce to practice, make or develop any information, inventions, innovations, ideas, discoveries, or products (whether copyrightable, patentable or not), (collectively “Intellectual Property”) resulting from use of the Treatment Regimen or any of AbbVie’s proprietary information. If I generate any Intellectual Property in violation of this section, I hereby assign all rights, title and interest in and to such Intellectual Property to AbbVie.   1. **Publications/Presentations.**   I agree to provide AbbVie with a draft of any proposed presentation and/or publication resulting from the use of the Treatment Regimen at least sixty (60) days prior to submission for presentation or publication.  I understand AbbVie reserves the right to review any such draft publication, provide comments and require removal of Confidential Information. I understand AbbVie’s review must be disclosed in the presentation/publication, in the interest of full transparency.   1. **No Warranty**   I understand that AbbVie provides the Treatment Regimen “AS IS”, WITH NO WARRANTY, EXPRESS OR IMPLIED, INCUDING WARRANTIES OF MERCHANTABILITY, OR FITNESS FOR A PARTICULAR PURPOSE, except where implied terms about the same cannot be excluded at law.  **8**. **Audit**  AbbVie reserves the right to audit Physician and institutional records and other data related to the use of the Treatment Regimen on a for cause basis and will schedule such audits during normal business hours.  **9. Debarment**  I represent and warrant that I am not Debarred, nor, to the best of my knowledge, am I the subject of a proceeding that could lead to my becoming Debarred. I understand “Debarred” means(A) debarred by the FDA under 21 U.S.C. § 335a or debarred by any other competent authority of another jurisdiction or under any other laws or regulations; (B) excluded, debarred, suspended, sanctioned or otherwise ineligible to participate in the Federal health care programs or in Federal procurement or non-procurement programs in the U.S.A. or similar programs under the corresponding laws or regulations of another jurisdiction; (C) listed on the FDA’s Disqualified and Restricted Lists for clinical investigators or a similar list of another jurisdiction;; or (D) convicted of a criminal offense that falls within the scope of 42 U.S.C. § 1320a-7(a), or applicable local laws or regulations of my jurisdiction that could lead to being excluded, debarred, suspended, sanctioned or otherwise declared ineligible. In the event I receive notice of, or if I otherwise become aware of, my Debarment, or proposed Debarment, I will notify AbbVie immediately and AbbVie will have the right to discontinue my participation in AbbVie’s Pre-Approval Access program |

This Declaration is hereby agreed to and executed by the Physician on the date specified below.

|  |
| --- |
| Signature:  Name:  Title:  **Date (DD-MMM-YYYY):** |

Appendix A. Sample List of Excluded and Cautionary Medications

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| --- |
| **Excluded During Ramp-Up Phase and Cautionary Afterwards: (Additional Guidance Noted):** |
| **Strong CYP3A inducers –––^––** avasimibe, carbamazepine (Tegretol®), phenytoin (Dilantin®), rifampin (Rifadin®), St. John's wort  **Moderate CYP3A inducers^** – bosentan, efavirenz, etravirine, modafinil, nafcillin  **Strong CYP3A inhibitors†** – Boceprevir, clarithromycin, conivaptan, indinavir, itraconazole, ketoconazole, mibefradil, lopinavir/ritonavir, nefazodone, nelfinavir, ritonavir, posaconazole, saquinavir, telaprevir, telithromycin, voriconazole  **Moderate CYP3A inhibitors††** – Amprenavir, aprepitant, atazanavir, ciprofloxacin, crizotinib\*, darunavir/ritonavir, diltiazem, dronedarone, erythromycin, fluconazole, fosamprenavir, imatinib\*, verapamil |
| **Cautionary** |
| **Coumarins (vitamin K antagonists):** Warfarin (Coumadin)\*\*, phenprocoumon (Marcumar)\*\*  **Weak CYP3A inducers:** Amprenavir, aprepitant, armodafinil, clobazamechinacea, pioglitazone, prednisone, rufinamide, vemurafenib\*  **Weak CYP3A inhibitors:** Alprazolam, amiodarone, amlodipine, atorvastatin, bicalutamide\*, cilostazol, cimetidine, cyclosporine\*, fluoxetine, fluvoxamine, ginkgo, goldenseal, isoniazid, nilotinib\*, oral contraceptives, pazopanib\*, ranitidine, ranolazine, tipranavir/ritonavir, ticagrelor, zileuton  **P-gp substrates:** Aliskiren, ambrisentan, colchicine, dabigatran etexilate, digoxin, everolimus\*, fexofenadine, lapatinib\*, loperamide, maraviroc, nilotinib\*, ranolazine, saxagliptin, sirolimus\*, sitagliptin, talinolol, tolvaptan, topotecan\*  **BCRP substrates:** Methotrexate\*, mitoxantrone\*, irrinotecan\*, lapatinib\*, rosuvastatin, sulfasalazine, topotecan\*  **OATP1B1/1B3 substrates:** Atrasentan, atorvastatin, ezetimibe, fluvastatin, glyburide, rosuvastatin, simvastatin acid, pitavastatin, pravastatin, repaglinide, telmisartan, valsartan, olmesartan  **P-gp inhibitors:** Amiodarone, azithromycin, captopril, carvedilol, felodipine, quercetin, ronalzine, quinidine, ronalzine, ticagrelor  **BCRP inhibitors:** Geftinib\*, cyclosporine\*  **OATP1B1/B3 inhibitors:** Gemfibrozil, eltrombopag, cyclosporine\*, tipranavir |

In addition to the medications listed in this table, the patient receiving venetoclax should not consume grapefruit, grapefruit products, Seville oranges (including marmalade containing Seville oranges) or Starfruits.

†      If the patient requires use of these medications, use with caution, and reduce the venetoclax dose at least by 4-fold.  After discontinuation of CYP3A inhibitor, wait for 3 days before venetoclax dose is increased back to the target dose.

††    If the patient requires use of these medications, use with caution, and reduce the venetoclax dose at least by 2-fold.  After discontinuation of CYP3A inhibitor, wait for 3 days before venetoclax dose is increased back to the target dose.