CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

213176Orig1Orig2s000

RISK ASSESSMENT and RISK MITIGATION REVIEW(S)

Division of Risk Management (DRM)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

Application Type	NDA
Application Number	213176
PDUFA Goal Date	February 15, 2021
OSE RCM #	20120-288 and 291
Reviewer Name	Mei-Yean Chen, Pharm.D.
Team Leader	Naomi Boston, Pharm.D.
Division Deputy Director (Acting)	Doris Auth, Pharm.D.
Review Completion Date	December 3, 2020
Subject	Evaluation of Need for a REMS
Established Name	Umbralisib
Trade Name	Ukoniq
Name of Applicant	TG Therapeutics, Inc.
Therapeutic Class	a kinase inhibitor
Formulation(s)	200 mg oral tablet
Dosing Regimen	800 mg orally once daily

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EXECUTIVE SUMMARY

This review evaluates whether a risk evaluation and mitigation strategy (REMS) for the new molecular entity umbralisib is necessary to ensure the benefits outweigh its risks. TG Therapeutics, Inc. submitted a New Drug Application (NDA) 213176 for umbralisib with the proposed indication for the treatment of adult patients with:

- Relapsed or refractory marginal zone lymphoma (MZL) who have received at least one prior anti-CD20-based regimen.
- Relapsed or refractory follicular lymphoma (FL) who have received at least three prior lines of systemic therapies.

These indications are proposed to be approved under accelerated approval based on overall response rate. Continued approval for these indications may be contingent upon verification and description of clinical benefit in a confirmatory trial.

The risks associated with umbralisib include infections, neutropenia, diarrhea or colitis, hepatotoxicity, severe cutaneous reactions, allergic reaction due to inactive ingredient FD&C Yellow No.5, and embryo-fetal toxicity. The applicant did not submit a proposed REMS or risk management plan with this application.

Division of Risk Management (DRM) and Division of Hematology Malignancy 2 (DHM2) has agreed that a REMS is not needed to ensure the benefits of umbralisib outweigh its risks. Relapsed and refractory (r/r) MZL and FL are serious diseases with substantial risks of morbidity and mortality. Umbralisib therapy provides an additional therapeutic option for patients with r/r MZL and FL. Umbralisib has demonstrated efficacy for patients who received multiple lines of therapy and has demonstrated less toxicity in patients who have received prior therapies.

This reviewer recommends that, if umbralisib is approved, a REMS is not necessary to ensure its benefits outweigh its risks. Infections, neutropenia, diarrhea or colitis, hepatotoxicity, severe cutaneous reactions, allergic reaction due to inactive ingredient FD&C Yellow No.5, and embryo-fetal toxicity will be communicated in Section 5 Warnings and Precautions of the labeling, as well as instructions on how to withhold and reduce the dose if necessary in Section 2 Dosage and Administration. A Medication Guide that is part of labeling will be provided to patients. At the time of this review, none of these risks warrants a boxed warning. The clinicians, typically oncologists/hematologists, who will prescribe umbralisib are familiar by their experience and training in the management of these toxicities.

1 Introduction

This review evaluates whether a risk evaluation and mitigation strategy (REMS) for the new molecular entity (NME)[a] umbralisib is necessary to ensure the benefits outweigh its risks. TG Therapeutics, Inc.

[a] Section 505-1 (a) of the FD&C Act: *FDAAA factor (F): Whether the drug is a new molecular entity.*

submitted a New Drug Application (NDA) 213176 for umbralisib with the proposed indication for the treatment of adult patients with:

- Relapsed or refractory marginal zone lymphoma (MZL) who have received at least one prior anti-CD20-based regimen.
- Relapsed or refractory follicular lymphoma (FL) who have received at least three prior lines of systemic therapies.

These indications are proposed to be approved under accelerated approval based on overall response rate. Continued approval for these indications may be contingent upon verification and description of clinical benefit in a confirmatory trial.
This application is under review in the Division of Hematology Malignancy 2 (DHM2). The applicant did not submit a proposed REMS or risk management plan with this application.

2 Background

2.1 Product Information

Umbralisib is an orally bioavailable inhibitor of PhosphoInositide 3-Kinase delta (PI3Kδ) and Casein Kinase l epsilon (CK1ε). PI3Kδ is strongly expressed in cells of hematopoietic origin, and often implicated in B-cell related lymphomas. CK1ε has been implicated in the pathogenesis of cancer cells, including lymphoid malignancies.

The recommended dose of umbralisib is 800 mg orally once daily until disease progression or unacceptable toxicity.[b] Umbralisib is not currently approved any jurisdiction.

2.2 Regulatory History

The following is a summary of the regulatory history for NDA 213176 relevant to this review:

- 12/28/2012: Investigation New Drug (IND) 116762 was activated and opened in the US.
- 01/17/2019: Breakthrough therapy designation granted for treatment of MZL.
- 04/11/2019: Orphan drug designation granted for treatment of MZL.
- 12/20/2019: Rolling review granted.
- 03/04/2020: Orphan drug designation granted for treatment of FL.
- 06/15/2020: Part 2 of 2 submitted and complete NDA submission.
- 09/28/2020: A Post Mid-cycle meeting was held between the Agency and the Applicant via teleconference. The Agency informed the Applicant that based on the currently available data, there were no safety issues that require a REMS for umbralisib.

3 Therapeutic Context and Treatment Options

3.1 Description of the Medical Condition

[b] Section 505-1 (a) of the FD&C Act: *FDAAA factor (D): The expected or actual duration of treatment with the drug.*

Marginal Zone Lymphoma (MZL)

MZL is the second most common indolent non-Hodgkin's lymphoma (NHL), accounting for 5% to 15% of all NHL. It is estimated that 7,500 cases are diagnosed each year in the United States (US)[c1] with patients having an average age of 64 years old. There are three types of MZL: the extranodal MZL of mucosa-associated lymphoid tissue (MALT or gastric GALT), the splenic MZL, and the nodal MZL, which respectively comprise 70%, 20%, and 10% of MZL cases. Five-year survival rates are reported as follows: 88.7% for MALT lymphoma, 79.7% for splenic MZL, and 76.5% for nodal MZL.[2] *Helicobacter pylori* and hepatitis C virus are precursors to many instances of gastric MALT and splenic MZL, respectively. The course of MZL is characterized by remitting and relapsing phases and most patients will require multiple regimens over the course of their disease. Median survival is generally between 8 and 12 years.

Follicular lymphoma (FL)

FL is the second most common NHL and the most common (70%) indolent NHL, with an estimated 15,000 new cases in the US every year[3], with patients having an average age of about 60. FL is derived from white blood cells that grow in an uncontrolled, slow manner. Although this slowly progressing disease can be managed, re-occurrence is common and new treatments are needed. The five-year survival rate is 87.7% with younger patients having a higher survival rate. Even though patients are initially asymptomatic, a majority have advanced-stage disease at diagnosis. Asymptomatic patients are typically managed with observation until they meet the criteria to warrant treatment. The introduction of rituximab has been an important factor behind improvement in FL survival rates. Despite therapeutic advances, FL remains incurable, with patients experiencing multiple relapses until ultimately succumbing to the disease.

3.2 DESCRIPTION OF CURRENT TREATMENT OPTIONS

Marginal Zone Lymphoma (MZL)

The national comprehensive cancer network (NCCN) offers second line and subsequent therapeutic options[4] including repeat chemoimmunotherapy, lenalidomide+rituximab, ibrutinib, radioimmunotherapy, PI3K inhibitors, or rituximab monotherapy. The only fully approved therapy for previously treated MZL is lenalidomide in combination with rituximab. Table 1 summarizes the FDA approved treatment option in the MZL relapsed setting.

[c] Section 505-1 (a) of the FD&C Act: *FDAAA factor (A): The estimated size of the population likely to use the drug involved.*

Table 1 Summary of FDA approved treatment options in the MZL relapsed setting

Generic Name (Trade name)	Indication	Dosing	Warnings & Precautions	Boxed Warning (BW)/REMS
Lenalidomide (REVLIMID)[5] full approval 05/2019	Treatment of adults with previously treated MZL in combination with a rituximab product	20 mg PO QD on day 1-21 of repeated 28-day cycles for up to 12 cycles	Toxicities of embryo-fetal /hematologic/ hepatic, venous/arterial thromboembolism, cutaneous reactions, tumor lysis syndrome, 2nd malignancies.	REMS for embryo-fetal toxicity; BW for embryo-fetal toxicity, hematologic toxicity, & veneous & arterial thromboembolism
Ibrutinib (IMBRUVICA)[6] accelerated approval 01/2017	Treatment of adults with MZL who require systemic therapy & who have received at least 1 prior anti-CD20 based therapy	560 mg oral once daily	Hemorrhage, infections, cytopenias, hypertension, 2nd primary malignancies, tumor lysis syndrome, embryo-fetal toxicity	No BW, no REMS

Follicular lymphoma (FL)

There is no standard of care treatment for FL following (b) (4) prior therapies at the current time. In the setting of relapse or refractory (r/r) FL, treatments vary depending on the presentation, age, previous treatments, and overall health. NCCN offers second-line options[4] including repeat chemo-immunotherapy, lenalidomide+rituximab, ibrutinib, radioimmuno-therapy, PI3K inhibitors, or rituximab monotherapy. Treatment options are limited for patients who have received two or more prior therapies, with no FDA approved options specifically for this patient population. A summary of FDA approved treatment options in the r/r FL setting is shown in Table 2.

Table 2 Summary of FDA approved treatment options in the r/r FL setting

Generic name (trade name)	Indication	Dosing	Warnings & Precautions	Boxed warning
Obinutuzumab (GAZYVA)[7], full approval 11/2017	In combination with bendamustine	1000 mg IV on days 1,8,& 15 of cycle 1,	Infusion related rx, hypersensitive rx including serum	Hepatitis B reactions & PML

	followed by Gazyva monotherapy to treat r/r FL to a rituximab containing regimen	1000 mg on day 1 of cycle 2-8, then 1000 mg every 2 months up to 2 years	sickness, TLS, infections, neutropenia, thrombocytopenia	
Lenalidomide (REVLIMID) full approval 05/2019	In combination with a rituximab product to treat previously treated FL	20 mg PO QD days 1-21 of repeated 28-day cycles up to 12 cycles	Same as Table 1	Same as Table 1
Tazemetostat (TAZVERIK)[8] accelerated approval 06/2020	r/r FL whose tumors are + for an EZH2 mutation or who have no satisfactory alternative treatment option	800 mg PO twice daily	Secondary malignancies & embryo-fetal toxicity	No BW, no REMS
Below are PI3K inhibitors				
Idelalisib (ZYDELIG)[9], accelerated approval 2014 then full approval 2018	relapsed FL in patients who received at least 2 prior systemic therapies	150 mg oral twice daily	Hepatoxicity, severe diarrhea or colitis, pneumonitis, infections, intestinal perforation, & severe cutaneous rx.	Communication plan (CP) REMS & BW for fatal and/or serious toxicities of hepatic/diarrhea or colitis/pneumonitis/ infections/intestinal perforation
Copanlisib (ALIQOPA)[10] accelerated approval 2017	Relapse FL in patients who have received at least 2 prior systemic therapies	60 mg intravenous infusion on days 1,8, & 15 of a 28-day cycle	Infections, hyperglycemia, hypertension, non-infectious pneumonitis, neutropenia, severe	No BW, No REMS

			cutaneous rx, & embryo-fetal toxicity	
Duvelisib (COPIKTRA)[11] accelerated approval 2018	r/r FL in patients with who have received least 2 prior systemic therapies	25 mg oral twice daily	Infections, diarrhea or colitis, cutaneous rx, pneumonitis, hepatoxicity, neutropenia, & embryo fetal toxicity	Communication plan (CP) REMS & BW for fatal and/or serious toxicities including infections, diarrhea or colitis, cutaneous rx, and pneumonitis

4 Benefit Assessment

4.1 Marginal Zone Lymphoma (MZL)

The efficacy of umbralisib was evaluated in a single-arm cohort of Study 205 (NCT02793583), an open-label, multi-center, multi-cohort trial.[12] This study enrolled patients with MZL who had received at least one prior therapy. The study excluded patients with prior exposure to a PI3K inhibitor. Patients received umbralisib 800 mg orally once daily until disease progression or unacceptable toxicity. There were 69 patients enrolled with a median age of 67 years (range 34 to 88 years), 52% were female, and 83% were White. Ninety seven percent of patients had a baseline Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1.The median number of prior lines of therapy was 2 (range 1 to 6), with 26% being refractory to their last therapy. The efficacy analysis included 69 patients with 3 sub-types of MZL: extranodal (N=38), nodal (N=20), and splenic (N=11).

Efficacy was measured by overall response rate as assessed by investigators and an independent review committee (IRC) using criteria adopted from the International Working Group criteria for malignant lymphoma. Overall response rates were 45%, 60%, and 46% for the 3 MZL sub-types (extranodal, nodal, and splenic, respectively). Table 3 demonstrated efficacy results per IRC.

Table 3 Efficacy results in patients with MZL (Study 205)

Endpoint	N=69
Overall Response Rate	34 (49%)
95% confidence interval	37.0, 61.6
Complete Response	11 (16%)
Partial Response	23 (33%)

Duration of Response (DOR)	
Median, months (95% confidence interval)	Not reached (9.3, not evaluable)

4.2 Follicular Lymphoma (FL)

The efficacy of umbralisib was evaluated in a single-arm cohort of Study 205 (NCT02793583), an open-label, multi-center multi-cohort trial. Study 2 enrolled patients with FL who had received at least two prior systemic therapies that included an anti-CD20 monoclonal antibody and an alkylating agent. The trial excluded patients with Grade 3b FL, large cell transformation, prior allogeneic transplant, history of CNS lymphoma, and prior exposure to a PI3K inhibitor. Patients received umbralisib 800 mg orally once daily until disease progression or unacceptable toxicity. There were 117 patients enrolled with the median age of 65 years (range 29 to 87 years). Patients had a median of 3 prior lines of therapy (range 1 to 10), with 36% refractory to their last therapy.

Efficacy was measured by overall response rate as assessed by investigators and an IRC using criteria adopted from the International Working Group criteria for malignant lymphoma. The median follow-up time was 20.1 months (13.5 to 29.6 months). Table 4 demonstrated efficacy results per IRC.

Table 4 Efficacy results in patients with relapsed or refractory FL(Study 205)

Endpoint	N=117
Overall Response Rate	50 (43%)
95% confidence interval	33.6, 52.2
Complete Response	4(3.4%)
Partial Response	46(39.3%)
Duration of Response (DOR)	
Median, months (95% confidence interval)	11.1 (8.3, 16.4)

5 Risk Assessment & Safe-Use Conditions

There were two deaths in Study 205 cohort for MZL, one death was due to disease progression and the cause of the other death is unknown.[13] There were 7 deaths in Study 205 cohort for FL, three were due to disease progression, one to respiratory failure, one to myelodysplastic syndromes, and two with an unknown cause.

The pooled safety population described in Warnings and Precautions reflects exposure to umbralisib as monotherapy at a dosage of 800 mg orally once daily in 335 adults with hematologic malignancies. All risks[d] associated with umbralisib listed below are currently included in the draft labeling in Section 5, Warnings and Precautions. [12]

5.1 INFECTIONS

Serious infections, including fatal infections, occurred in patients treated with umbralisib. Grade ≥ 3 infections occurred in 10% of 335 patients, with fatal infections occurring in <1%. The most frequent grade ≥ 3 infections included pneumonia, sepsis, and urinary tract infection. Healthcare providers (HCPs) will be advised to monitor for any new or worsening signs and symptoms of infection. Withhold umbralisib for grade ≥ 3 infection until the infection has resolved.

HCPs will also be advised to provide prophylaxis for *Pneumocystis jiroveci* pneumonia (PJP) during umbralisib therapy, and to monitor for cytomegalovirus (CMV) infection in patients with a history of CMV infection. Consider prophylactic antivirals to prevent CMV infection/reactivation. For clinical CMV infection or viremia, withhold umbralisib until the infection or viremia resolves.

5.2 NEUTROPENIA

Serious neutropenia occurred in patients treated with umbralisib. Grade 3 neutropenia was reported in (b) (4)% of patients and grade 4 neutropenia in 9% of patients. The median time to onset of grade 3 or 4 neutropenia was (b) (4) days.

HCPs will be advised to monitor neutrophil counts at least every 2 weeks for the first 2 month of therapy and at least weekly in patients with grade 3-4 neutropenia. Withhold, reduce dose, or discontinue umbralisib depending on severity and persistence of neutropenia.

5.3 DIARRHEA OR COLITIS

Serious diarrhea or colitis occurred in patients treated with umbralisib. Diarrhea or colitis was reported in (b) (4)% and grade 3 diarrhea in 9% of patients. HCPs will be advised to withhold umbralisib for patients with abdominal pain, stool with mucus or blood, change in bowel habits, peritoneal signs, or with severe diarrhea until resolved. Upon resolution, resume umbralisib at a reduced dose. Discontinue umbralisib for recurrent grade 3 diarrhea or recurrent colitis of any grade. Discontinue umbralisib for life-threatening diarrhea or colitis.

5.4 HEPATOTOXICITY

Serious hepatotoxicity occurred in patients treated with umbralisib. Grade 3 and 4 transaminase elevations (ALT and/or AST) was reported in 8% and <1%, respectively. The median time to onset for grade 3 or (b) (4) transaminase elevation was 2.2 months (range 15 days to 4.7 months). HCPs will be advised

[d] Section 505-1 (a) of the FD&C Act: *FDAAA factor (E): The seriousness of any known or potential adverse events that may be related to the drug and the background incidence of such events in the population likely to use the drug.*

to monitor hepatic function at baseline and during therapy. Withhold umbralisib (b) (4) (b) (4) and monitor at least weekly until return to less than 3 x upper limit of normal. Resume umbralisib at a reduced dose. For (b) (4) ALT/AST elevation, discontinue umbralisib.

5.5 SEVERE CUTANEOUS REACTIONS

Serious cutaneous reactions, including a fatal case of exfoliative dermatitis occurred in patients treated with umbralisib. Grade 3 cutaneous reactions occurred in 2% of 335 patients and included dermatitis exfoliative, erythema, and rash. HCPs will be advised to monitor patients for new or worsening cutaneous reactions. For patients with severe (grade 3) cutaneous reaction, withhold umbralisib and monitor at least weekly until resolution. After resolution, umbralisib can be resumed at a reduced dose. Umbralisib should be discontinued for life-threatening cutaneous reactions.

5.6 ALLERGIC REACTIONS DUE TO INACTIVE INGREDIENT FD&C YELLOW NO.5

Umbralisib contains FD&C Yellow No.5 (tartrazine), which may cause allergic type reactions (including bronchial asthma) in susceptible persons. In the general population, the incidence of FD&C Yellow No.5 sensitivity is low; it is frequently seen in patients who are also allergic to aspirin.

5.7 EMBRYO-FETAL TOXICITY

Umbralisib can cause fetal harm when administered to a pregnant woman based on findings from nonclinical studies and its mechanism of action. Administration of umbralisib to pregnant mice during the period of organogenesis caused adverse developmental outcomes at maternal exposure comparable to those in patients at the recommended dose of 800 mg.

The draft label states to advise pregnant women of the potential risk to a fetus. The draft label recommends to advise females of reproductive potential and males with female partners of reproductive potential to use effective contraception during therapy, and for one month after the last dose.

6 Expected Postmarket Use

If approved, it is expected that oncologists will be the likely health care providers to prescribe umbrasilib, in both inpatient and outpatient settings.

7 Risk Management Activities Proposed by the Applicant

The Applicant did not propose any risk management activities for umbrasilib beyond routine pharmacovigilance and labeling.

8 Discussion of Need for a REMS

The Clinical Reviewer recommends approval of umbralisib on the basis of the efficacy and safety information currently available.

MZL is a serious and incurable malignancy. The front-line therapies utilize rituximab plus chemotherapy. Lenalidomide plus a rituximab product (regular approval, 2017) and ibrutinib (accelerated approval, 2017) are second line options. There is no approved product for therapy after second line.

Currently, no standard of care treatment exists for FL following three prior therapies. Tazemetostat, an EZH2 inhibitor, which was granted accelerated approved in June 2020, and is indicated for r/r FL whose tumors are positive for an EZH2 mutation and who have received at least two prior therapies. Oral PI3K inhibitors idelalisib (accelerated approved 2014 and fully approved 2018) and duvelisib (accelerated approved 2018), both have a REMS program with a Communication Plan (CP), to address the risks of fatal and serious toxicities of infection, diarrhea/colitis, cutaneous reaction, and pneumonitis. Copanlisib, another PI3K inhibitor approved in 2017, is administered intravenously and does not have a REMS. The incidence of Grade 3 or higher adverse events appears to be lower for umbralisib. The following table compares the adverse event profile of these 4 products (presented in the midcycle meeting on 09/09/2020.) [13]

	Idelalisib, n=352 BW: hepatotoxicity, diarrhea/colitis, pneumonitis, infection, intestinal perforation	Copanlisib n=317	Duvelisib, n=442 BW: infection, diarrhrea/colitis, pneumonitis, rash	Umbralisib, n=371[a]	n=229[b]
Grade≥3 AE	73%	85%	84%	51%	52%
Grade (G) 5 AE	2%	1%	8%	1%	0
Serious AE	50%	26%	65%	26%	28%
discontinuation	20%	16%	35%	15%	16%
G≥3 hepatotoxicity	14%	2%	9%	7%	8%
G≥3 diarrhea/colitis	14%	5%	18%	8%	10%
G≥3 infection	21%	19%	31%	10%	10%
G≥3 neutropenia	25%	24%	42%	17%	16%
G≥3 rash	4%	4%	5%	3%	3%
G≥3 pneumonitis	4%	5%	5%	1%	≤1%

BW: boxed warning; AE: adverse event

N=371[a] : patients with hematologic malignancies; n=229[b]: patients with FL/MZL

While advances in treatment offered more options, r/r FL remains incurable and most patients relapse or progress. There remains an unmet need for new drugs that provide efficacy with different toxicity profiles. Umbralisib therapy provides an additional therapeutic option for patients with r/r MZL and FL. Umbralisib has demonstrated efficacy for patients who received multiple lines of therapy and has demonstrated less toxicity in patients who have received prior therapies.

This reviewer recommends that, if umbralisib is approved, a REMS is not necessary to ensure its benefits outweigh its risks. Compared to two other oral PI3K inhibitors with REMS programs, the medical team has decided that the risks associated with umbralisib are lower and do not warrant a REMS program. Infections, neutropenia, diarrhea or colitis, hepatotoxicity, severe cutaneous reactions, allergic reactions due to FD&C Yellow No.5, and embryo-fetal toxicity will be communicated in the labeling Section 5 Warnings and Precautions, as well as instructions how to withhold and reduce dose in Section 2 Dosage and Administration. A Medication Guide that is part of labeling will be provided to patients. At the time of this review, none of these risks warrants a boxed warning. The clinicians, typically oncologists, who will prescribe umbrasilib are familiar by their experience and training in the management of these toxicities.

9 Conclusion & Recommendations

Based on the clinical review, the benefit-risk profile is favorable therefore, DRM and DHM2 agree that a REMS is not necessary for umbralisib to ensure the benefits outweigh the risks. At the time of this review, evaluation of safety information and labeling was ongoing. Please notify DRM if new safety information becomes available that changes the benefit-risk profile; this recommendation can be reevaluated.

10 Appendices

10.1 References

[1] Assessment Aid Umbralisib for Marginal zone lymphoma, accessed 10/23/2020

[2] Leukemia & lymphoma society Marginal zone lymphoma, lls.org/research/mzl, accessed 10/23/2020

[3] Leukemia & lymphoma society Follicular lymphoma, lls.org/research/fl, accessed 10/23/2020

[4] National Comprehensive Cancer Network Guideline non-Hodgkin's Lymphoma, nccn.org, accessed 10/26/2020

[5] Revlimid prescribing information, revlimid.com, accessed 10/26/2020

[6] Imbruvica prescribing information, imbruvica.com, accessed 10/26/2020

[7] Gazyva prescribing information, gazyva.com, accessed 10/26/2020

[8] Tazverik prescribing information, tazverik.com, accessed 10/27/2020

[9] Zydelig prescribing information, zydelig.com, accessed 10/26/2020

[10] Aliqopa prescribing information, aliqopa.com, accessed 10/26/2020

[11] Copiktra prescribing information, copiktra.com, accessed 10/26/2020

[12] Umbralisib draft prescribing information, accessed 11/19/2020

[13] Umbralisib NDA 213176 midcycle clinical team slide presentation, 09/09/2020

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/s/

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