FDA Briefing Document

Pediatric Oncology Subcommittee of the Oncologic Drugs Advisory Committee (ODAC)

May 11, 2021

DISCLAIMER STATEMENT

The attached package contains background information prepared by the Food and Drug Administration (FDA) for the panel members of the advisory committee. The FDA background package often contains assessments and/or conclusions and recommendations written by individual FDA reviewers. Such conclusions and recommendations do not necessarily represent the final position of the individual reviewers, nor do they necessarily represent the final position of the Review Division or Office.

We have brought the following issues to this Advisory Committee in order to gain the Committee's insights and opinions, and the background package will not include issues relevant to any final regulatory recommendation and instead is intended to focus on issues identified by the Agency for discussion by the advisory committee.

The subcommittee will discuss the development and successful implementation of the Pediatric Patient-Reported Outcomes Version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE) as a tool for eliciting the patient's voice in oncology clinical trials to more accurately determine tolerability and toxicity of drugs under investigation. The subcommittee will also address the challenges of capturing this type of data across the age spectrum of the pediatric population and possible generalizability of data. It will consider approaches to address concerns about excluding the patient voice of young children deemed incapable of self-reporting. The subcommittee will also focus on approaches to investigators and commercial sponsors to use the Pediatric PRO-CTCAE in toxicity assessment moving forward.

The FDA will not issue a final determination on the issues at hand until input from the advisory committee process has been considered and all reviews have been finalized. The final determination may be affected by issues not discussed at the advisory committee meeting.

Memorandum

Date: April 23, 2021

To: Pediatric Oncology Subcommittee of the Oncologic Drugs Advisory Committee (ODAC) Members, Consultants, and Guests

From: Gregory Reaman, MD
Associate Director for Pediatric Oncology, Oncology Center of Excellence, Office of the Commissioner, FDA

Subject: FDA Background Package for May 11, 2021 Meeting

Thank you for agreeing to participate in the upcoming Pediatric Oncology Subcommittee of the ODAC meeting. The Subcommittee will consider the state of the science of the development and potentials for use of the recently developed Pediatric PRO-CTCAE (Patient-Reported Outcomes Version of the Common Terminology Criteria for Adverse Events) in the management of children with cancer, in the clinical research setting especially in the context of new drug development programs, developing strategies for supportive care interventions, and possibly in the setting of survivorship research.

The Pediatric Oncology Subcommitee of the ODAC will address the opportunities and challenges of using these measures and capturing this type of data across the age spectrum of the pediatric population. Identifying an acceptable assessment frequency, and a core group of symptomatic adverse events and self-reported severity, frequency and degree of interference with daily activities for incorporation in the Oncology Center of Excellence (OCE's) Project Patient Voice will be considered. The potential use of this measure to improve participant and family experience on clinical trials and to better inform patients and families regarding the tolerability of specific therapeutic interventions will be assessed by the committee.

As always, we appreciate your time and commitment and look forward to an informative meeting on May 11, 2021.

Development and successful implementation of the Pediatric Patient-Reported Outcomes Version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE) as a tool for eliciting the patient's voice in oncology clinical trials to more accurately determine tolerability and of drugs under investigation

The particular matter for this meeting will be a review of the development and validation of the recently released Pediatric PRO-CTCAE National Cancer Institute.
Common Terminology Criteria for Adverse Events (CTCAE) 2018
https://ctep.cancer.gov/protocoldevelopment/electronic_applications/ctc.htm#ctc_50)
and discussion of its successful implementation as a tool for eliciting the child's voice in understanding symptomatic Adverse Events in oncology clinical trials to more accurately determine tolerability. The Pediatric Oncology Subcommitee of the ODAC will address the opportunities and challenges of using these measures and capturing this type of data across the age spectrum of the pediatric population. Identifying an acceptable assessment frequency, and a core group of symptomatic adverse events and self-reported severity, frequency and degree of interference with daily activities for incorporation in the OCE's Project Patient Voice will be considered. The potential use of this measure to improve participant and family experience on clinical trials and to better inform patients and families regarding the tolerability of specific therapeutic interventions will be assessed by the committee. The analysis of the results of Pediatric PRO-CTCAE data to inform supportive care strategies both within and outside of clicical trials will be explored as well as the use of the Pediatric PRO-CTCAE in facilitating survivorship resrearch. The Pediatric Oncology Subcomittee of the ODAC will also focus on addressing how best to support investigators and commercial sponsors to use the Pediatric PRO-CTCAE in tolerability assessment of new cancer drugs and how best to make this information available to patients and families.

The 21st Century Cures Act directed the U.S. FDA to systematically incorporate patients' experiences, needs, perspectives, and priorities into drug development and evaluation. Due to their lived experiences with symptoms and treatment, patients are experts in their disease. This should include children. With succesful use of patient-reported outcome (PRO) measures that are fit-for-purpose, patients can provide unique and valuable information on symptoms and functional status that should inform FDAs benefit: risk assessment of new cancer therapies. Furthermore, this information, if well collected and informative, should be available to patients, caregivers, and providers at the point of care.

The use of PROs, standardized reports of a patient's symptom experience derived directly from the patient, has the potential to allow patients and their caregivers to feel more in control of those factors that impact their well-being, assist their healthcare team in better controlling symptoms in both cancer care and clinical research settings, and ultimately improve outcomes. Studies have reported that using PRO tools to monitor symptoms and toxic effects during chemotherapy can improve adult patients' quality of life, decreases their number of hospitalizations, and lengthens

their life. (1,2) In addition to their utility in clinical care, PRO data can add value to the assessment of the risk:benefit profile of new investigational therapies. The Oncology Center of Excellence (OCE) has highlighted the utility of PRO data to further characterize the tolerability of investigational anti-cancer therapies in adult cancer trials.
https://www.sciencedirect.com/science/article/pii/S1098301517335209

https://ascopubs.org/doi/full/10.1200/EDBK_159514

Despite the benefits seen in adult patients with cancer and the fact that multiple stakeholders, such as the Institute of Medicine and the American Cancer Society, have called the integration of PRO measures into pediatric research and care essential (3), the use of patient-reported outcomes to track symptoms and adverse effects in pediatric oncology is rare. The reason for the paucity of PRO use in pediatric clinical trials is likely multi-factorial. Regardless of the reasons for inadequate collection of PROs evaluation of treatment-emergent or related side effects, i.e. toxicity, in clinical trials of new drugs is equally important to the investigation of a therapy's effectiveness, and the two are critical to the contextualization of benefit:risk.

A recent review of the FDA's experience with the use of PROs in pediatric oncology product applications approved between 1997 and 2020 demonstrated that only 4 of 17 such pediatric applications included PRO data. In all 4 cases, PRO data was collected during small single arm studies that enrolled 28-88 patients. This data was used to support exploratory endpoints and was not incorporated in product labeling. In all studies, symptomatic adverse events (AEs) were characterized using clinician-reported measures of the Common Terminology Criteria for Adverse Events (CTCAE) without complementary patient self-report. PROs were infrequently utilized in clinical trials of new drugs that resulted in approval of the drug for pediatric use. When included in pediatric trials, PRO data were limited in theirutility by either the absence of a clear research objective and prospective statistical analysis, and were not specifically directed at assessment of symptomatic toxicity of therapy. Contemporary PRO symptom libraries such as the National Cancer Institute's (NCI's) Pediatric PRO-CTCAE provide an opportunity to better elicit the young patient's voice to better evaluate the incidence and impact of symptomatic AEs and complement standard clinician-reported safety data in children on clinical trials of new cancer drugs (4).

Evidence from multiple studies suggests that clinicians' and parents' ratings of children's symptoms do not reflect children's self-reported experiences. Specifically, previous studies have found poor agreement between what children and parents/clinicians report, with parents/clinicians more often underreporting the burden of cancer and treatment on the lives of the children and adolescents. (6-9) Even worse, AE grading is based on what is documented in patient charts and symptoms are thus more likely missed compared with clinical or laboratory based results. Despite these important findings and limitations, it has become the norm to accept clinicians' graded symptomatic AEs as the sole source of safety and toxicity data in pediatric oncology trials.

The Pediatric PRO-CTCAE was developed and validated to enhance the precision of AE grading in pediatric oncology trials by facilitating children and adolescents to self-report on the symptomatic AEs they experience. Its release extends previous work initiated by the NCI to design the Patient-Reported Outcomes version of the CTCAE (PRO-CTCAE) for adults in

oncology trials (10,11). The PRO-CTCAE system is different from the standard outcome measures used in research, such as the Patient-Reported Outcomes Measurement Information System® (PROMIS®), in that it screens patients over a broad range of symptom toxicities with the goal of informing CTCAE grading. Compared with other PRO measures, the Pediatric PRO-CTCAE uses a set of questions to identify the worst severity, frequency, and interference with normal activities of symptomatic toxicities of trial participants (see Pediatric Module below). Envisioned use of the PRO-CTCAE includes descriptive AE detection/screening, support of dose-finding work, and assessment of comparative tolerability. Of note, tolerability is unique from traditional safety data in that it reflects the degree to which symptomatic and non-symptomatic adverse events associated with a given product's administration affect the ability or desire of a patient to adhere to the treatment regimen, while reportable safety information involves clinical judgment and incorporates the overall AE profile including labs, radiographic and clinical events, as well as reported side effects.

Assessment of the Pediatric PRO-CTCAE was accomplished using one-on-one cognitive interviewing for content validity to establish, evaluate, and refine the 62 symptomatic PRO-CTCAE measures to be comprehensible to children and their caregivers and relevant for capturing AEs. The assessment included a stratification by age groups representing different developmental stages to determine whether children aged 7-8 years are able to understand and respond to the Pediatric PRO-CTCAE and at what age adolescents might be able to transition to the previously developed Adult PRO-CTCAE measure. CTCAE medical terminology was translated into child-friendly terms (e.g., epitaxis = nose bleeds). Questions were developed to capture the child's symptom experience. For a given AE, one to three questions were created to reflect attributes of the symptom experience including presence, frequency, worst severity, and interference with daily activities, all of which proved to be well understood by children and adolescents. The cognitive interviews were critical for content validation. Age-related differences in response to questions emerged related primarily to the ability to conceptualize temporal relationships with the index symptom and difficulty in responding to questions related to some symptoms that had not been previously experienced.

Pediatric Module of the Patient-Reported Outcomes version Of The Common Terminology Criteria For Adverse Events (Ped-PRO-CTCAE™)

QUICK GUIDE TO THE ITEM LIBRARY*

Oral	
Dry mouth	SI
Difficulty swallowing	S
Mouth/throat sores	FSI
Voice quality changes	PI
Hoarseness	FSI
Sore throat	SI

Gastrointestinal	
Taste changes	PI
Decreased appetite	F
Nausea	FSI
Vomiting	FI
Heartburn	FS
Gas	PI
Bloating	PI
Hiccups	FS
Constipation	FSI
Diarrhea	FI
Abdominal pain	FSI
Fecal incontinence	FI

Respiratory	
Shortness of breath	FSI
Cough	FSI
Wheezing	SI
Sneezing	S

Cardio/Circulatory	
Swelling	SI
Heart palpitations	FS

Cutaneous	
Skin dryness	P
Acne	S
Hair loss	P
Itching	SI
Hives	P
Sensitivity to sunlight	P
Skin ulceration	P

Neurological	
Numbness & tingling	SI
Dizziness	SI

Visual/Perceptual	
Blurred vision	PI
Flashing lights	FI
Watery eyes	FSI
Ringing in ears	SI
Dry eyes	FSI

Attention/Memory	
Concentration	SI
Memory	SI

Pain	
General pain	FSI
Headache	FSI
Muscle pain	FSI
Joint pain	FSI

Sleep/Wake	
Insomnia	FSI
Fatigue	SI

Mood	
Anxiety	FSI
Sad	SI
Suicidal ideation	P

Genitourinary	
Painful urination	SI
Urinary urgency	FI
Urinary frequency	FI
Change in usual urine color	P
Urinary incontinence	FI

Miscellaneous	
Bruising	P
Chills	FS
Increased sweating	FSI
Hot flashes	FSI
Nosebleed	FSI
Falls	F
Muscle weakness	FSI
Restlessness	SI

National Cancer Institute

*Complete library of items available at: https://healthcaredelivery.cancer.gov/pro-ctcae

Attributes	
F: Frequency	I: Interference
S: Severity	P: Presence/Absence

The PRO-CTCAE measurement system was further evaluated for construct validity, responsiveness, and test-retest reliability and released in March, 2020. More information about the measure is provided online (13) and in publications (8). Access to the Ped-PRO-CTCAE questions and additional information is available on the NCI website (https://healthcaredelivery.cancer.gov/pro-ctcae/). Evaluation of the measure's validity and reliability provides strong evidence to support use of the Ped-PRO-CTCAE measurement system with children and adolescents (7–18 years) receiving cancer treatment. Coupled with mounting support for the inclusion of patient-reported data for evaluating safety and efficacy of cancer treatments in trials, the demonstrated validity and reliability of the Ped-PRO-CTCAE support its incorporation into future pediatric oncology trials. Further, these items have been designed for ease of administration and interpretation and lend themselves well to longitudinal use in pediatric oncology care and clinical research. Details of the measurement system can be found at Ped-PRO-CTCAE Measurement System. https://populationhealth.duke.edu/ped-pro-ctcae-measurement-system and in the APPENDIX below.

The Oncology Center of Excellence has developed an online platform for patients and caregivers along with their healthcare providers to view patient-reported symptom data prospectively collected through validated PRO symptom libraries like the PRO-CTCAE from cancer clinical trials. The intent of Project Patient Voice is to make symptom data derived from patient self-

reporting from select clinical trials of approved cancer drug products available to patients and caregivers, as such data are generally not included in the U.S. Prescribing Information (drug label). This is yet another OCE response to the 21st Century Cures Act, supporting the systematic collection of patient self-report of treatment related symptoms and making it available in a format to benefit patients and prescribers. Patient reported symptomatic adverse events provide a complementary source of information about side effects of approved cancer drugs, which can assist patients and caregivers in making treatment decisions.

Details on the purpose, results of the pilot phase, and details for use of Project Patient Voice can be found at https://www.fda.gov/about-fda/oncology-center-excellence/project-patient-voice . Data from the clinical trials of approved drugs in which there is adequate, high-frequency, and longitudinal patient-reported symptomatic adverse event data can beviewed in tables, bar charts and pie charts. Symptom frequency, severity, or occurrence of a particular symptom can be accessed by opening a symptom-specific page, with pie charts and bar graphs of the first 6 month experience. Extending Project Patient Voice to children with cancer is expected to better inform patients, parents, caregivers and prescribers. Detailed longitudinal assessment has the potential to improve the patient and family experience, including during the clinical trial experience. In addition, detailed and accurate symptom reporting holds promise for the development of supportive care research strategies to prevent or mitigate symptoms associated with cancer therapies. Prolonged longitudinal assessment of symptom self-reports may facilitate survivorship care and research.

REFERENCES:

1. Basch E, Deal AM, Dueck AC, et al. Overall survival results of a trial assessing patient-reported outcomes for symptom monitoring during routine cancer treatment.JAMA. 2017;318(2):197-198. doi:10.1001/jama.2017.7156
2. Basch E, Deal AM, Kris MG, et al. Symptom monitoring with patient-reported outcomes during routine cancer treatment: a randomized controlled trial.J Clin Oncol. 2016;34(6):557-565. doi:10.1200/ JCO.2015.63.0830
3. Kirch R, Reaman G, Feudtner C, et al. Advancing a comprehensive cancer care agenda for children and their families: Institute of Medicine Workshop highlights and next steps. CA Cancer J Clin. 2016;66 (5):398-407. doi:10.3322/caac.21347
4. Murugappan M.N., King-Kallimanis B.L., Reaman G.H., Bhatnagar V., Horodniceanu E.G., Bouchkouj N., Kluetz P.G., "Patient Reported Outcomes in Commercial Pediatric Oncology Clinical Trials," Virtual ISPOR 2021. May 2021.
5. International Council for Harmonisation. *Medical Dictionary for Regulatory Activities (MedRA)* https://www.meddra.org. Accessed Feb. 21, 2021.
6. National Cancer Institute. Common Terminology Criteria for Adverse Events (CTCAE). 2018. https://ctep.cancer.gov/protocoldevelopment/electronic_applications/ctc.htm#ctc_. Accessed Feb. 21. 2021.
7. McFatrich M, Brondon J, Lucas NR, et al. Mapping child and adolescent self-reported symptom data to clinician-reported adverse event grading to improve pediatric oncology care and research. *Cancer*. 2020;126(1):140–147
8. Zhukovsky DS, Rozmus CL, Robert RS, et al. Symptom profiles in children with advanced cancer: patient, family caregiver, and oncologist ratings. *Cancer*. 2015;121(22):4080–4087.
9. Collins JJ, Devine TD, Dick GS, et al. The measurement of symptoms in young children with cancer: the validation of the Memorial Symptom Assessment Scale in children aged 7-12. *J Pain Symptom Manage*. 2002;23(1):10–167.
10. Reeve BB, Withycombe JS, Baker JN, et al. The first step to integrating the child's voice in adverse event reporting in oncology trials: a content validation study among pediatric oncology clinicians. *Pediatr Blood Cancer*. 2013;60(7):1231–1236
11. Basch E, Reeve BB, Mitchell SA, Clauser SB, et al. Development of the National Cancer Institute's patient-reported outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE). *J Nat Cancer Inst*. 2014;10,2910.
12. Dueck AC, Mendoza TR, Mitchell SA, et al. Validity and reliability of the US National Cancer Institute's patient-reported outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE). *JAMA Oncol*. 2015;1(8):1051–10594. .
13. Reeve BB, Withycombe JS, Baker JN, et al. The first step to integrating the child's voice in adverse event reporting in oncology trials: a content validation study among pediatric oncology clinicians. *Pediatr Blood Cancer*. 2013;60(7):1231–1236
14. Reeve BB, McFatrich M, Pinheiro LC, et al. Eliciting the child's voice in adverse event reporting in oncology trials: cognitive interview findings from the pediatric patient-reported outcomes version of the Common Terminology Criteria for Adverse Events initiative. *Pediatr Blood Cancer*. 2017;64(3):

15. Kluetz PG, Slagle A, Papadopoulos EJ, et al. Focusing on core patient-reported outcomes in cancer clinical trials: symptomatic adverse events, physical function, and disease-related symptoms. *Clin Cancer Res*. 2016;22(7):1553–1558
16. Reeve BB, McFatrich M, Pinheiro LC, et al. Eliciting the child's voice in adverse event reporting in oncology trials: cognitive interview findings from the pediatric patient-reported outcomes version of the Common Terminology Criteria for Adverse Events initiative. *Pediatr Blood Cancer*. 2017;64(3):e2626111. Duke University Department of Population Health Sciences. Ped-PRO-CTCAE Measurement System. https://populationhealth.duke.edu/ped-pro-ctcae-measurement-system. Accessed December 10, 2019.
17. Reeve BB, McFatrich M, Pinheiro LC, et al. Eliciting the child's voice in adverse event reporting in oncology trials: cognitive interview findings from the pediatric patient-reported outcomes version of the Common Terminology Criteria for Adverse Events initiative. *Pediatr Blood Cancer*. 2017;64(3):e26261.
18. Reeve BB, McFatrich M, Mac JW, et al. Validity and Reliability of the Pediatric Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse EventsJ Natl Cancer Inst. 2020 Nov; 112(11): 1143–1152 [PubMed] [Google Scholar] Cancer Inst. 2020 Nov; 112(11): 1143–1152.Published online 2020 Jan 30. doi: 10.1093/jnci/djaa016 PMCID: PMC7669229 PMID: 31999349
19. Basch, E., Campbell, A., Hudgens, S., Jones, L., King-Kallimanis, B., Kluetz, P., O'Connor, D., Rosen, O. (2020). *Broadening the definition of tolerability in cancer clinical trials to better measure the patient experience* [White paper]. Friends of Cancer Research. https://www.focr.org/sites/default/files/Comparative%20Tolerability%20Whitepaper_FINAL.pdf).https://www.focr.org/sites/default/files/Comparative%20Tolerability%20Whitepaper_FINAL.pdf

Discussion Issues Relating to the Development of Pediatric PRO-CTCAE

1. Consider how patient self-report by children of symptoms attributable to a drug in a clinical trial might inform patients, parents, and providers about its tolerability and decisions regarding use.

2. Since only children greater than 7 years of age are able to reliably self-report symptoms, discuss the role for supplementing experiences of younger children using care-giver reports of "observable" symptoms (frequency, severity, and interference)?

3. Consider the logistical and operational challenges to collecting and analysis of data from patient self-report of symptoms.

4. Consider how best the constellation of self-reported symptoms in children and adolescents should be selected to be used in extending FDA's Project Patient Voice to children.

5. Consider whether data obtained in real time from children's self-report of symptomatic AEs could possibly impact the conduct of a clinical trial or inform an individual study participant's clinical management. Consider specific assessment and reporting requirements to be included in the protocol.

6. Consider how pediatric PRO-CTCAE might contribute to planning and implementation of supportive care and survivorship research strategies in children.

APPENDIX

PRO-CTCAE™ Measurement System

Please see next page

NCI- PRO-CTCAE™ ITEMS-ENGLISH

Item Library Version 1.0

As individuals go through treatment for their cancer they sometimes experience different symptoms and side effects. For each question, please select the one response that best describes your experiences over the past 7 days…

1. PRO-CTCAE™ Symptom Term: Dry mouth				
a. In the last 7 days, what was the SEVERITY of your DRY MOUTH at its WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe

2. PRO-CTCAE™ Symptom Term: Difficulty swallowing				
a. In the last 7 days, what was the SEVERITY of your DIFFICULTY SWALLOWING at its WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe

3. PRO-CTCAE™ Symptom Term: Mouth/throat sores				
a. In the last 7 days, what was the SEVERITY of your MOUTH OR THROAT SORES at their WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe
b. In the last 7 days, how much did MOUTH OR THROAT SORES INTERFERE with your usual or daily activities?				
O Not at all	O A little bit	O Somewhat	O Quite a bit	O Very much

4. PRO-CTCAE™ Symptom Term: Cracking at the corners of the mouth (cheilosis/cheilitis)				
a. In the last 7 days, what was the SEVERITY of SKIN CRACKING AT THE CORNERS OF YOUR MOUTH at its WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe

5. PRO-CTCAE™ Symptom Term: Voice quality changes	
a. In the last 7 days, did you have any VOICE CHANGES?	
O Yes	O No

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NCI- PRO-CTCAE™ ITEMS-ENGLISH

Item Library Version 1.0

6. PRO-CTCAE™ Symptom Term: Hoarseness				
a. In the last 7 days, what was the SEVERITY of your HOARSE VOICE at its WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe

7. PRO-CTCAE™ Symptom Term: Taste changes				
a. In the last 7 days, what was the SEVERITY of your PROBLEMS WITH TASTING FOOD OR DRINK at their WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe

8. PRO-CTCAE™ Symptom Term: Decreased appetite				
a. In the last 7 days, what was the SEVERITY of your DECREASED APPETITE at its WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe
b. In the last 7 days, how much did DECREASED APPETITE INTERFERE with your usual or daily activities?				
O Not at all	OA little bit	O Somewhat	O Quite a bit	O Very much

9. PRO-CTCAE™ Symptom Term: Nausea				
a. In the last 7 days, how OFTEN did you have NAUSEA?				
O Never	O Rarely	O Occasionally	O Frequently	O Almost constantly
b. In the last 7 days, what was the SEVERITY of your NAUSEA at its WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe

10. PRO-CTCAE™ Symptom Term: Vomiting				
a. In the last 7 days, how OFTEN did you have VOMITING?				
O Never	O Rarely	O Occasionally	O Frequently	O Almost constantly
b. In the last 7 days, what was the SEVERITY of your VOMITING at its WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe

Version date: 4/26/2020

11. PRO-CTCAE™ Symptom Term: Heartburn				
a. In the last 7 days, how OFTEN did you have HEARTBURN?				
O Never	O Rarely	O Occasionally	O Frequently	O Almost constantly
b. In the last 7 days, what was the SEVERITY of your HEARTBURN at its WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe

12. PRO-CTCAE™ Symptom Term: Gas	
a. In the last 7 days, did you have any INCREASED PASSING OF GAS (FLATULENCE)?	
O Yes	O No

13. PRO-CTCAE™ Symptom Term: Bloating				
a. In the last 7 days, how OFTEN did you have BLOATING OF THE ABDOMEN (BELLY)?				
O Never	O Rarely	O Occasionally	O Frequently	O Almost constantly
b. In the last 7 days, what was the SEVERITY of your BLOATING OF THE ABDOMEN (BELLY) at its WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe

14. PRO-CTCAE™ Symptom Term: Hiccups				
a. In the last 7 days, how OFTEN did you have HICCUPS?				
O Never	O Rarely	O Occasionally	O Frequently	O Almost constantly
b. In the last 7 days, what was the SEVERITY of your HICCUPS at their WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe

15. PRO-CTCAE™ Symptom Term: Constipation				
a. In the last 7 days, what was the SEVERITY of your CONSTIPATION at its WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe

16. PRO-CTCAE™ Symptom Term: Diarrhea				
a. In the last 7 days, how OFTEN did you have LOOSE OR WATERY STOOLS (DIARRHEA/DIARRHOEA)?				
O Never	O Rarely	O Occasionally	O Frequently	O Almost constantly

17. PRO-CTCAE™ Symptom Term: Abdominal pain				
a. In the last 7 days, how OFTEN did you have PAIN IN THE ABDOMEN (BELLY AREA)?				
O Never	O Rarely	O Occasionally	O Frequently	O Almost constantly
b. In the last 7 days, what was the SEVERITY of your PAIN IN THE ABDOMEN (BELLY AREA) at its WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe
c. In the last 7 days, how much did PAIN IN THE ABDOMEN (BELLY AREA) INTERFERE with your usual or daily activities?				
O Not at all	O A little bit	O Somewhat	O Quite a bit	O Very much

18. PRO-CTCAE™ Symptom Term: Fecal incontinence				
a. In the last 7 days, how OFTEN did you LOSE CONTROL OF BOWEL MOVEMENTS?				
O Never	O Rarely	O Occasionally	O Frequently	O Almost constantly
b. In the last 7 days, how much did LOSS OF CONTROL OF BOWEL MOVEMENTS INTERFERE with your usual or daily activities?				
O Not at all	O A little bit	O Somewhat	O Quite a bit	O Very much

19. PRO-CTCAE™ Symptom Term: Shortness of breath				
a. In the last 7 days, what was the SEVERITY of your SHORTNESS OF BREATH at its WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe
b. In the last 7 days, how much did your SHORTNESS OF BREATH INTERFERE with your usual or daily activities?				
O Not at all	O A little bit	O Somewhat	O Quite a bit	O Very much

20. PRO-CTCAE™ Symptom Term: Cough				
a. In the last 7 days, what was the SEVERITY of your COUGH at its WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe
b. In the last 7 days, how much did COUGH INTERFERE with your usual or daily activities?				
O Not at all	O A little bit	O Somewhat	O Quite a bit	O Very much

21. PRO-CTCAE™ Symptom Term: Wheezing				
a. In the last 7 days, what was the SEVERITY of your WHEEZING (WHISTLING NOISE IN THE CHEST WITH BREATHING) at its WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe

22. PRO-CTCAE™ Symptom Term: Swelling				
a. In the last 7 days, how OFTEN did you have ARM OR LEG SWELLING?				
O Never	O Rarely	O Occasionally	O Frequently	O Almost constantly
b. In the last 7 days, what was the SEVERITY of your ARM OR LEG SWELLING at its WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe
c. In the last 7 days, how much did ARM OR LEG SWELLING INTERFERE with your usual or daily activities?				
O Not at all	O A little bit	O Somewhat	O Quite a bit	O Very much

23. PRO-CTCAE™ Symptom Term: Heart palpitations				
a. In the last 7 days, how OFTEN did you feel a POUNDING OR RACING HEARTBEAT (PALPITATIONS)?				
O Never	O Rarely	O Occasionally	O Frequently	O Almost constantly
b. In the last 7 days, what was the SEVERITY of your POUNDING OR RACING HEARTBEAT (PALPITATIONS) at its WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe

24. PRO-CTCAE™ Symptom Term: Rash	
a. In the last 7 days, did you have any RASH?	
O Yes	O No

25. PRO-CTCAE™ Symptom Term: Skin dryness				
a. In the last 7 days, what was the SEVERITY of your DRY SKIN at its WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe

26. PRO-CTCAE™ Symptom Term: Acne				
a. In the last 7 days, what was the SEVERITY of your ACNE OR PIMPLES ON THE FACE OR CHEST at its WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe

27. PRO-CTCAE™ Symptom Term: Hair loss				
a. In the last 7 days, did you have any HAIR LOSS?				
O Not at all	O A little bit	O Somewhat	O Quite a bit	O Very much

28. PRO-CTCAE™ Symptom Term: Itching				
a. In the last 7 days, what was the SEVERITY of your ITCHY SKIN at its WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe

29. PRO-CTCAE™ Symptom Term: Hives	
a. In the last 7 days, did you have any HIVES (ITCHY RED BUMPS ON THE SKIN)?	
O Yes	O No

30. PRO-CTCAE™ Symptom Term: Hand-foot syndrome				
a. In the last 7 days, what was the SEVERITY of your HAND-FOOT SYNDROME (A RASH OF THE HANDS OR FEET THAT CAN CAUSE CRACKING, PEELING, REDNESS OR PAIN) at its WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe

31. PRO-CTCAE™ Symptom Term: Nail loss	
a. In the last 7 days, did you LOSE ANY FINGERNAILS OR TOENAILS?	
O Yes	O No

32. PRO-CTCAE™ Symptom Term: Nail ridging	
a. In the last 7 days, did you have any RIDGES OR BUMPS ON YOUR FINGERNAILS OR TOENAILS?	
O Yes	O No

33. PRO-CTCAE™ Symptom Term: Nail discoloration	
a. In the last 7 days, did you have any CHANGE IN THE COLOR OF YOUR FINGERNAILS OR TOENAILS?	
O Yes	O No

34. PRO-CTCAE™ Symptom Term: Sensitivity to sunlight	
a. In the last 7 days, did you have any INCREASED SKIN SENSITIVITY TO SUNLIGHT?	
O Yes	O No

35. PRO-CTCAE™ Symptom Term: Bed/pressure sores	
a. In the last 7 days, did you have any BED SORES?	
O Yes	O No

36. PRO-CTCAE™ Symptom Term: Radiation skin reaction					
a. In the last 7 days, what was the SEVERITY of your SKIN BURNS FROM RADIATION at their WORST?					
O None	O Mild	O Moderate	O Severe	O Very severe	O Not applicable

37. PRO-CTCAE™ Symptom Term: Skin darkening	
a. In the last 7 days, did you have any UNUSUAL DARKENING OF THE SKIN?	
O Yes	O No

38. PRO-CTCAE™ Symptom Term: Stretch marks	
a. In the last 7 days, did you have any STRETCH MARKS?	
O Yes	O No

39. PRO-CTCAE™ Symptom Term: Numbness & tingling				
a. In the last 7 days, what was the SEVERITY of your NUMBNESS OR TINGLING IN YOUR HANDS OR FEET at its WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe
b. In the last 7 days, how much did NUMBNESS OR TINGLING IN YOUR HANDS OR FEET INTERFERE with your usual or daily activities?				
O Not at all	O A little bit	O Somewhat	O Quite a bit	O Very much

40. PRO-CTCAE™ Symptom Term: Dizziness				
a. In the last 7 days, what was the SEVERITY of your DIZZINESS at its WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe
b. In the last 7 days, how much did DIZZINESS INTERFERE with your usual or daily activities?				
O Not at all	O A little bit	O Somewhat	O Quite a bit	O Very much

41. PRO-CTCAE™ Symptom Term: Blurred vision				
a. In the last 7 days, what was the SEVERITY of your BLURRY VISION at its WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe
b. In the last 7 days, how much did BLURRY VISION INTERFERE with your usual or daily activities?				
O Not at all	O A little bit	O Somewhat	O Quite a bit	O Very much

42. PRO-CTCAE™ Symptom Term: Flashing lights	
a. In the last 7 days, did you have any FLASHING LIGHTS IN FRONT OF YOUR EYES?	
O Yes	O No

43. PRO-CTCAE™ Symptom Term: Visual floaters	
a. In the last 7 days, did you have any SPOTS OR LINES (FLOATERS) THAT DRIFT IN FRONT OF YOUR EYES?	
O Yes	O No

44. PRO-CTCAE™ Symptom Term: Watery eyes				
a. In the last 7 days, what was the SEVERITY of your WATERY EYES (TEARING) at their WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe
b. In the last 7 days, how much did WATERY EYES (TEARING) INTERFERE with your usual or daily activities?				
O Not at all	O A little bit	O Somewhat	O Quite a bit	O Very much

45. PRO-CTCAE™ Symptom Term: Ringing in ears				
a. In the last 7 days, what was the SEVERITY of RINGING IN YOUR EARS at its WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe

46. PRO-CTCAE™ Symptom Term: Concentration				
a. In the last 7 days, what was the SEVERITY of your PROBLEMS WITH CONCENTRATION at their WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe
b. In the last 7 days, how much did PROBLEMS WITH CONCENTRATION INTERFERE with your usual or daily activities?				
O Not at all	O A little bit	O Somewhat	O Quite a bit	O Very much

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47. PRO-CTCAE™ Symptom Term: Memory				
a. In the last 7 days, what was the SEVERITY of your PROBLEMS WITH MEMORY at their WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe
b. In the last 7 days, how much did PROBLEMS WITH MEMORY INTERFERE with your usual or daily activities?				
O Not at all	O A little bit	O Somewhat	O Quite a bit	O Very much

48. PRO-CTCAE™ Symptom Term: General pain				
a. In the last 7 days, how OFTEN did you have PAIN?				
O Never	O Rarely	O Occasionally	O Frequently	O Almost constantly
b. In the last 7 days, what was the SEVERITY of your PAIN at its WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe
c. In the last 7 days, how much did PAIN INTERFERE with your usual or daily activities?				
O Not at all	O A little bit	O Somewhat	O Quite a bit	O Very much

49. PRO-CTCAE™ Symptom Term: Headache				
a. In the last 7 days, how OFTEN did you have a HEADACHE?				
O Never	O Rarely	O Occasionally	O Frequently	O Almost constantly
b. In the last 7 days, what was the SEVERITY of your HEADACHE at its WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe
c. In the last 7 days, how much did your HEADACHE INTERFERE with your usual or daily activities?				
O Not at all	O A little bit	O Somewhat	O Quite a bit	O Very much

50. PRO-CTCAE™ Symptom Term: Muscle pain				
a. In the last 7 days, how OFTEN did you have ACHING MUSCLES?				
O Never	O Rarely	O Occasionally	O Frequently	O Almost constantly
b. In the last 7 days, what was the SEVERITY of your ACHING MUSCLES at their WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe
c. In the last 7 days, how much did ACHING MUSCLES INTERFERE with your usual or daily activities?				
O Not at all	O A little bit	O Somewhat	O Quite a bit	O Very much

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51. PRO-CTCAE™ Symptom Term: Joint pain				
a. In the last 7 days, how OFTEN did you have ACHING JOINTS (SUCH AS ELBOWS, KNEES, SHOULDERS)?				
O Never	O Rarely	O Occasionally	O Frequently	O Almost constantly
b. In the last 7 days, what was the SEVERITY of your ACHING JOINTS (SUCH AS ELBOWS, KNEES, SHOULDERS) at their WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe
c. In the last 7 days, how much did ACHING JOINTS (SUCH AS ELBOWS, KNEES, SHOULDERS) INTERFERE with your usual or daily activities?				
O Not at all	O A little bit	O Somewhat	O Quite a bit	O Very much

52. PRO-CTCAE™ Symptom Term: Insomnia				
a. In the last 7 days, what was the SEVERITY of your INSOMNIA (INCLUDING DIFFICULTY FALLING ASLEEP, STAYING ASLEEP, OR WAKING UP EARLY) at its WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe
b. In the last 7 days, how much did INSOMNIA (INCLUDING DIFFICULTY FALLING ASLEEP, STAYING ASLEEP, OR WAKING UP EARLY) INTERFERE with your usual or daily activities?				
O Not at all	O A little bit	O Somewhat	O Quite a bit	O Very much

53. PRO-CTCAE™ Symptom Term: Fatigue				
a. In the last 7 days, what was the SEVERITY of your FATIGUE, TIREDNESS, OR LACK OF ENERGY at its WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe
b. In the last 7 days, how much did FATIGUE, TIREDNESS, OR LACK OF ENERGY INTERFERE with your usual or daily activities?				
O Not at all	O A little bit	O Somewhat	O Quite a bit	O Very much

54. PRO-CTCAE™ Symptom Term: Anxious				
a. In the last 7 days, how OFTEN did you feel ANXIETY?				
O Never	O Rarely	O Occasionally	O Frequently	O Almost constantly
b. In the last 7 days, what was the SEVERITY of your ANXIETY at its WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe
c. In the last 7 days, how much did ANXIETY INTERFERE with your usual or daily activities?				
O Not at all	O A little bit	O Somewhat	O Quite a bit	O Very much

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55. PRO-CTCAE™ Symptom Term: Discouraged				
a. In the last 7 days, how OFTEN did you FEEL THAT NOTHING COULD CHEER YOU UP?				
O Never	O Rarely	O Occasionally	O Frequently	O Almost constantly
b. In the last 7 days, what was the SEVERITY of your FEELINGS THAT NOTHING COULD CHEER YOU UP at their WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe
c. In the last 7 days, how much did FEELING THAT NOTHING COULD CHEER YOU UP INTERFERE with your usual or daily activities?				
O Not at all	O A little bit	O Somewhat	O Quite a bit	O Very much

56. PRO-CTCAE™ Symptom Term: Sad				
a. In the last 7 days, how OFTEN did you have SAD OR UNHAPPY FEELINGS?				
O Never	O Rarely	O Occasionally	O Frequently	O Almost constantly
b. In the last 7 days, what was the SEVERITY of your SAD OR UNHAPPY FEELINGS at their WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe
c. In the last 7 days, how much did SAD OR UNHAPPY FEELINGS INTERFERE with your usual or daily activities?				
O Not at all	O A little bit	O Somewhat	O Quite a bit	O Very much

57. PRO-CTCAE™ Symptom Term: Irregular periods/vaginal bleeding		
a. In the last 7 days, did you have any IRREGULAR MENSTRUAL PERIODS?		
O Yes	O No	O Not Applicable

58. PRO-CTCAE™ Symptom Term: Missed expected menstrual period		
a. In the last 7 days, did you MISS AN EXPECTED MENSTRUAL PERIOD?		
O Yes	O No	O Not applicable

59. PRO-CTCAE™ Symptom Term: Vaginal discharge				
a. In the last 7 days, did you have any UNUSUAL VAGINAL DISCHARGE?				
O Not at all	O A little bit	O Somewhat	O Quite a bit	O Very much

60. PRO-CTCAE™ Symptom Term: Vaginal dryness				
a. In the last 7 days, what was the SEVERITY of your VAGINAL DRYNESS at its WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe

61. PRO-CTCAE™ Symptom Term: Painful urination				
a. In the last 7 days, what was the SEVERITY of your PAIN OR BURNING WITH URINATION at its WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe

62. PRO-CTCAE™ Symptom Term: Urinary urgency				
a. In the last 7 days, how OFTEN did you feel an URGE TO URINATE ALL OF A SUDDEN?				
O Never	O Rarely	O Occasionally	O Frequently	O Almost constantly
b. In the last 7 days, how much did SUDDEN URGES TO URINATE INTERFERE with your usual or daily activities?				
O Not at all	O A little bit	O Somewhat	O Quite a bit	O Very much

63. PRO-CTCAE™ Symptom Term: Urinary frequency				
a. In the last 7 days, were there times when you had to URINATE FREQUENTLY?				
O Never	O Rarely	O Occasionally	O Frequently	O Almost constantly
b. In the last 7 days, how much did FREQUENT URINATION INTERFERE with your usual or daily activities?				
O Not at all	O A little bit	O Somewhat	O Quite a bit	O Very much

64. PRO-CTCAE™ Symptom Term: Change in usual urine color	
a. In the last 7 days, did you have any URINE COLOR CHANGE?	
O Yes	O No

65. PRO-CTCAE™ Symptom Term: Urinary incontinence				
a. In the last 7 days, how OFTEN did you have LOSS OF CONTROL OF URINE (LEAKAGE)?				
O Never	O Rarely	O Occasionally	O Frequently	O Almost constantly
b. In the last 7 days, how much did LOSS OF CONTROL OF URINE (LEAKAGE) INTERFERE with your usual or daily activities?				
O Not at all	O A little bit	O Somewhat	O Quite a bit	O Very much

66. PRO-CTCAE™ Symptom Term: Achieve and maintain erection						
a. In the last 7 days, what was the SEVERITY of your DIFFICULTY GETTING OR KEEPING AN ERECTION at its WORST?						
O None	O Mild	O Moderate	O Severe	O Very severe	O Not sexually active	O Prefer not to answer

67. PRO-CTCAE™ Symptom Term: Ejaculation						
a. In the last 7 days, how OFTEN did you have EJACULATION PROBLEMS?						
O Never	O Rarely	O Occasionally	O Frequently	O Almost constantly	O Not sexually active	O Prefer not to answer

68. PRO-CTCAE™ Symptom Term: Decreased libido						
a. In the last 7 days, what was the SEVERITY of your DECREASED SEXUAL INTEREST at its WORST?						
O None	O Mild	O Moderate	O Severe	O Very severe	O Not sexually active	O Prefer not to answer

69. PRO-CTCAE™ Symptom Term: Delayed orgasm			
a. In the last 7 days, did you feel that it TOOK TOO LONG TO HAVE AN ORGASM OR CLIMAX?			
O Yes	O No	O Not sexually active	O Prefer not to answer

70. PRO-CTCAE™ Symptom Term: Unable to have orgasm			
a. In the last 7 days, were you UNABLE TO HAVE AN ORGASM OR CLIMAX?			
O Yes	O No	O Not sexually active	O Prefer not to answer

71. PRO-CTCAE™ Symptom Term: Pain w/sexual intercourse						
a. In the last 7 days, what was the SEVERITY of your PAIN DURING VAGINAL SEX at its WORST?						
O None	O Mild	O Moderate	O Severe	O Very severe	O Not sexually active	O Prefer not to answer

72. PRO-CTCAE™ Symptom Term: Breast swelling and tenderness				
a. In the last 7 days, what was the SEVERITY of your BREAST AREA ENLARGEMENT OR TENDERNESS at its WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe

73. PRO-CTCAE™ Symptom Term: Bruising	
a. In the last 7 days, did you BRUISE EASILY (BLACK AND BLUE MARKS)?	
O Yes	O No

74. PRO-CTCAE™ Symptom Term: Chills				
a. In the last 7 days, how OFTEN did you have SHIVERING OR SHAKING CHILLS?				
O Never	O Rarely	O Occasionally	O Frequently	O Almost constantly
b. In the last 7 days, what was the SEVERITY of your SHIVERING OR SHAKING CHILLS at their WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe

75. PRO-CTCAE™ Symptom Term: Increased sweating				
a. In the last 7 days, how OFTEN did you have UNEXPECTED OR EXCESSIVE SWEATING DURING THE DAY OR NIGHTTIME (NOT RELATED TO HOT FLASHES/FLUSHES)?				
O Never	O Rarely	O Occasionally	O Frequently	O Almost constantly
b. In the last 7 days, what was the SEVERITY of your UNEXPECTED OR EXCESSIVE SWEATING DURING THE DAY OR NIGHTTIME (NOT RELATED TO HOT FLASHES/FLUSHES) at its WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe

76. PRO-CTCAE™ Symptom Term: Decreased sweating	
a. In the last 7 days, did you have an UNEXPECTED DECREASE IN SWEATING?	
O Yes	O No

77. PRO-CTCAE™ Symptom Term: Hot flashes				
a. In the last 7 days, how OFTEN did you have HOT FLASHES/FLUSHES?				
O Never	O Rarely	O Occasionally	O Frequently	O Almost constantly
b. In the last 7 days, what was the SEVERITY of your HOT FLASHES/FLUSHES at their WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe

78. PRO-CTCAE™ Symptom Term: Nosebleed				
a. In the last 7 days, how OFTEN did you have NOSEBLEEDS?				
O Never	O Rarely	O Occasionally	O Frequently	O Almost constantly
b. In the last 7 days, what was the SEVERITY of your NOSEBLEEDS at their WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe

79. PRO-CTCAE™ Symptom Term: Pain and swelling at injection site		
a. In the last 7 days, did you HAVE ANY PAIN, SWELLING, OR REDNESS AT A SITE OF DRUG INJECTION OR IV?		
O Yes	O No	O Not applicable

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80. PRO-CTCAE™ Symptom Term: Body odor				
a. In the last 7 days, what was the SEVERITY of your BODY ODOR at its WORST?				
O None	O Mild	O Moderate	O Severe	O Very severe

OTHER SYMPTOMS					
Do you have any other symptoms that you wish to report?					
O Yes		O No			
Please list any other symptoms:					
1.	In the last 7 days, what was the SEVERITY of this symptom at its WORST?				
	O None	O Mild	O Moderate	O Severe	O Very Severe
2.	In the last 7 days, what was the SEVERITY of this symptom at its WORST?				
	O None	O Mild	O Moderate	O Severe	O Very Severe
3.	In the last 7 days, what was the SEVERITY of this symptom at its WORST?				
	O None	O Mild	O Moderate	O Severe	O Very Severe
4.	In the last 7 days, what was the SEVERITY of this symptom at its WORST?				
	O None	O Mild	O Moderate	O Severe	O Very Severe
5.	In the last 7 days, what was the SEVERITY of this symptom at its WORST?				
	O None	O Mild	O Moderate	O Severe	O Very Severe

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