DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2021-D-0691]

Pharmacokinetic-Based Criteria for Supporting Alternative Dosing Regimens of
Programmed Cell Death Receptor-1 or Programmed Cell Death-Ligand 1 Blocking
Antibodies for Treatment of Patients with Cancer; Draft Guidance for Industry;

Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the
availability of a draft guidance for industry entitled “Pharmacokinetic-Based Criteria for
Supporting Alternative Dosing Regimens of Programmed Cell Death Receptor-1 (PD-1) or
Programmed Cell Death-Ligand 1 (PD-L1) Blocking Antibodies for Treatment of Patients with
Cancer.” This draft guidance provides recommendations for sponsors of investigational new drug
applications (INDs) and biologics license applications (BLAs) on the use of pharmacokinetic
(PK)-based criteria to support the approval of alternative dosing regimens for programmed cell
death receptor-1 (PD-1) or programmed cell death-ligand 1 (PD-L1) blocking antibodies. This
draft guidance is based on accumulated scientific and regulatory experience for PD-1 and PD-L1
drugs, and as such, does not address development of alternative dosing regimens for any other
drugs or biologics, changes in route of administration, or novel formulations of previously
approved PD-1/PD-L1 products.

DATES: Submit either electronic or written comments on the draft guidance by [INSERT
DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER] to
ensure that the Agency considers your comment on this draft guidance before it begins work on
the final version of the guidance.
ADDRESSSES: You may submit comments on any guidance at any time as follows:

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: https://www.regulations.gov. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to https://www.regulations.gov will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else’s Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on https://www.regulations.gov.

- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see “Written/Paper Submissions” and “Instructions”).

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in “Instructions.”

Instructions: All submissions received must include the Docket No. FDA-2021-D-0691 for “Pharmacokinetic-Based Criteria for Supporting Alternative Dosing Regimens of
Programmed Cell Death Receptor-1 (PD-1) or Programmed Cell Death-Ligand 1 (PD-L1)
Blocking Antibodies for Treatment of Patients with Cancer.” Received comments will be placed
in the docket and, except for those submitted as “Confidential Submissions,” publicly viewable
at https://www.regulations.gov or at the Dockets Management Staff between 9 a.m. and 4 p.m.,
Monday through Friday, 240-402-7500.

- Confidential Submissions--To submit a comment with confidential information that you
do not wish to be made publicly available, submit your comments only as a written/paper
submission. You should submit two copies total. One copy will include the information
you claim to be confidential with a heading or cover note that states “THIS DOCUMENT
CONTAINS CONFIDENTIAL INFORMATION.” The Agency will review this copy,
including the claimed confidential information, in its consideration of comments. The
second copy, which will have the claimed confidential information redacted/blacked out,
will be available for public viewing and posted on https://www.regulations.gov. Submit
both copies to the Dockets Management Staff. If you do not wish your name and contact
information to be made publicly available, you can provide this information on the cover
sheet and not in the body of your comments and you must identify this information as
“confidential.” Any information marked as “confidential” will not be disclosed except in
accordance with 21 CFR 10.20 and other applicable disclosure law. For more
information about FDA’s posting of comments to public dockets, see 80 FR 56469,
September 18, 2015, or access the information at:

Docket: For access to the docket to read background documents or the electronic and
written/paper comments received, go to https://www.regulations.gov and insert the docket
number, found in brackets in the heading of this document, into the “Search” box and follow the
prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville,
MD 20852, 240-402-7500.
FDA is announcing the availability of a draft guidance for industry entitled “Pharmacokinetic-Based Criteria for Supporting Alternative Dosing Regimens of Programmed Cell Death Receptor-1 (PD-1) or Programmed Cell Death-Ligand 1 (PD-L1) Blocking Antibodies for Treatment of Patients with Cancer.” This draft guidance provides recommendations for sponsors of INDs and BLAs on the use of PK-based criteria to support the approval of alternative dosing regimens for PD-1 or PD-L1 blocking antibodies. The draft guidance is based on accumulated scientific and regulatory experience for PD-1 and PD-L1 drugs and, as such, does not address development of alternative dosing regimens for any other drugs or biologics, changes in route of administration, or novel formulations of previously approved PD-1/PD-L1 products.

Sponsors may seek approval of alternative intravenous (IV) dosing regimens that are different from those tested in clinical efficacy and safety trials. These alternative IV dosing regimens are typically designed to change doses (e.g., body weight adjusted doses to flat doses) and/or dosing intervals (e.g., once every 3 weeks to once every 6 weeks). Longer dosing interval
periods can minimize patient burden and reduce risks associated with more frequent administration (e.g., infusion reactions), as well as exposure to communicable diseases (e.g., SARS-CoV-2) associated with visits to hospitals or infusion centers. The draft guidance describes the criteria for using the PK-based approach and the documents that should be included in the submissions seeking approval.

This draft guidance is being issued consistent with FDA’s good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the current thinking of FDA on “Pharmacokinetic-Based Criteria for Supporting Alternative Dosing Regimens of Programmed Cell Death Receptor-1 (PD-1) or Programmed Cell Death-Ligand 1 (PD-L1) Blocking Antibodies for Treatment of Patients with Cancer.” It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.

II. Paperwork Reduction Act of 1995

While this guidance contains no collection of information, it does refer to previously approved FDA collections of information. Therefore, clearance by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501-3521) is not required for this guidance. The previously approved collections of information are subject to review by OMB under the PRA. The collections of information in 21 CFR part 312 have been approved under OMB control number 0910-0014 and the collections of information in 21 CFR part 601 have been approved under 0910-0338.

III. Electronic Access


Dated: August 17, 2021.
Lauren K. Roth,

*Acting Principal Associate Commissioner for Policy.*

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