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10 **UNITED STATES DISTRICT COURT**
11 **EASTERN DISTRICT OF WASHINGTON**

12 STATE OF WASHINGTON, et al.,

13 Plaintiffs,

14 v.

15 UNITED STATES FOOD AND
DRUG ADMINISTRATION, et al.,

16 Defendants.
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20
21
22

NO. 1:23-cv-03026-TOR

PLAINTIFF STATES'
RESPONSE TO NOTICE
OF SUPPLEMENTAL
INFORMATION

1 At the oral argument held in this matter on March 28, 2023, the Court asked
2 Defendants' counsel what other drugs require pharmacy certification. Counsel
3 responded that he did not have an example off the top of his head of such a drug.
4 On March 29, 2023, Defendants filed a Notice of Supplemental Information
5 (ECF No. 71) listing 43 medications. The Plaintiff States respectfully submit this
6 response to Defendants' Notice.

7 Although the drugs listed in Defendants' Notice are subject to some form
8 of pharmacy certification requirement, *none* of those requirements resemble the
9 uniquely onerous pharmacy requirements imposed by the mifepristone REMS.
10 The pharmacy certification requirement adopted by FDA for mifepristone in
11 January 2023 is unique to that drug alone because it is the only REMS that
12 requires individual pharmacies to independently create a secure system to verify
13 prescriber certification (and, moreover, only applies when the drug is used for
14 abortion or miscarriage care, not when a higher and more frequent dose is used
15 to treat Cushing's disease). *See* ECF No. 35 ¶ 146.

16 This distinction is crucial in terms of the burdens it imposes on patient
17 access and the healthcare delivery system. 21 U.S.C. §§ 355-1(f)(2)(C)-(D)
18 (providing that ETASU must not be "unduly burdensome on patient access to the
19 drug" and must "minimize the burden on the health care delivery system."). For
20 the drugs listed in Defendants' Notice, certified pharmacies may simply look up
21 the certified prescriber and/or the enrolled patient in a centralized database, which
22

1 is maintained by the drug's sponsor, to verify the provider's certification and/or
 2 the patient's enrollment in the REMS program. *See generally* Appendix A.
 3 Indeed, the REMS for these drugs establish these national, centralized
 4 clearinghouses. *Id.* This allows pharmacists nationwide to quickly and easily
 5 check the database when dispensing a prescription. *See id.* As reflected by the list
 6 of drugs in Defendants' Notice, these pharmacy-certification requirements are
 7 imposed only on drugs with significant risk profiles that require additional
 8 safeguards at the point of dispensing to ensure patient safety.¹ These life-
 9 threatening and often fatal risks include serious liver injury and severe birth
 10 defects (Tracleer); heart failure (Camzyos); sudden death (Caprelsa); rapidly life-
 11 threatening and fatal infections (empaveli); liver toxicity, liver failure, and severe
 12 birth defects (Filspari); pulmonary embolisms (Sublocade); addiction and
 13 overdose (fentanyl and Xyrem/Xyway); and valvular heart disease and
 14 pulmonary arterial hypertension (Fintepla), among others. *See id.* Yet despite
 15 these potentially fatal side effects, the pharmacy certification requirements
 16 imposed on mifepristone—an extremely safe drug that does not qualify for any
 17 REMS whatsoever—are uniquely burdensome.

18 _____
 19 ¹ Indeed, several of the drugs listed in Defendants' Notice cannot be
 20 dispensed directly to patients at all, but only to health care providers in a
 21 healthcare setting, such as Sublocade, Tecvayli, Tysabri, Zulresso, Xiaflex, and
 22 Zyprexa Relprevv. *See* Appendix A.

1 The mifepristone REMS alone impose the entire administrative burden
 2 solely on each individual certified pharmacy to create its own secure, dynamic
 3 system for tracking and storing providers' certification information. Unlike for
 4 the drugs listed in Defendants' Notice, there is no centralized system for
 5 pharmacists to check relevant information for purposes of a mifepristone
 6 prescription. Instead: (1) each provider must separately send their certification
 7 information to *each and every* certified pharmacy dispensing a prescription
 8 written by the provider; (2) each pharmacy must ensure it receives certification
 9 information from each prescriber on every mifepristone prescription; and (3) each
 10 pharmacy must separately track this information by creating its own secure,
 11 dynamic database of certified prescribers. *See* ECF No. 1-13 at 4; ECF No. 4-1:
 12 Colwill Decl. ¶ 19, DasGupta Decl. ¶¶ 8–9, Downing Decl. ¶ 8, Godfrey Decl.
 13 ¶ 26.

14 This is far more time-consuming and burdensome than for the high-risk
 15 drugs listed in Defendants' Notice. Instead of simply checking a centralized
 16 database, individual certified pharmacies must build and maintain their own
 17 secure, dynamic data-management systems to track and store the certification
 18 information they have received from each prescriber of mifepristone. DasGupta
 19 Decl. ¶ 15–16, Downing Decl. ¶¶ 10–11, Prager Decl. ¶ 35, Reed Decl. ¶ 6, Singh
 20 Decl. ¶¶ 12–13. And instead of sending their certifications and any other pertinent
 21 information to a single location, providers must likewise send them to *each and*
 22

1 every certified pharmacy before that pharmacy may dispense to their patients.
 2 Colwill Decl. ¶ 19, DasGupta Decl. ¶ 8, Downing Decl. ¶ 8, Godfrey Decl. ¶ 26,
 3 Gold Decl. ¶ 18, Shih Decl. ¶¶ 18, 23.

4 This decentralized, patchwork process negatively impacts patients, as well.
 5 Whereas the centralized systems that are in place for other REMS-restricted
 6 drugs allow *any* certified pharmacy to dispense a prescription written by *any*
 7 certified prescriber, the mifepristone REMS only allows a certified pharmacy to
 8 dispense a prescription written by a provider who has sent their certification to
 9 *that particular pharmacy*. Colwill Decl. ¶ 19, DasGupta ¶ 8, Downing Decl. ¶ 10,
 10 Godfrey Decl. ¶ 26, Gold Decl. ¶ 18, Shih Decl. ¶¶ 18, 23. This piles onto the
 11 complex and confusing requirements that patients already have to navigate to
 12 obtain a prescription for mifepristone in the first place, further delaying and
 13 blocking access to care to this time-sensitive medication. *See, e.g.,* Gold Decl.
 14 ¶ 24, Janiak Decl. ¶ 23, Lazarus Decl. ¶ 17, Shih Decl. ¶ 27. To be sure, a
 15 centralized database is not the answer for mifepristone, as the existence of any
 16 database poses threats to provider safety. *See* ECF No. 1-9 at 3–4; ECF No. 4-1:
 17 Godfrey Decl. ¶ 27, Gold Decl. ¶¶ 17–19, Janiak Decl. ¶ 20, Prager Decl. ¶¶ 38–
 18 40, Shih Decl. ¶¶ 23–25. The point is that the mifepristone pharmacy REMS are
 19 uniquely onerous and apply to a drug for which the imposition of *any* REMS is
 20 unlawful.

1 In sum, as indicated at oral argument, the mifepristone REMS is uniquely
 2 burdensome—indeed, no other drug is subject to its uniquely onerous pharmacy
 3 certification requirement. Given mifepristone’s proven safety record, FDA does
 4 not even attempt to argue the drug could possibly meet the statutory standard for
 5 a REMS in the first place. And, in square violation of the governing statute, FDA
 6 implemented the January 2023 REMS without ever considering how the REMS
 7 negatively impacted patient access, the blast radius from *Dobbs*, or the resulting
 8 (and compounding) effect of the REMS on rural and underserved patients. The
 9 mifepristone REMS—all three components of it—is contrary to law, arbitrary,
 10 and capricious.

11 DATED this 30th day of March, 2023.

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**Applications for pro hac vice admission
forthcoming*

CERTIFICATE OF SERVICE

I hereby certify that on March 30, 2023, I electronically filed the foregoing with the Clerk of the Court using the CM/ECF System, which in turn automatically generated a Notice of Electronic Filing (NEF) to all parties in the case who are registered users of the CM/ECF system. The NEF for the foregoing specifically identifies recipients of electronic notice.

DATED this 30th day of March, 2023, at Seattle, Washington.

/s/Kristin Beneski

KRISTIN BENESKI, WSBA #45478
First Assistant Attorney General

APPENDIX A

Drug	Goal of the REMS program	How this REMS is different from mifepristone REMS
Letairis (ambrisentan)	“mitigate the risk of embryo-fetal toxicity”	“To support REMS Program operations, Ambrisentan Applicants must: . . . <i>Provide certified pharmacies access to the database of certified prescribers and enrolled patients.</i> ” (p. 7-8)
Tracleer (bosentan)	“mitigate the risks of hepatotoxicity and embryo-fetal toxicity”	“To support REMS Program operations, Bosentan Applicants must: . . . <i>Provide certified pharmacies access to the database of certified prescribers and enrolled patients.</i> ” (p. 7-8)
Camzyos (mavacamten)	“mitigate the risk of heart failure due to systolic dysfunction”	“To support REMS operations, Bristol-Myers Squibb Company must: . . . <i>Provide certified pharmacies access to the database of certified healthcare providers and enrolled patients.</i> ” (p. 5-6)
Caprelsa (vandetanib)	“mitigate the serious risks of QT prolongation, Torsades de pointes, and sudden death”	“Genzyme must maintain a secure, validated, interactive, web-based database of all enrolled entities (prescribers, pharmacies, and distributors). . . . <i>Certified pharmacies can access the database to verify prescriber enrollment status as required by the REMS.</i> ” (p. 3)
Clozaril (clozapine)	“mitigate the risk of severe neutropenia”	“To support REMS program operations, Clozapine Applicants must: . . . <i>Provide certified pharmacies access to the database of certified prescribers and enrolled patients.</i> ” (p. 7-8)
Fazaclo ODT (clozapine)	Same as Clozaril (clozapine)	<i>Id.</i>
Versacloz (clozapine)	Same as Clozaril (clozapine)	<i>Id.</i>
Empaveli (pegcetacoplan)	“mitigate the occurrence and morbidity associated with encapsulated bacteria infections”	“To support REMS Program operations, Apellis Pharmaceuticals, Inc. must: . . . <i>Provide certified pharmacies access to the database of certified prescribers.</i> ” (p. 3-4)

<u>Filspari (sparsentan)</u>	“mitigate the risks of hepatotoxicity and embryo-fetal toxicity”	“To support REMS operations, Traveře Therapeutics, Inc. must: . . . <i>Provide certified pharmacies access to the database of certified prescribers and enrolled patients.</i> ” (p. 8-9)
<u>Fintepla (fenfluramine hydrochloride)</u>	“mitigate the risk of valvular heart disease and pulmonary arterial hypertension”	“To support REMS Program operations, Zogenix, Inc. must: . . . <i>Provide certified pharmacies access to the database of certified prescribers and enrolled patients.</i> ” (p. 5-6)
<u>Absorica (isotretinoin)</u>	“prevent fetal exposure to isotretinoin”	“To support REMS Program operations, Isotretinoin Applicants must: . . . <i>Provide pharmacies access to the database of enrolled patients and certified prescribers.</i> ” (p. 5-6)
Absorica LD (isotretinoin)	Same as <u>Absorica (isotretinoin)</u>	<i>Id.</i>
<u>Juxtapid (lomitapide)</u>	“mitigate the risk of hepatotoxicity”	“To support REMS Program operations, Amryt Pharmaceuticals DAC must: . . . <i>Provide certified pharmacies access to the database of certified prescribers and enrolled patients.</i> ” (p. 4)
<u>Jynarque (tolvaptan)</u>	“mitigate the risk of serious and potentially fatal liver injury”	“To support REMS Program operations, Otsuka Pharmaceutical Company, Ltd must . . . <i>Provide certified pharmacies access to the database of certified prescribers and enrolled patients.</i> ” (p. 6-7)
<u>Lemtrada (alemtuzumab)</u>	“mitigate the risks of autoimmune conditions, infusion reactions, stroke, and malignancies”	“To support REMS Program operations, Genzyme must: . . . <i>Provide certified pharmacies and certified healthcare facilities access to the database of certified prescribers and enrolled patients.</i> ” (p. 7)
<u>Revlimid (lenalidomide)</u>	“prevent the risk of embryo-fetal exposure”	“To support REMS Program operations, Lenalidomide Applicants must: . . . Establish and maintain a validated, secure database of all REMS participants who are enrolled and/or certified in the REMS Program. . . . <i>Provide certified pharmacies access to the REMS system.</i> ” (p. 9)

<u>Opsumit (macitentan)</u>	“mitigate the risk of embryo-fetal toxicity”	“To support the REMS operations, Macitentan REMS Applicants must: . . . <i>Provide certified pharmacies access to the database of certified prescribers and enrolled patients.</i> ” (p. 6-7)
<u>Myalept (metreleptin)</u>	“mitigate (1) the risks of serious adverse sequelae (such as severe infections, excessive weight gain, glucose intolerance, diabetes mellitus) due to the development of anti-metreleptin antibodies that neutralize endogenous leptin and/or Myalept, and (2) the risk of lymphoma”	“To support REMS Program operations, Amryt Pharmaceuticals DAC must: . . . <i>Provide certified pharmacies access to the database of certified prescribers.</i> ” (p. 3-4)
<u>Natpara (parathyroid hormone)</u>	“mitigate the potential risk of osteosarcoma”	“To support REMS Program operations, Shire-NPS Pharmaceuticals, Inc. must: <i>Provide certified pharmacies access to the database of certified prescribers and enrolled patients.</i> ” (p. 3-4)
<u>Palforzia (peanut (Arachis hyogaea) allergen powder dnfp)</u>	“mitigate the risk of anaphylaxis”	“To support REMS Program operations, Aimmune Therapeutics, Inc. must: <i>Provide certified pharmacies access to the database of certified prescribers, healthcare settings and enrolled patients.</i> ” (p. 6)
<u>Palynziq (pegvaliase- pqpz)</u>	“mitigate the risk of anaphylaxis”	“To support REMS Program operations, BioMarin must: . . . <i>Provide certified pharmacies access to the database of certified prescribers and enrolled patients.</i> ” (p. 4)
<u>Pomalyst (pomalidomide)</u>	“prevent the risk of embryo-fetal exposure”	“To support REMS Program operations, Celgene must: “Establish and maintain a validated, secure database of all REMS participants who are enrolled and/or certified in the REMS Program. . . . <i>Provide certified pharmacies access to the REMS system.</i> ” (p. 8-9)

<u>Probuphine (buprenorphine hydrochloride)</u>	“mitigate the risk of complications of migration, protrusion, expulsion and nerve damage associated with the insertion and removal of Probuphine”	“To support REMS Program operations, Titan Pharmaceuticals, Inc. must: . . . Establish and maintain a validated, secure database of all REMS participants who are certified in the Probuphine REMS Program. . . . <i>Provide certified prescribers, certified healthcare providers who insert Probuphine, certified pharmacies, and wholesalers-distributors access to the database of these participants.</i> ” (p. 5-6)
<u>Qsymia (phentermine and topiramate)</u>	mitigate the “increased risk of congenital malformations, specifically orofacial clefts, in infants exposed to Qsymia during the first trimester of pregnancy”	“To support REMS Program operations, VIVUS LLC must: . . . <i>Establish and maintain a validated, secure database of all REMS participants who are enrolled and/or certified in the Qsymia REMS Program.</i> ” (p. 2)
<u>Adempas (riociguat)</u>	“mitigate the risk of embryo-fetal toxicity”	“To support REMS Program operations, Riociguat Applicants must: <i>Provide certified pharmacies access to the database of certified prescribers and enrolled patients.</i> ” (p. 7-8)
<u>Siliq (brodalumab)</u>	“mitigate the observed risk of suicidal ideation and behavior, including completed suicides”	“To support REMS Program operations, Bausch Health US, LLC must: . . . <i>Provide certified pharmacies access to the database of certified prescribers and enrolled patients.</i> ” (p. 3-4)
<u>Spravato (esketamine)</u>	“mitigate the risks of serious adverse outcomes resulting from sedation and dissociation caused by SPRAVATO administration, and abuse and misuse of SPRAVATO”	“To support REMS Program operations, Janssen Pharmaceuticals, Inc. must: . . . <i>Provide certified pharmacies access to the database of certified healthcare settings.</i> ” (p. 5-6)
<u>Sublocade (buprenorphine extended-release)</u>	“mitigate the risk of serious harm or death that could result from intravenous self-administration”	“SUBLOCADE is dispensed directly to a healthcare provider,” not to a patient. (p. 1) “To support REMS Program operations, Indivior must: Establish and maintain a validated, secure database of all REMS participants who are enrolled and/or certified in the SUBLOCADE REMS.” (p. 3)

Tecvayli (teclistamab-cqyv)	“mitigate the risk of Cytokine Release Syndrome (CRS) and neurologic toxicity including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS)”	“To support REMS operations, Janssen Biotech, Inc. must: . . . <i>Provide certified pharmacies and healthcare settings access to the database of certified prescribers.</i> ” (p. 4-5)
Tegsedi (inotersen)	“mitigate the risk of serious bleeding with severe thrombocytopenia and the risk of glomerulonephritis”	“To support REMS operations, Akcea Therapeutics must: . . . <i>Provide certified pharmacies access to the database of certified prescribers and enrolled patients.</i> ” (p. 5-6)
Thalomid (thalidomide)	“prevent the risk of embryo-fetal exposure”	“To support REMS Program operations, Celgene must: . . . Establish and maintain a validated, secure database of all REMS participants who are enrolled and/or certified in the REMS Program. . . . <i>Provide certified pharmacies access to the REMS system.</i> ” (p. 8-9)
Actiq (fentanyl citrate)	“[m]itigate the risk of overdose”	“To support REMS program operations, TIRF Applicants must: . . . <i>Provide certified outpatient pharmacies access to the database of certified prescribers and enrolled patients.</i> ” (p. 7-8)
Fentora (fentanyl citrate)	Same as Actiq (fentanyl citrate)	<i>Id.</i>
Lazanda (fentanyl citrate)	Same as Actiq (fentanyl citrate)	<i>Id.</i>
Onsolis (fentanyl citrate)	Same as Actiq (fentanyl citrate)	<i>Id.</i>
Subsys (fentanyl)	Same as Actiq (fentanyl citrate)	<i>Id.</i>
Turalio (pexdartinib)	“mitigate the risk of serious and potentially fatal liver injury”	“To support REMS operations, Daiichi Sankyo, Inc. must: . . . <i>Provide certified pharmacies access to the database of certified prescribers and enrolled patients.</i> ” (p. 4-5)
Tysabri (natalizumab)	mitigate “the risk of progressive multifocal leukoencephalopathy (PML)”	Certified pharmacies may dispense only to authorized infusion sites, not to patients. (p. 3) “To support REMS Program operations, Biogen must: . . . <i>Provide certified pharmacies access to the database of certified infusion sites and enrolled patients.</i> ” (p. 5)

<u>Sabril (vigabatrin)</u>	“mitigate the risk of vision loss”	“To support REMS Program operations, the Vigabatrin Applicants must: . . . <i>Provide certified pharmacies access to the database of certified prescribers and enrolled patients.</i> ” (p. 5)
<u>Xiaflex (collagenase clostridium histolyticum)</u>	“mitigate the risks of corporal rupture (penile fracture) and other serious penile injuries”	“To support REMS Program operations, Endo Pharmaceuticals, Inc. must: . . . <i>Provide certified pharmacies and healthcare settings access to the database of certified prescribers.</i> ” (p. 3-4)
<u>Xyrem/Xywav (calcium, magnesium, potassium, and sodium oxybates)</u>	“mitigate the risks of serious adverse outcomes resulting from inappropriate prescribing, misuse, abuse, and diversion”	“To support REMS Program operations, Jazz Pharmaceuticals must: . . . <i>Provide the certified pharmacy access to the database of certified prescribers and enrolled patients.</i> ” (p. 7-8)
<u>Zulresso (brexanolone)</u>	“mitigate the risk of serious harm resulting from excessive sedation and sudden loss of consciousness during the ZULRESSO infusion”	Certified pharmacies may dispense only to a certified healthcare setting, not to a patient. (p. 4) “To support REMS Program operations, Sage Therapeutics, Inc. must: . . . <i>Provide certified pharmacies access to the database of certified healthcare settings and authorized wholesalers-distributors.</i> ” (p. 5-6)
<u>Zyprexa Relprevv (olanzapine)</u>	“mitigate the risk of negative outcomes associated with Zyprexa Relprevv post-injection delirium/sedation syndrome (PDSS)”	Zyprexa Relprevv “can only be dispensed for use in certain health-care settings that have ready access to emergency response services,” not to patients. (p. 4) “Lilly will ensure that certified dispensers will verify that each patient is eligible to receive Zyprexa Relprevv prior to dispensing each prescription/ refill of Zyprexa Relprevv <i>by accessing the Zyprexa Relprevv Patient Care Program and ensuring the patient is enrolled in the Zyprexa Relprevv Patient Care Program Registry and the prescriber is certified.</i> ” (p. 5)