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IN THE UNITED STATES DISTRICT COURT
DISTRICT OF ALASKA

UNITED STATES OF AMERICA *Ex rel.* Law Project for Psychiatric Rights, an Alaskan non-profit corporation, Plaintiff, vs. OSAMU H. MATSUTANI, MD, *et al*., Defendants.	)	Case No. 3:09-CV-00080-TMB

REFILED MOTION FOR PRELIMINARY INJUNCTION AGAINST DEFENDANTS HOGAN AND STREUR

Pursuant to the Court's Order Denying Motion for Preliminary Injunction Without Prejudice, Dkt. No. 79, *Qui tam* relator Law Project for Psychiatric Rights (PsychRights®) refiles its motion for a preliminary injunction prohibiting defendants William Hogan and William Streur, their agents, servants, employees and attorneys, and any persons who are in active concert or participation with them, from presenting claims or causing claims to be presented to Medicaid for reimbursement or payment of the

United States Government's federal financial participation (FFP) share[1] of outpatient prescriptions for psychotropic drugs to recipients under the age of 18 (children and youth) that are not for a medically accepted indication.

I. BACKGROUND

This is a case under the federal False Claims Act, 31 U.S.C. §3729, *et seq*., to:

(a) recover for false claims presented to and paid by Medicaid for outpatient psychiatric drugs prescribed to children and youth that were not for a "medically accepted indication;" and

(b) order the defendants to cease and desist from presenting or causing the presentment of such false claims.

This motion seeks to enjoin Defendants William Hogan and William Streur, their agents, servants, employees and attorneys, and any persons who are in active concert or participation with them, from presenting claims or causing claims to be presented to Medicaid[2] for outpatient prescriptions of psychotropic drugs to children and youth that are not covered under those programs. Defendant Hogan is the Commissioner of the Alaska Department of Health and Social Services (DHSS), and Defendant William Streur is the Director of the Division of Health Care Services (HCS) within DHSS which administers Alaska's Medicaid program. Defendant Streur is in charge of the administration of the Medicaid program by the State of Alaska under the direction and supervision of Defendant Hogan. In sum, Defendants Hogan and Streur are in charge of the administration of the Medicaid program by the State of Alaska.

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[1] "FFP" stands for "Federal Financial Participation," which means "the Federal Government's share of a State's expenditures under the Medicaid program." 42 CFR §400.203.

[2] As employed herein, Medicaid includes the "CHIP" program, which is a partnership between states and the United States to provide medical insurance for eligible children and youth who do not qualify for Medicaid, but who lack the economic means to afford private health insurance. *See*, First Amended Complaint, Dkt. No. 107, p. 33, ¶164.

Congress restricted reimbursement for outpatient drugs by the federal government under Medicaid to those that are for "medically accepted indications," defined as indications approved by the Food and Drug Administration (FDA), or the use of which is supported by one or more citations included or approved for inclusion in (i) American Hospital Formulary Service Drug Information, (ii) United States Pharmacopeia-Drug Information (or its successor publications), or (iii) DRUGDEX Information System (Covered Outpatient Drugs). 42 USC § 1396r-8(k)(3); 42 USC § 1396r-8(k)(6); 42 USC § 1396r-8(g)(1)(B)(i).

The parties sought to be enjoined continue to present claims or cause claims to be presented to Medicaid for payment of prescriptions to children and youth for psychotropic drugs that are not for a medically accepted indication. This motion thus seeks to preliminarily enjoin such continuing violation of federal law.

II. STANDARDS FOR PRELIMINARY INJUNCTIONS

In *California Pharmacists Ass'n v. Maxwell-Jolly*, 563 F.3d 847, 849 (9th Cir. 2009), citing to *Winter v. Natural Res. Def. Council, Inc.*, --- U.S. ----, 129 S.Ct. 365, 376, 172 L.Ed.2d 249 (2008), the 9th Circuit, recently had occasion to state the standard for obtaining a preliminary injunction where, as here, the public interest is involved:

> Plaintiffs seeking a preliminary injunction in a case in which the public interest is involved must establish that they are likely to succeed on the merits, that they are likely to suffer irreparable harm in the absence of preliminary relief, that the balance of equities tips in their favor, and that an injunction is in the public interest.

These factors will be discussed in turn.

III. THE STANDARDS FOR ISSUANCE OF A PRELIMINARY INJUNCTION ARE MET HERE

A. PsychRights is Likely to Succeed on the Merits

(1) Medicaid Coverage for Outpatient Drugs is Limited to "Medically Accepted Indications

42 USC 1396R-8(k)(3) provides in pertinent part, "The term 'covered outpatient drug' does not include any . . . drug . . . used for a medical indication which is not a medically accepted indication." 42 USC 1396R-8(k)(6) provides:

> The term “medically accepted indication” means any use for a covered outpatient drug which is approved under the Federal Food, Drug, and Cosmetic Act [21 U.S.C.A. § 301 et seq.], or the use of which is supported by one or more citations included or approved for inclusion in any of the compendia described in subsection (g)(1)(B)(i) of this section.

42 USC § 1396R-8(g)(1)(B)(i), in turn, designates the compendia as

> (I) American Hospital Formulary Service Drug Information;
> (II) United States Pharmacopeia-Drug Information (or its successor publications); and
> (III) the DRUGDEX Information System.

(Compendia).

In sum, Medicaid is only permitted by Congress to reimburse the states for expenditures on outpatient drugs for "medically accepted indications," defined as indications approved by the FDA or "supported by" a citation in any of the three Compendia. This was recognized in *US ex rel Rost v. Pfizer*, 253 F.R.D. 11, 13-14 (D.Mass 2008) where the Court held:

> Medicaid can only pay for drugs that are used for a “medically accepted indication,” meaning one that is either approved by the FDA or “supported by citations” in one of three drug compendia, including DRUGDEX. See 42 U.S.C. § 1396r8 (k)(3), (6); 42 U.S.C. § 1396r-8 (g)(1)(B)(I).

Similarly, in *U.S. ex rel. Franklin v. Parke-Davis*, 147 F.Supp. 2d 39, 44,45 (D.Mass 2001), the Court held:

> Whether a drug is FDA-approved for a particular use will largely determine whether a prescription for that use of the drug will be reimbursed under the federal Medicaid program. Reimbursement under Medicaid is, in most circumstances, available only for "covered outpatient drugs." 42 U.S.C. § 1396b(i)(10). Covered outpatient drugs do not include drugs that are "used for a medical indication which is not a medically accepted indication." Id. §1396r-8(k)(3). A medically accepted indication, in turn, includes a use "which is approved under the Federal Food Drug and Cosmetic Act" or which is included in specified drug compendia. Id. § 1396r-8(k)(6). See also id. § 1396r-8(g)(1)(B)(i) (identifying compendia to be consulted). Thus, unless a particular off-label use for a drug is included in one of the identified drug compendia, a prescription for the off-label use of that drug is not eligible for reimbursement under Medicaid.

(footnote omitted)

The Department of Justice agrees. For example, in September of 2009, the Department of Justice issued a news release announcing a $2.3 Billion settlement with Pfizer, stating, "[Pfizer] caused false claims to be submitted to government health care programs for uses that were not medically accepted indications and therefore not covered by those programs."[3] Similarly, the Government's February 13, 2009, Complaint in Intervention in *U.S. ex rel Gobble v. Forest Laboratories*, Case No. 03-cv-10395-NMG, District of Massachusetts, states that prescriptions presented to Medicaid that are not for medically accepted indications are false claims.[4] To the same effect is the settlement

[3] Dkt. No. 108-1, p.1.
[4] Dkt. No. 108-2, p. 9, at ¶s 26-30; p. 10, ¶37; p. 31 ¶97; p. 32, ¶100.

agreement in *U.S. ex rel Wetta v. AstraZeneca Pharmaceuticals*, Case No. 04-cv-3479-BMS, Eastern District of Pennsylvania.[5]

(2) Defendants Hogan and Streur Are Flouting Medicaid Requirements By Presenting or Causing the Presentment of Claims for Prescriptions of Psychotropic Drugs to Children and Youth That Are Not For A Medically Accepted Indication

In *ex rel Rost*, 253 F.R.D. at 14 the district court noted, "Each prospective Medicaid provider must agree that he will comply with all Medicaid requirements." To the same effect is *U.S. v. Mackby*, 261 F.3d 821, 828 (9th Cir. 2001). States must similarly agree to abide by Medicaid requirements as a condition of participation. Attached hereto as Exhibit 1 is a copy of the State of Alaska's Medicaid Plan where it agrees it will comply with all Medicaid requirements.

Among these requirements, under 42 USC §1396r-8 (g)(1)(A), the State of Alaska is required to have a drug use review program (DUR) "designed to educate physicians and pharmacists to identify and reduce the frequency of patterns of fraud," and at 42 USC §1396r-8 (g)(2)(A)(i), requires a "prospective drug review . . . before each prescription is filled or delivered."

Under 42 CFR §456.703:

> **42 CFR §456.705 Prospective drug review.**
>
> (a) General. Except as provided in Sec. Sec. 456.703 (b) and (c), the State plan must provide for a review of drug therapy before each prescription is filled or delivered to a recipient . . . . The State must provide pharmacies with detailed information as to what they must do to comply with prospective DUR requirements . . . . The pharmacies, in turn, must provide this information to their pharmacists.

In other words, through this prospective drug review, before each prescription is filled, the state Medicaid agency is required to review it to determine if it is eligible for reimbursement by Medicaid. Exhibit 2, is a copy of this provision in the State of

[5] Dkt. No. 108-3, p.6.

Alaska's State Plan under Medicaid, which at page 2, §E.1., provides that the State of Alaska's DUR includes prospective drug review.

42 CFR §456.722 allows for this prospective review of prescriptions to occur through a computerized system:

42 CFR §456.722 Electronic claims management system.

> (a) Point-of-sale system. Each Medicaid agency, at its option, may establish, as its principal (but not necessarily exclusive) means of processing claims for covered outpatient drugs, a point-of-sale electronic claims management (ECM) system to perform on-line, real-time (that is, immediate) eligibility verifications, claims data capture, adjudication of claims, and to assist pharmacists and other authorized persons (including dispensing physicians) in applying for and receiving payment. . . . If the State exercises this option and wishes to receive FFP for its ECM system, the system must meet the functional and additional procurement and system requirements in paragraphs (b) and (c) of this section.
>
> (b) Functional requirements. The ECM system developed by the State must include at least the on-line, real-time capabilities specified in paragraphs (b)(1) through (3) of this section. . . .
>
> (2) Claims data capture, including the following: . . .
>
> (iii) Minimum data set (as defined in Part 11 of the State Medicaid Manual).
>
> (3) Claims adjudication, including the following:
>
> (i) Performing all edits and audits contained in the State's Medicaid Management Information System (MMIS) applicable to prescription drugs.
>
> (ii) Notifying the pharmacist (or other authorized person, such as the dispensing physician) about the claim status.
>
> (iii) Taking steps up to, but not including, payment of the claim.

Included in the data set of Part 11 of the State Medicaid Manual[6] are:

> *6. Recipient's Date of Birth:
>
> The date of birth of the recipient. . .
>
> *61. Principal Diagnosis Code:

[6] From http://www.cms.hhs.gov/manuals/downloads/P45_11.zip, downloaded on March 17, 2010.

a. The diagnosis code for the principal condition requiring medical attention. . . .

62. Other Diagnosis Code:
    a. The diagnosis code of any condition other than the principal condition which requires supplementary medical treatment. . . .

88. Drug Code:
    Codes identifying particular drugs; e.g., National Drug Code, drug tables.

89. Diagnosis Code:
    A table of codes identifying medical conditions; i.e., ICD-9-CM.

90. Drug Name:
    The generally accepted nomenclature for a particular drug.

91. Drug Classification:
    The therapeutic group in to which a drug is categorized.

92. Minimum Days Supply of Drugs:
    The minimum units of a drug prescription eligible for payment.

93. Maximum Days Supply of Drug:
    The maximum units of a drug prescription eligible for a particular drug. . . .

95. Diagnosis Name:
    The generally accepted nomenclature for a diagnosis. Name is required only if not encoded by provider. (See Data Element No. 61.)

These statutory and regulatory provisions require the State of Alaska to screen prescriptions for compliance with the requirement that it not seek federal Medicaid payment for outpatient prescriptions to children and youth for psychotropic drugs that are not for a medically accepted indication.

To summarize: 42 USC §1396r-8 (g)(2)(A) requires the states to have a prospective drug review program, and 42 CFR §456.705 requires such prospective review to verify eligibility before the prescription is filled. Under 42 CFR §456.722, the State's electronic claims management system is required to collect the minimum data specified in Part 11 of the State Medicaid Manual, relevant elements of which are set

forth above. These elements can determine whether psychotropic drugs prescribed to children and youth are or are not for a medically accepted indication.

Under Defendants Hogan's and Steur's administration of Alaska's Medicaid program, these requirements are being flouted.

(3) Injunctive Relief is Available Against Defendants Hogan and Streur

Injunctive relief to enjoin a state official from violating a federal statute is proper and not barred by the 11th Amendment to the United States Constitution. *Armstrong v. Wilson*, 124 F.3d 1019 (9th Cir. 1997); *Independent Living Center of Southern California, Inc., v Maxwell-Jolly*, 572 F.3d 644 (9th Cir. 2009). Where a district court has the power to issue a permanent injunction, it also has authority to issue preliminary injunctions. *F.T.C. v. H. N. Singer, Inc.*, 668 F.2d 1107, 1111 (9th Cir. 1982).

B. The Plaintiff Will Suffer Irreparable Harm As a Matter of Law Without the Preliminary Injunction

(1) The Inability of This Court To Issue a Money Judgment Against the State Constitutes Irreparable Harm As a Matter of Law

In *California Pharmacists, supra*., 563 at 852, the 9th Circuit held that to the extent the 11th Amendment prevents a federal court from awarding a damages remedy against a state, irreparable harm is established as a matter of law:

> Because the economic injury doctrine rests only on ordinary equity principles precluding injunctive relief where a remedy at law is adequate, it does not apply where, as here, the Hospital Plaintiffs can obtain no remedy in damages against the state because of the Eleventh Amendment.

(citation and footnote omitted).

Defendants Hogan and Streur admit, indeed assert, that this Court can not grant a remedy in damages against the state of Alaska in its Motion to Dismiss Claims Against State of Alaska Officials, Dkt. No. 90, pp 4-5. Thus, under *California Pharmacists*, irreparable harm is established as a matter of law.

(2) The Continuing Violation of a Federal Statute is Irreparable Harm as a Matter of Law.

Similarly, it is respectfully suggested the continuing violation of a federal statute is irreparable harm as a matter of law. In *New Motor Vehicle Bd. v. Orrin W. Fox Co.*, 434 U.S. 1345, 1351, 98 S.Ct. 359, 363, 54 L.Ed.2d 439 (1977) (Rehnquist, J., in chambers), the U.S. Supreme Court held, "any time a State is enjoined by a court from effectuating statutes enacted by representatives of its people, it suffers a form of irreparable injury." In *Coalition for Economic Equity v. Wilson*, 122 F.3d 718, 719 (9th Cir. 1997), citing *New Vehicle*, the Ninth Circuit held, "it is clear that a state suffers irreparable injury whenever an enactment of its people or their representatives is enjoined." In *Independent Living Center*, *supra.*, 572 F.3d at 658, the Ninth Circuit clarified, that while that may be true, enforcing federal law pre-empts such irreparable harm suffered by a state, stating:

> As the cited authority suggests, a state may suffer an abstract form of harm whenever one of its acts is enjoined. To the extent that is true, however, it is not dispositive of the balance of harms analysis. If it were, then the rule requiring "balance" of "competing claims of injury," *Winter*, 129 S.Ct. at 376, would be eviscerated. Federal courts instead have the power to enjoin state actions, in part, because those actions sometimes offend federal law provisions, which, like state statutes, are themselves "enactment [s] of its people or their representatives,"

PsychRights respectfully suggests the Ninth Circuit has thus implicitly held that allowing continuing violation of federal law constitutes irreparable harm as a matter of law.

C. The Balance of Equities Tips in Favor of the Plaintiff and the Injunction is in the Public Interest as a Matter of Law

Under *California Pharmacists*, *supra*., 563 at 852-853, as a matter of law, the balance of equities tips in favor of the plaintiff and a prospective preliminary injunction is in the public interest if the requested preliminary injunction is to enjoin continuing violation of federal law ("it is clear that it would not be equitable or in the public's interest to allow the state to continue to violate the requirements of federal law"). Thus,

these two factors are satisfied as a matter of law. Where, as here, the violation of law is clear, the court must not allow it to continue.

IV. SCOPE OF THE REQUESTED PRELIMINARY INJUNCTION

A. Medically Accepted Indications for Use in Children and Youth for Specific Psychotropic Medications

As set forth above, Congress limited the federal government's payment under Medicaid for outpatient prescription drugs to medically accepted indications, defined as indications approved by the FDA or supported by one or more of the Compendia. Whether an indication is approved by the FDA is easily determinable, but some discussion of what it means to be "supported by" a citation in the Compendia seems necessary.

In the first instance, because as set forth above, all participants in Medicaid must agree to comply with all Medicaid requirements,[7] prior to presenting or causing the presentment of any claims to Medicaid for off-label use, i.e., for an indication not approved by the FDA, they are required to determine that such indication is "supported by" one or more of the Compendia. Or put another way, the default established by Congress is to prohibit reimbursement for off-label use, and any Medicaid participant who is presenting or causing presentment of claims to Medicaid for a prescription of a psychotropic drug to a child or youth for an off-label use, is required to determine that the prescription is for an indication which is supported by one or more of the Compendia.

PsychRights has analyzed commonly prescribed psychotropic drugs to determine medically accepted indications for children and youth, including off-label use that is

[7] *U.S. v. Mackby*, 261 at 828; *Ex rel Rost*, 253 F.R.D. at 14.

supported by DRUGDEX. DRUGDEX was used because it is universally recognized (and criticized) for being the most expansive.[8]

In the Government's May 12, 2008, Statement of Interest in *U.S. ex rel Rost v. Pfizer, Inc., et al.*, Docket No. 03-CV-11084-PBS, USDC Massachusetts, the United States Department of Justice explained what "supported by" a compendium means as follows:

> [W]hether a particular use is "supported by" a compendium depends on a variety of factors, including the type of drug and indication at issue, the compendium's assessment of the drug's efficacy in treating the indication, the content of the compendium citation, and the scope and outcome of the studies as described in the compendium.[9]

Exhibit 5, p. 7, is DRUGDEX's Recommendation, Evidence and Efficacy Ratings. Table 1, Strength of Recommendation is as follows:

Table 1. Strength Of Recommendation		
Class I	Recommended	The given test or treatment has been proven to be useful, and should be performed or administered.
Class IIa	Recommended, In Most Cases	The given test, or treatment is generally considered to be useful, and is indicated in most cases.
Class IIb	Recommended, In Some Cases	The given test, or treatment may be useful, and is indicated in some, but not most, cases.
Class III	Not Recommended	The given test, or treatment is not useful, and should be avoided.
Class Indeterminant	Evidence Inconclusive	

Exhibit 5, pp 1-6, is the color-coded chart titled, "Medically Accepted Indications for Pediatric Use of Certain Psychotropic Medications," which sets forth PsychRights' determination of the medically accepted indications for use in children and youth for commonly prescribed psychotropic drugs.

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[8] *See*, Ex. 3, p 1 ("Drugdex's listings are far more extensive than those of the other two guides -- making it the de facto standard-setter in authorizing payment for unapproved uses of prescription drugs.")

[9] Ex. 4, page 6.

This determination is based on the conclusion that indications with a Class IIb or below rating are not supported by DRUGDEX. The Class IIb rating is, 'The given test, or treatment may be useful, and is indicated in some, but not most, cases."

Thus, the following psychotropic drugs have no medically accepted indication for use in anyone under 18 years of age:

1. Ambien (zolipidem), Exhibit 5, page 1;
2. Buspar (buspirone), Exhibit 5, page 1;
3. Celexa (citalopram), Exhibit 5, page 1;
4. Clozaril (clozapine), Exhibit 5, page 2;
5. Cymbalta (duloxetine), Exhibit 5, page 2;
6. Desyrel (trazadone), Exhibit 5, page 2;
7. Effexor (venlafaxine), Exhibit 5, page 2;
8. Geodon (ziprasidone), Exhibit 5, page 2;
9. Invega (paliperidone), Exhibit 5, page 3;
10. Limbitrol (chlordiazepoxide/amitriptyline), Exhibit 5, page 3;
11. Lunesta (eszopiclone), Exhibit 5, page 3;
12. Paxil (paroxetine), Exhibit 5, page 4;
13. Pristiq (desvenlafaxine), Exhibit 5, page 4;
14. Restoril (temazepam), Exhibit 5, page 4;[10]
15. Rozerem (ramelteon), Exhibit 5, page 5;[11]
16. Sonata (zaleplon), Exhibit 5, page 5;
17. Symbyax (fluoxetine hydrochloride/olanzapine), Exhibit 5, page 5;
18. Wellbutrin (bupropion), Exhibit 5, page 6;
19. Xanax (alprozalam), Exhibit 5, page 6,[12]

and the following psychotropic drugs have only the following medically accepted indications for use in anyone under 18 years of age,

(a) Abilify (Aripiprazole), Exhibit 5, page 1
   (i) Bipolar I Disorder - Adjunctive therapy with lithium or valproate for Acute Manic or Mixed Episodes; 10 yrs old and up
   (ii) Bipolar I Disorder, monotherapy, Manic or Mixed Episodes; 10-17 years old for acute therapy
   (iii) Schizophrenia; 13-17 years old;

[10] Not included in ¶166 of First Amended Complaint, Dkt. No. 107.
[11] Not included in ¶166 of First Amended Complaint, Dkt. No. 107.
[12] Not included in ¶166 of First Amended Complaint, Dkt. No. 107.

(b) Adderall (amphetamine/dextroamphetamine), Exhibit 5, page 1
  (i) Attention Deficit Hyperactivity Disorder (ADHD); 3 years old and up for immediate-release and 6 years old and up for extended-release
  (ii) Narcolepsy; 6 years old and up for immediate release] drug);

(c) Anafranil (clomipramine), Exhibit 5, page 1
  (i) Obsessive-Compulsive Disorder; 10 years and up;

(d) Ativan (lorazepam), Exhibit 5, page 1
  (i) Anxiety; oral only, 12 years and older
  (ii) Chemotherapy-induced nausea and vomiting; Prophylaxis
  (iii) Insomnia, due to anxiety or situational stress
  (iv) Seizure
  (v) Status epilepticus;

(e) Concerta (methylphenidate), Exhibit 5, page 2
  (i) Attention Deficit Hyperactivity Disorder (ADHD); 6 years old to 12 years old
  (ii) Attention Deficit Hyperactivity Disorder (ADHD); 6 years old and up re ConcertaR;

(f) Dalmane (flurazepam), Exhibit 5, page 2
  (i) Insomnia; 15 years and older;

(g) Depakote (valproic acid), Exhibit 5, page 2
  (i) Absence Seizure, Simple and Complex and/or Complex Partial Epileptic Seizure; 10 years and older
  (ii) Complex Partial Epileptic Seizure; 10 years and older
  (iii) Seizure, Multiple sezure types; Adjunct; 10 years and older;

(h) Dexedrine (dextroamphetamine), Exhibit 5, page 2
  (i) Attention Deficit Hyperactivity Disorder (ADHD); 3 years to 16 years old (immediate-release) and age 6 years to 16 years old (sustained-release))
  (ii) Narcolepsy; 6 years old and up;

(i) Focalin (dexmethylphenidate), Exhibit 5, page 2
  (i) Attention Deficit Hyperactivity Disorder (ADHD); 6 years and older;

(j) Haldol (haloperidol), Exhibit 5, page 3
  (i) Hyperactive Behavior, (Short-term treatment) after failure to respond to non-antipsychotic medication and psychotherapy; 3 years old and up
  (ii) Problematic Behavior in Children (Severe), With failure to respond to non-antipsychotic medication or psychotherapy; 3 years old and up
  (iii) Psychotic Disorder; 3 years old and up but ORAL formulations only
  (iv) Schizophrenia; 3 years old and up but ORAL formulations only;

(k) Klonopin (clonazepam), Exhibit 5, page 3
  (i) Seizure; up to 10 years or up to 30 kg;

(l) Lamictal (lamotrigine), Exhibit 5, page 3
  (i) Convulsions in the newborn, Intractable
  (ii) Epilepsy, Refractory
  (iii) Lennox-Gastaut syndrome; Adjunct; yes (2 years and older)
  (iv) Partial seizure, Adjunct or monotherapy; 13 years and older, extended-release only; 2 years and older, chewable dispersible
  (v) Tonic-clonic seizure, Primary generalized; Adjunct; 2 years and older;

(m) Lexapro (escitalopram), Exhibit 5, page 3
  (i) Major Depressive Disorder; 12 years old and up;

(n) Luvox (fluvoxamine), Exhibit 5, page 3
  (i) Obsessive-Compulsive Disorder; 8 years old and up and immediate release formula only;

(o) Mellaril (thioridazine), Exhibit 5, page 4
  (i) Schizophrenia, Refractory;

(p) Moban (molindone) - antipsychotic, Dihydroindolone, Exhibit 5, page 4
  (i) Schizophrenia; 12 years and older;

(q) Neurontin (gabapentin) anticonvulsant, Exhibit 5, page 4
  (i) Partial seizure; Adjunct; 3-12 years old;

(r) Orap (pimozide), Exhibit 5, page 4
  (i) Gilles de la Tourette's syndrome; 12 years and older;

(s) Prozac (fluoxetine), Exhibit 5, page 4
  (i) Major Depressive Disorder; 8 years old and up
  (ii) Obsessive-Compulsive Disorder; 7 years old and up;

(t) Ritalin (methylphenidate), Exhibit 5, page 4
  (i) Attention Deficit Hyperactivity Disorder (ADHD); 6 years to 12 years old (extended release)
  (ii) Attention Deficit Hyperactivity Disorder (ADHD); 6 years old and up (immediate release)
  (iii) Narcolepsy; 6 years and up, and Ritalin(R) -SR only;

(u) Risperdal (risperidone), Exhibit 5, page 4
  (i) Autistic Disorder, Irritability; 5 years old and up
  (ii) Bipolar I Disorder; 10 years old and up
  (iii) Schizophrenia; 13 years old and up (Orally);

(v) Seroquel (quetiapine), Exhibit 5, page 5
  (i) Bipolar disorder, maintenance; 10-17 regular release only (12/4/09)

(ii) Manic bipolar I disorder; 10-17 regular release only (12/4/09)
(iii) Schizophrenia; 13-17, regular release only (12/4/09);

(w) Sinequan (doxepin), Exhibit 5, page 5
(i) Alcoholism - Anxiety - Depression; 12 years old and up
(ii) Anxiety - Depression; 12 years old and up
(iii) Anxiety - Depression - Psychoneurotic personality disorder; 12 years old and up;

(x) Strattera (atomoxetine), Exhibit 5, page 5
(i) Attention Deficit Hyperactivity Disorder (ADHD); 6 years old and up;

(y) Tegretol (carbamazepine), Exhibit 5, page 5
(i) Epilepsy, Partial, Generalized, and Mixed types;

(z) Tofranil (imipramine), Exhibit 5, page 5
(i) Nocturnal enuresis; 6 years old and up;

(aa) Topamax (topiramate), Exhibit 5, page 5
(i) Lennox-Gastaut syndrome, Adjunct; 2 years and older
(ii) Partial seizure, Initial monotherapy; 10 years and older
(iii) Partial seizure; Adjunct, 10 years and older
(iv) Tonic-clonic seizure, Primary generalized; Adjunct, 2 to 16 years old
(v) Tonic-clonic seizure, Primary generalized (initial monotherapy), 10 years and older;

(bb) Tranxene (clorazepate), Exhibit 5, page 6
(i) Partial seizure; Adjunct, 9 years and older;

(cc) Trileptal (oxcarbazepine), Exhibit 5, page 6
(i) Partial Seizure, monotherapy 4 years old and up
(ii) Partial seizure; Adjunct, 2 years old and up;

(dd) Vyvanse (lisdexamfetamine), Exhibit 5, page 6
(i) Attention Deficit Hyperactivity Disorder (ADHD); 6 years old to 12 years;

(ee) Zoloft (sertraline), Exhibit 5, page 6
(i) Obsessive-Compulsive Disorder; 6 years old and up;

(ff) Zyprexa (olanzapine), Exhibit 5, page 6
(i) Bipolar 1, Disorder, Acute Mixed or Manic Episodes, 13-17, oral only (12/4/09)
(ii) Schizophrenia 13-17, oral only (12/4/09).[13]

[13] In its original Motion for Preliminary Injunction, Dkt. No. 78, PsychRights attached copies of both the AHFS and DRUGDEX entries for all of the drugs identified in the

Except for an extremely limited number of psychotropic drugs, such as the use of Abilify in combination with lithium or valproate for manic or mixed episodes of Bipolar I disorder, polypharmacy is not for a medically accepted indication. Such drug combinations are neither approved by the FDA, nor supported by citations in any of the Compendia.

For psychotropic drugs not listed, PsychRights respectfully suggests the parties sought to be enjoined should be prohibited from approving for payment or reimbursement by Medicaid of the United States Government's FFP share of outpatient prescriptions for psychiatric drugs to anyone under 18 unless (a) it is for an indication approved by the FDA, or (b) upon application to the Court with notice to the other parties to determine whether such use is for a medically accepted indication.

V. BOND

Under F.R.C.P. 65(c) the United States is not required to give security. Since the United States is the real party in interest in this action, *Stoner, supra,* 502 F.3d at 1126, no security should be required.

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original Motion for Preliminary Injunction, albeit with many of the DRUGDEX citations cut off on the right margin. PsychRights has since acquired complete copies of the DRUGDEX entries for all of the drugs identified herein, but they run to over 5,000 pages and it seems more sensible to see to what extent if any, PsychRights' analysis of "supported by" is disputed and the evidence on this can be focused on what is actually disputed.

VI. CONCLUSION

For the foregoing reasons PsychRights' motion for a preliminary injunction should be granted.

RESPECTFULLY SUBMITTED this 14th day of May, 2010.

Law Project for Psychiatric Rights, an Alaskan non-profit corporation

By: /s/ James B. Gottstein
JAMES B. GOTTSTEIN, ABA #7811100

Attorney for *relator*, Law Project for Psychiatric Rights

CERTIFICATE OF SERVICE

The undersigned hereby certifies that on May 14, 2010, a true and correct copy of this document and accompanying proposed order was served electronically on all parties of record by electronic means through the ECF system as indicated on the Notice of Electronic Filing, or if not confirmed by ECF, by first class regular mail.

/s/ James B. Gottstein
JAMES B. GOTTSTEIN, ABA #7811100
Law Project for Psychiatric Rights

Revision: HCFA-PM-91-4 (BPD) OMB No. 0938-
AUGUST 1991

STATE PLAN UNDER TITLE XIX OF THE SOCIAL SECURITY ACT
MEDICAL ASSISTANCE PROGRAM

State/Territory: ALASKA

Citation

42 CFR
430.10

As a condition for receipt of Federal funds under title XIX of the Social Security Act, the

Department of Health and Social Services
(Single State Agency)

submits the following State plan for the medical assistance program, and hereby agrees to administer the program in accordance with the provisions of this State plan, the requirements of titles XI and XIX of the Act, and all applicable Federal regulations and other official issuances of the Department.

TN No. 91-13
Supersedes TN No. 76-31
Approval Date 4/10/92
Effective Date 10/1/91
HCFA ID: 7982E

Revision: HCFA-PM- (MB)

State/Territory: ALASKA

Citation		
1927(g) 42 CFR 456.700	4.26	Drug Utilization Review Program
	A.1.	The Medicaid agency meets the requirements of Section 1927(g) of the Act for a drug use review (DUR) program for outpatient drug claims.
1927(g)(1)(A)	2.	The DUR program assures that prescriptions for outpatient drugs are: -Appropriate -Medically necessary -Are not likely to result in adverse medical results
1927(g)(1)(a) 42 CFR 456.705(b) and 456.709(b)	B.	The DUR program is designed to educate physicians and pharmacists to identify and reduce the frequency of patterns of fraud, abuse, gross overuse, or inappropriate or medically unnecessary care among physicians, pharmacists, and patients or associated with specific drugs as well as: -Potential and actual adverse drug reactions -Therapeutic appropriateness -Overutilization and underutilization -Appropriate use of generic products -Therapeutic duplication -Drug disease contraindications -Drug-drug interactions -Incorrect drug dosage or duration of drug treatment -Drug-allergy interactions -Clinical abuse/misuse
1927(g)(1)(B) 42 CFR 456.703 (d)and(f)	C.	The DUR program shall assess data use against predetermined standards whose source materials for their development are consistent with peer-reviewed medical literature which has been critically reviewed by unbiased independent experts and the following compendia: -American Hospital Formulary Service Drug Information -United States Pharmacopeia-Drug Information -American Medical Association Drug Evaluations

TN No. 94-007
Supersedes TN No. —
Approval Date 7/21/94 Effective Date 4/1/94

Revision: HCFA-PM- (MB)

State/Territory: ALASKA

Citation		
1927(g)(1)(D) 42 CFR 456.703(b)	D.	DUR is not required for drugs dispensed to residents of nursing facilities that are in compliance with drug regimen review procedures set forth in 42 CFR 483.60. The State has never-the-less chosen to include nursing home drugs in: ___ Prospective DUR ___ Retrospective DUR.
1927(g)(2)(A) 42 CFR 456.705(b)	E.1.	The DUR program includes prospective review of drug therapy at the point of sale or point of distribution before each prescription is filled or delivered to the Medicaid recipient.
1927(g)(2)(A)(i) 42 CFR 456.705(b), (1)-(7))	2.	Prospective DUR includes screening each prescription filled or delivered to an individual receiving benefits for potential drug therapy problems due to: -Therapeutic duplication -Drug-disease contraindications -Drug-drug interactions -Drug-interactions with non-prescription or over-the-counter drugs -Incorrect drug dosage or duration of drug treatment -Drug allergy interactions -Clinical abuse/misuse
1927(g)(2)(A)(ii) 42 CFR 456.705 (c) and (d)	3.	Prospective DUR includes counseling for Medicaid recipients based on standards established by State law and maintenance of patient profiles.
1927(g)(2)(B) 42 CFR 456.709(a)	F.1.	The DUR program includes retrospective DUR through its mechanized drug claims processing and information retrieval system or otherwise which undertakes ongoing periodic examination of claims data and other records to identify: -Patterns of fraud and abuse -Gross overuse -Inappropriate or medically unnecessary care among physicians, pharmacists, Medicaid recipients, or associated with specific drugs or groups of drugs.

TN No. 94-007
Supersedes TN No. —
Approval Date 7/21/94 Effective Date 4/1/94

Revision: HCFA-PM- (MB)

State/Territory: ALASKA

Citation		
927(g)(2)(C) 42 CFR 456.709(b)	F.2.	The DUR program assesses data on drug use against explicit predetermined standards including but not limited to monitoring for: -Therapeutic appropriateness -Overutilization and underutilization -Appropriate use of generic products -Therapeutic duplication -Drug-disease contraindications -Drug-drug interactions -Incorrect drug dosage/duration of drug treatment -Clinical abuse/misuse
1927(g)(2)(D) 42 CFR 456.711	3.	The DUR program through its State DUR Board, using data provided by the Board, provides for active and ongoing educational outreach programs to educate practitioners on common drug therapy problems to improve prescribing and dispensing practices.
1927(g)(3)(A) 42 CFR 456.716(a)	G.1.	The DUR program has established a State DUR Board either: X Directly, or ___ Under contract with a private organization
1927(g)(3)(B) 42 CFR 456.716 (A) AND (B)	2.	The DUR Board membership includes health professionals (one-third licensed actively practicing pharmacists and one-third but no more than 51 percent licensed and actively practicing physicians) with knowledge and experience in one or more of the following: - Clinically appropriate prescribing of covered outpatient drugs. - Clinically appropriate dispensing and monitoring of covered outpatient drugs. - Drug use review, evaluation and intervention. - Medical quality assurance.
927(g)(3)(C) 42 CFR 456.716(d)	3.	The activities of the DUR Board include: - Retrospective DUR, - Application of Standards as defined in section 1927(g)(2)(C), and - Ongoing interventions for physicians and pharmacists targeted toward therapy problems or individuals identified in the course of retrospective DUR.

TN No. 94-007
Supersedes TN No. —
Approval Date 7/21/94 Effective Date 4/1/94

Revision: HCFA-PM- (MB) OMB No.

State/Territory: ALASKA

Citation		
1927(g)(3)(C) 42 CFR 456.711 (a)-(d)	G.4	The interventions include in appropriate instances: - Information dissemination - Written, oral, and electronic reminders - Face-to-Face discussions - Intensified monitoring/review of prescribers/dispensers
1927(g)(3)(D) 42 CFR 456.712 (A) and (B)	H.	The State assures that it will prepare and submit an annual report to the Secretary, which incorporates a report from the State DUR Board, and that the State will adhere to the plans, steps, procedures as described in the report.
1927(h)(1) 42 CFR 456.722	___ I.1.	The State establishes, as its principal means of processing claims for covered outpatient drugs under this title, a point-of-sale electronic claims management system to perform on-line: - real time eligibility verification - claims data capture - adjudication of claims - assistance to pharmacists, etc. applying for and receiving payment.
1927(g)(2)(A)(i) 42 CFR 456.705(b)	___ 2.	Prospective DUR is performed using an electronic point of sale drug claims processing system.
1927(j)(2) 42 CFR 456.703(c)	J.	Hospitals which dispense covered outpatient drugs are exempted from the drug utilization review requirements of this section when facilities use drug formulary systems and bill the Medicaid program no more than the hospital's purchasing cost for such covered outpatient drugs.

* U.S. G.P.O.:1993-342-239:80043

TN No. 94-007
Supersedes TN No. —
Approval Date 7/21/94 Effective Date 4/1/94

THE WALL STREET JOURNAL.
WSJ.com

LEADER (U.S.) | OCTOBER 23, 2003

How Drug Directory Helps Raise Tab for Medicaid and Insurers

They Pay for 'Off Label' Uses If Listed -- And Drugdex Lists Great Many of Them

By DAVID ARMSTRONG | Staff Reporter of THE WALL STREET JOURNAL

Alarmed by surging outlays for the drug Neurontin, Oklahoma's Medicaid agency last year sifted through patient records for clues. It found widespread prescriptions of the drug for uses not approved by the Food and Drug Administration.

Ninety-four percent of prescriptions for the Pfizer Inc. medicine were for these "off label" uses, the agency estimated, tripling its bill for the drug to $3.7 million from its 1998 level. The state pondered whether to curb payments for off-label uses but quickly concluded there was little it could do.

That's because nearly all of the off-label uses for Neurontin were listed in the Drugdex Information Service -- a little-known publication that has quietly become a powerful reason for rising drug costs.

Published online by Canada's Thomson Corp., Drugdex is one of three federally recognized directories for authorizing coverage under Medicaid, the federal-state insurance program for the poor and disabled. Medicaid payment for an off-label prescription can't be denied if the condition being treated is listed under the drug's name in any of the directories. At least 31 states also compel private insurers to cover some or all of the off-label uses listed in the directories, according to health-care researcher Verispan LLC.

Drugdex's listings are far more extensive than those of the other two guides -- making it the de facto standard-setter in authorizing payment for unapproved uses of prescription drugs. Such uses, recent studies suggest, account for 40% to 50% of all drug use. That translates into significant revenue for the pharmaceutical industry, which relies heavily on government and private insurance to support the $194 billion in annual sales of prescription drugs.

As government and employers see their drug tabs surge, more concerns are being raised about the efficacy and safety of so many prescriptions for treatments the FDA has never endorsed. Critics say the broad listings in Drugdex are a boost to drug-company efforts to get doctors to prescribe brand-name medicines for off-label uses. If insurance coverage didn't exist for these uses, they add, patients might take cheaper generic drugs, over-the-counter medicines, or nothing at all, saving the health-care system huge sums.

Michael Soares, director of editorial services for Micromedex, the Thomson unit that publishes the directory, says, "It is up to Medicaid to set the policies for what is reimbursed." He acknowledges that Drugdex's listings are wider than those of the other two directories, saying that reflects its larger staff, its effort to review more of the scientific literature and its desire to reflect what doctors are actually prescribing.

"Patients should not have effective, even life-saving, off-label-use drug therapies withheld from them simply because they are not reimbursed," Mr. Soares says.

Beyond Neurontin's two FDA-approved uses for epilepsy and pain related to shingles, Drugdex lists 48 other "therapeutic indications," or uses, for the drug, including bipolar disorder and other mental illnesses, headaches and hiccups. AHFS Drug Information, one of the other guides, lists only seven. The third guide, U.S. Pharmacopeia, lists

just one.

It's a broad pattern. Drugdex carries 203 off-label uses for the dozen top-selling drugs in the U.S. -- including Eli Lilly & Co.'s Zyprexa, Pfizer's cholesterol drug Lipitor and GlaxoSmithKline PLC's antidepressant Paxil. Drug Information carries only 68; U.S. Pharmacopeia, nine.

Drugdex publisher Thomson, the only private company to own one of the three guides, receives substantial revenue from the big drug companies that benefit from Drugdex listings. The company says that doesn't influence what Drugdex publishes. Similarly, Drugdex's status as an insurance authenticator "has no influence on us," Mr. Soares says.

Critics say Drugdex's criteria aren't strict enough. Drugdex often lists off-label uses based on one-patient observations or on studies that don't use the strict protocols of the FDA. And it sometimes disregards evidence showing that off-label uses aren't effective.

Arthur Levin, a member of the FDA's Drug Safety and Risk Management Advisory Committee, says that "simply being listed in a compendium" as a standard for coverage "makes no sense to me. It is overly permissive." Mr. Levin, who also runs the Center for Medical Consumers, a New York-based patient advocacy group, contends that "most often the evidence for off-label use isn't there."

Although drug companies are prohibited from promoting off-label uses, doctors can prescribe any FDA-approved drug for any ailment. One big reason for rising off-label use is patient demand. Many insurers liberalized their coverage standards for off-label uses in the early 1990s when desperate AIDS and cancer patients were dissatisfied with standard treatments.

The American Medical Association supports insurance coverage for any off-label prescription that represents "safe and effective therapy," as long as doctors pay attention to the scientific evidence and medical opinion. Off-label prescribing is "frankly just a way of life," says Edward Langston, an AMA board member and family physician in Lafayette, Ind., who says at least 10% to 15% of the prescriptions he writes are for off-label uses. "Patients would suffer without it."

Others say this standard is too lax. "If you go to Drugdex, they will include every use that has ever been written about for a drug," says Larry Sasich, a pharmacist and former outside editor for Drugdex, who now works for Public Citizen, a Washington advocacy group that typically looks for ways to broaden Medicaid coverage. "I'm not saying they do a bad job. They do what they advertise they are doing. But to use that as a standard to make reimbursement decisions is irresponsible."

Keeping Out Many Uses

Drugdex said it is selective in its listings and doesn't include every potential off-label use of a drug. In the case of Neurontin, for instance, Mr. Soares said the drug is the subject of 1,326 articles, but Drugdex has cited only 169 of them and didn't list many off-label uses cited in those additional articles. And in a small number of cases when Drugdex lists an off-label use, it rates the drug as "ineffective" for the condition.

FDA Commissioner Mark McClellan has said he wants to see more off-label uses subjected to the FDA approval process. "It is not the same kind of definitive evidence we would like to see," he said in an interview this summer. "I'd like to figure out a better way to get more information on the label."

Officials at several of the state agencies that dispense the $30 billion in annual Medicaid prescription outlays are searching for ways to control off-label spending. But Robert Reid, who runs pharmacy services for Ohio Medicaid, says he is unlikely to deny payment for an off-label prescription if there is a supportive reference in a directory -- even when the state doesn't think the use is warranted. If the patient appealed, "we would probably lose," he says.

A suit brought by a former Parke-Davis employee against Pfizer in U.S. district court in Boston seeks to recover some of the $421.6 million the suit says Medicaid spent on off-label use of Neurontin between 1994 and mid-2000. The Justice Department-backed suit alleges that Parke-Davis, which Pfizer acquired in 2000 in taking over Warner-Lambert Co., illegally marketed the drug for off-label uses.

Pfizer has denied responsibility for the alleged marketing activities because they occurred before it acquired Parke-

Davis. But it has also raised another defense: Because the off-label uses were listed in Drugdex, the government has no right to recover anything after 1997 when the directory became an official verifier. "You have to show the claims were for a use not in Drugdex," argues James Rouhandeh, a Pfizer attorney.

Is this true?

Before 1990, state Medicaid agencies decided on their own whether to cover off-label uses. But after an outcry from cancer and AIDS patients and their doctors that year, lawmakers took control of the process. Following an evaluation by the agency then overseeing Medicaid, Congress barred the states from denying coverage for a drug if the use was approved by the FDA or supported by a citation in one of three drug directories then operating.

Congress overcame concerns that the compendia would face pressure from the drug industry because all three publishers were controlled by nonprofit associations, says George Silberman, an Elm Services Inc. health economist who, while at the General Accounting Office, helped draft the bill.

But later, one of the nonprofit guides went out of business. In 1997, Congress named Thomson's Drugdex as an official reimbursement source. Thomson says it sought the designation to gain equal status with competitors. Drugdex says it applies the same standards to off-label listings today as it did then.

The three directories share similar, encyclopedic formats describing how a medicine works, its chemistry, dosing guidelines and side effects. But Drugdex covers about twice as many medicines as the others and is the only one whose editorial decisions are made by a for-profit entity. At AHFS Drug Information, a nonprofit association of hospital druggists, decisions are made by the American Society of Health-System Pharmacists. Another nonprofit, the U.S. Pharmacopeial Convention, elects and appoints 325 scientists and practitioners to make the calls in its U.S. Pharmacopeia.

Thomson's scientific and health-care division, which includes Drugdex, accounted for $780 million of the company's $7.8 billion in revenue last year. One of the division's biggest operations is running "continuing medical education" seminars for the pharmaceutical industry. Thomson doesn't disclose medical-education revenue. But Physician's World, one of its units pursuing this business, had revenue of $110 million last year, according to industry journal Medical Marketing & Media.

Thomson's medical-education customers include numerous companies whose drugs are listed in Drugdex -- including Pfizer, Glaxo and Lilly. Off-label uses of drugs are a frequent topic at medical-education seminars, which doctors often attend to fulfill state continuing-education requirements.

In its 2002 annual report, Thomson said its strategy in acquiring Physician's World and Gardiner-Caldwell, a similar company, was to "leverage" its other medical products in the medical-education market.

Mr. Soares says Drugdex makes decisions on off-label uses free of pharmaceutical-industry influence. "We would never risk any information business or the integrity of a product line for a leg up in another area," a Thomson spokeswoman adds.

Available only in online format, Drugdex appears to be eclipsing its two rival guides, traditionally available only in book form. Thomson over the last several years has noted the growth of its online-health data products and singled out Drugdex for special mention in 2000. The nonprofit group responsible for U.S. Pharmacopeia, by contrast, was having trouble making ends meet in 1998 and sold the publishing rights to the book to Thomson, while retaining editorial control.

Thomson won't discuss Drugdex pricing, but a salesman for the company quotes an annual subscription at $3,823. The U.S. Pharmacopeia book, used in many pharmacies, goes for $164, or $199 in CD form. Drug Information sells for $185; a more recent Internet version is $2,990 a year.

The three guides, whose primary audience is pharmacists, each have staffs of pharmacists, doctors and other medical professionals that review medical literature and conference presentations for possible new drug uses. But their views vary on the kind of research that qualifies as supporting evidence.

U.S. Pharmacopeia gives top points to clinical trials where patients are randomly assigned to take either a drug or a placebo, and where neither researchers nor subjects know who's in which group. It gives fewer points to studies that don't have control groups and to observational reports of a patient's response to a drug.

The American Hospital Formulary Service, which controls the AHFS Drug Information guide, says it looks for at least one, and often two randomized, double-blind and controlled studies before listing an off-label use.

These practices mirror FDA guidelines for evidence on new-drug approvals, which also give weight to larger numbers of studied patients.

At Drugdex, Mr. Soares says an article that justifies an off-label listing is one that is "reflective of a practice pattern and provides valuable insight to the clinician." Staffers are trained to know the difference between case studies and controlled trials. They place a higher value on certain studies, but also consider what was studied, the results and "what the value to the clinician will be," he says.

Support citations for Drugdex's off-label listings contain frequent examples of studies that don't involve control groups, of single-patient observations and of "open label" studies in which patients know which drug they are getting. Drugdex also supports some uses that were rejected by the FDA when the drugs' makers applied to have them approved. Mr. Soares says Drugdex includes such information as an aid to clinicians, and that they know the difference between the types of studies it cites.

One drug widely prescribed off-label is Botox, made by Allergan Inc., and approved by the FDA for treating wrinkles, the involuntary contracting of neck muscles and certain eye conditions. Beyond those, Drugdex lists 38 off-label uses, including the treatment of tension headaches, for which it is rated "effective." U.S. Pharmacopeia lists nine off-label Botox uses; AHFS Drug Information carries none.

In support of its Botox listing for tension headaches, Drugdex cites five studies. Two, the directory notes, showed negative results for effectiveness, but the other three "reported statistically significant reductions in headache pain." Two of the positive studies, published in European medical journals, were small, open-label trials, one with nine patients and the other with 10. The third positive study compared Botox with a steroid treatment in a group of 20 patients.

Drugdex doesn't mention that one of the studies it cites showing negative results was conducted at a higher research standard -- a randomized, placebo-controlled and double-blind study. Another study, unmentioned by Drugdex, was also conducted at this higher standard and found Botox to be ineffective in reducing headaches. As for why it excluded the second randomized study of Botox, Drugdex said it already listed one such study showing a lack of efficacy and that the authors of the second study "appear to be questioning" their own results.

The best-selling arthritis drug Bextra, a Pfizer product, is listed in Drugdex as effective for postoperative pain -- a use that doesn't appear in the other two indexes. Drugdex cites three 2001 studies as support, covering patients undergoing oral and foot surgery and hip replacements. The studies were conducted by the developer of the drug, Pharmacia Corp., which Pfizer acquired last year.

The FDA in November 2001 rejected the company's request to label Bextra as a treatment for acute pain, which is often equated in drug trials with post-operative pain. The FDA said the studies were "inadequate to establish safety and efficacy." A Pfizer spokeswoman wouldn't say whether the studies Drugdex cites were among those considered by the FDA. Drugdex says its staff of clinicians assessed the studies and found that Bextra was shown to be effective.

Neurontin, the drug that was a red flag to Oklahoma, is FDA-approved as an adjunctive, or add-on, treatment of partial seizures for epileptics and for postherpetic neuralgia, a painful complication of shingles. In listing 48 off-label uses, Drugdex calls Neurontin effective or possibly effective for 46 and ineffective for two.

The off-label uses include treatment of cocaine addiction and social phobia, or the fear of socializing. Many of the citations in support of the listings, as disclosed in the guide, involve a single person's experience with the drug, or otherwise fall short of the highest research standards. The listings also omit some studies that found Neurontin was ineffective for the off-label uses Drugdex carries.

One, a 1999 study funded by the National Institutes of Health, found Neurontin had about the same effect as a placebo when used as the primary treatment for bipolar-disorder patients previously resistant to other therapies. In a 2000 study, funded by Parke-Davis, a placebo was more effective than Neurontin when used as an adjunctive therapy. The company study said results "did not demonstrate" that Neurontin was effective as an adjunctive bipolar treatment.

Drugdex said it hasn't cited these studies in its Neurontin section because it was unaware of them. After reviewing them, Mr. Soares said they were flawed and wouldn't be added. Drugdex said the Parke-Davis study indicated that eight of 47 patients may not have been taking Neurontin as directed, potentially skewing results. The second study, Drugdex said, involved only 31 patients -- which it said was too small to be meaningful.

Many More 'Flaws'

Terrence Ketter, a Stanford University professor of psychiatry and co-author of the NIH study, said that "there are a hell of a lot more flaws" in Drugdex's policies than in his study, including "using uncontrolled data and endorsing something that is patently wrong." He added, "There is no way you can justify" including noncontrolled data "if you are excluding controlled data."

One of the six authors of the Drugdex section on the uses of Neurontin, Nina Graves, has had a long association with Neurontin's maker, Parke-Davis. According to Parke-Davis records produced by Pfizer in the Boston lawsuit, Ms. Graves, a former University of Minnesota pharmacy professor, traveled extensively on behalf of Parke-Davis speaking about Neurontin. Through 1997, according to the records, she received at least $75,000 in payments from the drug maker.

Ms. Graves, who now works for a medical-products company, declined to discuss her relationship with Parke-Davis or Drugdex. The Drugdex directory doesn't disclose any link between Ms. Graves and Parke-Davis or Pfizer online.

Thomson says Ms. Graves reviewed the original monograph, or passage, on Neurontin in the early 1990s. It says it was unaware of any association she might have had with the drug's maker.

Until a few weeks ago, Drugdex was the only guide that had an industry advisory board. It reviewed passages on specific drugs, though it didn't have a final say on what did or didn't get printed. After inquiries began for this article, Drugdex spokeswoman Jackie Reed said the industry advisory board "just recently has dissolved." Drugdex's Mr. Soares said the board was disbanded "because we want to get away from any look of impropriety."

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UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

UNITED STATES OF AMERICA ex rel. PETER ROST,	)	
Plaintiff,	)	Docket No. 03-CV-11084-PBS
v.	)	The Honorable Patti B. Saris
PFIZER, INC., et al.,	)	
Defendants	)	

UNITED STATES' STATEMENT OF INTEREST
IN RESPONSE TO DEFENDANT'S MOTION TO DISMISS
PLAINTIFF'S FIRST AMENDED COMPLAINT

The United States, real party in interest in this action, hereby moves to submit this Statement of Interest pursuant to 28 U.S.C. § 517 to respond to certain arguments raised in the context of defendants' Motion to Dismiss Relator's First Amended Complaint. The United States remains a real party in interest in this matter, even where it has not intervened in the action. United States ex rel. Karvelas v. Melrose-Wakefield Hosp., 360 F.3d 220, 231 (1st Cir. 2004). The False Claims Act (FCA), 31 U.S.C. § 3729 et seq., is the United States' primary tool used to redress fraud on the government. As such, the statute should be read broadly to reach all fraudulent attempts to cause the government to pay out sums of money. United States v. Neifert-White, 390 U.S. 228, 233 (1968). Thus, the United States has a keen interest in the development of the law in this area and in the correct application of the law in this, and similar, cases.[4]

[4] The brief of *amicus* Washington Legal Foundation (WLF) offers this Court its views as to what information manufacturers of medical devices and drugs may lawfully disseminate about the off-label uses of their products. Defendants, however, do not seek dismissal of this case on the grounds that the off-label marketing alleged in the First Amended Complaint was lawful.

The United States submits this brief to make four points. First, the fact that an off-label use is *listed in* a statutorily recognized compendium does not necessarily mean that the use is *supported by* the compendium citation, so that, in some circumstances, a use that is listed may not qualify as a "medically accepted indication" that is covered by law. Second, even if an off-label use is supported by a citation in a compendium, a claim nevertheless may be false for any other number of reasons (if sufficiently plead) and thus present an alternative ground for FCA liability. Third, as to section (a)(2) of the FCA, which requires the existence of a false record or statement to get a false or fraudulent claim paid or approved, a complaint need not allege that the defendants themselves made a false statement – the defendants may be liable if they caused a third party to make a false statement to get a false claim paid. In addition, false statements include not only affirmative misrepresentations but also material omissions so that the existence of either one may suffice to satisfy the false statement requirement of section (a)(2). Fourth, the identification of specific false claims is not an absolute prerequisite to satisfying the particularity requirement of Rule 9(b) in FCA cases. So long as the complaint as a whole is sufficiently particular to strengthen the inference of fraud beyond possibility, a court may conclude, as this one has in other cases, that Rule 9(b) is satisfied. Nonetheless, the United States submits that if

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WLF's arguments have not been raised or briefed by the parties, are not relevant to the instant motion to dismiss, and need not be addressed by this Court.

Indeed, WLF's assertion that it "successfully challenged the constitutionality of certain FDA restrictions on speech about off-label uses and has in place a permanent injunction against enforcement of those restrictions" is incorrect. There is no permanent injunction against the enforcement of FDA's guidance as WLF asserts. Washington Legal Foundation v. Henney, 128 F. Supp. 2d 11, 15-16 (D.D.C. 2000) (denying WLF's motion to confirm and enforce injunction, stating that the Court of Appeals "vacated all of this Court's previous constitutional rulings on the matter").

the Court finds that relator's complaint fails to meet that test and is subject to dismissal under Rule 9(b), then it need not reach the other issues addressed herein.

BACKGROUND

In order to participate in the Medicaid program, a State must have a plan for medical assistance that has been approved by the Centers for Medicare and Medicaid Services (CMS), which administers the program on behalf of the Secretary of Health and Human Services. The state plan must specify, among other things, the specific kinds of medical care and services that will be covered. 42 U.S.C. § 1396a(a)(10) and (17). If the plan is approved by the Secretary, the State thereafter is eligible for federal financial participation, *i.e.*, reimbursement by the federal government for a specified percentage of the amounts that qualify as medical assistance under the state plan. *Id.* at §§ 1396b(a)(1), 1396d(b).

States are accorded a broad measure of flexibility in tailoring the scope and coverage of their plans to meet the particular needs of their residents and their own budgetary and other circumstances. While the Medicaid Act requires States to provide certain basic services, the Act permits, but does not require, States to cover prescription drugs, although most States choose to do so. 42 U.S.C. § 1396d(a)(12).

In 1990, Congress enacted the Medicaid Drug Rebate Statute, codified at 42 U.S.C. §1396r-8, to "establish a rebate mechanism in order to give Medicaid the benefit of the best price for which a manufacturer sells a prescription drug to any public or private purchaser." H.R. Rep. No. 881, 101st Cong., 2d Sess. 96 (1990). That statute prohibits federal financial participation for covered outpatient drugs unless there is a rebate agreement in effect under section 1396r-8. See 42 U.S.C. §§ 1396b(i)(10)(A) and 1396r-8(a)(1). Once a drug manufacturer has entered into

a rebate agreement for a covered outpatient drug, a State is generally required to cover that drug under the state plan. However, there are several provisions of the Medicaid Act that permit a State to exclude or restrict coverage, at least two of which are potentially implicated in this case. 42 U.S.C. § 1396a(a)(54); H.R. Rep. No. 881 at 97, 98. A State may restrict from coverage or exclude altogether certain drugs or classes of drugs, or certain medical uses, such as drugs used for, among other things, cosmetic purposes. 42 U.S.C. § 1396r-8(d)(1)(B)(ii). A State also may exclude or restrict coverage of a drug where "the prescribed use is not for a medically accepted indication." 42 U.S.C. § 1396r-8(d)(1)(B)(i).[5]

Under the statute, a "covered outpatient drug" includes a drug dispensed by prescription and approved as safe and effective under the Federal Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. §§ 355 & 357, but does not include "a drug or biological used for a medical indication which is not a medically accepted indication." 42 U.S.C. § 1396r-8(k)(2), (3). The statute defines "medically accepted indication" as:

> any use for a covered outpatient drug which is approved under the [FDCA], or the use of which is supported by one or more citations included or approved for inclusion in any of the compendia described in subsection (g)(1)(B)(i) of this section.

Id. at § 1396r-8(k)(6). The three compendia described in subsection (g)(1)(B)(i) are the American Hospital Formulary Service Drug Information, the United States Pharmacopeia-Drug Information, and the Drugdex Information System. Id. at § 1396r-8(g)(1)(B)(i).

[5] In addition, under the terms set forth in the Medicaid Act, a State also may adopt a prior authorization program, maintain a formulary, impose limits on prescription quantities to discourage waste, and address instances of fraud or abuse by individuals. 42 U.S.C. § 1396r-8(d)(4)-(6). It does not appear that any of these potential restrictions are at issue in this matter.

I. The Term "Supported By" Requires That a Compendium Citation Corroborate a Particular Use.

One question raised by the parties here is what is necessary to satisfy the statutory requirement that a use is "supported by one or more citations" in a compendium. See id. at § 1396r-8(k)(6) (defining "medically accepted indication"). As both relator and defendants recognize, the mere existence of a compendium citation is not sufficient to meet this standard. Common usage of the term "supported by" generally requires some form of corroboration or validation. See American Heritage Dictionary of the English Language, 4th ed. (2000) ("to furnish corroborating evidence for"); Cambridge Dictionary of American English, 2d ed. (2006) ("to show (something) to be true . . . New evidence *supports* his theory"); see, e.g., In re Pharmaceutical Indus. Average Wholesale Price Litig., 460 F. Supp. 2d 277, 284 (D. Mass. 2006) ("Dictionaries of the English language are a fundamental tool in ascertaining the plain meaning of terms used in statutes and regulations."). Interpreting the definition of medically accepted indication to require only "citation in the compendia" would be problematic because it would fail to give meaning to the words "supported by," and would render that phrase superfluous. See United States v. Flores, 968 F.2d 1366, 1371 (1st Cir. 1992). Furthermore, CMS, the agency with responsibility to administer the statute at issue, has reiterated that the statutory definition of medically accepted indication "requires coverage of off-label uses of FDA-approved drugs for indications that are supported (as opposed to listed) in the compendia." See CMS Release No. 141 (emphasis added) (Attached to Relator Brief as Ex. 4). Because the agency's interpretation of this statutory provision is reasonable, it is entitled to deference by this Court. See Federal Express Corp. v. Holowecki, et al., 128 Sup. Ct. 1147, 1156 (2008). Moreover, a basic practical consideration is that Drugdex, the compendium relied on by

defendants here, classifies some indications as "not effective" and describes others as "controversial." See Def. Brief at Ex. A. Accordingly, whether a particular use is "supported by" a compendium citation may depend on a variety of factors, including the type of drug and indication at issue, the compendium's assessment of the drug's efficacy in treating the indication, the content of the compendium citation, and the scope and outcome of the studies as described in the compendium.

The only other case to have considered this provision, Edmonds v. Levine, 417 F. Supp. 2d 1323, 1339 (S.D. Fla. 2006), is distinguishable because of the circumstances in which the case was presented, and in particular because the decision predated CMS Release 141, which was released three months after the decision in Edmonds. The Edmonds case arose out of certain Medicaid beneficiaries challenging the State of Florida's adoption of a policy to make an independent evaluation of off-label uses for the drug Neurontin that resulted in the State's denying reimbursement for certain uses of the drug that were listed as effective in Drugdex, but allowing reimbursement for other uses listed as ineffective. The Court need not address the various issues raised in Edmonds stemming from whether the State's action was permissible. The relevant point here is that, as both relator and defendants recognize and CMS Release 141 has made clear, the statutory language of "supported by" means something other than merely "listed in."

As a final issue relating to coverage, it should be noted that the Medicaid statute permits a State to exclude or restrict reimbursement of an otherwise "covered outpatient drug" in certain circumstances.[6] See 42 U.S.C. § 1396r-8(d); supra at 3 & n. 1.

II. Coverage of an Off-label Indication Does Not Negate All Potential FCA Liability.

A claim may be false for any number of reasons regardless of whether it is submitted for a use supported by a citation in a compendium. For example, a claim may be ineligible for payment if a physician submitted a claim for reimbursement for which he received a kickback in exchange for prescribing a particular drug. See, e.g., United States v. Rogan, 517 F.3d 449 (7th Cir. 2008); Parke-Davis, 2003 WL 22048255, at *7. Likewise, a claim may be ineligible for payment if the prescription were signed by a person without a medical license or for a patient that did not exist. See, e.g., United States ex rel. Riley v. St. Luke's Episcopal Hosp., 355 F.3d 370, 378-79 (5th Cir. 2004) (allegation that services were performed by an unlicensed and unsupervised physician states a claim under FCA). Finally, a claim may be rendered false if a drug manufacturer falsified studies or engaged in other unlawful, fraudulent conduct in the promotion of a drug or to procure FDA approval or inclusion in a compendium. See, e.g., United States v. Dynamics Research Corp., 2008 WL 886035, *10 (D. Mass. Mar. 31, 2008) ("[W]here a claim for payment is the result of a fraudulent process-bid rigging, self-dealing, etc. such that the reliability and trustworthiness of a claim is compromised, the claim may be

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[6] Notably, this case does not present – at least not at this time – the question this Court left open in Parke-Davis as to whether States have discretion to cover off-label uses that are not supported by a citation in the compendia. See United States ex rel. Franklin v. Parke-Davis et al., 2003 WL 22048255, at *3 (D. Mass. Aug. 22, 2003). The Parke-Davis defendants argued that States are *permitted* to cover prescriptions for off-label uses even if those uses are *not* supported by a citation in the compendia. In this case, defendants contend that the off-label indication of "short stature" *is* supported by compendium citations.

considered false under the FCA despite its facial accuracy."); United States v. Incorporated Village of Island Park, 888 F. Supp. 419, 439 (E.D.N.Y. 1995) ("[T]he [FCA] is violated not only by a person who makes a false statement or a false record to get the government to pay a claim, but also by one who engages in a fraudulent course of conduct that causes the government to pay a claim for money."). Thus, the mere fact that a particular use is a "medically accepted indication" does not eliminate the possibility of fraudulent conduct or abuse that could render the claim false and ineligible for payment.

III. False Statements Under Section (a)(2) of the FCA.

This Court has held that illegal off-label marketing that results in the submission of impermissible claims for reimbursement states a claim under the FCA. Parke-Davis, 2003 WL 22048255, at *2. FCA liability exists so long as the defendants knowingly cause a false claim to be submitted by a provider to the United States. Id. Proof of falsity could entail a showing that the provider sought payment from a federal health care program for a use that was off-label and not covered by that program. Id. at *3. It is not necessary also to show (or allege) an express falsehood from the defendant to the provider to satisfy the "falsity" element of section (a)(1). Id. at *1.

Defendants correctly observe that to state a claim under section (a)(2), there must be a false record or statement. To satisfy this requirement, defendants assert that relator needed to allege "both that Pharmacia made a false statement and that this false statement was made to get a false claim paid by the government." See Def. Brief at 11. However, requiring a false statement to be made by the defendant drug company is contrary to the plain language of the FCA. Although section (a)(2) requires the existence of a false statement, it does not require the

false statement to be made *by the defendant*. Section (a)(2) imposes liability on a defendant so long as it "caused" another, such as a hired consultant, to make a false statement.

Contrary to what defendants' brief implies (Def. Br. at 11-12), for a statement to be "false," it need not be an affirmative misrepresentation; a material omission will suffice: "[H]alf the truth may obviously amount to a lie, if it is understood to be the whole." W. Page Keeton, Prosser & Keeton on the Law of Torts § 106, at 738 (5th ed. 1984); see Luckey v. Baxter Healthcare Corp., 183 F.3d 730, 732 (7th Cir. 1999) (observing that a half-truth may amount to a false statement under the FCA in certain circumstances); United States ex rel. Schwedt v. Planning Research Corp., 59 F.3d 196, 199 (D.C. Cir. 1995) (finding that false progress reports may constitute false statements under the FCA); United States ex rel. Fry v. Guidant Corp., 2006 WL 2633740, at *10-11 (M.D. Tenn. Sept. 3, 2006) (finding representation was rendered false by concealment of material information); United States ex rel. Kneepkins v. Gambro Healthcare, Inc., 115 F. Supp. 2d 35, 43 (D. Mass. 2000) (an "omitted material fact," such as the existence of illegal kickbacks, may be actionable under the FCA). Thus, a statement urging a physician to prescribe a drug for an unapproved, off-label use could well amount to a half-truth and satisfy the false statement requirement of section (a)(2), where, for example, the drug sales representative fails to mention that the evidence does not support the drug's efficacy for the use he or she is promoting or the FDA has specifically concluded that the drug is not safe or effective for that use.[7]

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[7] Notably, despite defendants' suggestion to the contrary (Def. Br. at 11, n. 8), the fact that the Medicaid Act provides for coverage for off-label uses that are supported by citation in certain compendia is irrelevant to whether a drug company made a false statement. To the extent that the FDA Modernization Act, 21 U.S.C. § 360aaa, provided a safe harbor for the dissemination of certain scientific information if a manufacturer complied with the requirements

IV. FCA Pleading Requirements.

Of course, if a relator is claiming that the defendant drug company *caused* the providers to submit these false claims, the relator must adequately allege such causation. See Parke-Davis, 2003 WL 22048255, at *4-5; United States ex rel. Cantekin v. University of Pittsburgh, 192 F.3d 402, 416 (3d Cir. 1999). The relator need not allege an express false statement to satisfy the causation element, though such evidence would be one way the relator could do so.[8]

Defendants argue that relator's complaint fails to set forth with sufficient particularity that conduct by defendants caused false claims to be submitted to federal health care programs. Defendants also argue the complaint does not sufficiently allege that the two off-label uses raised by relator (adult anti-aging and pediatric short stature) resulted in claims being submitted to federal health care programs that were false. Finally, Defendants further assert that relator has failed to identify specific adult anti-aging claims and that regardless of whether relator has identified specific pediatric short-stature claims submitted to federal health care programs, he

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set forth in the statute, the provision expired on September 30, 2006, and Congress has not renewed it. Moreover, the FDA draft guidance on *Good Reprint Practices for the Distribution of Medical Journal Articles and Medical or Scientific Reference Publications on Unapproved New Uses of Approved Drugs and Approved or Cleared Medical Devices* states that it contains "Nonbinding Recommendation, Draft – Not for Implementation" and that the FDA is accepting comments on the draft.

[8] WLF wrongly suggests that the defendant must have instructed or directed that claims be submitted or how to do so in order for liability to exist for "causing" the submission of a false or fraudulent claim. As the Supreme Court has recognized, the prototypical FCA case involving the "causing" of the submission of a false claim – when a subcontractor submits a false invoice to a prime contractor which, in turn, submits the invoice to the United States – rarely involves a subcontractor affirmatively instructing or directing the prime contractor to submit a false claim. See United States v. Bornstein, 423 U.S. 303, 309 (1976); Marcus v. Hess, 317 U.S.537, 544-45 (1943).

has failed to provide sufficient details about those claims.[9] To the extent that defendants contend that relator's complaint must fail because it did not identify specific false claims or do so with sufficient particularity, defendants seek to impose too rigid a pleading standard in FCA cases.

As a general matter, the allegation of a specific false claim is not an absolute prerequisite to pleading a viable FCA claim. Although FCA liability attaches to the claim for payment, the First Circuit and this Court have held that whether specific claims must be identified for a complaint to satisfy Rule 9(b)'s particularity requirement will depend on the circumstances of each case. See United States ex rel. Rost v. Pfizer, Inc., 507 F.3d 720, 732 (1st Cir. 2007); United States ex rel. West v. Ortho-McNeil Pharm., Inc., 2008 WL 435497, at *18 (D. Mass. Feb. 19, 2008). Thus, in off-label cases, where the alleged false claims were submitted not by the defendant, but instead by a third party, a relator "need not allege the details of particular claims, so long as 'the complaint as a whole is sufficiently particular to pass muster under the FCA.'" See Rost, 507 F.3d at 732 (quoting Karvelas, 360 F.3d at 225).[10] In evaluating such

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[9] Whether the requisite knowledge under the FCA was sufficiently plead does not appear to be a focus of defendants' brief and, in any event, questions relating to a defendant's knowledge typically cannot be resolved at the pleadings stage of a case. Accordingly, the Court need not address this issue. It bears noting here, however, that if a defendant knew or acted with reckless disregard as to the truth or falsity of claims that they caused to be submitted, "any possible ambiguity in the regulations is water under the bridge." Minnesota Ass'n of Nurse Anesthetists v. Allina Health System Corp., 276 F.3d 1032, 1053 (8th Cir. 2002).

[10] Such an analysis is consistent with FCA cases in which courts have found that when a complaint sets forth with particularity allegations of a fraudulent scheme or course of conduct, it is not also necessary to identify specific claims because doing so adds little to the sufficiency of the complaint as a whole. See, e.g., United States ex rel. Singh v. Bradford Regional Medical Center, 2006 WL 2642518, at *7 (W.D. Pa. 2006) ("[T]he falsity of the instant claims does not turn on anything unique to any individual claim or that would be revealed from an examination of any claim, but rather the claims 'are false because of the improper financial arrangements

matters, "the strength of the inference of fraud on the government" may be measured by, for example, factual or statistical evidence tending to show fraud beyond possibility. See West, 2008 WL 435497, at *18. Given the posture of this matter, the unique circumstances of the drug at issue in this case, and to assist the Court in applying the standard here, the United States submits that it is not aware of any billable diagnosis code for an anti-aging use that would be recognized or reimbursable by federal health care programs.

Conclusion

The United States submits this brief regarding how to interpret and apply certain aspects of the Medicaid Act and the FCA. The United States takes no position on the sufficiency of the complaint herein.

Respectfully submitted,

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between [defendant] and the physicians.'").

Washington, D.C. 20004
Phone: (202) 353-0426

Dated: May 12, 2008

Medically Accepted Indications for Pediatric Use of Certain Psychotropic Medications by The Law Project for Psychiatric Rights (PsychRights

Drug	Indication (diagnosis)	FDA Approval	DRUGDEX Support for Off-Label Use	DRUGDEX Recommendation Level
Key:	White Background: Medically Accepted Indication			
	Orange Background: Pediatric Indication cited, but not supported by DRUGDEX			
	Red Background: No Pediatric FDA Approval or DRUGDEX citation			
Abilify (Aripiprazole) - Antipsychotic				
	Autistic disorder-Psychomotor agitation	Yes (6-17)		
	Bipolar I Disorder - Adjunctive therapy with lithium or valproate for Acute Manic or Mixed Episodes	Yes (for 10 yrs old and up)		
	Bipolar I Disorder, monotherapy, Manic or Mixed Episodes	Yes (for 10-17 years old re acute therapy)		
	Schizophrenia	Yes (for 13-17 years old)		
Adderall (amphetamine/dextroamphetamine) - Central Nervous System Agent; CNS Stimulant				
	Attention Deficit Hyperactivity Disorder (ADHD)	Yes (for 3 years old and up re: [immediate-release] and 6 years old and up re: [extended-release] drug		
	Narcolepsy	Yes (for 6 years old and up (immediate release only)		
Ambien (zolipidem) - nonbartiturate Hypnotic				
	Insomnia, Short-term treatment	No		Class III
Anafranil (clomipramine) - Antidepressant; Antidepressant, Tricyclic; Central Nervous System Agent				
	Obsessive-Compulsive Disorder	Yes (for 10 years and up)		
	Depression	No		Class IIb
Ativan (lorazepam) - Antianxiety, Anticonvulsant, Benxodiazepine, Short or Intermediate Acting, Skeletal Muslgel Relaxant.				
	Anxiety	Yes, oral only, 12 years and older		
	Chemotherapy-induced nausea and vomiting; Prophylaxis	No	Class IIa	
	Insomnia, due to anxiety or situational stress	Yes		
	Seizure	No	Class IIa	
	Status epilepticus	No	Class IIa	
	Premedication for anesthetic procedure	No		Class IIb
	Sedation	No		Class IIb
	Seizure, drug-induced; Prophylaxis	No		Class IIb
Buspar (buspirone) - Antianxiety, Azaspirodeconedione				
	Anxiety	No		Class III
	Autistic disorder	No		Class IIb
	Behavioral syndrome	No		Class IIb
	Pervasive developmental disorder	No		Class IIb
Celexa (citalopram) - Antidepressant, Serotonin Reuptake Inhibitor				
	Depression	No		None
	Obsessive-compulsive disorder	No		Class IIb
	Panic disorder	No		Class IIb
	posttraumatic stress disorder	No		Class IIb

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Drug	Indication (diagnosis)	FDA Approval	DRUGDEX Support for Off-Label Use	DRUGDEX Recommendation Level
Clozaril (clozapine) – Antipsychotic; Dibenzodiazepine				
	Bipolar I Disorder	No		Class IIb
	Schizophrenia, Treatment Resistant	No		cited, with no recommendation level
Concerta (methylphenidate) - Amphetamine Related; Central Nervous System Agent; CNS Stimulant				
	Attention Deficit Hyperactivity Disorder (ADHD)	Yes (for 6 years old to 12 years old)		
	Attention Deficit Hyperactivity Disorder (ADHD)	Yes (for 6 years old and up) re ConcertaR		
	Autistic Disorder	No		Class IIb
	Impaired Cognition - inding related to coordination/ in coordination	No		Class IIb
	Schizophrenia	No		Class IIII
	Traumatic Brain Injury	No		Class IIb
Cymbalta (duloxetine) - Antidepressant; Central Nervous System Agent; Neuropathic Pain Agent; Serotonin/Norepinephrine Reuptake Inhibitor				
Dalmane (flurazepam) - Benzodiazepine, Long Acting, Hypnotic				
	Insomnia	Yes, 15 years and older		
Depakote/Depakene (valproate/valproic acid) – Anticonvulsant; Antimigraine; Valproic Acid (class)				
	Absence Seizure, Simple and Complex	Yes (10 years and older)		
	Complex Partial Epileptic Seizure	Yes (10 years and older)		
	Seizure, Multiple sezure types; Adjunct	Yes (10 years and older)		
	Bipolor I disorder, Maintenance	No		Class IIb
	Bipolor II disorder, Maintenance	No		Class IIb
	Chorea	No		Class IIb
	Febrile Seizure	No		Class IIb
	Mania	No		Class IIII
	Manic bipolar I disorder	No		Class IIb
	Mental Disorder - Mood Disorder	No		Class IIb
	Migraine; Prophylaxis	No		Class IIb
	Status epilepticus	No		Class IIb
	West syndrome	No		Class IIb
Desyrel (*trazodone*) - Antidepressant; Triazolopyridine				
	Migraine, Pediatric; Prophylaxis	No		Class III
Dexedrine (dextroamphetamine) - Amphetamine (class); CNS Stimulant				
	Attention Deficit Hyperactivity Disorder (ADHD)	Yes (for 3 years to 16 years old (immediate-release) and age 6 years to 16 years old (sustained-release))		
	Narcolepsy	Yes (for 6 years old and up)		
Effexor (venlafaxine) – Antidepressant; Antidepressant, Bicyclic; Phenethylamine (class); Serotonin/ Norepinephrine Reuptake Inhibitor				
	Attention Deficit Hyperactivity Disorder (ADHD)	No		Class IIb
	Generalized Anxiety Disorder	No		Class IIb
	Major Depressive Disorder	No		Class IIb
	Social Phobia	No		Class IIb
Focalin (dexmethylphenidate) - Amphetamine Related; CNS Stimulant				
	Attention Deficit Hyperactivity Disorder (ADHD)	Yes (for 6 years and older)		
Geodon (ziprasidone) - Antipsychotic; Benzisothiazoyl				

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Drug	Indication (diagnosis)	FDA Approval	DRUGDEX Support for Off-Label Use	DRUGDEX Recommendation Level
Haldol (haloperidol) - Antipsychotic; Butyrophenone; Dopamine Antagonis				
	Gilles de la Tourette's syndrome	Yes (for 3 years old and up)	It does not appear the injectible form (decanoate) is FDA approved for any pediatric use, nor is it supported by DRUGDEX for any indication.	
	Hyperactive Behavior, (Short-term treatment) after failure to respond to non-antipsychotic medication and psychotherapy	Yes (for 3 years old and up)		
	Problematic Behavior in Children (Severe), With failure to respond non-antipsychotic medication or psychotherapy	Yes (for 3 years old and up)		
	Psychotic Disorder	Yes (for 3 years old and up but ORAL formulations only)		
	Schizophrenia	Yes (for 3 years old and up but ORAL formulations only)		
	Agitation	No		Class IIb
	Migraine	No		Class III
Invega (paliperidone) - Antipsychotic; Benzisoxazole				
Klonopin (clonazepam) -antianxiety, Anticonvulsant, Bensodiazepine, Short or Intermediate Acting				
	Seizure	Yes, upt to 10 years or up to 30 kg		
	Gilles de la Tourette's syndrome	No		Class IIb
	Hyperexplexia	No		Class IIb
	Nocturnal epilepsy	No		Class IIb
	Panic disorder	No		Class IIb
	Status epilepticus	No		Class IIb
Lamictal (lamotrigine) - Anticonvulsant; Phenyltriazine				
	Convulsions in the newborn, Intractable	No	Class IIa	
	Epilepsy, Refractory	No	Class IIa	
	Lennox-Gastaut syndrome; Adjunct	yes (2 years and older)		
	Partial seizure, Adjunct or monotherapy	yes (13 years and older, extended-release only; 2 years and older, chewable dispersible		
	Tonic-clonic seizure, Primary generalized; Adjunct	yes (2 years and older)		
	Absence seizure; Adjunct	No		Class IIb
	Bipolar Disorder, Depressed Phase	No		Class IIb
	Infantile neuronal ceroid lipofuscinosis	No		Class IIb
	Juvenile myoclonic epilepsy	No		Class III
	Paroxysmal choreoathetosis, Paroxysmal	No		Class IIb
	Rett's disorder	No		Class IIb
	Status epilepticus	No		Class IIb
	West syndrome	No		Class IIb
Lexapro (escitalopram)- Antianxiety, Antidepressant, Serotonin Reuptake Inhibitor				
	Major Depressive Disorder	Yes (for 12 years old and up)		
Limbitrol (chlordiazepoxide/amitriptyline) - Tricyclic Antidepressant/Benzodiazepine Combination				
Lunesta (eszopiclone) - Nonbarbiturate Hypnotic				
Luvox (fluvoxamine) - Antidepressant; Central Nervous System Agent; Serotonin Reuptake Inhibitor				
	Obsessive-Compulsive Disorder	Yes (for 8 years old and up and immediate release formula only)		
	Asperger's Disorder	No		Class IIb

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Drug	Indication (diagnosis)	FDA Approval	DRUGDEX Support for Off-Label Use	DRUGDEX Recommendation Level
Mellaril (thioridazine) - Antipsychotic; Phenothiazine; Piperidine				
	Schizophrenia, Refractory	Yes		
	Behavioral Syndrome	No		Class III
Moban (molindone) - antipsychotic, Dihydroindolone				
	Schizophrenia	Yes, 12 years and older		
	Aggressive behavior, In children	No		Class IIb
Neurontin (gabapentin) anticonvulsant				
	Partial seizure; Adjunct	Yes (3- 12 years old)		
	Complex Regional Pain Syndrome, Type 1	No		Class IIb
	Neuropathic Pain	No		Class IIb
	Partial Seizure	No		Class IIb
	Partial Seizure, Refractory	No		Class III
	Phantom Limb Syndrome	No		Class IIb
Orap (pimozide) - Antipsychotic; Diphenylbutylpiperidine; Dopamine Antagonist				
	Gilles de la Tourette's syndrome	Yes (12 years and older)		
	Anorexia Nervosa	No		Class III
Paxil (paroxetine) - Antidepressant; Central Nervous System Agent; Serotonin Reuptake Inhibitor				
	Panic disorder	No		Class IIb
	Trichotillomania	No		Class IIb
Pristiq (desvenlafaxine) Antidepressant, Serotonin/Norepinephrine Reuptake Inhibitor				
Prozac (fluoxetine) - Antidepressant; Central Nervous System Agent; Serotonin Reuptake Inhibitor				
	Major Depressive Disorder	Yes (for 8 years old and up)		
	Obsessive-Compulsive Disorder	Yes (for 7 years old and up		
	Anxiety Disorder of Childhood	No		Class IIb
	Autistic disorder	No		None
	Bulimia nervosa	No		Class IIb
	Vasovagal syncope; Prophylaxis	No		Class III
Restoril (temazepam) - Antianxiety, Bensodiazepine, Short or Intermediate Acting, Hypnotic				
Ritalin (methylphenidate) - Amphetamine Related; Central Nervous System Agent; CNS Stimulant				
	Attention Deficit Hyperactivity Disorder (ADHD)	Yes (for 6 years to 12 years old)(exteded release)		
	Attention Deficit Hyperactivity Disorder (ADHD)	Yes (for 6 years old and up)(immediate release)		
	Narcolepsy	Yes (for 6 years and up, and Ritalin(R) -SR only)		
	Autistic disorder	No		Class IIb
	Finding related to coordination / incoordination - Impaired cognition	No		Class IIb
	Schizophrenia	No		Class III
	Traumatic Brain Injury	No		Class IIb
Risperdal (risperidone) - Antipsychotic; Benzisoxazole				
	Autistic Disorder – Irritability	Yes (for 5 years old and up)		
	Bipolar I Disorder	Yes (for 10 years old and up)		
	Schizophrenia	Yes (for 13 years old and up, ORALLY)		
	Behavioral syndrome - Mental retardation	No		Class IIb
	Gilles de la Tourette's syndrome	No		Class IIb
	Pervasive developmental disorder	No		Class IIb

Medically Accepted Indications for Pediatric Use of Certain Psychotropic Medications by The Law Project for Psychiatric Rights (PsychRights

Drug	Indication (diagnosis)	FDA Approval	DRUGDEX Support for Off-Label Use	DRUGDEX Recommendation Level
Rozerem (ramelteon) - Melatonin Receptor Agonist, Nanbarbiturate Hypnotic				
Seroquel (QUETIAPINE) - Antipsychotic; Dibenzothiazepine				
	Bipolar disorder, maintenance	Yes, 10-17 regular release only (12/4/09)		
	Manic bipolar I disorder	Yes, 10-17 regular release only (12/4/09)		
	Schizophrenia	Yes 13-17, regular release only (12/4/09)		
	Gilles de la Tourette's syndrome	No		Class IIb
Sinequan (doxepin) - Antianxiety Antidepressant; Antidepressant, Tricyclic; Antiulcer Dermatological Agent				
	Alcoholism - Anxiety – Depression	Yes (for 12 years old and up)		
	Anxiety – Depression	Yes (for 12 years old and up)		
	Anxiety - Depression - Psychoneurotic personality disorder	Yes (for 12 years old and up)		
	Pruritus (Moderate), Due to atopic dermatitis or lichen simplex chronicus	No		Class IIb
Sonata (zaleplon) - Nonbarbiturate Hypnotic				
Strattera (atomoxetine) - Central Nervous System Agent; Norepinephrine Reuptake Inhibitor				
	Attention Deficit Hyperactivity Disorder (ADHD)	Yes (for 6 years old and up)		
	Attention Deficit Hyperactivity Disorder (ADHD) - Social phobia	No		Class IIb
Symbyax (fluoxetine hydrochloride/olanzapine) - Antidepressant; Antipsychotic				
Tegretol (carbamazepine) - Anticonvulsant; Antimanic; Dibenzazepine Carboxamide; Neuropathic Pain Agent				
	Epilepsy, Partial, Generalized, and Mixed types	Yes		
	Apraxia			None
	Chorea			Class IIb
	Migraine; Prophylaxis			Class IIb
	Myokymia			Class IIb
	Neuropathy, General			Class IIb
	Schwartz-Jampel syndrome			Class IIb
Tofranil (imipramine) - Antidepressant; Antidepressant, Tricyclic; Urinary Enuresis Agent				
	Nocturnal enuresis	Yes (for 6 years old and up)		
	Attention Deficit Hyperactivity Disorder (ADHD), Predominantly Inattentive Type	No		Class III
	Depression	No		Class IIb
	Schizophrenia, Adjunct	No		Class III
	Separation Anxiety Disorder of Childhood	No		Class III
	Trichotillomania	No		Class IIb
	Urinary incontinence	No		Class IIb
Topamax (topiramate) - anticonvulsant, Fructopyranose Sulfamate				
	Lennox-Gastaut syndrome; Adjunct	Yes, 2 years and older		
	Partial seizure, Initial monotherapy	Yes, 10 years and older		
	Partial seizure; Adjunct	Yes, 10 years and older		
	Tonic-clonic seizure, Primary generalized; Adjunct	Yes, 2 to 16 years old		
	Tonic-clonic seizure, Primary generalized (initial monotherapy)	Yes, 10 years and older		
	Angelman syndrome	No		Class IIb
	Migraine; Prophylaxis	No		Class IIb

Medically Accepted Indications for Pediatric Use of Certain Psychotropic Medications by The Law Project for Psychiatric Rights (PsychRights

Drug	Indication (diagnosis)	FDA Approval	DRUGDEX Support for Off-Label Use	DRUGDEX Recommendation Level
	Status epilepticus	No		Class IIb
	West syndrome	No		Class IIb
Tranxene (clorazepate) - Antianxiety, Anticonfulsant, Benzodiazepine, Long Acting				
	Partial seizure; Adjunct	Yes, 9 years and older		
	Epilepsy	No		Class IIb
Trileptal (*oxcarbazepine*) - Anticonvulsant; Dibenzazepine Carboxamide				
	Partial Seizure, monotherapy	Yes (for 4 years old and up)		
	Partial seizure; Adjunct	Yes (for 2 years old and up)		
Vyvanse (lisdexamfetamine) - Amphetamine (class); CNS Stimulant				
	Attention Deficit Hyperactivity Disorder (ADHD)	Yes (for 6 years old to 12 years)		
Wellbutrin (bupropion) - Aminoketone, Antidepressant, Smoking Cessation Agent				
	Attention deficit hyperactivity disorder	No		None
Xanax (alprazolam) - Antianxiety, Benzodiazepine, Short or Intermediate Acting				
Zoloft (sertraline) - Antidepressant; Central Nervous System Agent; Serotonin Reuptake Inhibitor				
	Obsessive-Compulsive Disorder	Yes (6 years old and up)		
	Anorexia nervosa	No		Class III
	Generalized Anxiety Disorder	No		Class IIb
	Major Depressive Disorder	No		Class IIb
Zyprexa (olanzapine) - Antipsychotic; Thienobenzodiazepine				
	Bipolar 1, Disorder, Acute Mixed or Manic Episodes	Yes (ages 13-17), oral only, approved 12/4/09		
	Schizophrenia	Yes (ages 13-17), oral only, approved 12/4/09		
	Schizophrenia, Refractory	No		Class IIb
	Pervasive Developmental Disorder	No		Class IIb

DRUGDEX® Consults

RECOMMENDATION, EVIDENCE AND EFFICACY RATINGS

RESPONSE

The Thomson Efficacy, Strength of Evidence and Strength of Recommendation definitions are outlined below:

Table 1. Strength Of Recommendation		
Class I	Recommended	The given test or treatment has been proven to be useful, and should be performed or administered.
Class IIa	Recommended, In Most Cases	The given test, or treatment is generally considered to be useful, and is indicated in most cases.
Class IIb	Recommended, In Some Cases	The given test, or treatment may be useful, and is indicated in some, but not most, cases.
Class III	Not Recommended	The given test, or treatment is not useful, and should be avoided.
Class Indeterminant	Evidence Inconclusive	

Table 2. Strength Of Evidence	
Category A	Category A evidence is based on data derived from: Meta-analyses of randomized controlled trials with homogeneity with regard to the directions and degrees of results between individual studies. Multiple, well-done randomized clinical trials involving large numbers of patients.
Category B	Category B evidence is based on data derived from: Meta-analyses of randomized controlled trials with conflicting conclusions with regard to the directions and degrees of results between individual studies. Randomized controlled trials that involved small numbers of patients or had significant methodological flaws (e.g., bias, drop-out rate, flawed analysis, etc.). Nonrandomized studies (e.g., cohort studies, case-control studies, observational studies).
Category C	Category C evidence is based on data derived from: Expert opinion or consensus, case reports or case series.
No Evidence	

Table 3. Efficacy		
Class I	Effective	Evidence and/or expert opinion suggests that a given drug treatment for a specific indication is effective
Class IIa	Evidence Favors Efficacy	Evidence and/or expert opinion is conflicting as to whether a given drug treatment for a specific indication is effective, but the weight of evidence and/or expert opinion favors efficacy.
Class IIb	Evidence is Inconclusive	Evidence and/or expert opinion is conflicting as to whether a given drug treatment for a specific indication is effective, but the weight of evidence and/or expert opinion argues against efficacy.
Class III	Ineffective	Evidence and/or expert opinion suggests that a given drug treatment for a specific indication is ineffective.