



December 30, 2004

Mark B. McClellan, M.D., Ph.D.
Administrator, Centers for Medicare and Medicaid Services
Room 445-G, Hubert H. Humphrey Building
200 Independence Avenue, SW.
Washington, DC 20201

**RE: Draft Guidance—CMS Formulary Review
For the Medicare Prescription Drug Benefit
Comments on Rare Diseases and Orphan Drugs**

Dear Dr. McClellan:

On behalf of the National Organization for Rare Disorders (NORD), we are pleased to provide comments on the Draft Guidance on CMS Formulary Review for the Medicare Prescription Drug Benefits. NORD is a federation of approximately 130 voluntary health organizations and approximately 60,000 individual patients, healthcare providers and clinical researchers. We are all committed to the identification, treatment, and cure of rare disorders through programs of education, advocacy, research and service.

PRINCIPLES of Assured Access to Part D Benefits for Rare Disease Patients

As in our previous communications, we are concerned about the access of rare disease patients (estimated to be 10 percent of the overall Medicare population) to orphan drugs and biologicals under the Medicare Part D outpatient drug benefit. Orphan drugs are of little value to Medicare beneficiaries—both elderly and adult disabled with rare diseases—if they are not covered by the new prescription drug plans.

NORD had a grave concern with the USP's model classes and categories. The minimum of two drugs per category provided little likelihood that any orphan drug would be covered. Further, the typology itself failed the rare disease community by, for example, covering sleeping aids but not therapy for narcolepsy. We are especially grateful that CMS has chosen to propose guidelines that reach far beyond what the USP had offered.

CMS must continue to stress that the principles of Part D are not satisfied if beneficiaries lack access to the therapies appropriate to their medical condition. Because drug plans will have to compete on price, they have incentives to attract beneficiaries with few medical problems and no expensive drug regimens. Thus, concerns about discriminatory behavior are fully warranted and are a particular concern of NORD and beneficiaries with rare diseases.

There is one sentence on page 9 that we believe was intended to reinforce the specific importance of access to orphan drugs. It reads: "CMS will also assess the availability and tier position for commonly prescribed drugs for uncommon conditions." As stated, this sentence is ambiguous.

It is our hope that CMS meant either:

- "...whatever drugs are commonly used to treat rare diseases (uncommon conditions)." OR
- "CMS will also assess the availability and tier position of drugs that are the therapeutic standard for treatment of rare diseases."

We would appreciate clarification in the final guidance that this is meant to protect beneficiaries with rare diseases who need access to orphan drugs.

With regard to the guidance document as a whole, we are particularly comforted by a number of CMS' assertions, such as:

"...[K]ey requirements in the MMA are to assure that drug plans provide access to medically necessary treatments for all and do not discriminate against any particular types of beneficiaries..." (Page 1)

"The goal of this program, however, is not to save money on prescription drugs at the expense of appropriate medical care. Appropriate medical care would not be possible if plans sought to discourage enrollment by beneficiaries with high, expected drug costs." (Page 2)

"...because drug classes alone, whether detailed or general, are not sufficient to determine adequate access for all beneficiaries, we also will review the drug plans' formularies and benefits to identify discriminating practices." (Page 2)

"CMS has the discretion to find that failure to include a specific drug would substantially discourage enrollment by beneficiaries with a condition that may only be treated by that drug." (Page 3)

PRACTICALITIES of Assured Access to Part D Benefits for Rare Disease Patients

While the principles of assuring access to orphan drugs are repeatedly asserted in the guidance document, the practicalities remain a concern to NORD.

"CMS will compare plans' use of benefit management tools, like prior authorization, to the way these tools are used in existing plans, to ensure they are being applied in a clinically appropriate and non-discriminatory fashion." (Page 1)

This seems appropriate and consistent with the rest of the document. However, **it assumes that the model plans cited in the text are, in fact, models for access to orphan drugs.** Our preliminary analysis suggests that this assumption cannot be relied upon and may be incorrect.

The best practices formularies identified by CMS are: (1) Advance PCS for the Blue Cross and Blue Shield Federal Employee Program, (2) First Health, (3) Kaiser Permanente, (4) Massachusetts Medicaid, and (5) Florida Medicaid. We reviewed these formularies to determine coverage of orphan designated/approved drugs. Our preliminary findings are in the attached Excel workbook and are summarized below:

- Among 124 physician/provider injectable drugs (identified in our spreadsheet as Part B), coverage is very variable and ranges from a low of 7 and 12 on First Health's and Kaiser's listings, respectively, to a high of 69 on the Massachusetts Medicaid listing. We believe the low level of coverage on the private best practice models is because injectables are likely handled outside the "traditional" formulary.
- Among 81 other orphan drugs (identified in our spreadsheet as Part D), coverage is better, but still quite variable ranging from a low of 16 on the First Health listing to a high of 64 on the Massachusetts Medicaid listing.

Further, the best practice P&T Committee criteria cited by CMS are the American Society of Health-System Pharmacists (ASHP) and the Academy of Managed Care Pharmacy (AMCP) criteria. Neither of these mentions the need to ensure coverage for patients with rare disorders. Also mentioned as a best practice is the American Hospital Formulary System (AHFS) classification. The AHFS drug classification, which can accommodate most orphan drugs but would not be an appropriate alternative to the USP classification system, is based principally upon pharmacological classes and would not ensure coverage for rare disorders.

Our bottom line is that there still needs to be some additional practical pressures on prescription drug plans in order to assure beneficiaries with rare disorders that they will have access to the orphan drugs that they need.

Other Issues

There are three additional items on which NORD would appreciate correction or clarification. In the second to last bullet on page 5, NORD would amend the last part of the sentence to read: "...elderly, and people with rare diseases or people with disabilities."

This reflects our concern that rare diseases not be confused with disabilities. A large number of beneficiaries are in both categories, but the perspective is often quite different.

Second, we would appreciate some acknowledgement in the guidance document with regard to CMS' intent to consult with the FDA's Office of Orphan Product Development and the NIH Office of Rare Disease with regard to classification of rare diseases and coverage of orphan drugs and biologicals.

Mark B. McClellan, M.D., Ph.D.

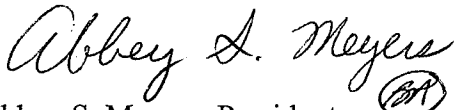
December 30, 2004

Page 4

Third, we believe that the need for consistent clinical care requires that drugs available under the Medicare demonstration should continue to be available to participating patients, even if their drug plan's formulary does not include that specific drug.

We appreciate the opportunity to provide comments on this draft guidance and to continue our dialogue about assuring access to orphan drugs and biologicals under all parts of the Medicare program.

Sincerely,

Handwritten signature of Abbey S. Meyers in cursive script, with a small circular stamp containing the initials 'AS' to the right.

Abbey S. Meyers, President
National Organization for Rare Disorders
55 Kenosia Avenue
Danbury, CT 06813
Phone: (203) 744-0100

cc: Diane Dorman
NORD Board of Directors
NORD Task Force on Public Affairs

Attachments

MIA 291402-1.020980.0048

Part B

	Nonproprietary name	Brand name	MassHealth Drug List	Florida Medicaid Preferred Drug List	First Health Rx Drug Guide	FEP Rx Drug Formulary	Kaiser-Permanente (DC)
1	Acetylcysteine	Acetadote	Y	N	N	Y	N
2	Agalsidase beta	Fabrazyme	Y	N	N	Y	N
3	Aldesleukin	Proleukin	N	Y	N	N	N
4	Alemtuzumab	Campath	N	N	N	N	N
5	Alglucerase Injection	Ceredase	N	N	N	Y	N
6	Allopurinol sodium	Aloprim for Injection	Y	N	N	N	Y
7	Alpha 1-proteinase Inhibitor Human	Prolastin	Y	Y	N	N	N
8	Amifostine	Ethyol	N	Y	N	N	N
9	Amphotericin B Lipid Complex	Abelcet	Y	Y	N	N	N
10	Liposomal Amphotericin B	AmBisome	Y	Y	N	N	N
11	Antihemophilic Factor (Porcine)	Hyate:C	N	N	N	N	N
12	Antihemophilic Factor (Human)	Alphanate* Hemofil M Koate-DVI Koate-HP Monarc-M Monoclate-P	Y	Y	N	N	N
13	Antihemophilic Factor (Recombinant)	Kogenate Kogenate FS ReFacto Helixate FS Recombinate	Y	Y	N	N	N
14	Antihemophilic Factor/von Willebrand Factor Complex Human, Dried	Humate-P	N	Y	N	N	N
15	Anti-inhibitor Coagulant complex, Heat Treated; Anti-inhibitor Coagulant Complex, Vapor Heated	Autoplex T FEIBA VH	Y	Y	N	N	N
16	Antithrombin III Human	ATnativ Thrombate III	N	N	N	N	N
17	Antivenin, crotalidae polyvalent immune Fab (ovine)	CroFab	N	N	N	N	N
18	Aprotinin	Trasylol	N	N	N	N	N
19	Arsenic Trioxide	Trisenox	N	N	N	N	N
20	Azacitidine	Vidaza	Y	N	N	N	N
21	Baclofen	Lioresal Intrathecal	Y	Y	N	Y	N
22	Basiliximab	Simulect	N	N	N	N	N
23	Bleomycin Sulfate	Blenoxane	Y	Y	N	N	N
24	Bortezomib	Velcade	Y	N	N	N	N
25	Botulinum Toxin Type A	BOTOX	Y	Y	N	Y	N
26	Botulinum Toxin Type B	Myobloc	Y	N	N	Y	N

Part B

	Nonproprietary name	Brand name	MassHealth Drug List	Florida Medicaid Preferred Drug List	First Health Rx Drug Guide	FEP Rx Drug Formulary	Kaiser-Permanente (DC)
27	Botulism immune globulin	BabyBIG	N	N	N	N	N
28	Buffered Intrathecal Electrolyte/Dextrose Injection	Elliot's B Solution	N	N	N	N	N
29	Busulfan	Busulfex	N	N	N	N	N
30	Caffeine	Cafcit	Y	N	N	N	N
31	Cladribine	Leustatin Injection	N	N	N	N	N
32	Clonidine	Duraclon	Y	N	N	N	Y
33	Coagulation Factor IX Complex	Bebulin VH Konyne 80 Proplex T Profilnine SD	Y	Y	N	N	N
34	Coagulation Factor IX Human	AlphaNine Mononine	Y	Y	N	N	N
35	Coagulation Factor IX Recombinant	Benefix	Y	Y	N	N	N
36	Coagulation Factor VIIa	Novoseven	Y	Y	N	N	N
37	Corticotropin Ovine Triflutate	Acthrel	N	N	N	N	N
38	Cytarabine Liposomal	DepoCyt	N	Y	N	N	N
39	Cytomegalovirus Immune Globulin Human	CytoGam	Y	Y	N	N	N
40	Daclizumab	Zenapax	Y	Y	N	N	N
41	Daunorubicin Citrate Liposome Injection	DaunoXome	N	Y	N	N	N
42	Denileukin Diftitox	Ontak	N	N	N	N	N
43	Dexrazoxane	Zinecard	N	Y	N	N	N
44	Digoxin Immune FAB Ovine	Digibind	N	N	N	N	N
45	Dornase alfa	Pulmozyme	Y	Y	N	Y	Y
46	Doxorubicin Liposome	Doxil	N	Y	N	N	N
47	Dronabinol	Marinol	Y	N	Y	Y	N
48	Eflornithine HCl	Ornidyl	N	N	N	N	N
49	Epirubicin	Ellence	Y	N	N	N	N
50	Epoetin Alfa	Epogen Procrit	Y	Y	N	Y	N
51	Epoprostenol	Flolan	Y	Y	N	N	N
52	Etanercept	Enbrel	Y	Y	N	Y	Y
53	Ethanolamine Oleate	Ethamolin	N	N	N	N	N
54	Etidronate Disodium	Didronel	Y	N	N	Y	Y
55	Filgrastim	Neupogen	Y	Y	N	Y	N
56	Fludarabine Phosphate	Fludara	N	N	N	N	N
57	Fomepizole	Antizole	N	N	N	N	N
58	Fosphenytoin	Cerebyx	N	Y	N	N	N
59	Gallium nitrate injection	Ganite	N	N	N	Y	N
60	Ganciclovir Intravitreal Implant	Vitrasert Implant	N	N	N	N	N

Part B

	Nonproprietary name	Brand name	MassHealth Drug List	Florida Medicaid Preferred Drug List	First Health Rx Drug Guide	FEP Rx Drug Formulary	Kaiser-Permanente (DC)
61	Ganciclovir sodium	Cytovene	Y	N	N	Y	Y
62	Gemtuzumab Zogamicin	Mylotarg	N	N	N	N	N
63	Glatiramer Acetate	Copaxone	Y	N	Y	Y	N
64	Gonadorelin acetate	Lutrepulse	N	N	N	Y	N
65	Hemin	Panhematin	N	N	N	N	N
66	Ibritumomab tiuxetan	Zevalin	Y	N	N	N	N
67	Icodextrin 7.5% with electrolytes peritoneal dialysis	Extraneal	N	N	N	N	N
68	Idarubicin HCl for Injection	Idamycin	N	N	N	N	N
69	Ifosfamide	Ifex	N	N	N	N	N
70	Imiglucerase	Cerezyme	Y	Y	N	Y	N
71	Immune Globulin Intravenous, Human	Gamimune N SD, Venoglobulin-S, Gammar-PIV, Gammagard S/D, Iiveegam-EN, Gamunex, Flebogamma, Carimune NF, Polygam S/D, Panglobulin	Y	Y	N	N	N
72	Infliximab	Remicade	Y	Y	N	Y	N
73	Interferon alfa-2a	Roferon A	Y	N	N	Y	N
74	Interferon alfa-2b	Intron A	Y	Y	Y	Y	N
75	Interferon beta-1a	Avonex	Y	Y	N	Y	N
76	Interferon beta-1b	Betaseron	Y	Y	N	Y	N
77	Interferon gamma-1b	Actimmune	Y	Y	N	N	N
78	Iobenguane Sulfate I-131	None	N	N	N	N	N
79	Laronidase	Aldurazyme	Y	N	N	Y	N
80	Lepirudin	Refluden	Y	N	N	N	N
81	Leucovorin	Leucovorin Calcium	Y	N	N	N	N
82	Leuprolide Acetate	Lupron Injection	Y	Y	Y	Y	N
83	Liothyronine sodium injection	Triostat	Y	N	N	N	Y
84	Levocarnitine	Carnitor	Y	N	N	Y	N
85	Melphalan	Alkeran for Injection	Y	N	Y	N	N
86	Mesna	Mesnex	Y	Y	N	N	N
87	Methotrexate Sodium	Methotrexate	Y	Y	N	Y	Y
88	Mitoxantrone	Novantrone	Y	Y	N	N	N
89	Monooctanoin	Moctanin	N	N	N	N	N
90	Morphine Sulfate Concentrate (preservative free)	Infumorph Atramorph/PF Duramorph Pres Free	Y	Y	N	Y	Y

Part B

	Nonproprietary name	Brand name	MassHealth Drug List	Florida Medicaid Preferred Drug List	First Health Rx Drug Guide	FEP Rx Drug Formulary	Kaiser-Permanente (DC)
91	Multi-vitamin infusion without vitamin K	M.V.I.-12	N	N	N	N	N
92	Octreotide	Sandostatin LAR Sandostatin	Y	Y	N	N	N
93	Oprelvekin	Neumega	Y	Y	N	N	N
94	Paclitaxel	Taxol	Y	Y	N	N	N
95	Pegademase Bovine	Adagen	N	Y	N	N	N
96	Pegaspargase	Oncaspar	N	N	N	N	N
97	Pemetrexed disodium	Alimta	Y	N	N	N	N
98	Pentamidine isethionate	Pentam 300 Nebupent	Y	N	N	N	N
99	Pentastarch	Pentaspán	N	N	N	N	N
100	Pentetate calcium trisodium injection/ pentetate zinc trisodium injection	None	N	N	N	N	N
101	Pentostatin for Injection	Nipent	N	N	N	N	N
102	Porfimer Sodium	Photofrin	N	N	N	N	N
103	Rasburicase	Elitek	Y	N	N	N	N
104	Respiratory syncytial virus immune globulin	Respigam	Y	N	N	N	N
105	Rho D immune globulin intravenous human	WinRho SDF	Y	Y	N	N	N
106	Rifampin	Rifadin IV	Y	Y	N	Y	Y
107	Rituximab	Rituxan	Y	Y	N	N	N
108	Sargramostim	Leukine	Y	Y	N	Y	N
109	Satumomab Pentetide	Oncoscint CR/OV	N	N	N	N	N
110	Sermorelin Acetate	Geref	N	Y	N	Y	N
111	Somatrem for Injection	Protropin	Y	N	Y	Y	N
112	Somatropin	Nutropin Genotropin Humatrope Saizen Norditropin Serostim	Y	N	N	Y	Y
113	Sterile talc powder	Sclerosol intrapleural aerosol	N	N	N	N	N
114	Synthetic porcine secretin		N	N	N	N	N
115	Temozolomide	Temodar	Y	N	Y	N	N
116	Teniposide	Vumon for Injection	N	N	N	N	N
117	Thyrotropin Alpha	Thyrogen	N	N	N	N	N
118	Tobramycin for inhalation	TOBI	N	Y	N	Y	Y
119	Tositumomab and iodine I131 tositumomab	Bexxar	Y	N	N	N	N

Part B

	Nonproprietary name	Brand name	MassHealth Drug List	Florida Medicaid Preferred Drug List	First Health Rx Drug Guide	FEP Rx Drug Formulary	Kaiser-Permanente (DC)
120	Tranexamic acid	Cyklokapron	N	N	N	N	N
121	Treprostinil	Remodulin	Y	N	N	Y	N
122	Trimetrexate Glucuronate	Neutrexin	N	N	N	N	N
123	Urofollitropin	Metrodin	N	N	N	N	N
124	Valrubicin	Valstar	N	Y	N	N	N
		Formulary	69	51	7	34	12
		Non-formulary	55	73	117	90	112

Part D

	Nonproprietary name	Brand name	MassHealth Drug List	Florida Medicaid Preferred Drug List	First Health Rx Drug Guide	FEP Rx Drug Formulary	Kaiser-Permanente (DC)
1	Albendazole	Albenza	Y	Y	N	N	N
2	Alitretinoin	Panretin	Y	N	N	Y	N
3	Altretamine	Hexalen	N	Y	Y	N	N
4	Aminosalicilic acid	Paser Granules	N	N	N	N	N
5	Amiodarone HCl	Cordarone	Y	N	N	Y	Y
6	Anagrelide	Agrylin	Y	Y	Y	Y	N
7	Apomorphine HCl	Apokyn	Y	N	N	Y	N
8	Atovaquone	Mepron	Y	Y	N	Y	Y
9	Benzoate and phenylacetate	Ucephan	N	N	N	N	N
10	Betaine	Cystadane	Y	N	N	N	N
11	Bexarotene	Targretin	Y	N	Y	N	N
12	Bosentan	Tracleer	Y	N	Y	Y	N
13	Buprenorphine hydrochloride	Subutex	Y	N	N	Y	N
14	Buprenorphine in combination with naloxone	Suboxone	Y	N	N	Y	Y
15	Calcitonon-human for injection	Cibacalcin	Y	N	N	N	N
16	Calcium acetate	Phos-Lo	Y	Y	N	Y	Y
17	Chenodiol	Chenix	N	N	N	N	N
18	Cinacalcet	Sensipar	Y	N	N	Y	N
19	Citric acid, glucono-delta-lactone and magnesium carbonate	Renacidin Irrigation	Y	N	N	N	N
20	Clofazimine	Lamprene	N	Y	N	N	N
21	Cromolyn sodium	Gastrocrom	Y	Y	N	N	Y
22	Cromolyn sodium 4% ophthalmic solution	Opticrom 4% ophthalmic solution	Y	Y	N	N	Y
23	Cysteamine	Cystagon	Y	N	N	N	N
24	Desmopressin acetate		Y	Y	N	Y	Y
25	Diazepam viscous solution for rectal administration		Y	Y	N	N	Y
26	Diethyldithiocarbamate	Imuthiol	N	N	N	N	N
27	Exemestane	Aromasin	Y	N	N	N	N
28	Felbamate	Felbatol	Y	N	N	Y	N
29	Follitropin alfa, recombinant		N	N	N	Y	Y
30	Glutamine	NutreStore	N	N	N	N	N
31	Halofantrine	Halfan	N	N	N	N	N
32	Histrelin acetate	Supprelin Injection	N	N	N	N	N
33	Hydroxyurea	Droxia	Y	Y	N	N	N
34	Imatinib	Gleevec	Y	N	Y	N	Y
35	Iron (III) - hexacyanoferrate (II)	Radiogardase	N	N	N	N	N
36	Lamotrigine	Lamictal	Y	Y	Y	Y	Y

Part D

	Nonproprietary name	Brand name	MassHealth Drug List	Florida Medicaid Preferred Drug List	First Health Rx Drug Guide	FEP Rx Drug Formulary	Kaiser-Permanente (DC)
37	Levomethadyl acetate hydrochloride	Orlaam	N	N	N	N	N
38	Lidocaine patch 5%	Lidoderm Patch	Y	Y	Y	Y	Y
39	Lodoxamide tromethamine	Alomide Ophthalmic Solution	Y	N	N	Y	N
40	Mafenide acetate solution	Sulfamylon solution	Y	N	N	N	N
41	Mefloquine HCl	Lariam	Y	Y	N	Y	Y
42	Megestrol acetate	Megace	Y	N	N	N	Y
43	Metronidazole (topical)	Metrogel	Y	Y	Y	Y	Y
44	Midodrine HCl	Amatine	Y	Y	N	Y	N
45	Miglustat	Zavesca	Y	N	N	Y	N
46	Modafinil	Provigil	Y	Y	Y	Y	N
47	Nafarelin acetate	Synarel nasal solution	Y	N	N	Y	N
48	Naltrexone HCl	Trexan	Y	N	N	N	Y
49	Nitazoxanide	Alinia	Y	N	N	Y	N
50	Nitisinone	Orfadin	Y	N	N	N	N
51	Ofloxacin	Ocuflox Ophthalmic Solution	Y	Y	N	Y	Y
52	Oxybate	Xyrem	N	N	N	Y	N
53	Pegvisomant	Somavert	Y	N	N	Y	N
54	Pentosan polysulfate sodium	Elmiron	Y	N	N	Y	N
55	Pilocarpine	Salagen	Y	Y	N	Y	N
56	Potassium citrate	Urocit-K	Y	Y	N	N	Y
57	Recombinant human luteinizing hormone	Luveris	N	N	N	N	N
58	Ribavirin	Rebetol	Y	Y	Y	Y	N
59	Rifabutin	Mycobutin	Y	Y	N	Y	Y
60	Rifampin, isoniazid, pyrazinamide	Rifater	Y	Y	N	N	Y
61	Rifapentine	Priftin	N	N	N	N	N
62	Riluzole	Rilutek	Y	Y	N	Y	Y
63	Sacrosidase	Sucraid	N	N	N	N	N
64	Selegiline HCl	Eldepryl	Y	N	N	N	Y
65	Sodium phenylbutyrate	Buphenyl	Y	N	N	N	N
66	Sotalol HCl	Betapace	Y	N	N	Y	Y
67	Succimer	Chemet capsules	Y	Y	N	N	N
68	Sulfadiazine		Y	Y	N	Y	Y
69	Teriparatide	Parathar	Y	N	N	N	Y
70	Thalidomide	Thalomid	Y	N	N	Y	N
71	Tinidazole	Tindamax	Y	Y	N	N	N
72	Tiopronin	Thiola	Y	N	N	N	N
73	Topiramate	Topamax	Y	Y	Y	Y	N
74	Toremifene	Fareston	Y	Y	Y	N	N
75	Tretinoin	Vesanoid	Y	Y	Y	N	Y

Part D

	Nonproprietary name	Brand name	MassHealth Drug List	Florida Medicaid Preferred Drug List	First Health Rx Drug Guide	FEP Rx Drug Formulary	Kaiser-Permanente (DC)
76	Trientine HCl	Syprine	Y	N	N	N	N
77	Ursodiol	URSO	Y	Y	Y	Y	N
78	Zalcitabine	Hivid	Y	Y	Y	Y	Y
79	Zidovudine	Retrovir	Y	Y	Y	Y	Y
80	Zinc acetate	Galzin	N	N	N	Y	N
81	Zoledronate	Zometa, Zabel	Y	N	N	Y	N
		Formulary	64	33	16	40	28
		Non-formulary	17	48	65	41	53