



November 18, 2010

Kent Lieginger  
Senior Vice President, Managed Care and Customer Operations  
Genentech  
1 DNA Way  
South San Francisco, CA 94080

Dear Dr. Lieginger:

We are writing on behalf of a broad coalition of hospitals participating in the federal 340B drug discount program. We have been advised that Genentech has begun to withhold 340B pricing for orphan drugs purchased by a subset of our membership, primarily children's and rural hospitals. We are aware that, under the Health Care and Education Reconciliation Act (HCERA), Congress established a statutory exclusion with respect to orphan drugs purchased by hospitals specifically added by the Patient Protection and Affordable Care Act (PPACA) to the 340B program under the Public Health Service Act, including freestanding cancer hospitals, children's hospitals, sole community rural referral centers, and critical access hospitals.<sup>1</sup> However, we are deeply concerned with Genentech's broad interpretation of the orphan drug exclusion, which Genentech has stated extends to all drugs that have been designated "orphan" by the FDA, regardless of the intended use of the drugs. We believe that, absent guidance from the Health Resources and Services Administration (HRSA) regarding the scope of the orphan drug exclusion, it is premature to withhold 340B pricing on orphan drugs. Accordingly, we request that Genentech resume its sale of orphan drugs to hospitals identified in PPACA at 340B prices until directed otherwise by HRSA. We understand that several manufacturers have decided to delay implementation until they receive further guidance from the government and ask that you follow their lead.

Our concerns regarding your company's interpretation are two-fold. First, the orphan drug exclusion is ambiguous in nature, and therefore requires further guidance from HRSA regarding its application. Specifically, the language of the exclusion, as stated in the HCERA, is unclear as to whether it is intended to apply to all indications for which orphan drugs may be used, or only orphan indications. As you know, orphan drug designation by the Food and Drug Administration (FDA) is always for a specified "indication," and the designated indication is usually but one of many illnesses or conditions for which the drug has been approved for use in

---

<sup>1</sup> Children's hospitals, though also included in PPACA, were in fact originally added to the list of covered entities in the 340B Drug Discount program through Section 6004 of the Deficit Reduction Act (DRA) of 2005 and have been receiving 340B discounts since 2009.

treatment. Orphan drugs are also often used for other FDA approved indications as well as off-label for non-orphan indications.<sup>2</sup>

HCERA does not define the scope of the orphan drug exclusion or expressly permit the application of the exclusion in circumstances where an orphan drug is used for a non-orphan indication. Further, HCERA does not specify whether the exclusion applies to the 361 “approved” orphan drugs or the 2,250 “designated” orphan drugs. Accordingly, the resolution of these ambiguities – which stands to have significant financial impact upon hospitals identified in PPACA – lies solely within the discretion of HRSA, the agency charged with the administration of the 340B program and empowered to create interpretive program guidance documents. As the Supreme Court has noted, where a statute is ambiguous or unclear, the interpretation of the administering agency is accorded deference.<sup>3</sup> Further, where a regulated entity undertakes to interpret an ambiguous statutory provision, the regulating agency’s subsequent interpretation will trump the alternative interpretation adopted by the entity.<sup>4</sup> In the case of the 340B program, HRSA has consistently issued interpretive guidance prior to the application of any statutory language that may impact upon the implementation of the 340B program.<sup>5</sup> Accordingly, Genentech should await guidance from HRSA prior to imposing its own interpretation of the orphan drug exclusion.

In addition to our concerns regarding Genentech’s premature and unilateral application of the orphan drug exclusion, we are concerned that Genentech’s broad interpretation of the orphan drug exclusion will deny hospitals identified in PPACA much of the benefit of 340B program eligibility. The drugs currently designated by the FDA as orphan drugs include many specialty oncology and pediatric drugs utilized heavily by cancer hospitals and freestanding children’s hospitals for both orphan and non-orphan conditions. Many rural hospitals buy orphan drugs to treat their cancer patients and other patients with a variety of FDA-approved indications, apart from those for which the orphan designated drugs are “indicated.” Genentech’s application of the orphan drug exclusion to *all* uses of an orphan drug, including non-orphan indications, thus stands to have far-reaching financial implications for all hospitals identified in PPACA. In fact, this overly-broad interpretation of the exclusion, as well as the exclusion itself, is driving new covered entities away from the very program that was intended to support them. New cancer and children’s hospitals, which are prohibited under 340B program requirements from purchasing covered outpatient drugs through a group purchasing organization (GPO), now face the prospect of having to purchase expensive orphan drugs at higher wholesale acquisition cost prices as an untenable condition of their participation in the 340B program. Such hospitals are therefore being compelled to forego the benefits of 340B program participation so that they may afford

---

<sup>2</sup> In fact, a recently published study indicated that orphan drugs may be used as much as 90 percent of the time for conditions or illnesses other than the designated orphan indication. Reforming Off-Label Promotion to Enhance Orphan Disease Treatment, Brian A. Liang and Tim Mackey, Science Magazine, Jan. 14, 2010, pp. 273-274.

<sup>3</sup> U.S. v. Mead Corp., 533 U.S. 218 (June 18, 2001).

<sup>4</sup> Howmet Corp. v. E.P.A., 614 F.3d 544 (D.C.Cir. 2010).

<sup>5</sup> For example, children’s hospitals were made eligible for participation in the 340B program pursuant to Section 6004 of the Deficit Reduction Act of 2005. However, it was not until September 2009, when HRSA issued final implementing guidelines, that children’s hospitals were permitted to enroll into the program. 74 Fed. Reg. 45206-45211 (September 1, 2009).

orphan drugs for their patients. Rural hospitals are finding that up to 75% of the savings they were expecting from this program are no longer available.

These results are in clear contravention of the purpose of the 340B program and the intent of Congress, which was to allow designated safety net health care providers – including new covered entities impacted by the orphan drug exclusion – to stretch scarce resources so that they may maximize their services and reach more patients.<sup>6</sup> Genentech’s expansive interpretation of the orphan drug exclusion will severely undermine this purpose and deprive safety net hospitals of the intended benefit of 340B program participation.

For the above reasons, we ask that Genentech reconsider its decision to terminate the sale of orphan drugs at 340B prices for hospitals identified in PPACA until HRSA issues implementing guidance providing clarification of the above uncertainties. If you have questions, please contact SNHPA President and General Counsel Bill von Oehsen at (202) 872-6765 or [william.vonoehsen@snhpa.org](mailto:william.vonoehsen@snhpa.org) if you have questions or NRHA’s Maggie Elehwany at (202) 639-0550 or [elehwany@nrharural.org](mailto:elehwany@nrharural.org).

Sincerely,

National Rural Health Association  
Safety Net Hospitals for Pharmaceutical Access

cc: Mary Wakefield, Administrator, Health Resources and Services Administration  
Krista Pedley, Director, Office of Pharmacy Affairs  
Marcus Farbstein, Director, Federal Accounts, Genentech, Inc.

---

<sup>6</sup> H.R. Rep. No. 102-384, pt. II, at 12 (1992).



November 18, 2010

Kenton Stewart  
Senior Director, Contracts & Pricing  
Astellas Pharma US, Inc.  
Three Parkway North  
Deerfield, IL 60015

Dear Mr. Stewart:

We are writing on behalf of a broad coalition of hospitals participating in the federal 340B drug discount program. We have been advised that Astellas Pharma US, Inc has begun to withhold 340B pricing for orphan drugs purchased by a subset of our membership, primarily children's and rural hospitals. We are aware that, under the Health Care and Education Reconciliation Act (HCERA), Congress established a statutory exclusion with respect to orphan drugs purchased by hospitals specifically added by the Patient Protection and Affordable Care Act (PPACA) to the 340B program under the Public Health Service Act, including freestanding cancer hospitals, children's hospitals, sole community rural referral centers, and critical access hospitals.<sup>7</sup> However, we are deeply concerned with Astellas Pharma US, Inc's broad interpretation of the orphan drug exclusion, which Astellas Pharma US, Inc has stated extends to all drugs that have been designated "orphan" by the FDA, regardless of the intended use of the drugs. We believe that, absent guidance from the Health Resources and Services Administration (HRSA) regarding the scope of the orphan drug exclusion, it is premature to withhold 340B pricing on orphan drugs. Accordingly, we request that Astellas Pharma US, Inc resume its sale of orphan drugs to hospitals identified in PPACA at 340B prices until directed otherwise by HRSA. We understand that several manufacturers have decided to delay implementation until they receive further guidance from the government and ask that you follow their lead.

Our concerns regarding your company's interpretation are two-fold. First, the orphan drug exclusion is ambiguous in nature, and therefore requires further guidance from HRSA regarding its application. Specifically, the language of the exclusion, as stated in the HCERA, is unclear as to whether it is intended to apply to all indications for which orphan drugs may be used, or only orphan indications. As you know, orphan drug designation by the Food and Drug Administration (FDA) is always for a specified "indication," and the designated indication is usually but one of many illnesses or conditions for which the drug has been approved for use in

---

<sup>7</sup> Children's hospitals, though also included in PPACA, were in fact originally added to the list of covered entities in the 340B Drug Discount program through Section 6004 of the Deficit Reduction Act (DRA) of 2005 and have been receiving 340B discounts since 2009.

treatment. Orphan drugs are also often used for other FDA approved indications as well as off-label for non-orphan indications.<sup>8</sup>

HCERA does not define the scope of the orphan drug exclusion or expressly permit the application of the exclusion in circumstances where an orphan drug is used for a non-orphan indication. Further, HCERA does not specify whether the exclusion applies to the 361 “approved” orphan drugs or the 2,250 “designated” orphan drugs. Accordingly, the resolution of these ambiguities – which stands to have significant financial impact upon hospitals identified in PPACA – lies solely within the discretion of HRSA, the agency charged with the administration of the 340B program and empowered to create interpretive program guidance documents. As the Supreme Court has noted, where a statute is ambiguous or unclear, the interpretation of the administering agency is accorded deference.<sup>9</sup> Further, where a regulated entity undertakes to interpret an ambiguous statutory provision, the regulating agency’s subsequent interpretation will trump the alternative interpretation adopted by the entity.<sup>10</sup> In the case of the 340B program, HRSA has consistently issued interpretive guidance prior to the application of any statutory language that may impact upon the implementation of the 340B program.<sup>11</sup> Accordingly, Astellas Pharma US, Inc should await guidance from HRSA prior to imposing its own interpretation of the orphan drug exclusion.

In addition to our concerns regarding Astellas Pharma US, Inc’s premature and unilateral application of the orphan drug exclusion, we are concerned that Astellas Pharma US, Inc’s broad interpretation of the orphan drug exclusion will deny hospitals identified in PPACA much of the benefit of 340B program eligibility. The drugs currently designated by the FDA as orphan drugs include many specialty oncology and pediatric drugs utilized heavily by cancer hospitals and freestanding children’s hospitals for both orphan and non-orphan conditions. Many rural hospitals buy orphan drugs to treat their cancer patients and other patients with a variety of FDA-approved indications, apart from those for which the orphan designated drugs are “indicated.” Astellas Pharma US, Inc’s application of the orphan drug exclusion to *all* uses of an orphan drug, including non-orphan indications, thus stands to have far-reaching financial implications for all hospitals identified in PPACA. In fact, this overly-broad interpretation of the exclusion, as well as the exclusion itself, is driving new covered entities away from the very program that was intended to support them. New cancer and children’s hospitals, which are prohibited under 340B program requirements from purchasing covered outpatient drugs through a group purchasing organization (GPO), now face the prospect of having to purchase expensive orphan drugs at higher wholesale acquisition cost prices as an untenable condition of their participation in the 340B program. Such hospitals are therefore being compelled to forego the benefits of 340B

---

<sup>8</sup> In fact, a recently published study indicated that orphan drugs may be used as much as 90 percent of the time for conditions or illnesses other than the designated orphan indication. Reforming Off-Label Promotion to Enhance Orphan Disease Treatment, Brian A. Liang and Tim Mackey, Science Magazine, Jan. 14, 2010, pp. 273-274.

<sup>9</sup> U.S. v. Mead Corp., 533 U.S. 218 (June 18, 2001).

<sup>10</sup> Howmet Corp. v. E.P.A., 614 F.3d 544 (D.C.Cir. 2010).

<sup>11</sup> For example, children’s hospitals were made eligible for participation in the 340B program pursuant to Section 6004 of the Deficit Reduction Act of 2005. However, it was not until September 2009, when HRSA issued final implementing guidelines, that children’s hospitals were permitted to enroll into the program. 74 Fed. Reg. 45206-45211 (September 1, 2009).

program participation so that they may afford orphan drugs for their patients. Rural hospitals are finding that up to 75% of the savings they were expecting from this program are no longer available.

These results are in clear contravention of the purpose of the 340B program and the intent of Congress, which was to allow designated safety net health care providers – including new covered entities impacted by the orphan drug exclusion – to stretch scarce resources so that they may maximize their services and reach more patients.<sup>12</sup> Astellas Pharma US, Inc’s expansive interpretation of the orphan drug exclusion will severely undermine this purpose and deprive safety net hospitals of the intended benefit of 340B program participation.

For the above reasons, we ask that Astellas Pharma US, Inc reconsider its decision to terminate the sale of orphan drugs at 340B prices for hospitals identified in PPACA until HRSA issues implementing guidance providing clarification of the above uncertainties. If you have questions, please contact SNHPA President and General Counsel Bill von Oehsen at (202) 872-6765 or [william.vonoehsen@snhpa.org](mailto:william.vonoehsen@snhpa.org) if you have questions or NRHA’s Maggie Elehwany at (202) 639-0550 or [elehwany@nrharural.org](mailto:elehwany@nrharural.org).

Sincerely,

National Rural Health Association  
Safety Net Hospitals for Pharmaceutical Access

cc: Mary Wakefield, Administrator, Health Resources and Services Administration  
Krista Pedley, Director, Office of Pharmacy Affairs

---

<sup>12</sup> H.R. Rep. No. 102-384, pt. II, at 12 (1992).



November 18, 2010

Gregg Lapointe  
Chief Executive Officer  
Sigma-Tau Pharmaceuticals, Inc.  
9841 Washingtonian Boulevard  
Suite 500  
Gaithersburg, MD 20878

Dear Mr. Lapointe:

We are writing on behalf of a broad coalition of hospitals participating in the federal 340B drug discount program. We have been advised that Sigma-Tau Pharmaceuticals, Inc has begun to withhold 340B pricing for orphan drugs purchased by a subset of our membership, primarily children's and rural hospitals. We are aware that, under the Health Care and Education Reconciliation Act (HCERA), Congress established a statutory exclusion with respect to orphan drugs purchased by hospitals specifically added by the Patient Protection and Affordable Care Act (PPACA) to the 340B program under the Public Health Service Act, including freestanding cancer hospitals, children's hospitals, sole community rural referral centers, and critical access hospitals.<sup>13</sup> However, we are deeply concerned with Sigma-Tau Pharmaceuticals, Inc's broad interpretation of the orphan drug exclusion, which Sigma-Tau Pharmaceuticals, Inc has stated extends to all drugs that have been designated "orphan" by the FDA, regardless of the intended use of the drugs. We believe that, absent guidance from the Health Resources and Services Administration (HRSA) regarding the scope of the orphan drug exclusion, it is premature to withhold 340B pricing on orphan drugs. Accordingly, we request that Sigma-Tau Pharmaceuticals, Inc resume its sale of orphan drugs to hospitals identified in PPACA at 340B prices until directed otherwise by HRSA. We understand that several manufacturers have decided to delay implementation until they receive further guidance from the government and ask that you follow their lead.

Our concerns regarding your company's interpretation are two-fold. First, the orphan drug exclusion is ambiguous in nature, and therefore requires further guidance from HRSA regarding its application. Specifically, the language of the exclusion, as stated in the HCERA, is unclear as to whether it is intended to apply to all indications for which orphan drugs may be used, or only orphan indications. As you know, orphan drug designation by the Food and Drug

---

<sup>13</sup> Children's hospitals, though also included in PPACA, were in fact originally added to the list of covered entities in the 340B Drug Discount program through Section 6004 of the Deficit Reduction Act (DRA) of 2005 and have been receiving 340B discounts since 2009.

Administration (FDA) is always for a specified “indication,” and the designated indication is usually but one of many illnesses or conditions for which the drug has been approved for use in treatment. Orphan drugs are also often used for other FDA approved indications as well as off-label for non-orphan indications.<sup>14</sup>

HCERA does not define the scope of the orphan drug exclusion or expressly permit the application of the exclusion in circumstances where an orphan drug is used for a non-orphan indication. Further, HCERA does not specify whether the exclusion applies to the 361 “approved” orphan drugs or the 2,250 “designated” orphan drugs. Accordingly, the resolution of these ambiguities – which stands to have significant financial impact upon hospitals identified in PPACA – lies solely within the discretion of HRSA, the agency charged with the administration of the 340B program and empowered to create interpretive program guidance documents. As the Supreme Court has noted, where a statute is ambiguous or unclear, the interpretation of the administering agency is accorded deference.<sup>15</sup> Further, where a regulated entity undertakes to interpret an ambiguous statutory provision, the regulating agency’s subsequent interpretation will trump the alternative interpretation adopted by the entity.<sup>16</sup> In the case of the 340B program, HRSA has consistently issued interpretive guidance prior to the application of any statutory language that may impact upon the implementation of the 340B program.<sup>17</sup> Accordingly, Sigma-Tau Pharmaceuticals, Inc should await guidance from HRSA prior to imposing its own interpretation of the orphan drug exclusion.

In addition to our concerns regarding Sigma-Tau Pharmaceuticals, Inc’s premature and unilateral application of the orphan drug exclusion, we are concerned that Sigma-Tau Pharmaceuticals, Inc’s broad interpretation of the orphan drug exclusion will deny hospitals identified in PPACA much of the benefit of 340B program eligibility. The drugs currently designated by the FDA as orphan drugs include many specialty oncology and pediatric drugs utilized heavily by cancer hospitals and freestanding children’s hospitals for both orphan and non-orphan conditions. Many rural hospitals buy orphan drugs to treat their cancer patients and other patients with a variety of FDA-approved indications, apart from those for which the orphan designated drugs are “indicated.” Sigma-Tau Pharmaceuticals, Inc’s application of the orphan drug exclusion to *all* uses of an orphan drug, including non-orphan indications, thus stands to have far-reaching financial implications for all hospitals identified in PPACA. In fact, this overly-broad interpretation of the exclusion, as well as the exclusion itself, is driving new covered entities away from the very program that was intended to support them. New cancer and children’s hospitals, which are prohibited under 340B program requirements from purchasing covered outpatient drugs through a group purchasing organization (GPO), now face the prospect of

---

<sup>14</sup> In fact, a recently published study indicated that orphan drugs may be used as much as 90 percent of the time for conditions or illnesses other than the designated orphan indication. Reforming Off-Label Promotion to Enhance Orphan Disease Treatment, Brian A. Liang and Tim Mackey, Science Magazine, Jan. 14, 2010, pp. 273-274.

<sup>15</sup> U.S. v. Mead Corp., 533 U.S. 218 (June 18, 2001).

<sup>16</sup> Howmet Corp. v. E.P.A., 614 F.3d 544 (D.C.Cir. 2010).

<sup>17</sup> For example, children’s hospitals were made eligible for participation in the 340B program pursuant to Section 6004 of the Deficit Reduction Act of 2005. However, it was not until September 2009, when HRSA issued final implementing guidelines, that children’s hospitals were permitted to enroll into the program. 74 Fed. Reg. 45206-45211 (September 1, 2009).

having to purchase expensive orphan drugs at higher wholesale acquisition cost prices as an untenable condition of their participation in the 340B program. Such hospitals are therefore being compelled to forego the benefits of 340B program participation so that they may afford orphan drugs for their patients. Rural hospitals are finding that up to 75% of the savings they were expecting from this program are no longer available.

These results are in clear contravention of the purpose of the 340B program and the intent of Congress, which was to allow designated safety net health care providers – including new covered entities impacted by the orphan drug exclusion – to stretch scarce resources so that they may maximize their services and reach more patients.<sup>18</sup> Sigma-Tau Pharmaceuticals, Inc’s expansive interpretation of the orphan drug exclusion will severely undermine this purpose and deprive safety net hospitals of the intended benefit of 340B program participation.

For the above reasons, we ask that Sigma-Tau Pharmaceuticals, Inc reconsider its decision to terminate the sale of orphan drugs at 340B prices for hospitals identified in PPACA until HRSA issues implementing guidance providing clarification of the above uncertainties. If you have questions, please contact SNHPA President and General Counsel Bill von Oehsen at (202) 872-6765 or [william.vonoehsen@snhpa.org](mailto:william.vonoehsen@snhpa.org) if you have questions or NRHA’s Maggie Elehwany at (202) 639-0550 or [elehwany@nrharural.org](mailto:elehwany@nrharural.org).

Sincerely,

National Rural Health Association  
Safety Net Hospitals for Pharmaceutical Access

cc: Mary Wakefield, Administrator, Health Resources and Services Administration  
Krista Pedley, Director, Office of Pharmacy Affairs

---

<sup>18</sup> H.R. Rep. No. 102-384, pt. II, at 12 (1992).



December 1, 2010

Angus Russell  
Chief Executive Officer  
Shire  
725 Chesterbrook Boulevard  
Wayne, PA 19087

Dear Mr. Russell:

We are writing on behalf of a broad coalition of hospitals participating in the federal 340B drug discount program. We have been advised that Shire has begun to withhold 340B pricing for orphan drugs purchased by a subset of our membership, primarily children's and rural hospitals. We are aware that, under the Health Care and Education Reconciliation Act (HCERA), Congress established a statutory exclusion with respect to orphan drugs purchased by hospitals specifically added by the Patient Protection and Affordable Care Act (PPACA) to the 340B program under the Public Health Service Act, including freestanding cancer hospitals, children's hospitals, sole community rural referral centers, and critical access hospitals.<sup>1</sup> However, we are deeply concerned with Shire's broad interpretation of the orphan drug exclusion, which Shire has stated extends to all drugs that have been designated "orphan" by the FDA, regardless of the intended use of the drugs. We believe that, absent guidance from the Health Resources and Services Administration (HRSA) regarding the scope of the orphan drug exclusion, it is premature to withhold 340B pricing on orphan drugs. Accordingly, we request that Shire resume its sale of orphan drugs to hospitals identified in PPACA at 340B prices until directed otherwise by HRSA. We understand that several manufacturers have decided to delay implementation until they receive further guidance from the government and ask that you follow their lead.

Our concerns regarding your company's interpretation are two-fold. First, the orphan drug exclusion is ambiguous in nature, and therefore requires further guidance from HRSA regarding its application. Specifically, the language of the exclusion, as stated in the HCERA, is unclear as to whether it is intended to apply to all indications for which orphan drugs may be used, or only orphan indications. As you know, orphan drug designation by the Food and Drug Administration (FDA) is always for a specified "indication," and the designated indication is usually but one of many illnesses or conditions for which the drug has been approved for use in

---

<sup>1</sup> Children's hospitals, though also included in PPACA, were in fact originally added to the list of covered entities in the 340B Drug Discount program through Section 6004 of the Deficit Reduction Act (DRA) of 2005 and have been receiving 340B discounts since 2009.

treatment. Orphan drugs are also often used for other FDA approved indications as well as off-label for non-orphan indications.<sup>2</sup>

HCERA does not define the scope of the orphan drug exclusion or expressly permit the application of the exclusion in circumstances where an orphan drug is used for a non-orphan indication. Further, HCERA does not specify whether the exclusion applies to the 361 “approved” orphan drugs or the 2,250 “designated” orphan drugs. Accordingly, the resolution of these ambiguities – which stands to have significant financial impact upon hospitals identified in PPACA – lies solely within the discretion of HRSA, the agency charged with the administration of the 340B program and empowered to create interpretive program guidance documents. As the Supreme Court has noted, where a statute is ambiguous or unclear, the interpretation of the administering agency is accorded deference.<sup>3</sup> Further, where a regulated entity undertakes to interpret an ambiguous statutory provision, the regulating agency’s subsequent interpretation will trump the alternative interpretation adopted by the entity.<sup>4</sup> In the case of the 340B program, HRSA has consistently issued interpretive guidance prior to the application of any statutory language that may impact upon the implementation of the 340B program.<sup>5</sup> Accordingly, Shire should await guidance from HRSA prior to imposing its own interpretation of the orphan drug exclusion.

In addition to our concerns regarding Shire’s premature and unilateral application of the orphan drug exclusion, we are concerned that Shire’s broad interpretation of the orphan drug exclusion will deny hospitals identified in PPACA much of the benefit of 340B program eligibility. The drugs currently designated by the FDA as orphan drugs include many specialty oncology and pediatric drugs utilized heavily by cancer hospitals and freestanding children’s hospitals for both orphan and non-orphan conditions. Many rural hospitals buy orphan drugs to treat their cancer patients and other patients with a variety of FDA-approved indications, apart from those for which the orphan designated drugs are “indicated.” Shire’s application of the orphan drug exclusion to *all* uses of an orphan drug, including non-orphan indications, thus stands to have far-reaching financial implications for all hospitals identified in PPACA. In fact, this overly-broad interpretation of the exclusion, as well as the exclusion itself, is driving new covered entities away from the very program that was intended to support them. New cancer and children’s hospitals, which are prohibited under 340B program requirements from purchasing covered outpatient drugs through a group purchasing organization (GPO), now face the prospect of having to purchase expensive orphan drugs at higher wholesale acquisition cost prices as an untenable condition of their participation in the 340B program. Such hospitals are therefore being compelled to forego the benefits of 340B program participation so that they may afford

---

<sup>2</sup> In fact, a recently published study indicated that orphan drugs may be used as much as 90 percent of the time for conditions or illnesses other than the designated orphan indication. Reforming Off-Label Promotion to Enhance Orphan Disease Treatment, Brian A. Liang and Tim Mackey, *Science Magazine*, Jan. 14, 2010, pp. 273-274.

<sup>3</sup> *U.S. v. Mead Corp.*, 533 U.S. 218 (June 18, 2001).

<sup>4</sup> *Howmet Corp. v. E.P.A.*, 614 F.3d 544 (D.C.Cir. 2010).

<sup>5</sup> For example, children’s hospitals were made eligible for participation in the 340B program pursuant to Section 6004 of the Deficit Reduction Act of 2005. However, it was not until September 2009, when HRSA issued final implementing guidelines, that children’s hospitals were permitted to enroll into the program. 74 Fed. Reg. 45206-45211 (September 1, 2009).

orphan drugs for their patients. Rural hospitals are finding that up to 75% of the savings they were expecting from this program are no longer available.

These results are in clear contravention of the purpose of the 340B program and the intent of Congress, which was to allow designated safety net health care providers – including new covered entities impacted by the orphan drug exclusion – to stretch scarce resources so that they may maximize their services and reach more patients.<sup>6</sup> Shire's expansive interpretation of the orphan drug exclusion will severely undermine this purpose and deprive safety net hospitals of the intended benefit of 340B program participation.

For the above reasons, we ask that Shire reconsider its decision to terminate the sale of orphan drugs at 340B prices for hospitals identified in PPACA until HRSA issues implementing guidance providing clarification of the above uncertainties. If you have questions, please contact SNHPA President and General Counsel William von Oehsen at (202) 872-6765 or [william.vonoehsen@snhpa.org](mailto:william.vonoehsen@snhpa.org) or NRHA Director of Government Relations Maggie Elehwany at (202) 639-0550 or [elehwany@nrharural.org](mailto:elehwany@nrharural.org).

Sincerely,

National Rural Health Association  
Safety Net Hospitals for Pharmaceutical Access

cc: Ron Ritter, Manager, Government Contracts, Pricing & Reporting, Shire

---

<sup>6</sup> H.R. Rep. No. 102-384, pt. II, at 12 (1992).



December 1, 2010

Henri Termeer  
Chairman of the Board, President, Chief Executive Officer  
Genzyme  
500 Kendall Street  
Cambridge, MA 2142

Dear Mr. Termeer:

We are writing on behalf of a broad coalition of hospitals participating in the federal 340B drug discount program. We have been advised that Genzyme has begun to withhold 340B pricing for orphan drugs purchased by a subset of our membership, primarily children's and rural hospitals. We are aware that, under the Health Care and Education Reconciliation Act (HCERA), Congress established a statutory exclusion with respect to orphan drugs purchased by hospitals specifically added by the Patient Protection and Affordable Care Act (PPACA) to the 340B program under the Public Health Service Act, including freestanding cancer hospitals, children's hospitals, sole community rural referral centers, and critical access hospitals.<sup>7</sup> However, we are deeply concerned with Genzyme's broad interpretation of the orphan drug exclusion, which Genzyme has stated extends to all drugs that have been designated "orphan" by the FDA, regardless of the intended use of the drugs. We believe that, absent guidance from the Health Resources and Services Administration (HRSA) regarding the scope of the orphan drug exclusion, it is premature to withhold 340B pricing on orphan drugs. Accordingly, we request that Genzyme resume its sale of orphan drugs to hospitals identified in PPACA at 340B prices until directed otherwise by HRSA. We understand that several manufacturers have decided to delay implementation until they receive further guidance from the government and ask that you follow their lead.

Our concerns regarding your company's interpretation are two-fold. First, the orphan drug exclusion is ambiguous in nature, and therefore requires further guidance from HRSA regarding its application. Specifically, the language of the exclusion, as stated in the HCERA, is unclear as to whether it is intended to apply to all indications for which orphan drugs may be used, or only orphan indications. As you know, orphan drug designation by the Food and Drug Administration (FDA) is always for a specified "indication," and the designated indication is usually but one of many illnesses or conditions for which the drug has been approved for use in

---

<sup>7</sup> Children's hospitals, though also included in PPACA, were in fact originally added to the list of covered entities in the 340B Drug Discount program through Section 6004 of the Deficit Reduction Act (DRA) of 2005 and have been receiving 340B discounts since 2009.

treatment. Orphan drugs are also often used for other FDA approved indications as well as off-label for non-orphan indications.<sup>8</sup>

HCERA does not define the scope of the orphan drug exclusion or expressly permit the application of the exclusion in circumstances where an orphan drug is used for a non-orphan indication. Further, HCERA does not specify whether the exclusion applies to the 361 “approved” orphan drugs or the 2,250 “designated” orphan drugs. Accordingly, the resolution of these ambiguities – which stands to have significant financial impact upon hospitals identified in PPACA – lies solely within the discretion of HRSA, the agency charged with the administration of the 340B program and empowered to create interpretive program guidance documents. As the Supreme Court has noted, where a statute is ambiguous or unclear, the interpretation of the administering agency is accorded deference.<sup>9</sup> Further, where a regulated entity undertakes to interpret an ambiguous statutory provision, the regulating agency’s subsequent interpretation will trump the alternative interpretation adopted by the entity.<sup>10</sup> In the case of the 340B program, HRSA has consistently issued interpretive guidance prior to the application of any statutory language that may impact upon the implementation of the 340B program.<sup>11</sup> Accordingly, Genzyme should await guidance from HRSA prior to imposing its own interpretation of the orphan drug exclusion.

In addition to our concerns regarding Genzyme’s premature and unilateral application of the orphan drug exclusion, we are concerned that Genzyme’s broad interpretation of the orphan drug exclusion will deny hospitals identified in PPACA much of the benefit of 340B program eligibility. The drugs currently designated by the FDA as orphan drugs include many specialty oncology and pediatric drugs utilized heavily by cancer hospitals and freestanding children’s hospitals for both orphan and non-orphan conditions. Many rural hospitals buy orphan drugs to treat their cancer patients and other patients with a variety of FDA-approved indications, apart from those for which the orphan designated drugs are “indicated.” Genzyme’s application of the orphan drug exclusion to *all* uses of an orphan drug, including non-orphan indications, thus stands to have far-reaching financial implications for all hospitals identified in PPACA. In fact, this overly-broad interpretation of the exclusion, as well as the exclusion itself, is driving new covered entities away from the very program that was intended to support them. New cancer and children’s hospitals, which are prohibited under 340B program requirements from purchasing covered outpatient drugs through a group purchasing organization (GPO), now face the prospect of having to purchase expensive orphan drugs at higher wholesale acquisition cost prices as an untenable condition of their participation in the 340B program. Such hospitals are therefore being compelled to forego the benefits of 340B program participation so that they may afford

---

<sup>8</sup> In fact, a recently published study indicated that orphan drugs may be used as much as 90 percent of the time for conditions or illnesses other than the designated orphan indication. Reforming Off-Label Promotion to Enhance Orphan Disease Treatment, Brian A. Liang and Tim Mackey, *Science Magazine*, Jan. 14, 2010, pp. 273-274.

<sup>9</sup> *U.S. v. Mead Corp.*, 533 U.S. 218 (June 18, 2001).

<sup>10</sup> *Howmet Corp. v. E.P.A.*, 614 F.3d 544 (D.C.Cir. 2010).

<sup>11</sup> For example, children’s hospitals were made eligible for participation in the 340B program pursuant to Section 6004 of the Deficit Reduction Act of 2005. However, it was not until September 2009, when HRSA issued final implementing guidelines, that children’s hospitals were permitted to enroll into the program. 74 Fed. Reg. 45206-45211 (September 1, 2009).

orphan drugs for their patients. Rural hospitals are finding that up to 75% of the savings they were expecting from this program are no longer available.

These results are in clear contravention of the purpose of the 340B program and the intent of Congress, which was to allow designated safety net health care providers – including new covered entities impacted by the orphan drug exclusion – to stretch scarce resources so that they may maximize their services and reach more patients.<sup>12</sup> Genzyme’s expansive interpretation of the orphan drug exclusion will severely undermine this purpose and deprive safety net hospitals of the intended benefit of 340B program participation.

For the above reasons, we ask that Genzyme reconsider its decision to terminate the sale of orphan drugs at 340B prices for hospitals identified in PPACA until HRSA issues implementing guidance providing clarification of the above uncertainties. If you have questions, please contact SNHPA President and General Counsel William von Oehsen at (202) 872-6765 or [william.vonoehsen@snhpa.org](mailto:william.vonoehsen@snhpa.org) or NRHA Director of Government Relations Maggie Elehwany at (202) 639-0550 or [elehwany@nrharural.org](mailto:elehwany@nrharural.org).

Sincerely,

National Rural Health Association  
Safety Net Hospitals for Pharmaceutical Access

cc: Pamela di Cenzo, Vice President, Patient & Product Services, Genzyme  
Andrew Rollauer, Senior Government Contract Analyst, Genzyme  
Randy Kipling, Senior Manager, Government Accounts, Genzyme

---

<sup>12</sup> H.R. Rep. No. 102-384, pt. II, at 12 (1992).



December 1, 2010

David Pyott  
Chairman of the Board and Chief Executive Officer  
Allergan  
2525 Dupont Drive,  
P.O. Box 19534  
Irvine, CA 92623

Dear Mr. Pyott:

We are writing on behalf of a broad coalition of hospitals participating in the federal 340B drug discount program. We have been advised that Allergan has begun to withhold 340B pricing for orphan drugs purchased by a subset of our membership, primarily children's and rural hospitals. We are aware that, under the Health Care and Education Reconciliation Act (HCERA), Congress established a statutory exclusion with respect to orphan drugs purchased by hospitals specifically added by the Patient Protection and Affordable Care Act (PPACA) to the 340B program under the Public Health Service Act, including freestanding cancer hospitals, children's hospitals, sole community rural referral centers, and critical access hospitals.<sup>13</sup> However, we are deeply concerned with Allergan's broad interpretation of the orphan drug exclusion, which Allergan has stated extends to all drugs that have been designated "orphan" by the FDA, regardless of the intended use of the drugs. We believe that, absent guidance from the Health Resources and Services Administration (HRSA) regarding the scope of the orphan drug exclusion, it is premature to withhold 340B pricing on orphan drugs. Accordingly, we request that Allergan resume its sale of orphan drugs to hospitals identified in PPACA at 340B prices until directed otherwise by HRSA. We understand that several manufacturers have decided to delay implementation until they receive further guidance from the government and ask that you follow their lead.

Our concerns regarding your company's interpretation are two-fold. First, the orphan drug exclusion is ambiguous in nature, and therefore requires further guidance from HRSA regarding its application. Specifically, the language of the exclusion, as stated in the HCERA, is unclear as to whether it is intended to apply to all indications for which orphan drugs may be used, or only orphan indications. As you know, orphan drug designation by the Food and Drug Administration (FDA) is always for a specified "indication," and the designated indication is

---

<sup>13</sup> Children's hospitals, though also included in PPACA, were in fact originally added to the list of covered entities in the 340B Drug Discount program through Section 6004 of the Deficit Reduction Act (DRA) of 2005 and have been receiving 340B discounts since 2009.

usually but one of many illnesses or conditions for which the drug has been approved for use in treatment. Orphan drugs are also often used for other FDA approved indications as well as off-label for non-orphan indications.<sup>14</sup>

HCERA does not define the scope of the orphan drug exclusion or expressly permit the application of the exclusion in circumstances where an orphan drug is used for a non-orphan indication. Further, HCERA does not specify whether the exclusion applies to the 361 “approved” orphan drugs or the 2,250 “designated” orphan drugs. Accordingly, the resolution of these ambiguities – which stands to have significant financial impact upon hospitals identified in PPACA – lies solely within the discretion of HRSA, the agency charged with the administration of the 340B program and empowered to create interpretive program guidance documents. As the Supreme Court has noted, where a statute is ambiguous or unclear, the interpretation of the administering agency is accorded deference.<sup>15</sup> Further, where a regulated entity undertakes to interpret an ambiguous statutory provision, the regulating agency’s subsequent interpretation will trump the alternative interpretation adopted by the entity.<sup>16</sup> In the case of the 340B program, HRSA has consistently issued interpretive guidance prior to the application of any statutory language that may impact upon the implementation of the 340B program.<sup>17</sup> Accordingly, Allergan should await guidance from HRSA prior to imposing its own interpretation of the orphan drug exclusion.

In addition to our concerns regarding Allergan’s premature and unilateral application of the orphan drug exclusion, we are concerned that Allergan’s broad interpretation of the orphan drug exclusion will deny hospitals identified in PPACA much of the benefit of 340B program eligibility. The drugs currently designated by the FDA as orphan drugs include many specialty oncology and pediatric drugs utilized heavily by cancer hospitals and freestanding children’s hospitals for both orphan and non-orphan conditions. Many rural hospitals buy orphan drugs to treat their cancer patients and other patients with a variety of FDA-approved indications, apart from those for which the orphan designated drugs are “indicated.” Allergan’s application of the orphan drug exclusion to *all* uses of an orphan drug, including non-orphan indications, thus stands to have far-reaching financial implications for all hospitals identified in PPACA. In fact, this overly-broad interpretation of the exclusion, as well as the exclusion itself, is driving new covered entities away from the very program that was intended to support them. New cancer and children’s hospitals, which are prohibited under 340B program requirements from purchasing covered outpatient drugs through a group purchasing organization (GPO), now face the prospect of having to purchase expensive orphan drugs at higher wholesale acquisition cost prices as an untenable condition of their participation in the 340B program. Such hospitals are therefore

---

<sup>14</sup> In fact, a recently published study indicated that orphan drugs may be used as much as 90 percent of the time for conditions or illnesses other than the designated orphan indication. Reforming Off-Label Promotion to Enhance Orphan Disease Treatment, Brian A. Liang and Tim Mackey, Science Magazine, Jan. 14, 2010, pp. 273-274.

<sup>15</sup> U.S. v. Mead Corp., 533 U.S. 218 (June 18, 2001).

<sup>16</sup> Howmet Corp. v. E.P.A., 614 F.3d 544 (D.C.Cir. 2010).

<sup>17</sup> For example, children’s hospitals were made eligible for participation in the 340B program pursuant to Section 6004 of the Deficit Reduction Act of 2005. However, it was not until September 2009, when HRSA issued final implementing guidelines, that children’s hospitals were permitted to enroll into the program. 74 Fed. Reg. 45206-45211 (September 1, 2009).

being compelled to forego the benefits of 340B program participation so that they may afford orphan drugs for their patients. Rural hospitals are finding that up to 75% of the savings they were expecting from this program are no longer available.

These results are in clear contravention of the purpose of the 340B program and the intent of Congress, which was to allow designated safety net health care providers – including new covered entities impacted by the orphan drug exclusion – to stretch scarce resources so that they may maximize their services and reach more patients.<sup>18</sup> Allergan’s expansive interpretation of the orphan drug exclusion will severely undermine this purpose and deprive safety net hospitals of the intended benefit of 340B program participation.

For the above reasons, we ask that Allergan reconsider its decision to terminate the sale of orphan drugs at 340B prices for hospitals identified in PPACA until HRSA issues implementing guidance providing clarification of the above uncertainties. If you have questions, please contact SNHPA President and General Counsel William von Oehsen at (202) 872-6765 or [william.vonoehsen@snhpa.org](mailto:william.vonoehsen@snhpa.org) or NRHA Director of Government Relations Maggie Elehwany at (202) 639-0550 or [elehwany@nrharural.org](mailto:elehwany@nrharural.org).

Sincerely,

National Rural Health Association  
Safety Net Hospitals for Pharmaceutical Access

cc: Gaelyn Pautsch, Senior Reimbursement Analyst, Allergan  
Inga Warren, Reimbursement Analyst, Allergan

---

<sup>18</sup> H.R. Rep. No. 102-384, pt. II, at 12 (1992).