CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-905

PHARMACOLOGY REVIEW(S)

CONSULTATION RESPONSE

DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF DRUG SAFETY
(DMETS; White Oak 22; Mail Stop 4447)

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TO: Mary Parks, MD
Acting Director, Division of Metabolism and Endocrinology Products (HFD- 510)

THROUGH: Alina Mahmud, RPh, MS, Team Leader
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Division of Medication Errors and Technical Support (HFD-420)

FROM: Nora Roselle, PharmD, Safety Evaluator
Division of Medication Errors and Technical Support (HFD-420)

PRODUCT NAME: **Valtropin**
(Somatropin (rDNA origin) for Injection, USP)
5 mg

NDA#: 21-905
NDA SPONSOR: LG Life Sciences, Ltd.

RECOMMENDATIONS:

1. DMETS does not recommend the use of the proprietary name, Valtropin. ✓
2. DMETS recommends implementation of the label and labeling revisions outlined in section III of this review to minimize potential errors with the use of this product.
3. DDMAC finds the proprietary name, Valtropin, acceptable from a promotional perspective. ✓

DMETS would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Diane Smith, project manager, at 301-796-0538.

Division of Medication Errors and Technical Support (DMETS)
Office of Drug Safety
White Oak 22, Mail Stop 4447
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE OF REVIEW: January 18, 2006

NDA#: 21-905

NAME OF DRUG: **Valtropin**
(Somatropin (rDNA origin) for Injection, USP)

NDA HOLDER: LG Life Sciences, Ltd.

I. INTRODUCTION:

This consult was written in response to a request from the Division of Metabolism and Endocrinology Products (HFD-510), for assessment of the proprietary name "Valtropin", regarding potential name confusion with other proprietary or established drug names. Draft container labels, carton and insert labeling were provided for review and comment.

PRODUCT INFORMATION

Valtropin (Somatropin (rDNA origin) for Injection, USP) is indicated in adults for replacement therapy in growth hormone deficiency (GHD) [redacted] Valtropin will be available in cartons containing one vial of powder with 5 mg somatropin for reconstitution and one pre-filled syringe with 1.5 mL diluent consisting of the preservative metacresol in Water for Injection. After reconstitution with the provided solvent, the solution contains 3.33 mg/mL of somatropin. The recommended dose of Valtropin is shown below:

b(4)

Growth Hormone Deficiency in Children	0.023 – 0.043 mg/kg/day given 6-7 times a week by subcutaneous injection
Children with Turner Syndrome	0.054 mg/kg/day given 6-7 times a week by subcutaneous injection
Growth Hormone Deficiency in Adults	Initial: 0.33 mg/day (equivalent to 0.005 mg/kg/day) given as a subcutaneous injection; the dosage is usually increased but not more than 0.66 mg/day (equivalent to 0.01 mg/kg/day) after 4 weeks depending upon patient's tolerance of treatment.

II. RISK ASSESSMENT:

The medication error staff of DMETS conducted a search of several standard published drug product reference texts[1,2], as well as several FDA databases[3,4] for existing drug names which sound-alike or look-alike to Valtropin to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's Text and Image Database was also conducted[5]. The Saegis[6] Pharma-In-Use database was searched for drug names with potential for confusion. An expert panel discussion was conducted to review all findings from the searches. In addition, DMETS conducted three prescription analysis studies consisting of two written prescription studies (inpatient and outpatient) and one verbal prescription study, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name.

A. EXPERT PANEL DISCUSSION (EPD)

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name, Valtropin. Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of DMETS Medication Errors Prevention Staff and representation from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

1. DDMAC finds the proprietary name, Valtropin, acceptable from a promotional perspective.
2. Several product names were identified in the Expert Panel Discussion (EPD) that were thought to have potential for confusion with Valtropin. These products are listed in table 1 (see page 4), along with the dosage forms available and usual dosage.

[1] MICROMEDEX Integrated Index, 2006, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.
[2] Facts and Comparisons, 2006, Facts and Comparisons, St. Louis, MO.
[3] The Division of Medication Errors and Technical Support [DMETS] database of proprietary name consultation requests, Drugs@FDA, and the electronic online version of the FDA Orange Book.
[4] Phonetic and Orthographic Computer Analysis (POCA)
[5] Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at www.thomson-thomson.com
[6] WWW location http://www.uspto.gov/tmdb/index.html.

Table 1: Potential Sound-Alike/Look-Alike Names Identified by EPD

Product Name	Established name, Dosage form(s)	Usual adult dose*	Other
Valtropin	Somatropin (rDNA origin) for Injection – Powder for Injection: 5 mg	Growth Hormone Deficiency in Adults: Initial: 0.03 mg/day (equivalent to 0.005 mg/kg/day) given as SC injection; dosage is usually increased but not more than 0.66 mg/day (equivalent to 0.01 mg/kg/day) after 4 weeks depending tolerance of tx. Growth Hormone Deficiency in Children: 0.023 – 0.043 mg/kg/day given 6-7 times a week by SC injection Children with Turner Syndrome: 0.054mg/kg/day given 6-7 times a week by SC injection	
Nutropin Nutropin Depot Nutropin AQ	Somatropin Powder for Injection, lyophilized (Nutropin): 5 mg/vial and 10 mg/vial Powder for Injection (Nutropin Depot): 13.5 mg/vial, 18 mg/vial, and 22.5 mg/vial Injection (Nutropin AQ): 10 mg/vial	Nutropin and Nutropin AQ (GHD - adults): *initial* – 0.006 mg/kg given as a daily SC injection; maximum of 0.025 mg/kg/day (in patients <35 yo) and 0.0125 mg/kg/day in patients >35 yo); (GHD - children) – weekly dosage of up to 0.3 mg/kg of body weight divided into daily SC injection (up to 0.7 mg/kg divided daily over a week) (Turner syndrome – children): weekly dosage of up to 0.375 mg/kg of body weight divided into equal doses 3 to 7 times per week by SC injection Nutropin Depot: 1.5 mg/kg administered SC on the same day of each month or 0.75 mg/kg administered SC twice each month on the same days of each month	Look-alike
Atropine *(marketed under the generic name atropine as well as various other brand names)*	Atropine Sulfate Ophthalmic Ointment: 1% Ophthalmic Solution: 0.5%, 1%, and 2% Tablets: 0.4 mg Injection: 0.05 mg/mL, 0.1 mg/mL, 0.3 mg/mL, 0.4 mg/mL, 0.5 mg/mL, 0.8 mg/mL, and 1 mg/mL	Ophthalmic Ointment: apply a small amount in the conjunctival sac once or twice a day Ophthalmic Solution: 1 or 2 drops in the eye(s) 3 times a day Tablet and Injection (SC, IM, or IV): 0.4 to 0.6 mg with the average adult dose of 0.5 mg	Look-alike
Atropen	Atropine Injection 0.25 mg, 0.5 mg, 1 mg, and 2 mg	Mild symptoms of nerve agent or insecticide exposure: one intramuscular injection Severe symptoms: two additional IM injections given in rapid succession 10 minutes after receiving the 1st injection	Look-alike
Voltaren Voltaren XR	Diclofenac Sodium Enteric Coated Tablets: 25 mg, 50 mg, and 75 mg Extended Release Tablets (XR): 100 mg Ophthalmic Solution: 0.1% (2.5 mL)	Tablets: Osteoarthritis: 50 mg 2 – 3 times daily or 75 mg twice daily; 100 mg (XR) once daily Rheumatoid arthritis: 50 mg 3-4 times daily or 75 mg twice daily; 100 mg (XR) once daily Ankylosing spondylitis: 100 -125 mg daily in 4-5 divided doses Ophthalmic Solution: Cataract Surgery – 1 drop in affected eye(s) 4X/day for 2 weeks following postop Corneal Refractive Surgery – 1-2 drops 4X/day for up to 3 days following surgery	Look-alike, Sound-alike

*Frequently used, not all-inclusive.

B. PRESCRIPTION ANALYSIS STUDIES

1. Methodology:

Three separate studies were conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of Valtropin with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. These studies employed a total of 122 health care professionals (pharmacists, physicians, and nurses). These exercises were conducted in an attempt to simulate the prescription ordering process. An inpatient order and outpatient prescriptions were written, each consisting of a combination of marketed and unapproved drug products and a prescription for Valtropin (see below). These prescriptions were optically scanned and one prescription was delivered to a random sample of the participating health professionals via e-mail. In addition, the outpatient orders were recorded on voice mail. The voice mail messages were then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants sent their interpretations of the orders via e-mail to the medication error staff.

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
Written Outpatient: Valtropin 1cc Vial Inject SQ 6-7 times a week utd.	Valtropin Dispense one vial. Inject subcutaneously six to seven times a week as directed.
Written Inpatient: Valtropin 1cc Inject SQ 6-7 times a week utd.	

2. Results:

None of the interpretations of the proposed name overlap, sound similar, or look similar to any currently marketed U.S. product. See appendix A for the complete listing of interpretations from the verbal and written studies.

C. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name Valtropin, the primary concerns related to look-alike and sound-alike confusion with Nutropin, Atropine, Atropen, and Voltaren.

DMETS conducted prescription studies to simulate the prescription ordering process. In this case, there was no confirmation that the proposed name could be confused with any of the aforementioned names. However, negative findings are not predicative as to what may occur once the drug is widely prescribed, as these studies have limitations primarily due to small sample size. The majority of misinterpretations were misspelled/phonetic variations of the proposed name, Valtropin.

1. Nutropin was identified as a name with similar appearance to Valtropin. Nutropin is marketed under several tradenames and strengths: Nutropin (5 mg/vial and 10 mg/vial), Nutropin Depot (13.5 mg/vial, 18 mg/vial, and 22.5 mg/vial), and Nutropin AQ (10 mg/vial). The Nutropin products are indicated for the replacement of endogenous growth hormone in patients with growth hormone deficiency and for the long-term treatment of short stature associated with Turner syndrome (children).

Nutropin and Valtropin may look-alike when scripted because they share the ending letters "-tropin". In addition, a capital letter "N" can look similar to a capital letter "V" when scripted (see below). The drugs each share an overlapping dosage form (injectable), route of administration (subcutaneous injection), frequency of administration (once daily), strength (5 mg/vial), active ingredient (somatropin), and indication for use (growth hormone deficiency). In addition, both drugs are dosed based on a patient's weight in kilograms. Even though, Nutropin and Valtropin have different usual adult versus children daily doses (see Table 1 on page 4), the numerical doses may be similar. For example, Nutropin can be dosed as 0.025 mg/kg/day for adults with growth hormone deficiency while Valtropin can be dosed as 0.023 mg/kg/day for children with growth hormone deficiency. Thus, due to the written similarities and numerous overlapping product characteristics, DMETS believes there is potential for confusion and error between Nutropin and Valtropin.

Nutropen Valtropin

2. Atropine was identified as a name with similar appearance to Valtropin. Atropine is available in several dosage forms and strengths, and has various indications for use. Atropine (marketed under the names Atropine Sulfate Ophthalmic, Isopto Atropine, and Atropine-1) is available as an ophthalmic ointment (1%) and solution (0.5%, 1%, and 2%), indicated for mydriasis or cycloplegia. Atropine tablets (0.4 mg), marketed under the brand name 'Sal-Tropine', and Atropine Injection (0.05 mg/mL, 0.1 mg/mL, 0.3 mg/mL, 0.4 mg/mL, 0.5 mg/mL, 0.8 mg/mL, and 1 mg/mL) are used for a variety of indications including as a preanesthetic medication to prevent or reduce secretions of the respiratory tract, treatment of parkinsonism, and to restore cardiac rate and arterial pressure during anesthesia.

   Atropine and Valtropin may look-alike when scripted because the letters "Atropine" and "-altropin" differ only by the addition of the upstroke letter "l" in Valtropin and the ending letter "e" in Atropine. In addition, the letter "V" may look like a stray mark on a prescription order and be overlooked inadvertently (see below). The drugs each share an overlapping dosage form (injectable), route of administration (subcutaneous injection), frequency of administration (one dose vs. once daily), and have a numerically similar strength (0.5 mg/mL vs. 5 mg). Furthermore, Atropine and Valtropin may have an overlapping dose of 0.5 mg. A child weighing approximately 25.5 pounds (equivalent to 11.6 kg) may receive a 0.5 mg dose of Valtropin (0.043 mg/kg/day x 11.6 kg = 0.5 mg/day). Atropine, on the other hand, has a usual IV adult dose of 0.5 mg with a range from 0.4 mg to 0.6 mg. Due to the similarity of the scripted names, if an inpatient order for "Atropine .5 mg SC x 1" is written omitting the leading zero before the 0.5 mg, one may inadvertently misinterpret the prescription order as "Valtropin .5 mg SC x 1". DMETS believes that due to the similar appearance of the names as well as the overlapping product characteristics, there is increased risk for confusion and error between Atropine and Valtropin.

Atropine .5mg SC x1 Valtropin .5mg SC x 1

3. Atropen was identified as a name with similar sound and appearance to Valtropin. Atropen is indicated for the treatment of poisoning by susceptible organophosphorous nerve agents having cholinesterase activity as well as organophosphorous or carbamate insecticides. Atropen currently is made available only to federal, state, and local governments and emergency responders. Atropen is a prefilled atropine auto-injector pen available in four strengths: 0.25 mg, 0.5 mg, 1 mg, and 2 mg. Atropen is dosed based on a patient's weight and age: 0.25 mg for infants weighing less than 15 pounds and generally less than 6 months of age; 0.5 mg for children weighing 15 to 40 pounds, generally 6 months to 4 years of age; 1 mg for children weighing from 40 to 90 pounds, generally 4 to 10 years of age; and 2 mg for adults and children weighing over 90 pounds who generally are over 10 years of age.

One Atropen intramuscular injection is recommended if two or more mild symptoms of nerve agent or insecticide exposure appear. Two additional injections given in rapid succession are recommended ten minutes after receiving the first injection if the victim develops any severe symptoms.

Atropen and Valtropin may look alike when scripted because the letters "Atropen" and "-altropin" differ only by the addition of the upstroke letter "l" in Valtropin. However, the letter "V" at the beginning of Valtropin helps differentiate one name from the other (see below). While the two drugs are both injectable products, there are many characteristics which help distinguish between Atropen and Valtropin. In addition, Valtropin can sound similar to Atropen if the "V" in Valtropin is spoken softly. Likewise, Valtropin and Atropen each have a parenteral route of administration (intramuscular injection vs. subcutaneous injection) and an overlapping numerical strength (0.5 mg vs. 5 mg). Furthermore, it is possible to have an overlapping dose of Valtropin and Atropen. For example, a 15 to 40 pound child will be administered an Atropen dose of 0.5 mg. While a child weighing approximately 25.5 pounds (equivalent to 11.6 kg) may also receive a 0.5 mg dose of Valtropin (0.043 mg/kg/day x 11.6 kg = 0.5 mg/day). However, the drugs each have a different frequency of administration (one time dose vs. 6-7 times a week) and indication for use (nerve agent and insecticide poisoning vs. growth hormone deficiency). Moreover, Atropen has a specialized setting of use as it is intended for use by individuals who have had training in the recognition and treatment of chemical and nerve agent poisoning and currently is made available only to federal, state, and local governments and emergency responders. While there are similarities between the two drugs, DMETS believes the different product characteristics and Atropen's limited distribution of use decrease the risk for confusion and error between Atropen and Valtropin.

atropen Valtropen

4. Voltaren has a look- and sound-alike similarity to Valtropin. Voltaren is a non-steroidal anti-inflammatory agent indicated for the treatment of osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, and for the treatment of ocular inflammation and pain following cataract extraction and corneal refractive surgery. Voltaren is supplied as delayed release tablets (25 mg, 50 mg, and 75 mg), extended-release tablets (Voltaren XR – 100 mg), and as an ophthalmic solution (0.1%).

   Voltaren and Valtropin can look-alike because the names begin with four similar looking letters (Volta- vs. Valto). However, when scripted the ending letters help differentiate one name from the other (-ren vs. –pin) as Valtropin has a downstroke letter "p". Furthermore, the two names share similar verbal characteristics in that they each contain three syllables and begin with similar sounds (Vol- vs. Val-). Yet, when spoken, the ending letters of each name sound different when compared to one another (-taren vs. -tropin). Voltaren and Valtropin have a different dosage form (tablets and ophthalmic solution vs. injectable powder for reconstitution), route of administration (oral and ophthalmic vs. subcutaneous injection), strength (25 mg, 50 mg, 75 mg, 100 mg, and 0.1% vs. 5 mg), and indication for use (arthritis and ocular inflammation/pain vs. growth hormone deficiency). In addition, each drug has a different dose and dosing regimen. For the treatment of osteoarthritis and rheumatoid arthritis, Voltaren can be dosed as 50 mg by mouth two to three times daily, 75 mg twice daily, or as 100 mg (Voltaren XR) once daily. Voltaren is dosed as 100 mg to 125 mg daily in four to five divided doses for the treatment of ankylosing spondylitis. Voltaren is also available as an ophthalmic solution and dosed as one to two drops in the affected eye(s) four times daily. Valtropin, on the other hand, is dosed based on weight in kilograms in children and as a milligram per day dose in adults. For example, for the treatment of growth hormone deficiency in children the dose is 0.023 to 0.043 mg/kg/day and for adults 0.33 mg/kg/day (up to a maximum of 0.66 mg/day). Due to the differences in look-alike, sound-alike, and

product characteristics, DMETS believes that there is minimal risk for confusion and error between Voltaren and Valtropin.

Voltaren Valtropin

III. COMMENTS TO THE SPONSOR:

A. DMETS does not recommend the use of the proprietary name Valtropin. In reviewing the proprietary name, the primary concerns related to look-alike confusion with Nutropin and Atropine.

1. Nutropin was identified as a name with similar appearance to Valtropin. Nutropin is marketed under several tradenames and strengths: Nutropin (5 mg/vial and 10 mg/vial), Nutropin Depot (13.5 mg/vial, 18 mg/vial, and 22.5 mg/vial), and Nutropin AQ (10 mg/vial). The Nutropin products are indicated for the replacement of endogenous growth hormone in patients with growth hormone deficiency and for the long-term treatment of short stature associated with Turner syndrome (children).

   Nutropin and Valtropin may look-alike when scripted because they share the ending letters "-tropin". In addition, a capital letter "N" can look similar to a capital letter "V" when scripted (see below). The drugs each share an overlapping dosage form (injectable), route of administration (subcutaneous injection), frequency of administration (once daily), strength (5 mg/vial), active ingredient (somatropin), and indication for use (growth hormone deficiency). In addition, both drugs are dosed based on a patient's weight in kilograms. Even though, Nutropin and Valtropin have different usual adult versus children daily doses (see Table 1 on page 4), the numerical doses may be similar. For example, Nutropin can be dosed as 0.025 mg/kg/day for adults with growth hormone deficiency while Valtropin can be dosed as 0.023 mg/kg/day for children with growth hormone deficiency. Thus, due to the written similarities and numerous overlapping product characteristics, DMETS believes there is potential for confusion and error between Nutropin and Valtropin.

   Nutropin Valtropin

2. Atropine was identified as a name with similar appearance to Valtropin. Atropine is available in several dosage forms and strengths, and has various indications for use. Atropine (marketed under the names Atropine Sulfate Ophthalmic, Isopto Atropine, and Atropine-1) is available as an ophthalmic ointment (1%) and solution (0.5%, 1%, and 2%), indicated for mydriasis or cycloplegia. Atropine tablets (0.4 mg), marketed under the brand name 'Sal-Tropine', and Atropine Injection (0.05 mg/mL, 0.1 mg/mL, 0.3 mg/mL, 0.4 mg/mL, 0.5 mg/mL, 0.8 mg/mL, and 1 mg/mL) are used for a variety of indications including as a preanesthetic medication to prevent or reduce secretions of the respiratory tract, treatment of parkinsonism, and to restore cardiac rate and arterial pressure during anesthesia.

   Atropine and Valtropin may look-alike when scripted because the letters "Atropine" and "-altropin" differ only by the addition of the upstroke letter "l" in Valtropin and the ending letter "e" in Atropine. In addition, the letter "V" may look like a stray mark on a prescription order and be overlooked inadvertently (see page 9). The drugs each share an overlapping dosage form (injectable), route of administration (subcutaneous injection), frequency of administration (one dose vs. once daily), and have a numerically similar strength (0.5 mg/mL vs. 5 mg). Furthermore, Atropine and Valtropin may have an overlapping dose of 0.5 mg. A child weighing approximately 25.5 pounds (equivalent to 11.6 kg) may receive a 0.5 mg dose of Valtropin (0.043 mg/kg/day x 11.6 kg = 0.5 mg/day). Atropine, on the other hand, has a usual IV adult dose of 0.5 mg with a range from 0.4 mg to 0.6 mg. Due to the similarity of the scripted names, if an inpatient order for "Atropine .5 mg SC x 1" is written omitting the leading zero before the 0.5 mg, one may inadvertently misinterpret the

prescription order as "Valtropin .5 mg SC x 1". DMETS believes that due to the similar appearance of the names as well as the overlapping product characteristics, there is increased risk for confusion and error between Atropine and Valtropin.

Atropine .5mg SC x 1 Valtropin .5mg SC x 1

B. In the review of the labels and labeling, DMETS has attempted to focus on safety issues relating to possible medication errors. DMETS has identified the following areas of possible improvement, which might minimize potential user error.

1. CONTAINER LABEL (Valtropin 5 mg)

   a. The proprietary and established names should be the most prominent information on the label. Please ensure that the information is prominent and legible. We recommend increasing the prominence of the proprietary and established names as they tend to blend in with the other information listed in black font on the vial label.

   b. In order to provide clear and accurate information on the label, a space should be inserted between the "5" and "mg" following the proprietary name.

   c. The statement "Once reconstituted with solvent..." should be more clearly worded to include the name of diluent and the amount needed for reconstitution (i.e., XX mL of XXX solvent).

   d. It appears that the product is the subject of a USP monograph. Please ensure that the appropriate USP designation appears in the established name.

   e. We recommend differentiating the route of administration "Subcutaneous use only" with a contrasting color, boxing, or some other means as it currently blends in with the other information listed in black font on the vial label.

   f. If space permits, include a quantitative and qualitative list of inactive ingredients.

   g. If space permits, we recommend the "Rx only" statement appear on the principal display panel.

   h. The "LG Life Sciences" logo that appears in red distracts from the label and should be deleted. As currently presented, this logo is more prominent than the established name, storage, and reconstitution information.

2. CONTAINER LABEL (Diluent for Valtropin)

   a. The diluent is packaged in a syringe and labeled with the proprietary name Valtropin. Because it is packaged in a syringe it could be inadvertently administered by direct infusion we recommend repackaging in a vial.

   b. We note the sponsor proposes to label the diluent of solvent with the proprietary name Valtropin and the established name. Labeling the diluent as Valtropin is misleading as it implies that the Valtropin drug is already prepared and ready for use, and therefore does not require reconstitution. In addition to repackaging the product into a vial, as described above, we recommend clearly labeling the syringe as follows and completely removing the name "Valtropin" from the label:

      Metacresol (0.3%w/v) in Water for Injection
      Diluent Only

      Additionally, the word "solvent" should be replaced with the above term.

c. The statement "Single use syringe" should appear on the principal display panel of the diluent.

d. See comments 1b, 1f, and 1h.

3. CARTON LABELING

a. See comments 1a, 1b, 1d, 1e, and 1h.

b. The statement '[redacted]' should be deleted from the principal display panel as the total strength of the drug powder already appears in conjunction with the proprietary name. However, if the statement is kept on the labeling the abbreviation IU should be written as International Unit to avoid confusion and error. b(4)

c. The principal display panel of the carton should be revised to include a statement such as "Each carton contains: 1 multiple dose vial containing somatropin...
1 pre-filled syringe containing 1.5 mL of Metacresol (0.3% w/v) in Water for Injection."

d. The instructions found on the carton labeling are not clear and could lead to confusion. Revise as follows: "Reconstitute each vial with 1.5 mL of the enclosed diluent of Metacresol (0.3% w/v) in Water for Injection. After reconstituting with 1.5 mL of Metacresol (0.3% w/v) in Water for Injection the solution contains 3.33 mg/mL of somatropin."

4. INSERT LABELING

1. See comment 2b.

2. The Dosage and Administration Section

This section of the labeling is not clear and could lead to confusion. Revise to include the drug preparation instructions, final concentration, and other information important to the proper dosing and administration of the drug product.

3. The Stability and Storage, After Reconstitution With Water for Injection Subsection

We note this product when reconstituted with Metacresol (0.3% w/v) in Water for Injection is stable for 21 days. However, when reconstituted with Sterile Water for Injection without preservative, the product can only be used for one single dose and the remainder must be immediately discarded. Therefore, Metacresol (0.3% w/v) in Sterile Water for Injection is the optimal diluent and use of Sterile Water for Injection without preservative should be reserved only for patients who have an allergy or sensitivity to Metacresol or when the supplied diluent is unavailable. DMETS recommends that this section note that Sterile Water for Injection without preservative should only be used in these scenarios. This will prevent practitioners and/or patients from using Sterile Water for Injection without preservative to reconstitute the drug and storing the bottle for 21 days.

Appendix A. Valtropin

Written Outpatient	Written Inpatient	Verbal
Valtropin	Valtropin	Vatinpin
Valtropin	Valtropin	Vatiapin
Valtropen	Valtropin	Vatiapin
Valtryn	Valtropin	Vatinpin
Valtropin	Valtropin	Vatiapin
Maltropin	Valtropin	Vatiapin
Valtropin	Valtropin	Vatenpin
Valtropin	Valtropin	Vatinpin
Valtropin	Valtropin	Vatiaprin
Valtropin	Valtropin	Vatiapin
valtropen	Valtropin	Vatiapin
Valtropan	Valtropin	Vatinpin
Valtropen	Valtropin	Vatinpen
Valtropin	Valtropin	Vatenpin
Vatepin	Valtropin	Vatinpin
	Valtropin	Vatinpin
	Valtropin	Vateapir
	Valtropin	Vatenpin
	Valtropin	Vatiapin
		Vateapin
		Vatinpin

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