Review of the List of High-Cost Medicines used by the Dominican Republic's Protected Diseases Program and Planning of Purchases for 2015

July 2014

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This report was made possible by the support provided by the United States Agency for International Development (USAID) under the terms of Cooperative Agreement No. AID-OAA-A-11-00021. The contents of the report do not necessarily reflect the views of USAID or the United States Government.

About the SIAPS Program

The goal of the Systems for Improved Access to Pharmaceuticals and Services (SIAPS) Program is to assure the availability of quality pharmaceutical products and effective pharmaceutical services in order to achieve desired health outcomes. Toward this end, the SIAPS results areas include improving governance, building capacity for pharmaceutical management and services, addressing information needed for decision-making in the pharmaceutical sector, strengthening financing strategies and mechanisms for improving access to medicines, and increasing the quality of pharmaceutical services.

Recommended Citation

This report may be produced provided that credit is given to the author. Please use the following citation:

Narváez E, Valdez C, Barillas E. 2014. *Review of the List of High-Cost Medicines Used by the Dominican Republic's Protected Diseases Program and Planning of Purchases for 2015*. Santo Domingo, Dominican Republic, July 2014. Presented to the US Agency for International Development by the Systems for Improved Access to Pharmaceuticals and Services (SIAPS) Program. Arlington, VA: Management Sciences for Health.

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ACKNOWLEDGMENTS

The tasks of gathering information and analyzing the costs and effectiveness of the items included on the list of medicines were carried out by Dr. Edgard Narváez, short-term consultant to the Systems for Improved Access to Pharmaceuticals and Services (SIAPS) Program. The data were provided by Dr. Sandra Fermín, Director of the Ministry of Public Health's Protected Diseases Program, and her technical team. Participating in the workshop to review the list were the scientific committees on Oncology, Hemato-oncology, Nephrology and Transplants, Gastroenterology and Liver Diseases, Rheumatology, and Hemophilia.

Procurement planning for 2015 was carried out by the Protected Diseases Program team, with support from SIAPS. Claudia Valdez and Edgar Barillas, SIAPS consultants, conducted the final review and validation of the information and were also responsible for editing this report.

ACRONYMS AND ABBREVIATIONS

COMISCA	*Consejo de Ministros de Salud de Centroamérica y República Dominicana* (Council of Ministers of Health of Central America and the Dominican Republic)
CTSM	*Comisión Técnica Subregional de Medicamentos* (Subregional Technical Commission on Medicines)
DOP	Dominican pesos
MPH	Ministry of Public Health
PAHO	Pan American Health Organization
PP	*Programa de Enfermedades Protegidas* (Protected Diseases Program)
PROMESE/CAL	*Programa de Medicamentos Esenciales/Central de Abastecimiento Logístico* (Program of Essential Medicines/Center for Logistical Support)
SIAPS	Systems for Improved Access to Pharmaceuticals and Services Program
SUGEMI	*Sistema Único de Gestión de Medicamentos e Insumos* (Integrated System for Medicine and Supply Management)
USD	US dollars

BACKGROUND

The Dominican Republic's Ministry of Public Health (MPH) is currently implementing, within the framework of its health sector reform program, an Integrated System for Medicine and Supply Management (known as SUGEMI, for its Spanish acronym) as part of the Ministry's Public Service Network. Its objective is to improve public access to essential medicines and quality health supplies while promoting the decentralized management and optimum use of available resources.

Since 2010, the Strengthening Pharmaceutical Systems and Systems for Improved Access to Pharmaceuticals and Services (SIAPS) programs, both of which are implemented by Management Sciences for Health and funded by the US Agency for International Development, have been providing support focused on the organization of SUGEMI. SUGEMI is designed to bring about the gradual integration of all MPH programs, including the Protected Diseases Program (*Programa de Enfermedades Protegidas*; PP), into a single supply management system. The PP is responsible for providing high-cost clinical interventions, such as treatment for hepatitis B and C, renal insufficiency, kidney transplants, leukemias, and certain low-incidence diseases, such as Crohn's disease, multiple sclerosis, and myelodysplastic syndrome, among others. By 2013, coverage had reached 11,868 patients.

In May 2013, the PP participated in the national planning exercise for procurement of medicines for 2014. The total purchase price of those medicines was DOP 4.8 billion (USD 107 million), accounting for 51% of the MPH budget for medicines for that year.[1] Resources allocated for medicine procurement totaled DOP 2.116 billion (USD 49 million), leaving a shortfall of DOP 2.8 billion (USD 62 million). Because of the high cost of the medicines included in this group, the substantial percentage of MPH budget funds required for their purchase, and the limited amount of budget funds available, the PP requested technical assistance from SIAPS in conducting a review of the list of medicines to be made available and in subsequently planning medicine purchases for 2015.

[1] *Informe de brechas financieras para la compra de medicamentos e insumos médicos en el 2014.* Unidad Nacional de Gestión de Medicamentos del Ministerio de Salud Pública y SIAPS/USAID. Dominican Republic.

OBJECTIVES

1. To facilitate for the various PP scientific committees the selection of medicines to be procured in 2015, using medical criteria based on evidence and cost-effectiveness.

2. To estimate and plan for purchases to be made for 2015 of medicines recommended for permanent inclusion on the PP list of medicines.

METHODOLOGY

Stage I. Gathering of Evidence and Preliminary Analysis of the Medicine List

A SIAPS consultant analyzed the therapeutic benefits and cost of the 95 medicines included on the PP's list (Annex 1). Information sources used included the following:

- British National Formulary: http://www.bnf.org/bnf/index.htm
- Martindale; Trip Database: http://www.tripdatabase.com/
- NICE (National Institute for Health and Care Excellence): http://www.nice.org.uk/
- Cochrane: http://www.cochrane.org/
- Clinical Evidence: http://clinicalevidence.bmj.com/x/index.html?displaySurveys=&portfolioHost=portfolio.bmj.com
- National Cancer Institute: http://www.cancer.gov/
- National Guidelines Clearinghouse: http://www.guideline.gov/
- PubMed: http://www.ncbi.nlm.nih.gov/pubmed/

The information gathered was used to prepare a "Technical Report: Review of the List of Medicines used by the Dominican Republic's Protected Diseases Program," which could then be used to support discussions with the various PP scientific committees.

The report proposes four levels of prioritization for the 95 medicines analyzed:

- *Priority 1*: Medicines included on the Model Lists of Essential Medicines of the World Health Organization (WHO)[2] and in the Report of the Expert Committee for the Selection and Inclusion of Medicines in the Pan American Health Organization (PAHO) Strategic Fund.

- *Priority 2*: Medicines included on the list for joint purchases to be made through the Council of Ministers of Health of Central America and the Dominican Republic (*Consejo de Ministros de Salud de Centroamérica y República Dominicana*; COMISCA).[3]

- *Priority 3*: Medicines not included in the preceding groups (1 and 2) but with scientific evidence supporting their use for specific health problems. The ultimate inclusion in, or

[2] WHO. 2013. Model List of Essential Medicines, 18th edition; Model List of Essential Medicines for Children, 4th list.

[3] In 2005, COMISCA launched the process for joint purchase of medicines. In 2006, it created the Subregional Technical Commission on Medicines (*Comisión Técnica Subregional de Medicamentos*; CTSM), made up of experts in pharmaceuticals appointed by member countries and supported by advisory assistance provided by PAHO. The CTSM provides advisory assistance in preparing harmonized lists of medicines, preparing technical datasheets, consolidating estimates of needs, and negotiating prices. In 2007, the process of standardizing the list of medicines was carried out at the regional level, using as points of reference the lists of essential medicines in effect in member countries. The result of this effort was a list of 37 medicines deemed to be of priority importance for the region, by virtue of their therapeutic importance, their high cost, and the limited potential for their procurement in the local market. The list was revised in 2013.

exclusion from, the medicines in this group depends on market availability, marketing authorization given by regulatory agencies such as the European Medicines Agency and the US Food and Drug Administration, and the priority accorded them by clinicians based on therapeutic guidelines or protocols, the prevalence of cases, and the availability of funds for their purchase. The consensus reached by the scientific committees at the workshop would allow these medicines to be moved to a different priority group.

- *Priority 0:* Medicines for which scientific evidence is insufficient to support their use for the purpose intended, or for which better or equivalent alternatives are available.

Stage 2. Facilitation in the Selection of Medicines to be Purchased

On May 23 and 24, 2014, a workshop was held with the scientific committees. To allow reaching a consensus in a relatively short period of time, the following methodology was developed:

Presentation of Key Concepts for Reviewing Scientific Evidence Supporting a Medicine List and Prioritization Proposal

- Presentation of basic concepts regarding the rational use of medicines and elements of pharmoeconomics, with emphasis on the cost-effectiveness of the medicines. The goal was to provide the clinical specialists with systematic methods to use in reviewing the list of medicines.

- Presentation of the prioritization proposal referred to in the preceding section together with the medicines tentatively classified in each group.

Group Consensus to Modify the Prioritization Proposal

- Four working groups were created for specific clinical specialties, as follows: (1) hemato-oncology (including hemophilias); (2) gastroenterology; (3) rheumatology; and (4) nephrology and transplants. The following resources were made available to the working groups:

    - Technical Report: Review of the PP list of medicines (draft Technical Report, in both print and electronic versions)
    - Scientific evidence supporting the recommendations provided in the Technical Report (electronic)
    - Internet access to facilitate a search for evidence supporting proposals for modification
    - Working matrix containing 98[4] medicines classified in accordance with the proposed priority group, with columns to record consensus reached on modifications agreed to by the working groups

[4] The list of medicines in effect as of the date of the workshop contained a total of 95 items (annex 1). During the workshop, three additional medicines were added: 2 for hemophilias and 1 for oncology (Factor IX, Factor VIII and pertuzumab 420 mg). Accordingly, the number of medicines ultimately analyzed totaled 98.

- Arriving at their conclusions by consensus, the work groups validated the proposed prioritization of the medicines or suggested modifications to the assigned priority group based on the agreements reached by the group and identified supporting literature.

Plenary Session to Discuss and Validate Group Proposals

- Proposal for modifications were presented by each group at a plenary session, together with the evidence supporting the group's recommendations. Discussions moderated by a SIAPS facilitator made it possible to agree upon, and record by consensus, the priority group for each medicine.

- For one group of medicines, the work groups requested a short extension for presenting the evidence supporting the modification recommended. These medicines were classified as *lacking evidence* or *evidence pending*.

Final selection of medicines for programming of purchases

- A small committee made up of technical personnel from both the PP and SIAPS conducted a comparative analysis of the working group recommendations and the prioritization proposal included in the Technical Report. In arriving at the final selection of medicines to be included in the purchase planning exercise, the following criteria were taken into account:

    - Inclusion of medicines on which there was agreement between the Technical Report and the consensus reached by the specialists.
    - Inclusion of medicines not considered in the Technical Report, but for which scientific evidence existed to support their inclusion.
    - Exclusion of those medicines proposed by specialists for which no evidence was presented or for which the evidence did not support their inclusion.
    - Exclusion of medicines providing proven therapeutic benefit but which were not deemed to be high cost. These medicines (three) will be procured by the Program of Essential Medicines/Center for Logistical Support (*Programa de Medicamentos Esenciales y Central de Abastecimiento Logístico*; PROMESE/CAL)[5] or by a social program operated by a government agency.
    - Exclusion of medicines having an extremely low level of consumption, for diseases classified as *rare.* Given the exceptional nature of the demand for such medicines, it was proposed that they be procured under social programs operated by the MPH or some other government agency.

- The application of these criteria led to the establishment of three categories that would make it possible to adapt programming to budget ceilings.

[5] By Presidential Decree, this program is responsible for procuring all public health sector medicines and commodities.

Category A:

Medicines that must remain with the PP, based on the three established priorities:

Priority 1: Included on the WHO/PAHO model list and ratified by the group of experts

Priority 2: Included on the COMISCA list and ratified by the group of experts

Priority 3: Not included on the above lists but backed by scientific evidence supporting their use and ratified by the group of experts

Category B:

Medicines lacking evidence or with a final decision still pending

Category C:

Medicines completely excluded or proposed for inclusion in PROMESE or a social program operated by the MPH or some other government agency

Stage 3. Planning of 2015 Purchases

Estimates and planning of purchases for 2015 took place for categories A (medicines that must remain with the PP) and B (medicines pending a final decision). Medicines excluded or proposed for procurement by another agency (category C) were not included in the planning exercise.

Based on data availability and reliability, the historic consumption and morbidity methods were used to develop estimates. For valuation purposes, local purchase prices provided by the MPH Procurement Directorate and prices for procurements made through COMISCA were used.

RESULTS

Of the 98 medicines analyzed, 22 (22.45%) were on the WHO/PAHO Model List (priority 1) and 17 (17.35%) were on the COMISCA list (priority 2). These were included in category A. For the 59 remaining medicines, a review was conducted of existing scientific evidence. For 17 additional medicines (17.35%), evidence was found to support their inclusion in category A. A cost analysis reduced this group (priority 3) to 14 medicines (14.29%).[6] A total of 53 medicines (45 active ingredients) included in category A would be included in the planning exercise for 2015 purchases; 45 medicines would be excluded (figure 1).

Even with this significant reduction in the PP list of medicines, the cost exceeds the budget historically allotted to the PP. Accordingly, it was agreed that two alternative scenarios for 2015 purchases would be proposed (figure 1):

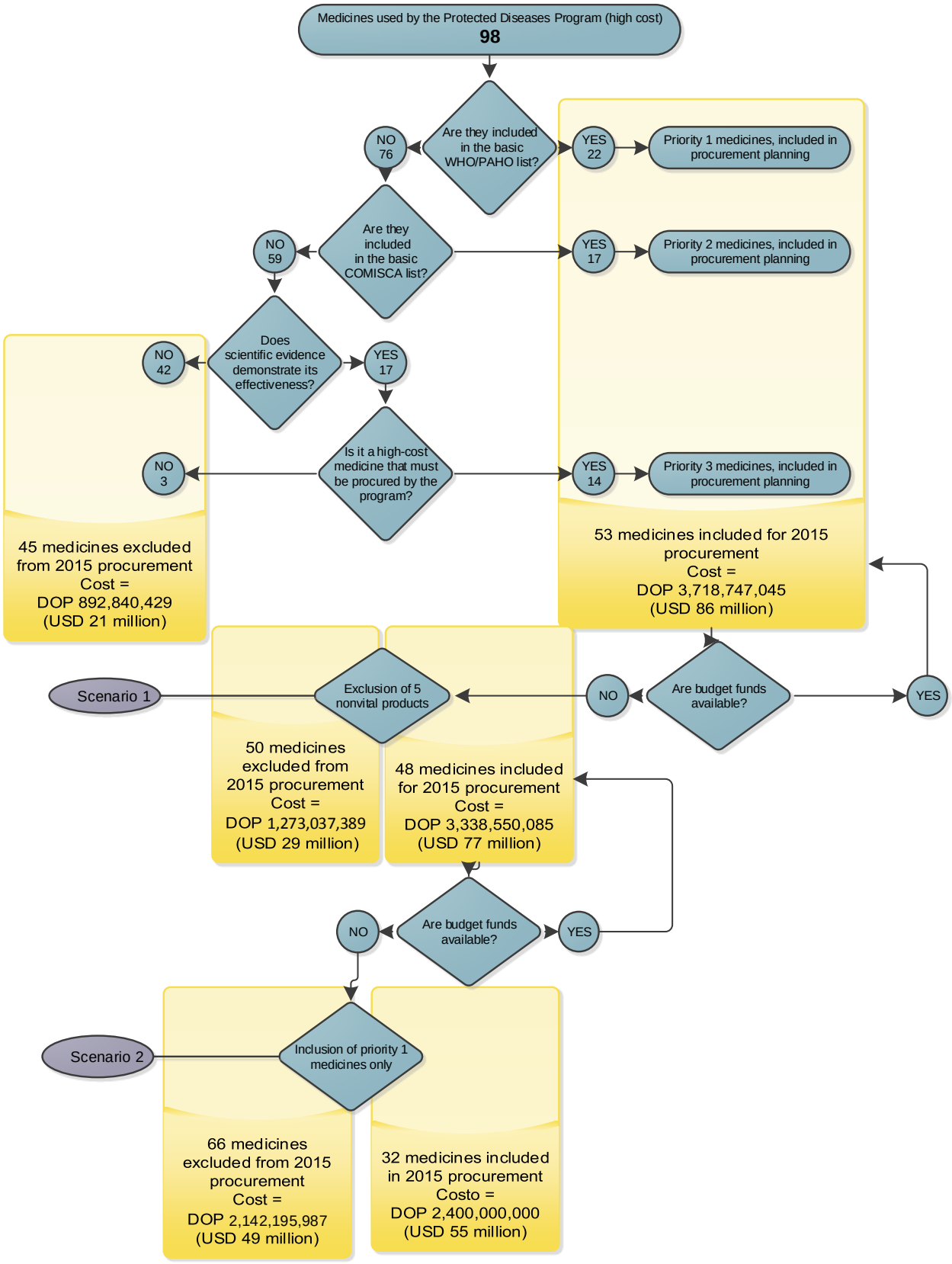
1. **Scenario 1:** Only those products included in priorities 1 and 2 would be included in the purchase planning exercise. In this scenario, 50 products from the list would be excluded. The budget for procuring the remaining 48 medicines would be reduced to DOP 3.338 billion (USD 77 million), but even so would exceed the budget allocated for 2014 purchases.

2. **Scenario 2:** Only priority 1 medicines would be included in the purchase planning exercise. In this scenario, 66 medicines from the list would be excluded. The budget for procuring the remaining 32 medicines would decrease to DOP 2.4 billion (USD 29 million), an amount similar to the budget allocated for the procurement of medicines in 2014.

In this way, the consensus-based order of priority and the scenarios developed on the basis of availability of budgeted funds would enable MPH authorities to conduct evidence-based funding negotiations with the Ministry of Finance and, in the event that the final allotment was insufficient to meet all requirements, to determine the budget to be assigned to the group of medicines providing the greatest therapeutic benefit for the cost involved.

[6] Three medicines (iron sucrose, erythropoietin, and oxaliplatin) were found to have low unit costs, as a result of which their inclusion on the list of high-cost medicines could not be justified. They will be procured through PROMESE/CAL.

Figure 1. Decision flowchart for reviewing the PP list of medicines



ANNEX 1: MEDICINES USED BY THE PROTECTED DISEASES PROGRAM

1. Pulmonary surfactant 25 mg/8 ml
2. Leuprolide acetate 7.5 mg
3. Leuprolide acetate 22.5 mg
4. Trabectedin 1 Gr
5. Abiraterone acetate 250 mg
6. Crizotinib 250 mg
7. Pemetrexed 500 mg
8. Trastuzumab 440 mg
9. Lapatinib 250 mg
10. Capecitabine 500 mg
11. Letrozole 2.5 mg
12. Sunitinib 50 mg
13. Sunitinib 25 mg
14. Sunitinib 12.5 mg
15. Erlotinib 150 mg
16. Octreotide 20 mg
17. Irinotecan 100 mg
18. Oxaliplatin 100 mg
19. Oxaliplatin 50 mg
20. Temozolomide 100 mg
21. Temozolomide 20 mg
22. Vemurafenib
23. Gemcitabine 1 Gr
24. Bevacizumab 100 mg
25. Bevacizumab 400 mg
26. Cetuximab 100 mg
27. Sorafenib 200 mg
28. Zoledronic acid 4 mg
29. Ibandronic acid 6 mg
30. Imatinib 400 mg
31. Dasatinib 100 mg
32. Nilotinib 200 mg
33. Deferasirox 500 mg
34. Octaplex 500 IU
35. Factor VIII 500–600 IU
36. Azacitidine 100 mg
37. Lenalidomide 25 mg
38. Bortezomib 3.5 mg
39. Levetiracetam 1000 mg
40. Levetiracetam 100 mg
41. Human immunoglobulin 5 Gr 5%
42. Human immunoglobulin 10 Gr 10%
43. Interferon beta 1A 30 µg
44. Interferon beta 1B 8 IU
45. Natalizumab 300 mg
46. Bosentan 125 mg
47. Somatropin 5-5.3 mg/15 IU x ml
48. Zoledronic acid 5 mg
49. Teriparatide 250 mg
50. Leuprolide acetate 3.75 mg
51. Leuprolide acetate 11.25 mg
52. Human epidermal growth factor-R
53. Imiglucerase 200 IU
54. Tenofovir Disoproxil Fumarate 300 mg
55. Peginterferon alfa-2a 180 mcg
56. Peginterferon alfa-2b 120 mcg + ribavirin
57. Peginterferon Alfa 2b 100 mcg + ribavirin
58. Peginterferon Alfa 2b 80 mcg + ribavirin
59. Boceprevir 200 mg
60. Telaprevir 375 mg
61. Basiliximab 20 mg
62. Cyclosporine 25 mg
63. Cyclosporine 100 mg
64. Everolimus 0.50 mg
65. Everolimus 0.75 mg
66. Mycophenolate mofetil 500 mg
67. Mycophenolate sodium 360 mg
68. Mycophenolate sodium 180 mg
69. Tacrolimus monohydrate XL 0.5 mg
70. Tacrolimus monohydrate XL 1.0 mg
71. Tacrolimus monohydrate XL 5 mg
72. Valganciclovir 450 mg
73. Thymoglobulin 250 mg
74. Sirolimus 1mg
75. Human albumin 20%
76. Methoxy polyethylene glycol-epoetin beta 200 mcg
77. Methoxy polyethylene glycol-epoetin beta 100 mcg
78. Methoxy polyethylene glycol-epoetin beta 75 mcg
79. Methoxy polyethylene glycol-epoetin beta 50 mcg
80. Sevelamer hydrochloride 800 mg
81. Alfacalcidol 0.25 mcg
82. Alfacalcidol 0.1 mcg
83. Iron sucrose
84. Heparin sodium
85. Calcium polystyrene sulfonate 15 G
86. Erythropoietin 4000 IU
87. Hemodialysis kit
88. Etanercept 25 mg
89. Adalimumab 40 mg
90. Infliximab 100 mg
91. Tocilizumab 200 mg
92. Tocilizumab 80 mg
93. Rituximab 100 mg
94. Rituximab 500 mg
95. Ranibizumab 10 mg/ml