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Biological drugs for the treatment of psoriasis in a public health system

Medicamentos biológicos para o tratamento de psoríase em sistema público de saúde

ABSTRACT

OBJECTIVE: To analyze the access and utilization profile of biological medications for psoriasis provided by the judicial system in Brazil.

METHODS: This is a cross-sectional study. We interviewed a total of 203 patients with psoriasis who were on biological medications obtained by the judicial system of the State of Sao Paulo, from 2004 to 2010. Sociodemographics, medical, and political-administrative characteristics were complemented with data obtained from dispensation orders that included biological medications to treat psoriasis and the legal actions involved. The data was analyzed using an electronic data base and shown as simple variable frequencies. The prescriptions contained in the lawsuits were analyzed according to legal provisions.

RESULTS: A total of 190 lawsuits requesting several biological drugs (adalimumab, efalizumab, etanercept, and infliximab) were analyzed. Patients obtained these medications as a result of injunctions (59.5%) or without having ever demanded biological medication from any health institution (86.2%), i.e., public or private health services. They used the prerogative of free legal aid (72.6%), even though they were represented by private lawyers (91.1%) and treated in private facilities (69.5%). Most of the patients used a biological medication for more than 13 months (66.0%), and some patients were undergoing treatment with this medication when interviewed (44.9%). Approximately one third of the patients discontinued treatment due to worsening of their illness (26.6%), adverse drug reactions (20.5%), lack of efficacy, or because the doctor discontinued this medication (13.8%). None of the analyzed medical prescriptions matched the legal prescribing requirements. Clinical monitoring results showed that 70.3% of the patients had not undergone laboratory examinations (blood work, liver and kidney function tests) for treatment control purposes.

CONCLUSIONS: The plaintiffs resorted to legal action to get access to biological medications because they were either unaware or had difficulty in accessing them through institutional public health system procedures. Access by means of legal action facilitated long-term use of this type of medication through irregular prescriptions and led to a high rate of adverse drug reactions as well as inappropriate clinical monitoring.

DESCRIPTORS: Psoriasis. Antibodies, Monoclonal, therapeutic use. Pharmaceutical Services, legislation & jurisprudence. Judicial Decisions. Equity in Access.

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RESUMO

OBJETIVO: Analisar o acesso e o perfil de utilização, por via judicial, de medicamentos biológicos para o tratamento de psoríase.

MÉTODOS: Estudo transversal descritivo. Foram entrevistados 203 pacientes com psoríase que demandaram medicamentos biológicos, por via judicial, ao Estado de São Paulo, entre 2004 e 2010. Informações sobre características sociodemográficas, médico-sanitárias e político-administrativas foram complementadas com dados obtidos das respectivas ordens de dispensação quanto a medicamento biológico para tratamento de psoríase e autos correspondentes. Os dados foram analisados em banco eletrônico e as variáveis sumarizadas por frequência simples. As prescrições contidas nos processos foram analisadas quanto aos preceitos legais contidos na lei.

RESULTADOS: Foram analisados 190 autos referentes aos medicamentos biológicos: adalimumabe, efalizumabe, etanercepte e infliximabe. Os proponentes obtiveram o medicamento por mandado de segurança (59,5%), sem nunca ter solicitado o medicamento biológico para outra instituição (86,2%), por sistema de saúde público ou privado. Utilizaram-se da prerrogativa de gratuidade de justiça (72,6%), embora fossem representados por advogado particular (91,1%) e atendidos em consultórios médicos privados (69,5%). Utilizaram o medicamento biológico por período > 13 meses (66,0%) e 44,9% faziam uso do medicamento no momento da entrevista. Quase um terço daqueles que deixaram de usar os medicamentos abandonou o tratamento por piora do quadro (26,6%), efeitos adversos (20,5%), falta de eficácia ou suspensão pelo médico (13,8%). Nenhuma prescrição médica atendeu aos preceitos legais; 70,3% dos pacientes não haviam realizado exames laboratoriais (hemograma, função hepática e renal) para controle do tratamento.

CONCLUSÕES: Os demandantes recorreram à via judicial para obtenção de medicamentos biológicos por desconhecimento ou por dificuldades de acesso pelas vias institucionais do sistema público de saúde O acesso facilitado pela via judicial favorece o uso do medicamento por tempo prolongado por meio de prescrições não conformes, frequência elevada de efeitos adversos e monitoramento clínico inadequado.

DESCRITORES: Psoríase. Anticorpos Monoclonais, uso terapêutico. Assistência Farmacêutica, legislação & jurisprudência. Decisões Judiciais. Equidade no Acesso.

INTRODUCTION

Psoriasis (PSO) is a recurrent, inflammatory, genetic, and chronic disease characterized by epidermal proliferation and inflammation. This disease causes scaly and erythematous lesions that target the skin, nails, and joints. The prevalence rates vary between 0.6% and 4.8% and equally affect men and women of all races.[a]

Despite showing benign progression, worsening of the conditions causes significant physical and psychological morbidity and has a major impact on the patient's quality of life. The treatment is based on the criteria of the Psoriasis Area Severity Index (PASI) and in the impact on the quality of life with respect to disease remission or increase in the period free of skin lesions.[b]

According to the national therapeutic guidelines[c] and international guidelines, the treatment of moderate to severe PSO should begin with phototherapy.[16,a,b] In case of failure,

[a] Scottish Intercollegiate Guidelines Network. Diagnosis and management of psoriasis and psoriatic arthritis in adults: a national clinical guideline. Edinburgh: SIGN; 2010 [cited 2014 Mar 31]. Available from: http://www.sign.ac.uk/pdf/sign121.pdf

[b] National Institute for Health and Clinical Excellence. Psoriasis: the assessment and management of psoriasis. London; 2012 [cited 2014 Mar 31]. Available from: http://guidance.nice.org.uk/cg153

[c] Sociedade Brasileira de Dermatologia. Consenso Brasileiro de Psoríase 2012: guias de avaliação e tratamento. 2. ed. Rio de Janeiro; 2012 [cited 2014 Mar 31]. Available from: http://www.ufrgs.br/textecc/traducao/dermatologia/files/outros/Consenso_Psoriase_2012.pdf

treatment should be continued with systemic medications (e.g., methotrexate, acitretin, and cyclosporine) before proceeding with the biological medications (e.g., etanercept, infliximab, and adalimumab). The *Protocolo Clínico e Diretrizes Terapêuticas* (PCDT – Clinical Protocol and Therapeutic Guidelines) for the treatment of PSO in the Public Health System (SUS) was published in 2013.[d] The treatment excludes biological medications and follow-up includes clinical monitoring of the evolution of disease and analysis of adverse drug reactions.

The access to biological medicines is achieved through the judicial system or via administrative means, which makes it difficult to plan and manage the expenses involved.[2,6,16] The latter is implemented by some health departments to request medications that are not available at SUS but both generate a conflict regarding the principle of comprehensiveness proposed by SUS.

The process that plaintiffs undergo to obtain access to biological medications is challenging, and the data pertaining to drug use, prescription, and effects (results and safety) are scarcely available. In addition, the documentation regarding the judicialization process is rarely disclosed in this type of study. Therefore, the purpose of our study was to analyze the access and utilization profile, obtained by judicial means, of biological medications for the treatment of PSO in Brazil.

METHODS

We performed a descriptive cross-sectional study with patients with PSO who were either undergoing treatment or had been treated with biological medications by means of judicial actions against the state of Sao Paulo between 2004 and 2010.

The dispensation orders (DO) containing the biological medication to be supplied per patient with PSO (International Classification of Diseases – ICD-L40), which was made available by the court control system of the Sao Paulo State Health Department (SCJ/SES-SP), provided an estimate of the population under treatment in the referred period. The following variables were collected: contested medication, author and type of action, and sociodemographic characteristics of the plaintiff and prescriber.

After locating corresponding records, we analyzed the documents presented to the court with information regarding the medical report, prescription, legal representation, type of injunction, appointed justice system, defendant, civil or district court, and the origin of prescription.

Patients who had retrieved and used biological medication during our study period and were willing to participate were included. They were found through injunctions filed against the state government, with a judicial decision in favor of the authors in any instance that were submitted to 14 public circuit courts of the capital of the State of Sao Paulo. We excluded patients who provided their contact as their lawyer's office number, those who were not located after five attempts, and deceased patients.

Telephone contact was elected because it is effective and inexpensive.[10] All interviews were performed using the computer-assisted telephone interviewing technique, with the use of a microcomputer coupled to a telephone device with a headset; specific management and recording software were connected simultaneously. This apparatus allows monitoring interviews, avoiding inconsistencies in the questionnaire and developing features related with research management such as automatic control of follow-up calls, control of time per interview/interviewer, remote listening system, and real time control.

We developed a Microsoft Office Access® electronic form, based on the instrument used for the interviews with 16 screens to record the data. The language of the questionnaire was adapted for a telephone conversation. The team of interviewers was previously trained to standardize language and interview time.

The questionnaire included the following information: patient, type of medical assistance, access to medication for the treatment of PSO before the injunction, participation in a support group, meetings with the lawyer, contact with the pharmaceutical manufacturer, evolution of the disease, and use of medicine (time involved in diagnosis and treatment), provided pharmacotherapy follow-up, and suspected adverse drug reactions. This instrument[e] was previously validated by rheumatology and public health experts. The SCJ/SES-SP data, regarding injunctions and interviews, were organized in an electronic spreadsheet. The data was analyzed with the 2013 version of Excel® software, and the results were shown as simple variable frequencies. The quality control of data collection was achieved by periodic crosschecking of information, which was performed by one of the researchers who was not part of the on-the-spot data collection.

The prescriptions involved in the proceedings were analyzed in terms of legal provisions of the Law 5.991/1973.[f]

Data collection was authorized by the Health Department of Sao Paulo State. This study was approved by the Research Ethics Committee of the University of Sorocaba (Protocol 011/2009 of August 17, 2009), according to

[d] Ministério da Saúde, Secretaria de Atenção à Saúde. Portaria nº 1.229, de 5 de novembro de 2013. Aprova o Protocolo Clínico e Diretrizes Terapêutica da Psoríase. *Diario Oficial Uniao*. 6 nov 2013;Seção 1:52.

[e] For those interested in the questionnaire, please contact the authors.

[f] Presidência da República. Lei nº 5.991, de 17 de dezembro de 1973. Dispõe sobre o Controle Sanitário do Comércio de Drogas, Medicamentos, Insumos Farmacêuticos e Correlatos, e dá outras Providências. Brasília (DF); 1973[cited 2014 Mar 31]. Available from: http://www.planalto.gov.br/ccivil_03/leis/L5991.htm

Resolution 196/96 of the National Health Council. All participants signed the informed consent form.

RESULTS

A total of 25,184 DO were analyzed regarding the lawsuits filed to obtain medication and other health products between 2004 and 2010. Of 218 identified patients, 11 did not meet the inclusion criterion and 4 were excluded. Of 203 interviewed plaintiffs, 190 processes were located (Figure).

Adalimumab, etanercept, infliximab, and efalizumab were part of these DO. The sociodemographic characteristics and the process toward access to a biological medicine are described in Table 1. A total of 44.9% patients used a biological medicine, of which 89.7% never requested the medicine to SUS before filing a lawsuit. Patients with access to private medical care (69.5%) were assisted by SUS (3.5%). Among SUS patients (30.5%), 12.9% were treated at University Hospitals (*Hospital São Paulo*, Puccamp, HU-USP, ABC Santo André University and Unicamp) (Table 1).

All patients treated with efalizumab (banned in Brazil since 2009) (n = 43) were not taking this medicine any longer when interviewed. Approximately 20.5% of the patients discontinued the use of biological medicines due to suspicion of adverse drug reactions which was confirmed by doctors. Adverse drug reactions included local reactions (70.0%), hospitalization after use of medicine, cardiovascular events (arrhythmia and high blood pressure), liver disease, blood dyscrasia, pneumonia, and kidney injury. The majority of patients discontinued using the biological medicine due to dropout (26.6%) or suspension by the physician (13.8%), which was caused by their worsening condition or lack of efficacy of medication (Table 2).

The highest request rate was for infliximab (57.4%), followed by efalizumab (21.6%), etanercept (16.3%), and adalimumab (4.7%). The *Associação dos Portadores de Vitiligo e Psoríase do Estado de São Paulo* (APVPESP – Association of Vitilligo and Psoriasis Patients of Sao Paulo State) provided legal representation to 12.6% patients (Table 3).

Of the 42 lawyers that represented the 203 plaintiffs in 90 lawsuits, three lawyers (7.1%; Group A) filed 88 (46.3%) lawsuits; four lawyers (9.5%; Group B) filed 42 lawsuits (22.1%); and 35 lawyers (83.3%; Groups C and D) filed between one and seven lawsuits each.

A total of 189 medical prescriptions attached to the lawsuits (n = 190) were analyzed. One lawsuit did not provide a prescription for the medicine etanercept. Legible names of patients were also absent in 5.3% of prescriptions. Neither the generic name of the medicine nor the pharmaceutical dosage form were reported in 59.8% of cases, among other missing or incomplete information that are required by law, totaling 94.7% of cases (Table 4).

DISCUSSION

The majority of the analyzed lawsuits (n = 190) did not explicitly justify the prescription of a biological medicine or provide information regarding previous treatment, evolution of the disease, supplementary exams, or diagnoses according to the ICD-10. Applicants used biological medicines for periods of more than 13 months (4.0% of the patients have been using this medicine for > 49 months), which extrapolates any follow-up of a high-quality clinical study up to this date.[8,14] As for medicine discontinuation, 11.3% of the patients were discontinued because of either suspicion of an adverse drug reaction or by their own or their physician's decision, which was always related with worsening of the condition or lack of efficacy of the medicine. Ninety-one patients were still using a biological medicine when interviewed.

Patients (n = 203) were mostly male, age ranging from 19 to 59 years, and residing in Sao Paulo. They acquired the medicine through an injunction, obtained in 7-10 days (average time). They used the prerogative of free legal aid, despite having legal representation by a private lawyer and having been assisted in private care facilities. Three private lawyers represented patients in more than 40.0% of these lawsuits filed against the state.

Instructions to obtain medicines via judicial process came from the medical doctors who assisted these patients (approximately three clinical practitioners prescribed 80.0% of requested medicines). Approximately 60.0% of patients never had a meeting with their lawyers, having signed power of attorneys at the doctor's office. In 20.0% of lawsuits, a Non-governmental organization (patient associations) was responsible for instructing patients to request a medicine through the courts.

All patients visited their doctors once a year, but 70.3% of them visited for follow-up laboratory examinations (blood work, liver and kidney function tests), which would help them to detect possible adverse drug reactions.[a]

Whilst the use of biological medication for the treatment of moderate to severe PSO is considered a therapeutic breakthrough with some short-term effectiveness and tolerance,[a] meta-analyses[1,17] and field synopses[g] advise caution in terms of long-term effectiveness and safety. National and international references[3,15,a,c] recommend these medicines as a third line of action, followed by careful monitoring for early identification of adverse drug reactions.

[g] Naldi L, Rzany B. Psoriasis (chronic plaque). *Clin Evid(Online)*. 2009[cited 2014 Mar 31];2009:1706. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2907770/pdf/2009-1706.pdf

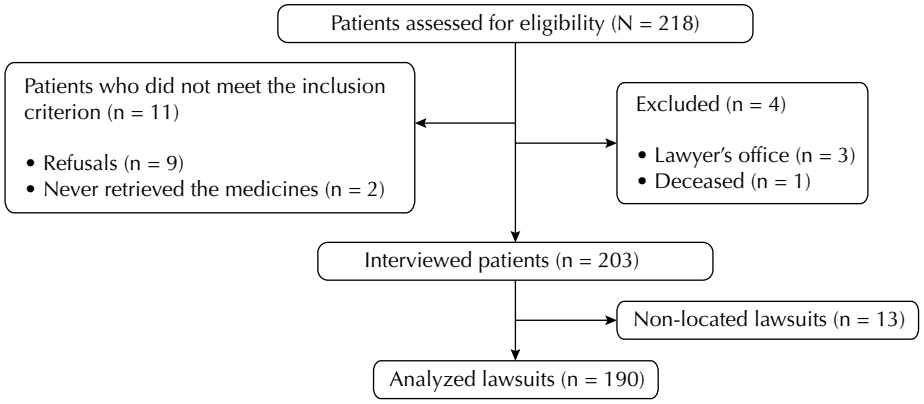

Figure. Flowchart of the phases of sample composition. State of Sao Paulo, 2004-2010.

Biological medications are administered via the IV route,[9] which can cause several local reactions, which were experienced by the patients in our study. Adverse drug reactions differ from those caused by conventional chemical compounds because they are heterogeneous[5,11,18] and may appear years after patients discontinue their use.[4] Adverse drug reactions resulting from 1 year of use include malignancies, opportunist infections caused by fungi, tuberculosis, hypertension, among others.[13,14] Clinical monitoring of patient, as well as of the way to use the medication, duration of use, dose, and recommendations to patients are all essential ways to reduce and control these events.

The fact that the court granted petitions containing prescriptions lacking not only relevant legal requirements (almost 100% of this study) but also important data (name of patient, name of the prescribing practitioner registered in local Regional Medical Board, date, duration of treatment, dose, generic name, among others), which are fundamental elements for proper prescribing and compulsory under current legislation, highlights the faulty drug use rationale evident in these petitions. Moreover, the situation exposes these plaintiffs to risks (disability, death) and also leads to other health issues (use of hospital beds, chronic treatments due to disability, among others) for the Health System, including direct and indirect costs.

The (i) recommendations of the *Comissão Nacional de Incorporação e Tecnologias* (National Committee of Technology Incorporation) of SUS; (ii) Law 12.401/2011[h] regarding therapeutic assistance and health technology incorporation in the scope of SUS; (iii) Decree 7.508/2011,[i] with provisions related to planning, health assistance, and joint federal actions; and (iv) the current PCDT,[d] do not recommend the use of these agents for the treatment of PSO. Brazilian physicians, even those working in SUS (30.5%) (Table 1), do not comply with the official recommendations and prescribe these agents to patients with PSO.

The supply of biological medicines used to treat PSO in the state of Sao Paulo is offered via registration of administrative requests in the *Componente Especializado da Assistência Farmacêutica* (CEAF – Specialized Pharmaceutical Care Program) but it does not require a proper clinical protocol follow-up of patients. After the publication of Resolution SS-54, of May 11, 2012,[j] a *Comissão de Farmacologia* (Pharmacology Committee) was established in SES-SP to provide a computerized processing of administrative requests. It is the prescribing practitioner's responsibility to justify the need for a biological medicine. However, although the above measures have favored the management of requests and granted them a technical nature (based on scientific eligibility for the use of medicines), they have not lowered the number of lawsuits requesting biological medicines.

The majority of patients with PSO (69.5%) pursue a biological medicine through the public system, but their prescription is generated by a private system. Doctors' visits and monitoring are performed at private facilities and medicines are supplied by the public system. Patient care is not comprehensive in any of the pathways, which does not comply with the principles of SUS.

[h] Presidência da República. Lei nº 12.401, de 28 de abril de 2011. Altera a Lei nº 8.080, de 19 de setembro de 1990, para dispor sobre a assistência terapêutica e a incorporação de tecnologia em saúde no âmbito do Sistema Único de Saúde - SUS. Brasília (DF); 2011 [cited 2014 Mar 31]. Available from: http://www.planalto.gov.br/ccivil_03/_Ato2011-2014/2011/Lei/L12401.htm

[i] Presidência da República. Decreto nº 7.508, de 28 de junho de 2011. Regulamenta a Lei nº 8.080, de 19 de setembro de 1990, para dispor sobre a organização do Sistema Único de Saúde - SUS, o planejamento da saúde, a assistência à saúde e a articulação interfederativa, e dá outras providências. Brasília (DF); 2011 [cited 2014 Mar 31]. Available from: http://www.planalto.gov.br/ccivil_03/_ato2011-2014/2011/decreto/D7508.htm

[j] Secretaria de Estado da Saúde de São Paulo. Resolução SS-54, de 11 de maio de 2012. Aprova, no âmbito da Pasta, estrutura e funcionamento da Comissão de Farmacologia da Secretaria de Estado da Saúde de São Paulo, e dá outras providências. *Diario Oficial Estado Sao Paulo*. 12 maio 2012;Seção 1:37. [cited 2014 Mar 31]. Available from: www.adj.org.br/download/pdf/2012jur_resol54.pdf

Table 1. Sociodemographic characteristics and ways used to gain access to biological medicines to treat PSO by the authors of injunction filed against the state of Sao Paulo, 2004-2010.

Variable	Adalimumab		Efalizumab		Etanercept		Infliximab		Total	
	%	n	%	n	%	n	%	n	%	n
	6.8	14	21.2	43	17.3	35	54.7	111	100.0	203
Gender										
Male	64.3	9	60.5	26	60.0	21	65.8	73	63.6	129
Female	35.7	5	38.6	17	40.0	14	34.2	38	36.4	74
City										
Sao Paulo	85.7	12	46.5	20	71.4	25	58.6	65	60.1	122
Other locations	14.3	2	53.5	23	26.6	10	41.4	46	39.9	81
Age (years)										
19 to 59	57.1	8	81.4	35	74.3	26	78.4	87	76.8	156
≥ 60	42.9	6	18.6	8	25.7	9	21.6	24	23.2	47
Type of medical assistance										
Non-SUS	92.9	13	62.8	27	65.7	23	70.3	78	69.5	141
SUS	7.1	1	37.2	16	34.3	12	29.7	33	30.5	62
Registered at CEAF										
Information provided by the patient (Yes)	42.9	6	65.1	28	40.0	14	51.4	57	51.7	105
Information confirmed in the system (Yes)	71.4	10	0.0	0	34.3	12	4.5	5	13.3	27
Patient was being treated by a biological medicine[a]	50.0	7	0.0	0	25.7	9	0.9	1	8.4	17
Guidance to obtain a biological medicine via lawsuit										
Doctor	71.4	10	79.1	34	80.0	28	72.1	80	74.9	152
NGO, Family, and others	14.3	2	11.6	5	34.3	12	37.0	41	6.9	60
Lawyer	0.0	0	4.7	2	0.0	0	2.7	3	2.5	5
Pharmaceutical Laboratory	7.1	1	4.7	2	0.0	0	1.8	2	2.5	5
NI	7.1	1	0.0	0	0.0	0	0.9	1	1.0	2
Use of biological medicine before lawsuit										
Yes	92.9	13	93.0	40	65.7	23	95.5	106	89.7	182
NI	0.0	0	0.0	0	0.0	0	3.6	4	2.0	4
Form of acquisition of medicine beforelawsuit										
Pharmaceutical laboratory	7.1	1	6.8	3	14.3	5	0.0	0	4.4	9
Other (city hall, State, NGO)	0.0	0	0.0	0	8.6	3	0.9	1	2.0	4
Supplied by doctor	0.0	0	0.0	0	5.7	2	0.0	0	1.0	2
Own resources	0.0	0	0.0	0	2.9	1	0.0	0	0.5	1
NI	0.0	0	0.0	0	2.9	1	0.0	0	0.5	1
Request of medication for an institution[b] before filing the lawsuit										
No	92.9	13	95.3	41	77.1	27	84.7	94	86.2	175
NI	0.0	0	0.0	0	0.0	2	1.8	2	2.0	4
Institution activated for provision of medicine before lawsuit										
Private[c]	0.0	0	0.0	0	5.7	2	9.0	10	5.9	12
Public	7.1	1	2.3	1	17.1	6	2.7	3	5.4	11
NGO	0.0	0	2.3	1	0.0	0	0.0	0	1.5	1
Request fulfilled										
Yes	7.1	1	0.0	0	2.9	1	1.8	2	1.5	3
Supply of biological medication by another institution (time in months)										
< 6	0.0	0	0.0	0	0.0	0	1.8	2	0.5	2
> 6	7.1	1	0.0	0	2.9	1	0.0	0	0.5	1

Continue

Continuation										
Participation in a support group for patients										
Yes	14.3	2	11.6	5	17.1	6	9.0	10	11.3	23
Number of meetings with the lawyer										
None	64.3	9	58.1	25	62.9	22	62.2	69	61.6	125
One or more	35.7	5	34.9	15	34.3	12	37.9	42	36.5	74
NI	0.0	0	7.0	3	2.9	1	0.9	0	2.5	4
Contacted by the pharmaceutical laboratory										
Yes	64.3	9	62.8	27	62.9	22	37.9	42	49.3	100

NI: not informed; SUS: Public Health System; NGO: Non-governmental organizations; CEAF: Specialized Pharmaceutical Care Program
[a] Patients who were receiving a biological medicine because they were registered at CEAF.
[b] Any public or private institution (City hall, NGO, laboratory, and others).
[c] Laboratory, private hospitals.

Table 2. Features of the pharmacotherapy follow-up provided to the plaintiff. Sao Paulo, SP, Southeastern Brazil, 2004-2010.

Variable	Adalimumab		Efalizumab		Etanercept		Infliximab		Total	
	%	n	%	n	%	n	%	n	%	n
	6.8	14	21.2	43	17.3	35	54.7	111	100.0	203
Diagnosis time										
≥ 6 years	85.7	12	90.7	39	85.7	30	86.5	96	87.2	177
2 to 5 years	14.3	2	9.3	4	14.3	5	12.6	14	12.3	25
Up till 6 months	0.0	0	0.0	0	0.0	0	0.9	1	0.5	1
Concurrent disease										
Yes	50.0	7	51.1	22	37.1	13	29.8	33	37.0	75
Treatment time with biological medicine (months)										
Up to 12	35.7	5	51.2	22	22.9	8	30.6	34	34.0	69
13 to 48	35.7	5	48.9	21	74.3	26	66.7	74	62.0	126
49 to 72	28.6	4	0.0	0	2.9	1	2.7	3	4.0	8
Average (SD)	31.4 (22.2)		16.8 (10.2)		26.4 (14.4)		25.2 (14.6)		24.0 (14.9)	
Patient was using obtained biological medicine										
Yes	64.3	9	0.0	0	62.9	22	54.0	60	44.9	91
Clinical monitoring[a]										
Medical visit	100.0	9	0.0	0	100.0	22	100.0	60	100.0	91
Laboratory exams	55.5	5	0.0	0	68.2	15	73.3	44	70.3	64
Reasons to discontinue the use of biological medicine										
Stopped using[b]	0.0	0	100	43	5.7	2	8.1	9	26.6	54
Suspension by the doctor	14.3	2	0.0	0	22.9	8	16.2	18	13.8	28
Suspicion of ADR	21.4	3	0.0	0	5.7	2	16.2	18	11.3	23
Suspended by a court decision	0.0	0	0.0	0	2.9	1	6.4	6	34.5	7
Perception of the efficacy of the biological medicine										
Yes	71.4	10	76.2	32	91.4	32	82.0	91	81.3	165
No	28.6	4	21.0	9	8.6	3	17.1	19	17.2	35
NI	0.0	0	4.7	2	0.0	0	0.9	1	2.7	3
Perception of the evolution of the disease with the use of biological medicines										
Improved/Cured	57.1	8	60.5	26	71.4	25	67.6	75	66.0	134
Stationary	28.6	4	23.3	10	20.0	7	21.7	24	22.2	45
Worsened	14.3	2	11.7	5	2.9	1	10.9	12	9.9	20
NI	0.0	0	4.7	2	5.7	2	0.0	0	2.0	4

NI: not informed; ADR: adverse drug reactions, SD: standard deviation
[a] According to recommendations of therapeutic guidelines.
[b] Other reasons.

Table 3. Technical characteristics of injunctions filed against the state of Sao Paulo, 2004-2010.

Variable	Adalimumab		Efalizumab		Etanercept		Infliximab		Total	
	%	n	%	n	%	n	%	n	%	n
	4.7	9	21.6	41	16.3	31	57.4	109	100.0	190
Number of authors per injunction										
1	11.1	1	95.1	39	93.5	29	100.0	109	93.7	178
2 to 6	88.9	8	4.9	2	6.5	2	0.0	0	6.3	12
Type of injunction										
CI	88.9	8	48.8	20	58.1	18	61.5	67	59.5	113
RO	11.1	1	51.2	21	41.9	13	37.5	41	40.0	76
Public Defender	0.0	0	0.0	0	0.0	0	0.9	1	0.5	1
Civil Society Representation										
No	100.0	9	51.2	21	96.8	30	92.7	101	84.7	161
Yes	0.0	0	48.8	20	3.2	1	7.3	8	15.3	29
Defendant										
State	88.9	8	100.0	41	100.0	31	100.0	109	99.5	189
Union	11.1	1	0.0	0	0.0	0	0.0	0	0.5	1
Judicial Representation										
Private	100.0	9	48.8	20	96.8	30	92.7	101	84.2	160
APVPESP	0.0	0	48.8	20	3.4	1	2.8	3	12.6	24
MP	0.0	0	2.4	1	0.0	0	1.8	2	1.6	3
PD	0.0	0	0.0	0	0.0	0	2.8	3	1.6	3
Free Legal Aid										
Yes	56.6	5	75.6	31	64.5	20	75.2	82	72.6	138
No	11.1	1	12.2	5	9.7	3	16.5	18	14.2	27
NI	33.3	3	12.2	5	25.8	8	8.3	9	13.2	25
Primary injunction										
Yes	88.9	8	53.7	22	61.3	19	56.0	61	57.9	110
No	11.1	1	31.7	13	25.8	8	24.4	32	28.4	54
NI	0.0	0	14.6	6	12.9	4	14.7	16	13.7	26
District injunction /Civil injunction of Sao Paulo/Osasco										
1 to 5	55.6	5	43.9	18	35.5	11	30.3	33	35.3	67
6 to 10	44.4	4	29.3	12	41.9	13	46.8	51	42.1	80
11 to 14	0.0	0	26.8	11	22.6	7	21.1	23	21.6	41
Osasco (1 to 2)	0.0	0	0.0	0	0.0	0	1.8	2	1.1	2
Legal representation of author(s) – OAB										
A	88.9	8	48.8	20	0.0	0	55.0	60	46.3	88
B	11.1	1	4.9	2	35.5	11	25.7	28	22.1	42
C	0.0	0	39.0	16	22.6	7	4.6	5	14.7	28
D	0.0	0	2.4	1	41.9	13	11.9	13	14.2	27
PD	0.0	0	2.4	1	0.0	0	2.8	3	2.1	4
NI	0.0	0	2.4	1	0.0	0	0.0	0	0.5	1

CI: court injunction; RO: ordinary proceedings; PD: Public Defender; MP: Public Prosecutor's Office or Public Ministry; APVPESP: Association of Vitilligo and Psoriasis of the state of Sao Paulo; NI: not informed; OAB: Brazilian Bar Association; A: three lawyers had between 21 and 35 representations; B: four lawyers had between 10 and 13 representations; C: 12 lawyers had between two and seven representations; D: 22 lawyers had at least one representation per medicine

Table 4. Medical prescriptions linked to lawsuits, according to legal precepts(Law 5.991/1973).[a] Sao Paulo, SP, Southeastern Brazil, 2004-2010.

Variable	Adalimumab		Efalizumab		Etanercept		Infliximab		Total	
	%	n	%	n	%	n	%	n	%	n
	4.8	9	21.7	41	15.9	30	57.7	109	100.0	189
Legible name of author (patient)										
No	0.0	0	2.4	1	6.7	2	6.4	7	5.3	10
Author's address (patient)										
No	100.0	9	100.0	41	100.0	30	100.0	109	100.0	189
Generic name										
No	77.8	7	39.0	16	66.7	20	64.2	70	59.8	113
Trade name										
No	22.2	2	0.0	0	23.3	7	21.1	23	16.9	32
Pharmaceutical form										
No	88.9	8	100.0	41	86.7	26	95.4	104	94.7	179
Concentration										
No	44.4	4	58.5	24	13.3	4	19.3	21	28.0	53
Administration route										
No	11.1	1	12.2	5	13.3	4	20.2	22	16.9	32
Dosage										
No	11.1	1	53.7	22	66.7	20	56.0	61	55.0	104
Duration of treatment										
No	77.8	7	85.4	35	90.0	27	89.9	98	88.4	167
Interval between doses										
No	11.1	1	7.3	3	16.7	5	13.8	15	12.7	24
Total quantity										
No	77.8	7	85.4	35	90.0	27	89.9	98	88.4	167
Name of the Doctor										
No	0.0	0	2.4	1	3.3	1	3.7	4	3.2	6
CRM										
No	0.0	0	0.0	0	0.0	0	0.9	1	0.5	1
Illegible	0.0	0	7.3	3	16.7	5	11.9	13	11.1	21
Address of prescribing practitioner's medical institution										
No	0.0	0	4.9	2	3.3	1	10.1	11	7.4	14
Date										
No	0.0	0	4.9	2	0.0	0	11.0	12	7.4	14
Illegible	0.0	0	0.0	0	0.0	0	0.9	1	0.5	1

Source: lawsuits. Coordination of Strategic Demands of SUS (Codes). Health Department of Sao Paulo State.
CRM: *Conselho Regional de Medicina* (Regional Council of Medicine)
[a] Presidência da República. Lei nº 5.991, de 17 de dezembro de 1973. Dispõe sobre o Controle Sanitário do Comércio de Drogas, Medicamentos, Insumos Farmacêuticos e Correlatos, e dá outras Providências. Brasília (DF); 1973 [cited 2014 Mar 31]. Available from: http://www.planalto.gov.br/ccivil_03/leis/L5991.htm

The pharmaceutical manufacturers maintained frequent contact with more than 50.0% of patients. This suggests possible influence on patients' needs, transforming them into legal demands.

The legal request of medicines without scientific evidence weakens pharmaceutical services because it exposes the patient to risks and promotes the financing of technologies devoid of proper proof of efficacy and safety.[6,8] Efalizumab was approved for the treatment of PSO in the USA and Europe in 2003. Its marketing was suspended due to safety concerns in 2009 (three cases of progressive multifocal leukoencephalopathy), in addition to efficacy issues, rending it inferior to other biological medicines.[5] Then, the access to this drug was obtained via lawsuits in Brazil.

Approximately 21.2% of patients in our study gained access to efalizumab via lawsuits deferred by the state of Sao Paulo.

Most of the interviewees were diagnosed more than six years ago. Some of the data may have suffered from recall bias. Patients who are still being treated with a biological medicine have been receiving it for more than 24 months. On the other hand, most of the data was crosschecked with the SES-SP database and with the clinical lab results provided by the patients themselves during interviews. The utilization data of biological medications were confirmed by the pharmacy from which each of the patients received these medicines.

Considering the limitations of any observational study, the results of this study may play an important role in the process of decision making in Public Health in Brazil. To the best of our knowledge, this is the first set of data on the use of biological medicines by patients with PSO financed by judicial demands in Brazil. This is important information for dermatologists, because it provides a real-life view of clinical practice, a goal that is hard to achieve with randomized controlled clinical trials.

Some treatments are associated with potentially serious adverse drug reactions. Therefore, in the long-term observational studies may provide additional and important information for doctors, users, manufacturers and researchers to assess the risks and benefits of treatments.

To perceive the public health system as one that may provide services without the requirements of in-place regulation, planning, forecasting of financial resources or epidemiological background is imprudent and can collapse the system.

The plaintiffs selected the judicial procedures to obtain biological medicines because they are either unaware of other routes or find difficulty in accessing the institutional pathways of SUS. Easy access provided by courts favors the use of biological medicines for an extended period of time through irregular prescriptions, the high frequency of adverse drug reactions and inappropriate clinical monitoring. Strict compliance to PCDT may guarantee access, effectiveness, and safety of an appropriate therapy for PSO.

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HIGHLIGHTS

This study aimed to analyze the legal access to and usage profile of biological drugs for the treatment of psoriasis. The legal access to medications distorts planning and spending and undermines the principle of a comprehensive health care system proposed by the Brazilian Unified Health System (SUS).

A total of 203 applicants were interviewed, and 190 patients requiring biological drugs for psoriasis (adalimumab, efalizumab, etanercept, and infliximab) were examined. The patients obtained the drugs through a writ of mandamus (59.5%); without the need to request the drugs from another institution, either private or through SUS (86.2%); and using the prerogative of gratuity justice (72.6%). However, 91.1% of the patients were represented by a private attorney, 69.5% received assistance in private medical offices, and 60.0% had never met with their attorneys and therefore needed to sign proxies at the doctor's office.

In addition, 20.5% of the patients discontinued the use of biological drugs because they reported suspected adverse reactions previously confirmed by doctors – reactions at the application site, hospitalization after medication use, cardiovascular events (arrhythmia, hypertension), liver disease, blood dyscrasia, pneumonia, renal injury, etc. Most patients discontinued the use of these drugs on their own (26.6%) or following doctor's recommendation (13.8%) because of the worsening of the clinical status or lack of efficacy.

Important differences between clinical practice and guideline recommendations are evident in the treatment of these patients.

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Scientific Editor