Endokrynologia Polska
DOI: 10.5603/EP.2015.0022
Tom/Volume 66; Numer/Number 2/2015
ISSN 0423–104X

Dosage and costs of lanreotide Autogel 120 mg administered as part of routine acromegaly care in Poland — two years of data from Lanro-Study

Dawkowanie i koszt lanreotydu Autogel 120 mg stosowanego w leczeniu akromegalii w Polsce — wyniki 2-letniego badania Lanro-Study

Ewa Orlewska[1], Beata Kos-Kudła[2], Jerzy Sowiński[3], Krzysztof Sworczak[4], Wojciech Zgliczyński[5] and the Lanro-Study Group*

[1]Faculty of Health Sciences, the Jan Kochanowski University, Kielce, Poland
[2]Division of Endocrinology, Department of Pathophysiology and Endocrinology, SMDD Zabrze, Medical University of Silesia, Katowice, Poland
[3]Chair and Department of Endocrinology, Metabolism and Internal Diseases, Poznan University of Medical Sciences, Poland
[4]Endocrinology and Internal Diseases Department, Medical University, Gdansk
[5]Centre of Postgraduate Medical Education, Warsaw, Poland

**Lanro-Study investigators: Elżbieta Andrysiak-Mamos (Szczecin), Anna Babińska (Gdańsk), Agata Bałdys-Waligórska (Kraków), Elżbieta Bandurska-Stankiewicz (Olsztyn), Krzysztof Błaut (Gdańsk), Paweł Bolko (Plewiska), Wanda Foltyn (Katowice), Danuta Jakubczyk (Białystok), Aleksandra Jawiarczyk-Przybyłowska (Wrocław), Roman Junik (Bydgoszcz), Olga Juraniec (Bydgoszcz), Ewelina Lewkowicz (Kraków), Anna Lewczuk (Gdańsk), Beata Matyjaszek-Matuszek (Lublin), Krzysztof Michałek (Poznań), Sławomir Mucha (Łódź), Renata Orłowska-Florek (Rzeszów), Marta Peszel-Barlik (Tarnowskie Góry), Sławomir Pynka (Szczecin), Violetta Rosiek (Katowice), Marek Ruchała (Poznań), Joanna Rutkowska (Olsztyn), Julia Słynko-Krzyzostaniak (Poznań), Agnieszka Stefańska (Kraków), Janusz Strzelczyk (Katowice), Anhelli Syrenicz (Szczecin), Małgorzata Trofimiuk-Müldner (Kraków), Joanna Waligórska-Stachura (Poznań), Ryszard Waśko (Poznań), Przemysław Witek (Warszawa), Danuta Zalewska-Rydzkowska (Bydgoszcz), Piotr Zdunowski (Warszawa), Anna Zemczak (Katowice)*

Abstract

Introduction: to evaluate, over 24 months of prospective follow-up, the dosage and costs of lanreotide AUTOGEL 120 mg (ATG120) administered as part of routine acromegaly care in Poland.

Material and methods: A multicentre, non-interventional, observational prospective study on resource utilisation in Polish acromegalic patients treated with ATG120 at 4-week or extended (> 4 weeks) dosing interval. The study population consisted of adult acromegalic patients treated for at least 3 injections of ATG120. The endpoints were: percentage of patients treated with ATG120 at an extended dosing interval (> 4 weeks), mean time between injections, and the cost of ATG120 during a 24-month prospective observation. Costs were calculated in PLN from the public health-care payer and patient perspective for the year 2014.

Results: 143 patients were enrolled in, and 132 completed (70% women, 81% macroadenoma, 75% previous surgery) the analysis. During two years, changes in the treatment pattern were reported in 41 patients: 17% of them had increased injection interval and 10% switched to octreotide LAR and then returned to ATG120. Sixty-three patients (48%) received ATG120 at an extended dosing interval. ATG120 was predominantly administered in an out-patient setting (84%) by a health care professional (97%).

Conclusions: The results demonstrated that extended dosing interval of ATG120 is used in a substantial proportion of patients in routine clinical practice in Poland. Such findings support the potential for ATG120 in reducing treatment burden in the real-world clinical environment. **(Endokrynol Pol 2015; 66 (2): 142–148)**

Key words: *acromegaly; lanreotide Autogel; clinical study; cost of treatment*

Streszczenie

Wstęp: Ocena schematu dawkowania i kosztu lanreotydu Autogel 120 mg (ATG120) stosowanego w leczeniu akromegalii w Polsce.

Materiał i metody: Wieloośrodkowe, nieinterwencyjne, obserwacyjne badanie prospektywne oceniające zużycie zasobów ochrony zdrowia w populacji polskich pacjentów z akromegalią leczonych ATG120 z zastosowaniem 4-tygodniowego lub wydłużonego (> 4 tygodni) odstępu między dawkami leku. Do badania włączani byli dorośli pacjenci, którzy otrzymali co najmniej 3 dawki ATG120. Horyzont czasowy badania wynosił 24 miesięcy. Koszt leku obliczono z perspektywy płatnika publicznego i pacjenta w 2014 roku.

Wyniki: Do badania włączono 143 pacjentów, 132 z nich ukończyło badanie (70% kobiet, u 81% makrogruczolak, 75% było wcześniej leczonych chirurgicznie). W czasie 2 lat zmiany schematu leczenia dokonano u 41 chorych, u 17% z nich wydłużono odstęp między dawkami, u 10% - zmieniono lek na oktreotyd LAR a potem ponownie zastosowano ATG120. U 63 pacjentów (48%) odstęp pomiędzy dawkami ATG120 wynosił > 4 tygodnie. ATG120 był przeważnie podawany ambulatoryjnie (84%) przez fachowy personel medyczny (97%).

Ewa Orlewska M.D., Ph.D., Faculty of Health Sciences, the Jan Kochanowski University, Al. IX wieków Kielc, 25–317 Kielce, tel.: 601 151 989, e-mail: ewaorlewska@tlen.pl

Wnioski: Badanie wykazało, że w codziennej praktyce klinicznej u znaczącego odsetka pacjentów odstęp czasowy pomiędzy kolejnymi dawkami ATG120 jest dłuższy niż 4 tygodnie. Wynik ten potwierdza tezę, że dzięki stosowaniu ATG120 można obniżyć koszty leczenia akromegalii. **(Endokrynol Pol 2015; 66 (2): 142–148)**

Słowa kluczowe: *akromegalia; lanreotyd Autogel; badanie kliniczne; koszt leczenia*

The study was founded by Ipsen Poland.

Introduction

Lanreotide, one of two commercially available somatostatin receptor ligands (SRLs), is an established treatment for patients with acromegaly following unsuccessful pituitary surgery, in preparation for surgical treatment, and as a long-term therapy if surgical treatment cannot be used [1]. A recent European study, PRIMARYS, designed to assess if ATG120 used as first-line therapy in patients with macroadenoma could reduce tumour volume, confirmed that in such therapy ATG120 not only improved symptoms and attenuated or normalised growth hormone (GH) and insulin-like growth factor 1 (IGF-1) hypersecretion, but also reduced tumour volume and improved quality of life [2]. The results showed a clinically relevant effect as expressed by the 63% of patients with a 20% or more tumour volume reduction [2].

Both SRL agents, lanreotide and octreotide, have been approved as depot formulations and are administered monthly, with an approved extension of a 6- to 8-week injection interval possible for lanreotide [1]. The possibility of extending dosing intervals of drugs administered in injections may positively influence patients' preference to treatment, compliance, and quality of life [1]. Studies have been conducted to investigate the efficacy and acceptability of extending the dosing interval beyond monthly [3, 4]. One study, conducted in Germany, enrolled patients who were previously treated with octreotide LAR doses of 10 mg, 20 mg, and 30 mg monthly and then switched to lanreotide AUTOGEL 120 mg (ATG120) at intervals of every 56, 42, and 28 days, respectively [3], and the other was an international study enrolling patients well controlled on octreotide 10 or 20 mg (LEAD study) [4]. The results demonstrated for both studies that extended dosing is effective at achieving biochemical control with at least similar rates of control in patients who responded to the somatostatin analogues. Investigators judged the injections with lanreotide to be easier than using octreotide LAR, and patients preferred receiving injections less frequently. A recent study evaluating the efficacy and safety of extended dosing intervals with ATG120 in patients with acromegaly previously controlled with conventional doses of octreotide LAR every four weeks demonstrated that extended dosing intervals were associated with patient preference over octreotide [5].

So far, limited data have been published concerning dosing patterns and the cost of somatostatin analogues used for treatment of acromegalic patients in routine clinical practice [5, 6]. Findings that in a one-year time horizon approximately 50% of patients could be treated with dose intervals of longer than 28 days document the potential of ATG 120 to reduce treatment burden [5, 6].

The aim of this study was to evaluate, over 24 months of prospective follow-up, the dosage and costs of lanreotide AUTOGEL 120 mg administered as part of routine acromegaly care in Poland. In this type of study the decision to prescribe the given medical product, treatment monitoring, dose adjustment, and all other medical decisions were made at the responsible physician's discretion, according to the routine practice at the clinical site.

Material and methods

Lanro-Study was a national, multicentre, non-interventional, observational, prospective study conducted in accordance with the Declaration of Helsinki [7] and the International Ethical Guidelines for Epidemiological Studies, CIOMS, Feb 2008 [8]. This study also followed the recommendations of the International Epidemiological Association Guidelines for Proper Conduct in Epidemiologic Research (GEP) — Nov 2007 [9], and the International Society for Pharmacoepidemiology (ISPE) Good Pharmacoepidemiological Practices (GPP) Guidelines, April 2007 [10]. All patients gave written informed consent before entering the study.

Patients were included in the study during routine out-patient visits. All sites that treat acromegaly patients meeting the study inclusion criteria were selected and contracted. Site selection was based on the ability to collect the data in electronic format, motivation to participate, and fulfilment of all requirements of the protocol.

Eligible patients were adults (≥ 18 years of age) with symptomatic acromegaly treated with ATG120 in routine practice for at least three months before inclusion. The decision to prescribe ATG120 was made prior to and independently of the decision to enrol the subject in this non-interventional study. Patients were excluded if they actively participated in any clinical study.

Relevant data collected prospectively during 24-months were captured on an electronic Case Report Form (eCRF). The following data were gathered:

baseline patient characteristics (demographic information, clinical assessment, relevant medical history, prior therapies) and data of current treatment. The primary objective was to evaluate over the 24-month prospective follow-up - in everyday clinical practice — resource utilisation and effectiveness of the treatment of acromegalic patients in Poland with ATG120, including extended injection intervals.

The measured endpoints were: percentage of patients treated with ATG120 at an extended dosing interval (> 4 weeks), mean time between injections, and cost of ATG120 during the 24-month prospective observation.

Cost evaluation was performed from the perspective of the public payer, e.g. National Health Fund, and patients in 2014 (1 PLN = 0.25 EURO). Costs were assessed using a micro-costing approach, applying unit cost multipliers to the quantity of each type of resource consumed. Given the exploratory nature of the study, no formal statistical analysis was performed.

Results

Characteristics of the population

A total of 151 patients, suffering from acromegaly for at least 1 year, were screened and 143 enrolled in 35 centres across Poland between 29 Oct 2010 and 31 March 2012. Of those, 11 patients were excluded from the analysis: 2 patients because of missing follow-up visits and 9 patients because they did not complete the treatment period (24 months); thus there were 132 patients in the completers group included into analysis (Table I). The baseline demographic characteristics of the population included into analysis (n = 132) are summarised in Table II. At the time of inclusion 54% of patients with GH data (n = 101) achieved biochemical control of their disease, defined as GH ≤ 2.5 ng/mL. The most commonly reported symptoms of the disease were headache (84% of patients) and arthralgia (82% of patients), predominantly mild/moderate. Excessive sweating, easy fatigue, swelling of the area around joints, and wheezing were reported in 76%, 67%, 55%, and 69% of patients, respectively (Table III). In 13–15% of patients fatigue, arthralgia, and hoarseness were of high intensity.

Treatment history

With regard to previous acromegaly treatment, 99 patients (75%) had undergone pituitary surgery. Twenty-three patients (17.4%) had received pituitary radiotherapy (Table IV). The mean time since surgery/radiotherapy was 7.7/8.1 years, respectively. Different combined treatment (somatostatin analogue + cabergoline or bromocriptine, or pegvisomant) was

Table I. *Duration of time for which the population was followed (n = 143)*

Tabela I. *Czas obserwacji (tygodnie) populacji pacjentów włączonych do badania (n = 143)*

Time (weeks)	No. of patients
104	132
122	1
98	1
97	1
78	1
76	1
75	1
68	1
59	1
52	1
0	2

Table II. *Baseline characteristics of population included into analysis (n = 132)*

Tabela II. *Charakterystyka pacjentów włączonych do analizy (n = 132)*

Variable	Population
Age: mean (SD) (years)	51.7 (14.3)
Weight: mean (SD) [kg]	82.8 (17.7)
BMI: mean (SD) [kg/m^2]	29.4 (5.4)
Gender	
Male: n (%)	39 (29.6)
Female: n (%)	93 (70.5)
Tumour size	
Macroadenoma (≥ 10 mm in diameter): n (%)	108 (81.8)
Microadenoma (< 10 mm in diameter): n (%)	18 (13.6)
Not known: n (%)	6 (4.6)
Tumour diameter: mean (SD) [mm]	19.2 (11.2)
Diabetes mellitus, n (%)	40 (42.1)
Hypertension, n (%)	78 (82.1)
Cholelithiasis, n (%)	26 (27.4)

Table III. *Acromegaly-related symptoms of the population included into the analysis (n = 132)*

Tabela III. *Objawy kliniczne akromegalii w populacji pacjentów włączonych do analizy (n = 132)*

Symptom	% of population
Headache	84
Arthralgia	82
Sweating	76
Fatigue	67
Swelling of joint areas	55
Wheezing	69

Table IV. *Treatment history at baseline in the population included into the analysis (n = 132)*

Tabela IV. *Leczenie stosowane w przeszłości u pacjentów włączonych do analizy (n = 132)*

Variable	Population
Pituitary surgery, n (%)	99 (75)
Time span since surgery: mean (SD) (years)	7.7 (6.7)
Radiotherapy, n (%)	23 (17.4)
Time span since radiotherapy: mean (SD) (years)	8.1 (6.5)
Bromocriptine, n (%)	6 (4.5)
Cabergoline, n (%)	8 (6.1)
Pegvisomant, n (%)	1 (0.8)

Table V. *Concomitant treatments in the population included into the analysis (n = 132)*

Tabela V. *Leki dodatkowe stosowane w populacji pacjentów włączonych do analizy (n = 132)*

Antidiabetic drugs n (%)	41 (42.3)
Oestrogens n (%)	18 (29.0)
Androgens n (%)	10 (16.1)
Hydrocortisone n (%)	43 (69.4)
Levothyroxine n (%)	52 (83.9)
Desmopressin n (%)	4 (6.5)

used in 15 patients (11.4%). As additional treatment, 6 patients (4.5%) received bromocriptine, 8 patients (6.1%) — cabergoline and 1 (0.8%) — pegvisomant (Table IV). Almost 43% of patients were treated due to diabetes. Due to concomitant pituitary insufficiency, 52 patients (39.4%) were using levothyroxine, 43 patients (32.6%) — hydrocortisone, 4 patients (3.0%) — desmopressin, and 28 patients (21.2%) — sex hormones (Table V).

Treatment with lanreotide ATG120 during the 24-month follow-up

During the 24-month prospective phase, 63 patients (48%) received ATG120 at an extended dosing interval (> 4 weeks), predominantly every 5 weeks (n = 28) or every 6 weeks (n = 19) (Table VI). The mean/median number of days between injections during 24 months was 35.1 (SD 8.2)/31. The dosing intervals set at the beginning of the study remained the same for 91 patients (69.6%) until the end of the study; ATG120 was administered every 4, 5, 6, 7, 8, and 9 weeks in 67%, 14%, 10%, 2%, 5%, and 1% of patients, respectively. Changes in dosing regimen of ATG120 in clinical practice were reported in 41 patients (30.4%): for 7 subjects the interval was increased, for 12 subjects the interval was shortened, for 18 patients the interval was alternately extended or shortened, and in 4 patients the treatment was switched: from ATG120 every 4 weeks to octreotide LAR 30 mg every 4 weeks and then to ATG120 every 4 weeks (1 patient), from ATG120 every 5 weeks to octreotide LAR 30 mg every 4 weeks and then to ATG120 every 4 weeks (1 patient), from ATG120 every 4 weeks to octreotide LAR 30 mg every 4 weeks (1 patient), and from ATG120 every 4 weeks to octreotide LAR 20 mg every 4 weeks, then to octreotide LAR 30 mg every 4 weeks and then to ATG 120 every 4 weeks (1 patient).

ATG120 was predominantly administered in an outpatient setting (84% of injections) by a health care professional (97% of injections): a nurse (80% of injections) or physician (17% of injections) (Table VI). The number of unsupervised home injections was only 76 (2.6% of the total number of injections). The mean/median time needed for preparation and administration of ATG120 was 4.1 (SD 2.5)/4 minutes and 1.6 (SD 1.4)/1 minutes, respectively; mean/median product wastage was 0.2 (SD 0.7)/0 mg.

The cost of ATG120 calculated based on reimbursement status and retail price of the drug being in force from 1 November 2014 [11] was 4066.1 PLN/month/1016.5 EURO (the amount covered by the public payer and paid by patient was 4062.5 PLN/1015.6 EURO and 3.6 PLN/0.9 EURO, respectively) (Table VII). This monthly cost is lower than the retail price per pack — 4770.5 PLN/1192.6 EURO because of the possibility of extending dosing intervals of ATG120 in a substantial proportion of patients.

Table VI. *Administration of ATG120 in 24-month time frame (setting, person administering ATG120)*

Tabela VI. *Warunki podawania ATG 120 w ciągu 24 miesięcy obserwacji (miejsce i osoba podająca lek)*

Physician		Person administering ATG120				Total
		Care-giver	Patient	Nurse		
Setting of administration	House	–	48	28	30	106
	Outpatient setting	430	9	1	2053	2493
	Inpatient setting	63	3	1	289	356
Total		493	60	30	2372	2955

Table VII. *Dosing regimen and cost of ATG120 during 24-month observation (n = 132)*
Tabela VII. *Schemat dawkowania i koszt ATG 120 w ciągu 24 miesięcy obserwacji (n = 132)*

	Dose	Interval (weeks)	N. of patients		Cost/PLN/month*		
					Public payer + patient	Public payer	Patient
Lanreotide Autogel	120 mg	4	69	132	4066.13	4062.49	3.64
		5	28				
		6	19				
		7	7				
		8	8				
		9	1				

*the cost of ATG120 was calculated based on reimbursement status and retail price of ATG120 being in force from 1 November 2014 [11]

Discussion

This real-life, observational study investigated dosage pattern and cost of ATG120 in the population of Polish patients with active acromegaly. The results showed that during two years 48% of patients were treated with a dose interval longer than 28 days. Approximately one third of patients required dosing adjustment, while in 15% of them it was possible to increase the injection interval. ATG120 was predominantly administered in an outpatient setting by a health care professional. The results obtained during two years were consistent with those described in interim analysis with follow-up of one year [6]. This analysis revealed that 50% of patients received ATG120 at an extended dosing interval, and the mean number of days between injections was 35.6 (SD 8.4). ATG120 was predominantly administered in an outpatient setting (77%) by a health care professional (94%) [6].

When interpreting the results of this study it is important to note the three following assets: First, the results have been obtained from a prospective study. These studies are considered to yield the most reliable real-world economic data that can contribute to the evidence base needed for coverage and payment decisions [12]. Second, the time horizon of Lanro-Study was two years, and a high proportion of patients (92.3% of enrolled population) were followed-up, thus the results can be presumed reliable. Third, the study population, from 35 centres in different Polish regions, represents a wide cross-section of acromegalic patients in our country. About 80% of patients with a documented tumour size had a macroadenoma at diagnosis indicating that the analysed cohort was representative for the disease [13–23]. In the current analysis the prevalence of acromegaly in women is higher than in other registries [13–23], but the female predominance is in accordance with literature.

The percentage of patients treated previously with surgery is in the range of that reported from the Spanish and German registry (81% and 89%, respectively) [14,21], but higher than those reported from the Belgian cohort (68%) [16] or the UK National Acromegaly Register (68.7%) [20]. In the present cohort, irradiation had been applied in 17% of cases. This is less than the numbers in the Belgian register (34%) [16] and about half of those published from the UK or Spain (48% and 45%, respectively) [13, 14]. A very recent publication from the Spanish Acromegaly Registry, however, documented a decline in the use of radiotherapy to 11.9% in patients diagnosed after 2000 [19].

Very limited data have been published concerning the dosing of SRLs in routine clinical practice [20, 21, 23]. The UK Acromegaly Register collected routine biochemical and clinical data on patients with acromegaly from 31 UK centres with GH data covering more than 30 years [20]. In terms of medical treatment for acromegaly, 1549 patients (60.2%) had received some sort of medical therapy, and 40.6% had received SRLs (34.9% as monotherapy).

Doses of lanreotide ATG and octreotide LAR were examined in cases where this information had been entered in the database. There were 437 courses of octreotide LAR and 161 courses of lanreotide ATG. The mean/median dose for octreotide LAR was 22 mg/20 mg per month. Lanreotide ATG was given at the dose of 30 mg (2%), 60 mg (35%), 90 mg (29%), 120 mg (34%), and 150 mg (1%). These data represent the dosages of each injection (typically monthly), but the data on the frequency of injection were recorded inconsistently in the original database and therefore were not analysed in the publication. Assuming that the doses presented above were per month, the mean/median dose of lanreotide ATG in the UK population was 89 mg/90 mg per month. Retrospective data analysis from 1344 patients followed in 42 centres of the German Acromegaly Register showed that in patients who were controlled by drug monotherapy, the median dose for octreotide LAR was 20 mg every 28 days (n = 182), and for lanreotide ATG 60 mg every 4 weeks (n = 27) [21]. The

median doses for uncontrolled patients treated by drug monotherapy were, for octreotide LAR 30 mg every 28 days (n = 78), and for lanreotide ATG 90 mg every 28 days (n = 10) [21]. There were no differences in doses between patients with a long-standing (> 2 years) or a more recent (< = 2 years) diagnosis of acromegaly [21]. In the Somatuline Depot for Acromegaly (SODA) study carried out in the US, lanreotide ATG dose information was available for 146 patients at 12 months [23]. The majority of patients were taking lanreotide ATG 90 mg. Almost all patients (95%) received lanreotide ATG injections every 28 days, and one was receiving 120 mg at the extended dosing interval of every 42 days or longer. In total, 42 (29%) had dose adjustments in the first year of the study. The proportion of patients taking 90 mg decreased in the first year (from 57% to 43%), while the proportion taking 120 mg increased (from 27% to 43%), representing a general trend towards dose increase: mean/median dose at enrolment and after 12 months was 93.3 mg/90 mg and 98.7 mg/90 mg, respectively. The majority of patients (89%) received injections every 28 days after 12 months of treatment [23]. In conclusion, the UK, German, and US real-life data revealed that the mean dose of lanreotide ATG per month was lower than 120 mg, which is consistent with results of Lanro-Study, showing that 48% of patients could be treated with a dose of 120 mg given at an extended dosing interval.

Only the SODA study provided information on the aspects of drug administration [23]. Lanreotide ATG has the unique formulation of a prefilled self-injectable device, which offers a quick method of administration and allows for self- or partner-administration in the home or clinical setting. The proportion of patients in this study receiving injections from health professional (58/166; 35 %) was much lower than those reported from Lanro-Study. In the US study 16 % of patients self-injected lanreotide, and the remaining 50% were evenly split between those who had injections administered by their partner and those who used a combination of methods [23]. In Polish routine practice the proportion of unsupervised home injections was 2.6%. The SODA study demonstrated that administration of lanreotide ATG at home by oneself or partner provides similar biochemical control to injections administered in the healthcare provider's office, with similar tolerability and greater convenience. Such findings support the potential for lanreotide ATG to reduce treatment burden in the real-world clinical environment and indicate that in the future unsupervised home injections might also be a viable alternative to healthcare professional injections for Polish patients.

The recently finished LEAD study evaluated the efficacy and safety of ATG120 extended dosing intervals in 124 patients from 14 countries previously controlled with conventional doses of octreotide LAR (10 or 20 mg every 4 weeks) [4]. At week 48, three-quarters of patients maintained IGF-1 control after switching to ATG120 every 6 to 8 weeks. The benefits of ATG120, including the patients' preference of this drug in extended dosing intervals, were achieved without safety or tolerability issues [4].

In conclusion, the Lanro-Study 2-year observation of a representative group of patients suffering from acromegaly indicates that ATG120 is economically preferable due to its extended dosing interval used in almost half of patients. The subcutaneous, convenient method of administration via a prefilled syringe represents an additional benefit of this drug.

References

1. Bolanowski M, Ruchała M, Zgliczyński W et al. Acromegaly — a novel view of the patient. Polish proposals for diagnostic and therapeutic procedures in the light of recent reports. Endokrynol Pol 2014; 65: 326–331. doi 10.5603/EP.2014.0045
2. Caron PJ, Bevan JS, Petersenn S et al. Tumor Shrinkage With Lanreotide Autogel 120 mg as Primary Therapy in Acromegaly: Results of a Prospective Multicenter Clinical Trial. J Clin Endocrinol Metab 2014; 99: 1282–1290. doi:10.1210/jc.2013-3318.
3. Schopohl J, Strasburger CJ, Caird D et al. Efficacy and acceptability of lanreotide Autogel 120 mg at different dose intervals in patients with acromegaly previously: treated with octreotide LAR. Exp Clin Endocrinol Diabetes. 2011; 119: 156–162.
4. van der Lelij AJ, Neggers S, Pronin V. Extended dosing intervals with lanreotide Autogel/Depot 120 mg can be effective in acromegalic patients biochemically controlled with octreotide LAR 10 or 20 mg: the LEAD study. Presented at the 96th ENDO/16th ICE meeting 2014, Chicago, IL, USA, June 21–24, 2014. https://endo.confex.com/endo/2014endo/webprogram/Paper16052.html; accessed 1 Dec 2014.
5. Orlewska E, Kos-Kudła B, Sowiński J et al. Results of the retrospective phase of an observational study Lanro-Study evaluating the use of health care resources in the population of Polish patients with acromegaly, treated with Somatuline AUTOGEL. (Polish) Nowa Medycyna 2012; 3: 39–46.
6. Orlewska E, Kos-Kudła B, Sowiński J et al. Assessment of real-world usage of lanreotide AUTOGEL 120 in Polish acromegalic patients — results from the prospective 12-month phase of Lanro-Study. Contemp Oncol 2013; 17: 460–465.
7. Declaration of Helsinki, 2008. http://www.wma.net/en/30publications/10policies/b3/17c.pdf; accessed 1 Dec 2014.
8. International Ethical Guidelines for Epidemiological Studies, CIOMS, Feb.2008. http://www.ufrgs.br/bioetica/cioms2008.pdf; accessed 1 Dec 2014.
9. International Epidemiological Association Guidelines for the Proper Conduct in Epidemiologic Research (GEP) — Nov 2007. http://ieaweb.org/wp-content/uploads/2012/06/cioms.pdf; accessed 1 Dec 2014.
10. International Society for Pharmacoepidemiology (ISPE) Good Pharmaco Epidemiological Practices (GPP) Guidelines, April 2007. https://www.pharmacoepi.org/resources/guidelines_08027.cfm; accessed 1 Dec 2014.
11. Statement of the Minister of Health of 22 October 2014 on the list of reimbursed drugs, foodstuffs intended for particular nutritional and medical devices. Dz. Urz. Min. Zdr. 2014.71.
12. Garrison LP, Neumann PJ, Erickson P et al. Using real-world data for coverage and payment decisions: the ISPOR Real-World Data Task Force Report. Value in Health 2007; 10: 326–335.
13. Jenkins PJ, Bates P, Carson MN et al. Conventional pituitary irradiation is effective in lowering serum growth hormone and insulin-like growth factor-I in patients with acromegaly. J Clin Endocrinol Metab 2003; 88: 5258–5265.
14. Mestron A, Webb SM, Astorga R et al. Epidemiology, clinical characteristics, outcome, morbidity and mortality in acromegaly based on the Spanish Acromegaly Registry (Registro Espanol de Acromagalia, REA). Eur J Endocrinol 2004; 151: 439–446.
15. Knauppinen-Makelin R, Sane T, Reunanen A et al. A nationwide survey of mortality in acromegaly. J Clin Endocrinol Diab 2006; 114: 498–505.
16. Bex M, Abs R, T'Sjoen G et al. AcroBel — the Belgian registry on acromegaly: a survey of the 'real-life' outcome in 418 acromegalic subjects. Eur J Endocrinol 2007; 157: 399–409.

17. Arosio M, Reimondo G, Malchiodi E et al. Predictors of morbidity and mortality in acromegaly: an Italian survey. Eur J Endocrinol 2012; 167: 189–198.
18. Kwon O, Song YD, Kim SY et al. Nationwide survey of acromegaly in South Korea. Clin Endocrinol 2013; 78: 577–585.
19. Sesmilo, G. Gaztambide S, Venegas E et al. Changes in acromegaly treatment over four decades in Spain: analysis of the Spanish Acromegaly Registry (REA). Pituitary 2013; 16: 115–121.
20. Trevor AH, Willis D, Walker G et al. and the UK Acromegaly Register Study Group (UKAR-3). Control of growth hormone and IGF1 in patients with acromegaly in the UK: responses to medical treatment with somatostatin analogues and dopamine agonists. Clin Endocrinol 2013; 76: 689–699.
21. Schöfl C, Franz H, Grussendorf M et al.; participants of the German Acromegaly Register. Long-term outcome in patients with acromegaly: analysis of 1344 patients from the German Acromegaly Register. Eur J Endocrinol 2012; 168: 39–47.
22. Burton T, Le Nestour E, Bancroft T et al. Real-world comorbidities and treatment pattern of patients with acromegaly in two large US health plan databases. Pituitary 2013; 16: 354–362.
23. Salvatori R, Woodmansee MM, Gordon MB et al. Lanreotide extended-release aqueous-gel formulation, injected by patient, partner or healthcare provider in patients with acromegaly in the United States: 1-year data from the SODA registry. Pituitary 2014; 17: 13–21.
24. Holdaway IM, Rayasoorya C. Epidemiology of acromegaly. Pituitary 1999; 2: 29–41.