2 SYNOPSIS

Name of Sponsor/Company: Ipsen Ltd	Individual Study Table Referring to Part	*(For national authority use only)*
Name of Product: Somatuline® Autogel®	of the Dossier	
Name of Active Ingredient(s): Lanreotide acetate	Volume: Page:	

Title of study: An observational, multicentre, open label, post-marketing surveillance programme to assess the long-term safety and efficacy of Somatuline® Autogel® in the treatment of acromegaly when administered by patients or their partners ("Home Injection Group") or administered by healthcare professionals.

Investigators: Five hospital clinicians in Australia

Study centre(s): PPD

Publication (reference): None at the time of writing this report

Studied period (years): Date of first enrolment: 14 April 2009 Date of last completed: 05 April 2013	**Phase of development**: Post marketing

Objectives:

Primary:

To assess the safety and local tolerability of the long-term use of Somatuline Autogel when administered by patients or their partners ("Home Injection Group") and the safety and local tolerability in patients receiving their injection from a healthcare professional (HCP) ("Reference Group").

Secondary:

To assess the efficacy of the long-term use of Somatuline Autogel in both groups.

To evaluate the training requirements for patients / partners to perform home injection of Somatuline Autogel.

To evaluate the acceptability of home injections to patients, partners and healthcare professionals.

Methodology:This was an observational (non-interventional), multicentre post marketing surveillance programme. Patients who had been established on a stable dose of Somatuline Autogel for at least 4 months before entering the programme were asked if they wished to commence home (self or partner) injections. The decision was taken prior to, and independently of, the decision to participate in this post-marketing surveillance (PMS) programme. Patients who were enrolled in this PMS programme and chose to have their injections at home were included in the Home Injection Group, and patients who chose to

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receive their injections from a healthcare professional (HCP) were included in the Reference (HCP) Group. Patients could switch from home injection to HCP injection or from HCP injection to home injection during the observation period.

Number of patients (planned and analysed):

It was planned that approximately 30 patients would be enrolled in this PMS programme. The number of patients enrolled into each group was not mandated. At the end of the data collection period, 38 patients were enrolled, and all 38 patients had post-baseline data (intention-to-treat [ITT]/Safety Population). Of these, 11 patients were included in the Home Injection Group and had at least one injection recorded; and 27 patients were included in the Reference (HCP) Group and had at least one injection recorded.

Diagnosis and criteria for inclusion:

Eligible patients were at least 18 years of age and had a diagnosis of acromegaly for which they had received treatment with Somatuline Autogel at a stable dose for at least 4 months. All patients gave written informed consent for their data to be included in the database for this PMS programme and any subsequent analysis. Patients who chose to be in the Home Injection Group had to be able to store Somatuline Autogel safely in a refrigerator in their own home, and either to collect it from their General Practitioner (GP) or Pharmacy on a monthly basis, or to receive the medication by a home delivery service.

Patients who were pregnant or breast-feeding were excluded from the study unless the treating clinician determined that continued treatment with Somatuline Autogel was clearly needed.

Study product dose, mode of administration and batch numbers:

Somatuline Autogel was supplied in pre-filled ready-for-use syringes containing 60, 90 or 120 mg lanreotide as acetate. Study medication was administered by deep subcutaneous injection into either the superior external quadrant of the buttock (HCP or partner injections) or upper, outer thigh (self-injections). Injections could be given by a HCP or by an appropriately trained friend or relative of the patient. Patients who were well motivated and had received appropriate training could self-administer the product.

Injections were generally administered every 28 days, although the 120 mg injection could be given at intervals of up to 56 days to patients whose condition was well controlled. The dose and frequency of administration was determined by the treating clinician in accordance with usual medical practice.

Study medication was obtained from commercial stock and batch numbers were not recorded.

Duration of treatment: Somatuline Autogel is a long-term treatment and no duration of

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treatment was defined. Participation in the PMS programme for each patient could be up to 4 years, depending on the timing of their enrolment. Participation in the programme ended for all patients 2 years after the last patient was enrolled in the programme.

Reference therapy dose, mode of administration and batch numbers:

There was no comparator compound in this study. The Reference Group consisted of patients whose Somatuline Autogel (60, 90, or 120 mg) was administered by their usual HCP.

Criteria for evaluation:

Safety endpoints:

- Incidence of related treatment-emergent adverse events (TEAEs).
- Incidence of related serious adverse events (SAEs).
- Concomitant medications, therapies and surgical procedures.
- Liver and gall bladder ultrasound imaging, vital signs (heart rate, blood pressure, weight, height), where available.

Efficacy endpoints:

- Growth hormone (GH) plasma levels.
- Insulin-like growth factor (IGF)-1 plasma levels.
- Acromegaly symptoms

Tumour size was also an efficacy endpoint. However, tumour size data was not collected after baseline and this analysis was not done.

Additional endpoints:

- Training evaluations for patients in the Home Injection Group, including
  - Number of training sessions required.
  - Nature of training sessions required.
  - Supportive material or documentation used.
  - Length of training sessions.
  - Outcome of training session (patient/partner qualified or not qualified to perform home injections).
- Tolerability evaluations through patient reported comments.
- Acceptability evaluations, including:
  - The proportion of patients/partners who successfully qualified to perform home

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injections.

- The proportion of patients who discontinued home injection after successfully qualifying to perform them.
- Treatment compliance.
- Any other issues with administration of injections

Statistical methods:

This was an observational programme. Therefore, no formal statistical analysis was planned or performed. All data were summarised descriptively by administration group and/or by dose and injection interval as appropriate.

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Results:

Patients:

Thirty-eight patients were enrolled in the PMS programme and had post-baseline data: 11 patients in the Home Injection Group and 27 patients in the Reference (HCP) Group. Eighteen patients (47.4%) were female and 20 patients (52.6%) were male. Mean age was 52.9 years and ranged between 19 and 85 years. Most patients were Caucasian/White (34 patients, 89.5%).

Safety:

Overall exposure to treatment in this PMS programme ranged between 5.4 weeks and 200.3 weeks (approximately 3.9 years). Median exposure was approximately 2 years 8 months (139.4 weeks) in the Home Injection Group and 3 years 3 months (171.1 weeks) in the Reference (HCP) Group.

A total of 43 related TEAEs were reported for 15 patients (39.5%). Fourteen related TEAEs were reported for 4 patients (36.4%) in the Home Injection Group, and 29 related TEAEs were reported for 11 patients (40.7%) in the Reference (HCP) Group.

The related TEAEs in the Home Injection Group were injection site reactions (pain, burning, redness, and swelling), fever, tiredness, diarrhoea, nausea, dizziness, and joint ache (1 patient for each related TEAE). Dizziness was severe; the other related TEAEs were mild or moderate. One patient who experienced moderate injection site pain, erythema, and swelling, and mild pyrexia, had a dose delay but continued in the PMS programme for 18 months.

In the Reference (HCP) Group, the most frequently reported related TEAEs were injection site pain, and diarrhoea (4 patients, 14.8% for each TEAE); and injection site burning, and nausea (2 patients, 7.4% for each TEAE). The other TEAEs were all single cases. Four related TEAEs were severe in intensity: nausea, vomiting, diarrhoea, and chest pain. The patient with severe diarrhoea discontinued treatment with Somatuline Autogel.

There was no apparent relationship between duration of treatment and onset of related TEAEs.

There were no serious related TEAEs and no related TEAEs with fatal outcome.

Injection tolerance data at last visit were available for 4 patients in the Home Injection Group and 18 patients in the Reference (HCP) Group. None of these patients reported injection site rash or itching. Injection site reactions of tenderness, erythema, haematoma, and pain were all mild or moderate. Severe injection site reactions were reported for swelling (1 patient in each group), and other symptoms (1 patient in the Reference (HCP) Group with a large lump).

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There were no consistent clinically significant changes in laboratory values or physical examinations, including vital signs. But, in the Reference (HCP) group, the haematology result for 1 patient was clinically significant at baseline compared to normal at the last recorded visit. One patient had a clinically significant biochemistry result at the last 2 reported visits compared with normal at baseline. Two patients had clinically significant baseline urinalysis results but no other urinalysis results were recorded for these patients. One patient in the Reference (HCP) group had clinically significant biochemistry and physical examination results at 6 months, but no other results were reported for this patient. There were no apparent significant changes in the Home Injection Group.

Other information:

Patients in the Home Injection Group required a median of 2 training sessions (range 1 to 3). The median duration of each training session was 30 minutes (range 20 to 60 minutes). All 11 patients and their partners were considered to have received adequate training for home injection and were qualified to perform it.

Overall, mean (standard deviation [SD]) GH levels were unchanged between pre active study and the last visit (change of 0.04 µg/L [0.95 µg/L]). The change between pre active study and last visit was a decrease in the Home Injection Group (-0.59 µg/L [0.76 µg/L]), and an increase in the Reference (HCP) Group (0.20 µg/L [0.93 µg/L]). One patient in each group had abnormal, clinically significant GH values at the last visit.

Mean (SD) IGF-1 values normalised for age and sex were 13.1 nmol/L (38.7 nmol/L) higher at the last visit than pre active study. The change between pre active study and last visit was a decrease in the Home Injection Group (-5.9 nmol/L [26.2 nmol/L]), and an increase in the Reference (HCP) Group (19.6 nmol/L [40.5 nmol/L). Abnormal, clinically significant IGF-1 values at the last visit were reported for 2 patients (22.2%) in the Home Injection Group, and for 3 patients (11.1%) in the Reference (HCP) Group.

Acromegaly symptoms were absent in most patients both at baseline and at the last visit. Patients in both groups had shifts in acromegaly symptoms; both improvements and worsening were recorded with no indications of a trend either way.

Three patients in the Reference (HCP) Group permanently switched to home injection during the PMS Programme, whereas none of the patients in the Home Injection Group switched permanently to HCP administration. The predominant reasons for continuing with home injection were convenience and flexibility.

There were no other findings of note.

Conclusion:

There were no new safety findings in this PMS Programme.

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Home injection of Somatuline Autogel was convenient for those patients who chose it. **Date of report:** 17 March 2015		