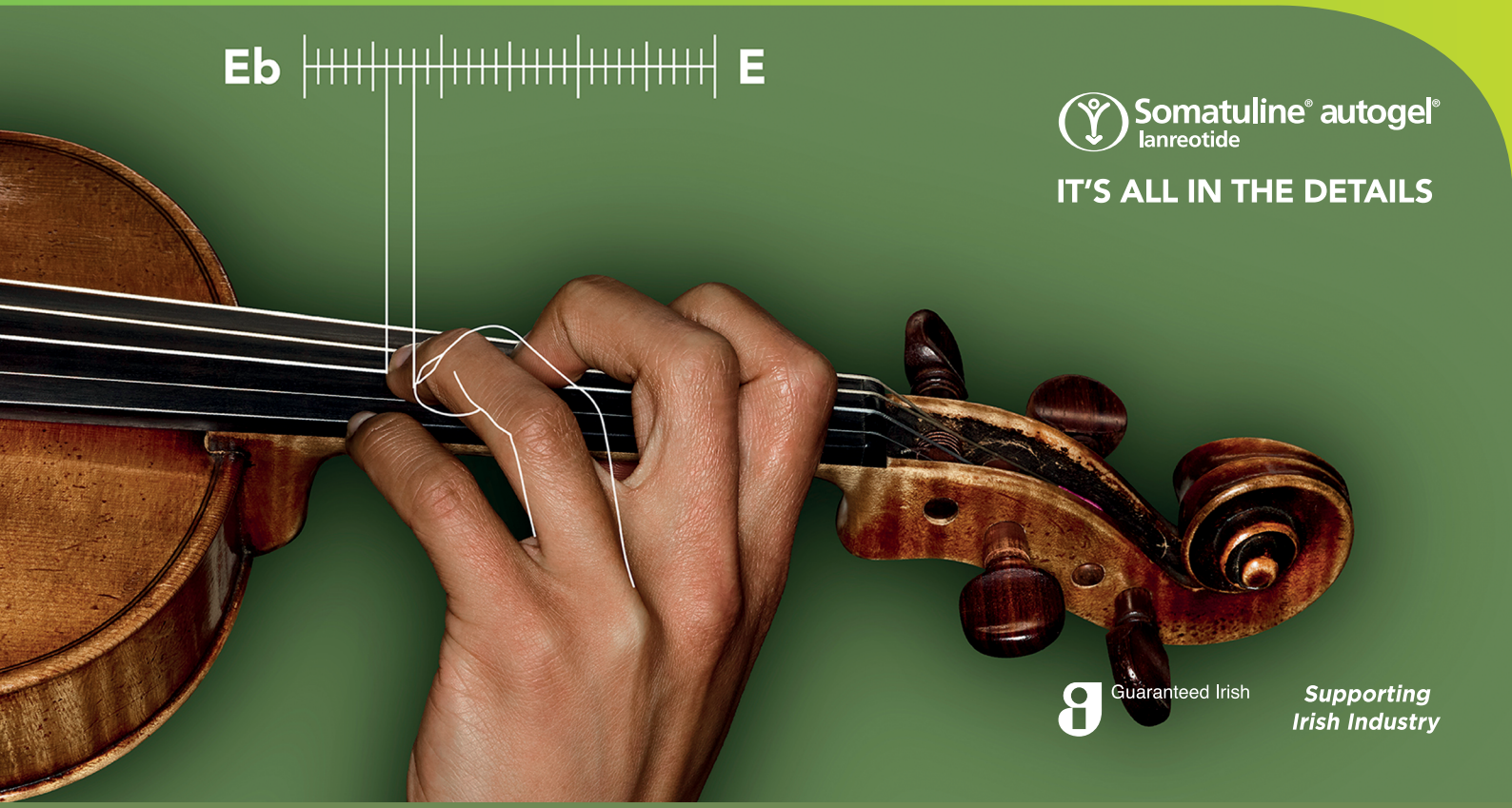
IPSEN

NEUROENDOCRINE TUMOURS



Somatuline® autogel®
lanreotide

IT'S ALL IN THE DETAILS

Guaranteed Irish

Supporting Irish Industry

Somatuline® Autogel® is indicated for:[1]

- The treatment of individuals with acromegaly when the circulating levels of Growth Hormone (GH) and/or Insulin-like Growth Factor-1 (IGF-1) remain abnormal after surgery and/or radiotherapy, or in patients who otherwise require medical treatment. The goal of treatment in acromegaly is to reduce GH and IGF-1 levels and where possible to normalise these values
- The treatment of Grade 1 and a subset of Grade 2 (Ki67 index up to 10%) gastroenteropancreatic neuroendocrine tumours (GEP-NETs) of midgut, pancreatic or unknown origin where hindgut sites of origin have been excluded, in adult patients with unresectable locally advanced or metastatic disease
- The treatment of symptoms associated with neuroendocrine (particularly carcinoid) tumours

This material is intended for healthcare professionals only. Prescribing Information can be found on the back page of this booklet.

Adverse events should be reported.

Reporting forms and information can be found at www.hpra.ie or email medsafety@hpra.ie. The HPRA can also be contacted on 016764971.
Adverse events should also be reported to Ipsen via email at pharmacovigilance.uk-ie@ipsen.com or phone on +441753 627777, IE phone 018098256.

EFFICACY IN TUMOUR CONTROL

Somatuline® Autogel® offers significantly prolonged PFS for patients with NETs[2]

The CLARINET trial was a 96-week, Phase 3, randomised, double-blind, placebo-controlled, multinational study that assessed PFS in patients with NETs who administered Somatuline® Autogel®.[2] An OLE extension* assessed long-term efficacy and safety in these patients[3]

PFS, according to subgroups (ITT population)

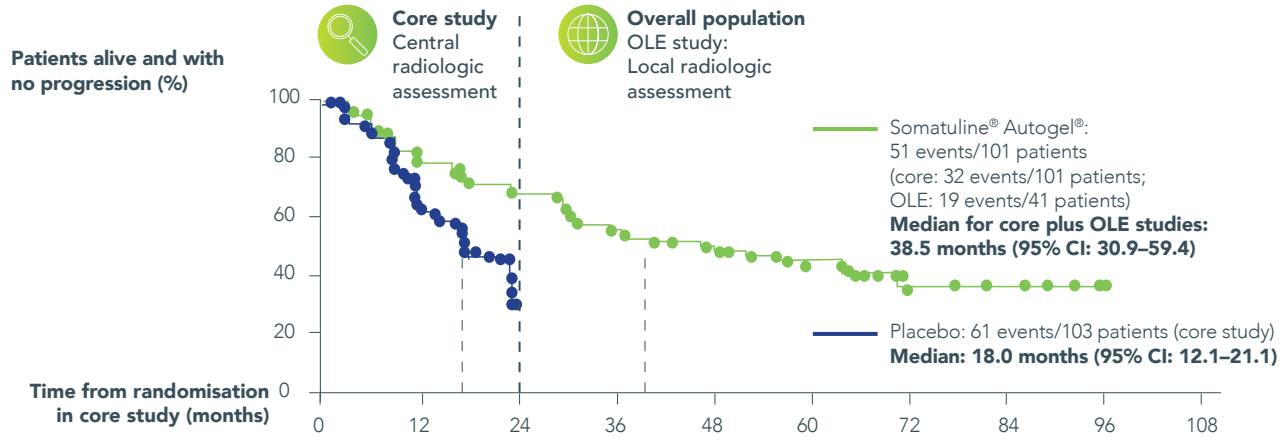


Figure adapted from Caplin ME, *et al.* 2014[2] and Caplin ME, *et al.* 2021.[3]

In patients eligible for the core and OLE studies, Somatuline® Autogel® significantly increased mPFS vs placebo in:[3,4]

Midgut NETs:
61.5 vs 21.1 months (P=0.030)†

Pancreatic NETs:
29.7 vs 12.1 months (P=0.036)†

Significant increases vs placebo in mPFS were also demonstrated in patients with high (>25%) and low (≤25%) tumour volume, and Grade 1 and 2 tumours†[4]

*At the end of the core study, 41 patients with stable disease while receiving Somatuline® Autogel® were eligible for enrolment in the OLE study.[3]
†mPFS was compared between groups using log-rank tests.[4]

REDUCTION IN CARCINOID SYNDROME SYMPTOMS

Somatuline® Autogel® provides statistically significant improvements in the control of diarrhoea and flushing symptoms vs placebo in the 48-week ELECT trial[5]

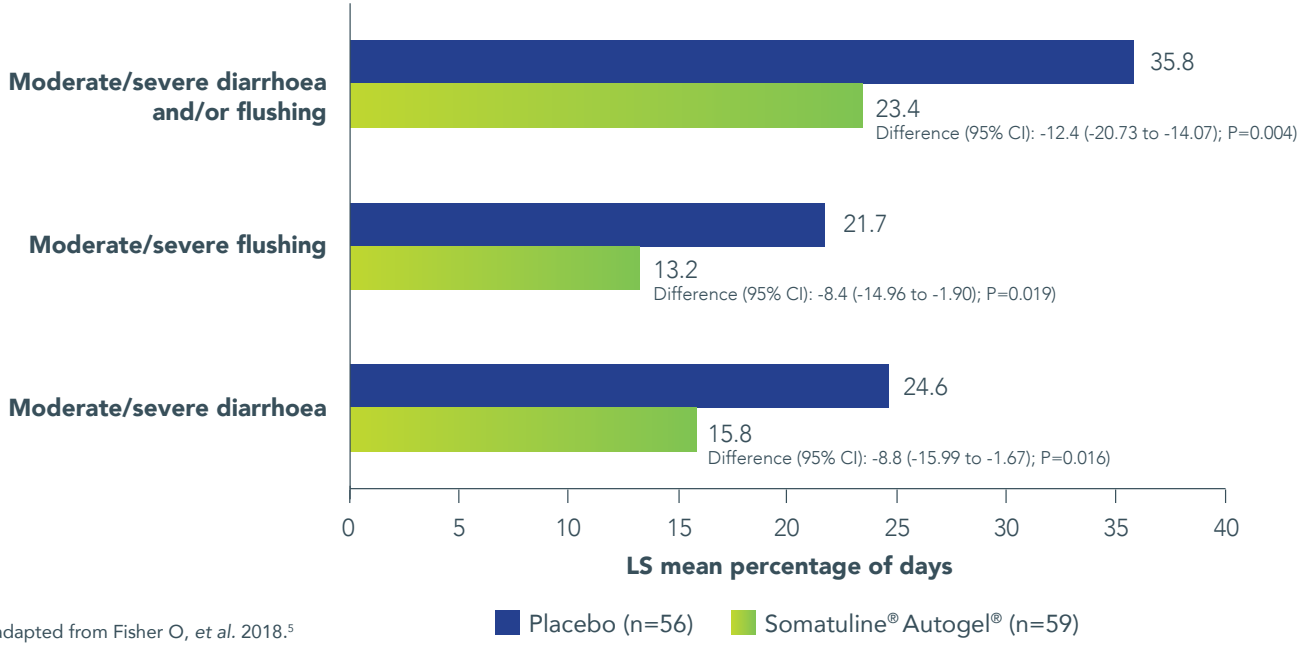


Figure adapted from Fisher O, *et al*. 2018.[5]

Patient-reported outcomes in an international, open-label, observational study of adults with NETs receiving Somatuline® Autogel® demonstrated:[6]

76%

were **completely** or **rather satisfied** with **diarrhoea control** (n=203/268)

73%

were **completely** or **rather satisfied** with **flushing control** (n=107/147)

IMPROVED PATIENT EXPERIENCE

Fewer patients experienced pain lasting >2 days, resulting in less interference in daily life with Somatuline® Autogel® vs octreotide LAR in the international PRESTO 2 patient-experience survey[7]

59% of patients reported no interference at all in their daily life as a result of injection-site pain from Somatuline® Autogel®[7]

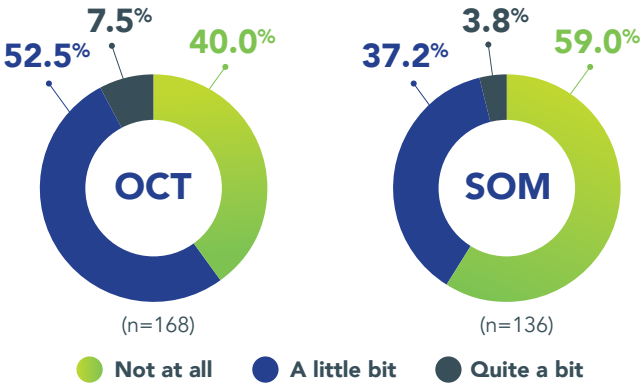
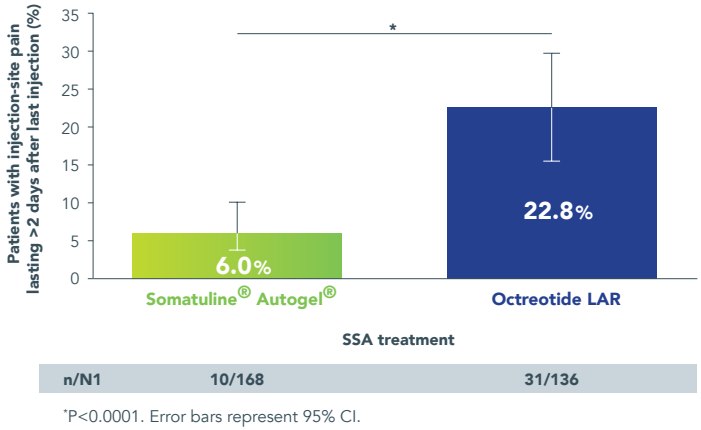


Figure adapted from O'Toole D, *et al.* 2023.[7]

Significantly fewer patients reported post-injection pain lasting >2 days with Somatuline® Autogel® vs octreotide LAR[7]



n/N1	10/168	31/136

*P<0.0001. Error bars represent 95% CI.

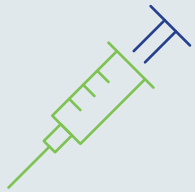
Figure adapted from O'Toole D, *et al.* 2023.[7]

Somatuline® Autogel® is a long-acting SSA licensed for injection independently of an HCP[1]

In a Phase 4, open-label, crossover patient-reported study:

88%

(n=22/25) of patients preferred injecting independently of an HCP vs injection by an HCP[8]



ENETS recommends Somatuline® Autogel® for syndrome control in functional NETs[9]

Recommendations for the preferential use of Somatuline® Autogel® as a first-line therapy[9]

Primary site		MIDGUT				PANCREAS			
Grading		G1		G2 (Ki67 <10%)		G1		G2 (Ki67 <10%)	
Liver tumour burden		Low	High (>25%)	Low	High (>25%)	Low	High (>25%)	Low	High (>25%)
Preferred SSA for use as first-line therapy	Somatuline® Autogel®	✓	✓	✓	✓	✓	✓	✓	✓
	Octreotide LAR	✓							

Table adapted from Pavel M, *et al.* 2016.[9]

Somatuline® Autogel® Patient Support Programme

At Ipsen, we are committed to ensuring patients feel informed about their NETs diagnosis and comfortable to administer Somatuline® Autogel® at home. Our nursing support service, provided by TCP Healthcare, has a dedicated team of nurses who provide face-to-face training to patients on how to optimally self-administer Somatuline® Autogel® in their own home.

For more information, please contact your local Ipsen representative.

Abbreviations

CI, confidence interval; ENETS, European Neuroendocrine Tumour Society; G1, Grade 1; G2, Grade 2; HCP, healthcare professional; ITT, intention-to-treat; LAR, long-acting release; mPFS, median progression-free survival; NET, neuroendocrine tumour; OLE, open label extension; PFS, progression-free survival; SSA, somatostatin analogue.

References

1. Somatuline® Autogel® Summary of Product Characteristics; **2.** Caplin ME, *et al. N Engl J Med.* 2014;371(3):224–233; **3.** Caplin ME, *et al. Endocrine.* 2021;71(2):502–513; **4.** Phan AT, *et al.* Presented at the 14th Annual ENETS Conference; 8–10 March 2017; Barcelona, Spain; **5.** Fisher GA, *et al. Oncologist.* 2018;23(1):16–24; **6.** Ruszniewski P, *et al. Dig Liver Dis.* 2016;48(5):552–558; **7.** O'Toole D, *et al. Adv Ther.* 2023;40(2):671–690; **8.** Johanson V, *et al. Patient Prefer Adherence.* 2012:6:703–710; **9.** Pavel M, *et al. Neuroendocrinology.* 2016;103(2):172–185.

Abbreviated Prescribing Information

Somatuline® Autogel® (lanreotide acetate) solution for injection in a pre-filled syringe. See full Summary of Product Characteristics before prescribing. Available at: www.medicines.ie Presentation: Pre-filled syringe containing a solution of lanreotide acetate 60, 90 or 120mg per syringe. **Indications: (1)** The long-term treatment of acromegaly when the circulating levels of growth hormone (GH) and/or Insulin-like Growth Factor-1 (IGF-1) remain abnormal after surgery and/or radiotherapy, or in patients who otherwise require medical treatment. **(2)** Relief of symptoms associated with acromegaly. **(3)** The treatment of Grade 1 and a subset of Grade 2 (Ki67 index up to 10%) gastroenteropancreatic neuroendocrine tumours (GEP- NETs) of midgut, pancreatic or unknown origin (where hindgut have been excluded), in adults with unresectable locally advanced or metastatic disease. **(4)** Treatment of symptoms associated with carcinoid tumours. **Dosage:** *Acromegaly:* Starting dose 60 to 120mg administered via deep subcutaneous injection every 28 days. Dose individualised according to patient's response (judged by reduction in symptoms and/or reduction in GH and/or IGF-1 levels). If complete control is obtained, the dose may be decreased. Patients well controlled on a somatostatin analogue can be treated with Somatuline Autogel 120 mg every 42 or 56 days. *Neuroendocrine Tumours (NET) treatment:* The recommended dose is one injection of Somatuline Autogel 120mg administered every 28 days. Continue treatment for as long as needed for tumour control. *NET (carcinoid) symptoms:* Starting dose 60 to 120mg administered via deep subcutaneous injection every 28 days. Dose adjusted according to degree of symptomatic relief obtained. Patients well controlled on a somatostatin analogue can be treated with Somatuline Autogel 120mg every 42-56 days. There should be close monitoring of symptoms when treatment is switched to the extended dosing interval. *Elderly, renal and/or hepatic impairment:* No dose adjustment necessary due to the wide therapeutic window. *Paediatrics:* not recommended in children/adolescents due to lack of safety and efficacy data. **Method of Administration:** Somatuline Autogel should be injected via deep subcutaneous route into the superior external quadrant of the buttock or in the upper outer thigh. For patients who receive a stable dose of Somatuline Autogel and after appropriate training, the injection may be given by the patient themselves or another trained person. In the case of self-injection, the injection should be given in the upper outer thigh. A healthcare professional should decide who should administer the injections. Regardless of the injection site, the skin should not be folded, and the needle should be inserted rapidly and to its full length, perpendicularly to the skin. The injection site should alternate between the right and left side. **Contraindications:** Hypersensitivity to lanreotide, somatostatin or related peptides or any of the excipients. **Warnings/Precautions:** May reduce gallbladder motility and lead to gallstone formation. Patients may require periodic monitoring. It is advised, during prolonged treatment, to perform before treatment and every 6 months, an echography of the gallbladder. There have been post-marketing reports of gallstones resulting in complications, including cholecystitis, cholangitis, and pancreatitis, requiring cholecystectomy in patients taking lanreotide. If complications of cholelithiasis are suspected, discontinue lanreotide and treat appropriately. Patients treated with Somatuline Autogel may experience hypo- or hyperglycaemia. Blood glucose levels should be monitored at the start of the treatment or when the dose is altered; and any anti-diabetic medication should be adjusted accordingly. Slight decreases in thyroid function have been observed in patients with acromegaly. Thyroid function tests are recommended where clinically indicated. Somatuline Autogel may lead to a decrease of heart rate in patients without underlying cardiac problems. Sinus bradycardia may occur in patients with pre- existing cardiac disorders. Care should be taken when initiating treatment in patients with bradycardia. Symptoms of pancreatic exocrine insufficiency (PEI) including steatorrhea, loose stools, abdominal bloating, and weight loss have been observed in patients receiving lanreotide treatment for GEP-NETs. Screening and and appropriate treatment for PEI should be considered for symptomatic patients. In patients with acromegaly, use of lanreotide is not exempt from the monitoring of the volume of the pituitary tumour. **Interactions:** The pharmacological gastrointestinal effects of lanreotide may result in a reduction of the intestinal absorption of co- administered drugs including ciclosporin. Concomitant administration of ciclosporin with lanreotide may decrease the relative bioavailability of ciclosporin and therefore may necessitate the adjustment of ciclosporin dose to maintain therapeutic levels. Concomitant administration of bromocriptine may increase the bioavailability of bromocriptine. Concomitant administration of bradycardia inducing drugs (e.g., beta blockers) may have an additive effect on the slight reduction of heart rate associated with lanreotide. Dose adjustments of such concomitant medications may be necessary. The limited published data available indicate that somatostatin analogues may decrease clearance of drugs metabolised via CYP450 enzymes. Drugs with a low therapeutic index mainly metabolised via CYP3A4 (e.g. quinidine, terfenadine) should be used with caution. Dose adjustments of insulin and antidiabetics may be necessary when Somatuline is administered simultaneously. Risk of hypoglycaemia or hyperglycaemia: decrease in the needs of anti-diabetic treatment following decrease or increase in endogen glucagon secretions. The glycaemic self-monitoring must be reinforced and the posology of anti-diabetic treatment during treatment by lanreotide should be adapted as required. **Pregnancy/Lactation:** *Pregnancy:* Limited data indicate no adverse effects; only use in pregnancy if lanreotide is clearly needed. *Lactation:* Unknown whether lanreotide is excreted in breast milk; caution when administered during lactation. **Undesirable effects:** ***Very common:*** Diarrhoea, loose stools, abdominal pain, cholelithiasis. **Common:** Hypoglycaemia, decreased appetite, hyperglycaemia, diabetes mellitus, dizziness, headache, lethargy, sinus bradycardia, nausea, vomiting, constipation, flatulence, abdominal distension, abdominal discomfort, dyspepsia, steatorrhea, biliary dilatation, musculoskeletal pain, myalgia, alopecia, hypotrichosis, asthenia, fatigue, injection site reactions, ASAT increased, ASAT abnormal, ALAT abnormal, blood bilirubin increased, blood glucose increased, glycosylated hemoglobin increased, weight decreased, pancreatic enzymes decreased. **Uncommon:** Insomnia, hot flushes, faeces discoloured, ASAT increased, blood alkaline phosphatase increased, blood bilirubin abnormal, blood sodium decreased. Post- marketing safety experience (frequency not known): Pancreatic exocrine insufficiency, pancreatitis, cholecystitis, cholangitis, injection site abscess, allergic reactions (including angioedema, anaphylaxis, hypersensitivity). *Prescribers should consult the Summary of Product Characteristics in relation to other side effects.* **Pharmaceutical Particulars:** Store in a refrigerator (2°C to 8°C) in the original package. Box of one 0.5ml prefilled syringe with automatic safety system and one needle. **Legal category:** POM. **Marketing Authorisation Number(s):** 60mg PA869/4/2, 90mg PA869/4/3, 120mg PA869/4/4. **Marketing Authorisation Holder:** Ipsen Pharmaceuticals Ltd, Blanchardstown Industrial Park, Blanchardstown, Dublin 15. Further information can be obtained from IPSEN Pharmaceuticals Ltd, Blanchardstown Industrial Park, Blanchardstown, Dublin 15, Ireland, Tel: (01)8098256. Somatuline® and Autogel® are registered trademarks. **Date of Preparation of PI:** July 2024. SOM-IE-000623.

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