Reconstitution and preparation of Sandostatin® LAR® (octreotide acetate)

Sandostatin LAR is recommended for tumour control in advanced midgut NETs by ENETS guidelines[1]

Sandostatin LAR is indicated in:[2]

- Treatment of patients with acromegaly in whom surgery is inappropriate or ineffective, or in the interim period until radiotherapy becomes fully effective
- Treatment of patients with symptoms associated with functional gastro-entero-pancreatic endocrine tumours, e.g. carcinoid tumours with features of the carcinoid syndrome
- Treatment of patients with advanced NETs of the midgut or of unknown primary origin where non-midgut sites of origin have been excluded
- Treatment of TSH-secreting pituitary adenomas:
  - when secretion has not normalised after surgery and/or radiotherapy
  - in patients in whom surgery is inappropriate;
  - in irradiated patients, until radiotherapy is effective

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Novartis online through the pharmacovigilance intake (PVI) tool at www.novartis.com/report or alternatively email medinfo.uk@novartis.com or call 01276 698370.

ENETS, European Neuroendocrine Tumor Society; NET, neuroendocrine tumours; TSH, thyroid stimulating hormone.

Prescribing information and Adverse Event Reporting can be found at the end of this booklet.

Promotional material funded and produced by Novartis Pharmaceuticals Ltd.

For UK healthcare professionals.

UK | October 2024 | FA-11276280

Sandostatin® LAR®
octreotide / IM INJECTION

NOVARTIS

UK | October 2024 | FA-11276280

Preparation and administration critical actions[2]

ROOM TEMPERATURE	FULLY SATURATED	UNIFORM SUSPENSION
The injection kit must reach room temperature	Ensure powder is fully saturated by letting vial stand for 5 minutes	Shake vial moderately for a minimum of 30 seconds, until uniform suspension forms

Suspension must only be prepared immediately before administration

Sandostatin LAR should only be administered by a trained healthcare professional.

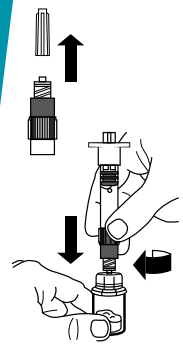
STEP 1

1. Remove Sandostatin LAR injection kit from refrigeration
2. Allow to stand for minimum of 30 minutes to allow the kit to reach **room temperature**, but do not exceed 24 hours (kit can be replaced in refrigerated storage if needed)
3. Remove the plastic cap from the vial and clean the rubber stopper of the vial with an alcohol wipe

STEP 2

1. Peel off lid film of blister tray containing vial adapter. Do NOT remove vial adapter from tray
2. Holding blister tray, position vial adapter on top of vial and push it fully down so that it snaps in place, confirmed by an audible 'click'
3. Lift blister tray off of vial adapter

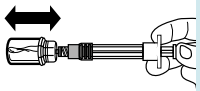
STEP 3



1. Remove cap from prefilled syringe and screw syringe onto vial adapter
2. Slowly push plunger all the way down to transfer all the diluent into vial
3. Let vial stand for **5 minutes** to ensure that the diluent has fully saturated the powder. Prepare patient for injection
4. Visually **inspect the vial to ensure powder is thoroughly wetted**

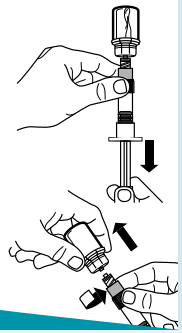
Note: It is normal for plunger rod to move up, as there might be a slight overpressure in the vial

STEP 4



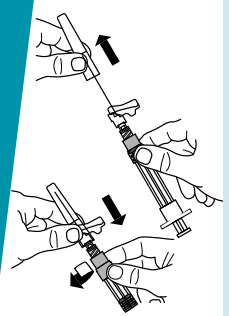
1. After wetting period, press plunger all the way down into syringe
2. Keep plunger pressed and **shake vial moderately** in a horizontal direction for a **minimum of 30 seconds**
3. Check visually that powder is completely suspended in vehicle (uniform milky suspension). **Repeat moderate shaking** for another 30 seconds if powder is not completely suspended

STEP 5



1. Turn syringe and vial upside down
2. Slowly pull plunger back and draw entire content from vial into syringe
3. Unscrew syringe from vial adapter

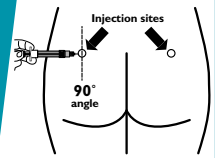
STEP 6



1. Screw safety injection needle onto syringe
2. Prepare injection site with an alcohol wipe
3. Pull protective cover straight off needle and gently invert syringe to maintain a uniform suspension
4. Perform a final visual check
5. Gently tap syringe to remove any visible bubbles and remove them from the syringe. Reconstituted Sandostatin LAR is now ready for **IMMEDIATE ADMINISTRATION**

Note: If immediate administration is delayed gently re-shake the syringe to ensure a milky uniform suspension

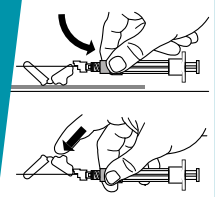
STEP 7



1. Insert needle fully into right or left gluteus at 90° angle
2. Slowly pull back the plunger to check that no blood vessel has been penetrated (reposition if a blood vessel has been penetrated)
3. Using steady pressure, depress plunger until syringe is empty
4. Withdraw needle from injection site

Note: Sandostatin LAR must be given only by **deep intramuscular injection**, NEVER intravenously.

STEP 8



1. Activate safety guard using single-handed technique:

a) Press hinged section of safety guard onto rigid surface

or

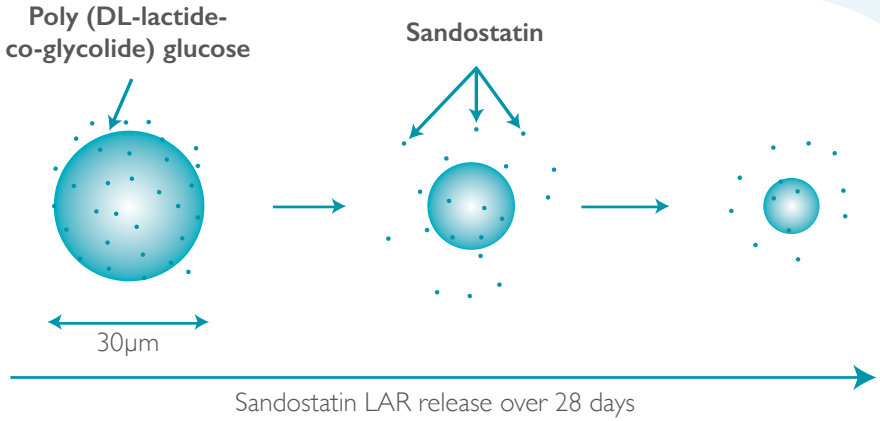
b) Push hinge forward with forefinger

2. **Audible 'click' confirms proper activation** of safety mechanism
3. Immediately dispose of syringe, with needle, in sharps container

All steps adapted from Sandostatin LAR (octreotide acetate) Summary of Product Characteristics.[2]

Sandostatin LAR mechanism of action

Microspheres containing Sandostatin gradually dissolve, causing a steady release of octreotide LAR over 28 days.[3,4]



Adapted from Anezi A, et al. 2016.[5]

Resources

To view a video on How to administer and prepare Sandostatin LAR, please scan the QR code below.

SANDOSTATIN® LAR® *(octreotide)*

Please refer to the Summary of Product Characteristics (SmPC) before prescribing Sandostatin LAR.

Indications: Treatment of patients with symptoms associated with functional gastro-entero-pancreatic endocrine tumours e.g. carcinoid tumours with features of the carcinoid syndrome. Treatment of patients with advanced neuroendocrine tumours of the midgut or of unknown primary origin where non-midgut sites of origin have been excluded. Treatment of patients with acromegaly in whom surgery is inappropriate or ineffective, or in the interim period until radiotherapy becomes fully effective. Treatment of TSH-secreting pituitary adenomas: when secretion has not normalised after surgery and/or radiotherapy; in patients in whom surgery is inappropriate; in irradiated patients, until radiotherapy is effective. **Presentation:** Long-acting injection form of octreotide (as acetate): 10, 20 or 30mg per vial. Each supplied with solvent for suspension. **Dosage and Administration:** Sandostatin LAR may only be administered by deep intramuscular injection. The site of repeat intragluteal injections should be alternated between the left and right gluteal muscle. **Gastro-entero-pancreatic endocrine tumours**: ***Treatment of patients with advanced neuroendocrine tumours of the midgut or of unknown primary origin where non-midgut sites of origin have been excluded:*** The recommended dose of Sandostatin LAR is 30 mg administered every 4 weeks. Treatment with Sandostatin LAR for tumour control should be continued in the absence of tumour progression. ***Treatment of patients with symptoms associated with functional gastro-entero-pancreatic neuroendocrine tumours:*** It is recommended to start treatment with the administration of 20 mg Sandostatin LAR at 4-week intervals. Patients on treatment with s.c. Sandostatin should continue at the previously effective dosage for 2 weeks after the first injection of Sandostatin LAR. For patients in whom symptoms and biological markers are well controlled after 3 months of treatment, the dose may be reduced to 10 mg Sandostatin LAR every 4 weeks. For patients in whom symptoms are only partially controlled after 3 months of treatment, the dose may be increased to 30 mg Sandostatin LAR every 4 weeks. For days when symptoms associated with gastro-entero-pancreatic tumours may increase during treatment with Sandostatin LAR, additional administration of s.c. Sandostatin is recommended at the dose used prior to the Sandostatin LAR treatment. This may occur mainly in the first 2 months of treatment until therapeutic concentrations of octreotide are reached. **Acromegaly:** It is recommended to start treatment with the administration of 20 mg Sandostatin LAR at 4-week intervals for 3 months. Patients on treatment with s.c. Sandostatin can start treatment with Sandostatin LAR the day after the last dose of s.c. Sandostatin. Subsequent dosage adjustment should be based on serum growth hormone (GH) and insulin-like growth factor 1/somatomedin C (IGF-1) concentrations and clinical symptoms. For patients in whom, within this 3-month period, clinical symptoms and biochemical parameters (GH; IGF-1) are not fully controlled (GH concentrations still above 2.5 microgram/L), the dose may be increased to 30 mg every 4 weeks. If after 3 months, GH, IGF-1, and/or symptoms are not adequately controlled at a dose of 30 mg, the dose may be increased to 40 mg every 4 weeks. For patients whose GH concentrations are consistently below 1 microgram/L, whose IGF-1 serum concentrations normalised, and in whom most reversible signs/symptoms of acromegaly have disappeared after 3 months of treatment with 20 mg, 10 mg Sandostatin LAR may be administered every 4 weeks. However, particularly in this group of patients, it is recommended to closely monitor adequate control of serum GH and IGF-1 concentrations, and clinical signs/symptoms at this low dose of Sandostatin LAR. For patients on a stable dose of Sandostatin LAR, assessment of GH and IGF-1 should be made every 6 months. **Treatment of TSH-secreting adenomas:** Treatment with Sandostatin LAR should be started at a dose of 20 mg at 4-weekly intervals for 3 months before considering dose adjustment. The dose is then adjusted on the basis of the TSH and thyroid hormone response. **Children:** Limited data available. **Use in patients with impaired renal function**. No dose adjustment of Sandostatin LAR is necessary in patients with impaired renal function. **Use in the elderly**. No dose adjustment of Sandostatin LAR is necessary in elderly patients (≥ 65 years of age) **Contraindications:** Known hypersensitivity to the active substance or any of the excipients. **Special Warnings & Precautions for Use:** All patients with GH secreting pituitary tumours should be monitored carefully in case complications occur with tumour expansion (e.g. visual field defects). If evidence of tumour expansion appears, alternative procedures may be advisable. Females of childbearing potential should be advised to use adequate contraception if necessary during treatment with octreotide. Thyroid function should be monitored in patients receiving prolonged treatment with octreotide. Hepatic function should be monitored during octreotide therapy and in certain cases patients with impaired hepatic function may require dose adjustment. Cardiovascular related events: Common cases of bradycardia have been reported and dose adjustment of any cardiac medication may be necessary. Gallbladder and related events: Cholelithiasis is a very common event during Sandostatin treatment and may be associated with cholecystitis and biliary duct dilatation. Additionally, cases of cholangitis have been reported as a complication of cholelithiasis in patients taking Sandostatin in the post-marketing setting. Ultrasonic examination of the gallbladder is recommended before and at 6 month intervals during Sandostatin LAR therapy. Glucose metabolism: Glucose tolerance and antidiabetic treatment should be monitored in all patients receiving LAR; and adjustment of insulin or oral hypoglycaemic requirements may be necessary in diabetics due to hyper and hypoglycaemic effect of Sandostatin LAR. Post prandial glucose tolerance may be impaired. The depth and duration of hypoglycaemia may be increased in insulinoma. These patients should be carefully monitored Nutrition: Sandostatin LAR may alter absorption of dietary fats and vitamin B_{12}. Monitoring of levels is recommended during therapy, especially for those patients that have a history of vitamin B_{12} deprivation. Pancreatic function: Pancreatic exocrine insufficiency (PEI) has been observed in some patients receiving octreotide therapy for gastroenteropancreatic neuroendocrine tumours. Symptoms of PEI can include steatorrhea, loose stools, abdominal bloating and weight loss. Screening and appropriate treatment for PEI according to clinical guidelines should be considered in symptomatic patients. Sodium Content: Sandostatin LAR contains less than 1 mmol (23 mg) sodium per vial, that is to say essentially 'sodium-free'. Pregnancy & Breastfeeding: It is preferable to avoid the use of Sandostatin LAR during pregnancy. Patients should not breastfeed during Sandostatin LAR treatment. Fertility: It is not known whether octreotide has an effect on human fertility. **Interactions:** Dose adjustment of medicinal products such as beta blockers, calcium channel blockers, or agents to control fluid and electrolyte balance may be necessary when Sandostatin LAR is administered concomitantly. Dose adjustments of insulin and antidiabetic medicinal products may be required when Sandostatin LAR is administered concomitantly. Sandostatin reduces absorption of cyclosporine and delays that of cimetidine. Concomitant administration of octreotide and bromocriptine increases bioavailability of bromocriptine. Somatostatin analogues may decrease the clearance of drugs metabolised by CYP3A4. Drugs metabolised by CYP3A4 with a low therapeutic index should be used with caution (e.g. quinidine and terfenadine). Somatostatin and its analogues such as Octreotide competitively bind to somatostatin receptors and may interfere with the efficacy of radioactive somatostatin analogues. The administration of Sandostatin LAR should be avoided for at least 4 weeks prior to the administration of lutetium (177 Lu) oxodotreotide. If necessary, patients may be treated with short acting somatostatin analogues until 24 hours prior to the administration of lutetium (177Lu) oxodotreotide. After administration of lutetium (177Lu) oxodotreotide, treatment with Sandostatin LAR can be resumed within 4 to 24 hours and should be discontinued again 4 weeks prior to the next administration of lutetium (177Lu) oxodotreotide. Sandostatin LAR has no or negligible influence on the ability to drive and use machines. Patients should be advised to be cautious when driving or using machines if they experience dizziness, asthenia/fatigue, or headache during treatment with Sandostatin LAR. **Side-Effects:** Adverse drug reactions reported in clinical studies: **Very Common:** Injection site reactions, diarrhoea, abdominal pain, nausea, constipation, flatulence, cholelithiasis, headache, hyperglycaemia **Common:** Asthenia, dyspepsia, vomiting, abdominal bloating, steatorrhoea, loose stools, discolouration of faeces, elevated transaminase levels, hypothyroidism, thyroid disorder, hypoglycaemia, impaired glucose tolerance, anorexia, bradycardia, dyspnoea, dizziness, pruritus, rash, alopecia, cholecystitis, biliary sludge, hyperbilirubinaemia **Uncommon:** Tachycardia, dehydration. **Adverse drug reactions** reported spontaneously (causality & frequency unknown): Thrombocytopenia, Anaphylaxis, allergy/hypersensitivity reactions, Urticaria, Acute pancreatitis, acute hepatitis without cholestasis, cholestatic hepatitis, cholestasis, jaundice, cholestatic jaundice, Arrhythmias, Increased alkaline phosphatase levels, increased gamma glutamyl transferase levels. Please refer to the SmPC for full details of all adverse reactions. **Package Quantities and Basic NHS Cost:** 10mg per vial (+ vehicle): £549.71 20mg per vial (+ vehicle): £799.33 30mg per vial (+ vehicle): £998.41 **Product Licence Numbers:** 10mg: PL 23860/0033 20mg: PL 23860/0034 30mg: PL 23860/0035 **Legal Category:** POM. **Marketing Authorisation Holder:** Novartis Ireland Limited, Vista Building, Elm Park, Merrion Road, Ballsbridge, Dublin 4, Ireland. Tel: 01276 692255.

Date of last revision of prescribing information: Sept 2024

UK | Sept 2024 | 168725-3

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References
1. Pavel M, et al. *Neuroendocrinology* 2016;103(2):172–185.
2. Sandostatin LAR (octreotide acetate) Summary of Product Characteristics, 2022.
3. Astruc B, et al. *J Clin Pharmacol* 2005;45:836–844.
4. Chen T, et al. *J Clin Pharmacol* 2000;40(5):475–481.
5. Anezi A, et al. *Endocrinol Metab Int J* 2016;3(4):98–99.

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