Medicines & Healthcare products
Regulatory Agency

Public Assessment Report

National Procedure

Atomoxetine 10 mg hard capsules
Atomoxetine 18 mg hard capsules
Atomoxetine 25 mg hard capsules
Atomoxetine 40 mg hard capsules
Atomoxetine 60 mg hard capsules
Atomoxetine 80 mg hard capsules
Atomoxetine 100 mg hard capsules

atomoxetine

PL 43542/0190-0196

Euro-Link Pharma Ltd

LAY SUMMARY

Atomoxetine 10 mg, 18 mg, 25 mg, 40 mg, 60 mg, 80 mg and 100 mg hard capsules atomoxetine

This is a summary of the Public Assessment Report (PAR) for Atomoxetine 10 mg, 18 mg, 25 mg, 40 mg, 60 mg, 80 mg and 100 mg hard capsules. It explains how these products were assessed and their authorisation recommended, as well as their conditions of use. It is not intended to provide practical advice on how to use these products.

These products will be referred to as Atomoxetine in this lay summary for ease of reading.

For practical information about using Atomoxetine, patients should read the Patient Information Leaflet (PIL) or contact their doctor or pharmacist.

What is Atomoxetine and what is it used for?
These products are generic medicines. This means that these medicines are the same as, and considered interchangeable with, reference medicines already authorised, called Strattera 10, 18, 25, 40, 60 mg hard capsules.

Atomoxetine is used to treat attention deficit and hyperactivity disorder (ADHD).
It is used:
- in children over six years of age
- in young people
- in adults

It is used only as a part of the total treatment of the disease which also requires treatments which do not involve medicines, such as counselling and behavioural therapy.
Atomoxetine is not for use as a treatment for ADHD in children under 6 years of age as it is not known if the drug works or is safe in these people.
In adults, Atomoxetine is used to treat ADHD when the symptoms are very troublesome and affect the patient's work or social life and when the patient has had symptoms of the disease as a child.

How does Atomoxetine work?
Atomoxetine hard capsules contain atomoxetine.
Atomoxetine increases the amount of noradrenaline in the brain. This is a chemical that is produced naturally and increases attention and decreases impulsiveness and hyperactivity in patients with ADHD. These medicines have been prescribed to help control the symptoms of ADHD. This medicine is not a stimulant and is therefore not addictive.

About ADHD
Children and young people with ADHD find it:
• hard to sit still and
• hard to concentrate.
It is not their fault that they cannot do these things.
Many children and young people struggle to do these things. However, with ADHD this can cause problems with everyday life. Children and young people with ADHD may have difficulty

learning and doing homework. They find it hard to behave well at home, at school or in other places. ADHD does not affect the intelligence of a child or young person.
Adults with ADHD find it difficult to do all the things that children find difficult; however, this may mean they have problems with:
• work
• relationships
• low self esteem
• education

How is Atomoxetine used?
The pharmaceutical form of these medicines is hard capsules, and the route of administration is oral (by mouth).

How much to take
If the patient is a child or teenager (6 years or older):
The child's doctor will tell the child how much Atomoxetine to take and will calculate this according to child's weight. He/she will normally start on a lower dose before increasing the amount of Atomoxetine the child needs to take according to the body weight.
- Body weight up to 70kg: a starting total daily dose of 0.5mg per kg of body weight for a minimum of 7 days. The patient's doctor may then decide to increase this to the usual maintenance dose of about 1.2mg per kg of body weight daily.
- Body weight over 70kg: a starting total daily dose of 40 mg for a minimum of 7 days. The patient's doctor may then decide to increase this to the usual maintenance dose of 80mg daily. The maximum daily dose the doctor will prescribe is 100 mg.

Adults
- Atomoxetine should be started at a total daily dose of 40 mg for a minimum of 7 days. Your doctor may then decide to increase this to the usual maintenance dose of 80mg-100mg daily. The maximum daily dose the patient's doctor will prescribe is 100 mg.
If the patient has problems with their liver the doctor may prescribe a lower dose.

For further information on how Atomoxetine is used, refer to the PIL and Summaries of Product Characteristics (SmPCs) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

These medicines can only be obtained with a prescription.

The patient should always take this medicine exactly as their doctor/pharmacist has told them. The patient should check with their doctor or pharmacist if they are not sure.

What benefits of Atomoxetine have been shown in studies?
Atomoxetine hard capsules are generic medicines that fulfil the criteria, meaning that no additional studies are required. Atomoxetine hard capsules have been considered generic medicines of the reference medicines based on the BCS (Biopharmaceutics Classification System)-based biowaiver approach, by satisfactory *in vitro* data comparison of their physical and chemical characteristics.

What are the possible side effects of Atomoxetine?
For the full list of all side effects reported with these medicines, see Section 4 of the PIL or the SmPCs available on the MHRA website.

If a patient gets any side effects, they should talk to their doctor, pharmacist or nurse. This includes any possible side effects not listed in the product information or the PIL that comes with the medicine. Patients can also report suspected side effects themselves, or a report can be made on their behalf by someone else who cares for them, directly via the Yellow Card scheme at https://yellowcard.mhra.gov.uk or search for 'MHRA Yellow Card' online. By reporting side effects, patients can help provide more information on the safety of this medicine.

Because Atomoxetine are a generic medicines, its benefits and possible side effects are considered to be the same as for the reference medicines.

Why was Atomoxetine approved?
It was concluded that, Atomoxetine has been shown to be comparable to the reference medicine. Therefore, the MHRA decided that, as for the reference medicine, the benefits are greater than the risks and recommended that it can be approved for use.

What measures are being taken to ensure the safe and effective use of Atomoxetine?
As for all newly-authorised medicines, a Risk Management Plan (RMP) has been developed for Atomoxetine. The RMP details the important risks of Atomoxetine, how these risks can be minimised, any uncertainties about Atomoxetine (missing information), and how more information will be obtained about the important risks and uncertainties.

The following safety concerns have been recognised for Atomoxetine:

Summary of safety concerns	
Important identified risks	• Suicidal ideation • Hepatic injury • Increased blood pressure an increased heart rate • Peripheral vascular instability (Raynaud's phenomenon)
Important potential risks	• Cardiovascular and cerebrovascular outcomes - myocardial ischaemia - tachyarrhythmia - cerebrovascular accident • QTc prolongation • Aggression/hostility • Seizures
Missing information	• Use in pregnancy and lactation

The information included in the SmPC and the PIL is compiled based on the available quality, non-clinical and clinical data, and includes appropriate precautions to be followed by healthcare professionals and patients. Side effects of Atomoxetine are continuously monitored and reviewed including all reports of suspected side-effects from patients, their carers, and healthcare professionals.

An RMP and a summary of the pharmacovigilance system have been provided with these applications and are satisfactory.

Other information about Atomoxetine
Marketing authorisations for Atomoxetine were granted in the United Kingdom (UK) on 30 May 2025.

The full PAR for Atomoxetine follows this summary.

This summary was last updated in June 2025.

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I INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) considered that the applications for Atomoxetine 10 mg, 18 mg, 25 mg, 40 mg, 60 mg, 80 mg and 100 mg hard capsules (PL 43542/0190-0196) could be approved.

The products are approved for the following indications:

Atomoxetine is indicated for the treatment of Attention-Deficit/Hyperactivity Disorder (ADHD) in children of 6 years and older, in adolescents and in adults as part of a comprehensive treatment programme. Treatment must be initiated by a specialist in the treatment of ADHD, such as a paediatrician, child/adolescent psychiatrist, or psychiatrist. Diagnosis should be made according to current DSM criteria or the guidelines in ICD.

In adults, the presence of symptoms of ADHD that were pre-existing in childhood should be confirmed. Third-party corroboration is desirable, and Atomoxetine should not be initiated when the verification of childhood ADHD symptoms is uncertain. Diagnosis cannot be made solely on the presence of one or more symptoms of ADHD. Based on clinical judgment, patients should have ADHD of at least moderate severity as indicated by at least moderate functional impairment in 2 or more settings (for example, social, academic, and/or occupational functioning), affecting several aspects of an individual's life.

Additional information for the safe use of this product:

A comprehensive treatment programme typically includes psychological, educational and social measures and is aimed at stabilising patients with a behavioural syndrome characterised by symptoms which may include chronic history of short attention span, distractibility, emotional lability, impulsivity, moderate to severe hyperactivity, minor neurological signs and abnormal EEG. Learning may or may not be impaired.

Pharmacological treatment is not indicated in all patients with this syndrome and the decision to use the drug must be based on a very thorough assessment of the severity of the patient's symptoms and impairment in relation to the patient's age and the persistence of symptoms.

The name of the active substance is atomoxetine which belongs to the pharmacotherapeutic group of psychoanaleptics, centrally acting sympathomimetics.

Mechanism of action and Pharmacodynamic effects

Atomoxetine is a highly selective and potent inhibitor of the pre-synaptic noradrenaline transporter, its presumed mechanism of action, without directly affecting the serotonin or dopamine transporters. Atomoxetine has minimal affinity for other noradrenergic receptors or for other neurotransmitter transporters or receptors. Atomoxetine has two major oxidative metabolites: 4- hydroxyatomoxetine and N-desmethylatomoxetine. 4-Hydroxyatomoxetine is equipotent to atomoxetine as an inhibitor of the noradrenaline transporter but unlike atomoxetine, this metabolite also exerts some inhibitory activity at the serotonin transporter. However, any effect on this transporter is likely to be minimal as the majority of 4-hydroxyatomoxetine is further metabolised such that it circulates in plasma at much lower

concentrations (1% of atomoxetine concentration in extensive metabolisers and 0.1% of atomoxetine concentration in poor metabolisers). N-Desmethylatomoxetine has substantially less pharmacological activity compared with atomoxetine. It circulates in plasma at lower concentrations in extensive metabolisers and at comparable concentrations to the parent drug in poor metabolisers at steady state.

Atomoxetine is not a psychostimulant and is not an amphetamine derivative. In a randomised, double-blind, placebo-controlled, abuse-potential study in adults comparing effects of atomoxetine and placebo, atomoxetine was not associated with a pattern of response that suggested stimulant or euphoriant properties.

These applications were approved under Regulation 51B of The Human Medicines Regulation 2012, as amended (previously Article 10(1) of Directive 2001/83/EC, as amended), as generic medicines of a suitable originator medicinal products, Strattera 10, 18, 25, 40, 60 mg hard capsules that has been licensed for a suitable time, in line with the legal requirements.

No new non-clinical studies were conducted, which is acceptable given that the applications are for generic medicinal products of a suitable reference products.

A biowaiver was submitted with these applications, which was accepted. No bioequivalence study was required, and no new clinical studies were provided with these applications.

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for these products at all sites responsible for the manufacture, assembly and batch release of these products.

A Risk Management Plan (RMP) and a summary of the pharmacovigilance system have been provided with these applications and are satisfactory.

Advice was sought from the Commission of Human Medicines (CHM) on 19th December 2024, following provision of additional data the CHM were reassured on the quality of the product.

Marketing authorisations for Atomoxetine were granted in the United Kingdom (UK) on 30 May 2025.

II QUALITY ASPECTS

II.1 Introduction

These products consist of hard capsules; each hard capsule contains atomoxetine hydrochloride equivalent to 10 mg, 18 mg, 25 mg, 40 mg, 60 mg, 80 mg and 100mg of atomoxetine, respectively.

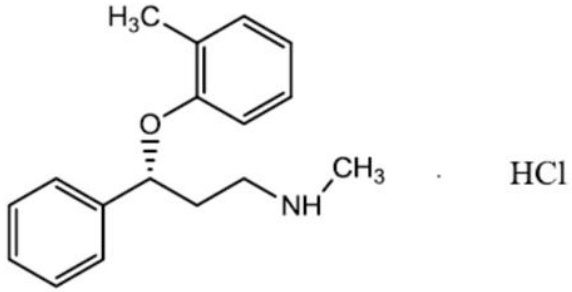
In addition to atomoxetine, these products also contain the following excipients:
Capsule contents:
Pregelatinized Starch
Dimeticone.
Capsule shell contents:
Gelatin
Titanium dioxide (E171)
Capsule Shell Cap colourants:
FD&C Blue 2 (Indigo Carmine) (E 132)
Indigotine
Iron oxide red (E172)
Yellow iron oxide
Titanium dioxide (E 171)
Printing ink:
Shellac (E904)
Dehydrated alcohol
(E1510) Isopropyl alcohol
Butyl alcohol
Propylene glycol (E1520)
Strong Ammonia solution (E527)
Black Iron Oxide (E172)
Potassium hydroxide (E525)

The finished products are packaged in PVDC/PVC/PE/PVDC-Alu blister of pack size of 28 capsules.

Satisfactory specifications and Certificates of Analysis have been provided for all packaging components. All primary packaging complies with the current regulations concerning materials in contact with food.

II.2 ACTIVE SUBSTANCE(S)

rINN: atomoxetine
Chemical Name:
(3R)-N-methyl -3-(2-methyl phenoxy)-3-phenylpropane-1-amine hydrochloride
Molecular Formula: $C_{17}H_{21}NO.HCl$
Chemical Structure:



Molecular Weight: 291.82
Appearance: A white to practically white powder
Solubility: Sparingly soluble in water, soluble in anhydrous ethanol, practically insoluble in heptane.

Atomoxetine is the subject of a European Pharmacopoeia monograph.

All aspects of the manufacture and control of the active substance are covered by a European Directorate for the Quality of Medicines and Healthcare (EDQM) Certificate of Suitability.

II.3 DRUG PRODUCT(S)

Pharmaceutical development

A satisfactory account of the pharmaceutical development was provided.

Comparative *in vitro* dissolution and impurity profiles were provided for the proposed and reference products.

All excipients comply with either their respective European/national monographs, or a suitable in-house specification. Satisfactory Certificates of Analysis were provided for all excipients.

No excipients of animal or human origin are used in the final products.

These products do not contain or consist of genetically modified organisms (GMO).

Manufacture of the product(s)

A description and flow-chart of the manufacturing method has been provided.

Satisfactory batch formulation data have been provided for the manufacture of the product(s), along with an appropriate account of the manufacturing process. The manufacturing process has been validated and has shown satisfactory results.

Finished Product Specifications

The finished product specifications at release and shelf-life are satisfactory. The test methods have been described and adequately validated. Batch data have been provided that comply with the release specifications. Certificates of Analysis have been provided for any working standards used.

Stability

Finished product stability studies have been conducted in accordance with current guidelines, using batches of the finished product stored in the packaging proposed for marketing. Based

on the results, a shelf-life of 3 years with no special storage conditions requirements, is acceptable.

II.4 Discussion on chemical, pharmaceutical and biological aspects
The grant of marketing authorisations was recommended.

III NON-CLINICAL ASPECTS

III.1 Introduction
As the pharmacodynamic, pharmacokinetic and toxicological properties of atomoxetine are well-known, no new non-clinical studies are required, and none have been provided. An overview based on the literature review is, thus, appropriate.

III.2 Pharmacology
No new pharmacology data were provided, and none were required for these applications.

III.3 Pharmacokinetics
No new pharmacokinetic data were provided, and none were required for these applications.

III.4 Toxicology
No new toxicology data were provided, and none were required for these applications.

III.5 Ecotoxicity/Environmental Risk Assessment
A suitable justification was provided for non-submission of an Environmental Risk Assessment. As the applications is for generic versions of an already authorised products, an increase in environmental exposure is not anticipated following approval of the marketing authorisations for the proposed products.

III.6 Discussion on the non-clinical aspects
The grant of marketing authorisations was recommended.

IV CLINICAL ASPECTS

IV.1 Introduction
The clinical pharmacology, efficacy and safety of atomoxetine are well-known. According to the regulatory requirements, the applicant has provided a suitable BCS-based biowaiver and a bioequivalence study is not required for this product. An overview based on a literature review is, thus, satisfactory.

IV. 2 Pharmacokinetics
No new pharmacokinetic data were submitted for these applications and none were required.

IV.3 Pharmacodynamics
No new pharmacodynamic data were submitted for these applications and none were required.

IV.4 Clinical efficacy
No new efficacy data were submitted with these applications and none were required.

IV.5 Clinical safety

No new safety data were submitted with these applications and none were required. The safety profile for these products is considered to be the same as Strattera 10, 18, 25, 40, 60 mg hard capsules.

IV.6 Risk Management Plan (RMP)

The applicant has submitted an RMP, in accordance with the requirements of Regulation 182 of The Human Medicines Regulation 2012, as amended. The applicant proposes only routine pharmacovigilance and routine risk minimisation measures for all safety concerns. This is acceptable.

IV.7 Discussion on the clinical aspects

The grant of marketing authorisations was recommended for these applications.

V USER CONSULTATION

A full colour mock-up of the Patient Information Leaflet (PIL) was provided with the application in accordance with legal requirements, including user consultation.

VI OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The quality of the products is acceptable, and no new non-clinical or clinical safety concerns have been identified. Extensive clinical experience with atomoxetine is considered to have demonstrated the therapeutic value of the compound. The benefit/risk is, therefore, considered to be positive.

The Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and labelling are satisfactory, in line with current guidelines and consistent with the reference products.

In accordance with legal requirements, the current approved UK versions of the SmPCs and PIL for these products are available on the MHRA website.

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Steps taken after the initial procedure with an influence on the Public Assessment Report (non-safety variations of clinical significance).

Please note that only non-safety variations of clinical significance are recorded below and in the annexes to this PAR. The assessment of safety variations where significant changes are made are recorded on the MHRA website or European Medicines Agency (EMA) website. Minor changes to the marketing authorisation are recorded in the current SmPC and/or PIL available on the MHRA website.

Application type	**Scope**	**Product information affected**	**Date of grant**	**Outcome**	**Assessment report attached Y/N**