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25 February 2015

Dear Sir/Madam

CONSULTATION DOCUMENT: ARM 90 OTRIVINE EXTRA DUAL RELIEF NASAL SPRAY SOLUTION

REQUEST TO RECLASSIFY A MEDICINAL PRODUCT FROM PRESCRIPTION ONLY MEDICINE (POM) TO PHARMACY (P)

This consultation seeks your views on the reclassification from POM to P of Otrivine Extra Dual Relief Nasal Spray Solution. The Commission on Human Medicines has advised that this product can be available as a pharmacy medicine. Consultation document ARM 90 which includes the applicant's Reclassification Summary, the carton label, the Patient Information Leaflet and response document has been posted on GOV.UK, the new home on the web for all consultations from central government.

You are invited to comment on the proposal and the response form can be found within the consultation document. Comments should be sent to me either by post to Floor 4-O, 151 Buckingham Palace Road, London SW1W 9SZ or by email (reclassification@mhra.gsi.gov.uk) to arrive by **18 March 2015**. Contributions received after that date cannot be included in the exercise.

To help informed debate on the issues raised by this consultation exercise, and within the terms of the Freedom of Information Act, the Agency intends to make copies of comments received publicly available. Unless you state otherwise we will assume that you have no objections to your comments being publicly available on the Agency's website.

Yours faithfully

Abiodun Aderogba
Self Medication Unit

REPLY FORM: ARM 90; OTRIVINE EXTRA DUAL RELIEF NASAL SPRAY SOLUTION

To: Abiodun Aderogba

From: _____

MHRA
Room 4-O
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ALL RESPONDENTS MUST TICK ONE OF THE FOLLOWING BOXES

- My reply may be made freely available
- I wish my reply to remain confidential*
- I wish parts of my reply to remain confidential*

*Please use the space below to explain why you feel the information in your reply should be treated as confidential. In line with the Freedom of Information Act 2000, if we receive a request for disclosure of the information we will take full account of your explanation, but we cannot give an assurance that confidentiality can be maintained in all circumstances. Responses to consultation will not normally be released under FOI until the regulatory process is complete

Explanation regarding why your response should remain confidential

Name:

Signature

Date:

Regulatory Affairs

**Otrivine[®] Extra Dual Relief Nasal Spray, solution
0.5 mg/ml + 0.6 mg/ml**

Xylometazoline hydrochloride, Ipratropium bromide

**POM to P reclassification summary of a medicinal
product for human use**

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RM2

RECLASSIFICATION SUMMARY for POM to P APPLICATIONS

1. Applicant details

Novartis Consumer Health UK Ltd.

Park View, Riverside Way, Watchmoor Park, Camberley, Surrey, GU15 3YL UK.

2. Product Details

Name and where applicable MA number

Otrivine Extra Dual Relief, 0.05% w/v, 0.06% w/v, Nasal Spray.

PL 00030/0462

Active ingredients

Xylometazoline hydrochloride, 0.5 mg/ml

Ipratropium bromide, 0.6 mg/ml

Indications

Symptomatic treatment of nasal congestion and rhinorrhoea in connection with common colds.

Dosage including age-limits and restrictions on length of treatment

Adults: 1 puff in each nostril up to 3 times daily. At least 6 hours should elapse between two doses.

The treatment duration should not exceed 7 days (see section 4.4).

It is recommended to stop treatment, when the symptoms have diminished, even before the maximum duration of treatment of 7 days, in order to minimise the risk of adverse reactions (see section 4.8).

Paediatric population:

Otrivine Extra Dual Relief is not recommended for use in children and adolescents below 18 years of age due to lack of sufficient documentation.

Elderly:

There is only limited experience of use in patients above 70 years of age.

Method of administration

Before the first application, prime the pump by actuating 4 times. Once primed, the pump will normally remain charged throughout regular daily treatment periods. Should the spray not be ejected during the full actuation stroke, or if the product has not been used for longer than 6 days, the pump will need to be reprimed with 4 actuations as initially performed.

Pack size

10ml

3. Introduction and Rationale for the Reclassification

Otrivine Extra Dual Relief Nasal Spray is a new fixed combination nasal metered-dose spray, solution, containing the active ingredients ipratropium bromide 0.6 mg/ml and xylometazoline hydrochloride 0.5 mg/ml, supplied in a 10ml metered-dose spray bottle. It is indicated for the relief of nasal congestion and rhinorrhoea associated with the common cold in adults.

The recommended dose in adults is one spray per nostril, up to three times daily for up to a maximum of 7 days. One spray dose contains 84 µg ipratropium bromide and 70µg xylometazoline hydrochloride.

Although this combination product has not previously been available in the UK, the individual ingredients ipratropium bromide and xylometazoline are in currently authorised products as Prescription Only Medicine (POM) and General Sales List (GSL) products respectively.

As additional supporting evidence, Otrivine Extra Dual Relief Nasal Spray is available as a non-prescription medicine in other member states of the European Union in the same fixed dose combination (ipratropium bromide 0.6 mg/ml and xylometazoline hydrochloride 0.5 mg/ml).

Role of the active ingredients and their role in combination

Ipratropium bromide is a synthetic quaternary amine with anticholinergic activity. Nasal application of ipratropium decreases nasal mucus secretion by competitive inhibition of cholinergic receptors on the serous and seromucous glands in the nasal epithelium. Ipratropium was shown to be effective and safe in the treatment of rhinorrhoea

In the UK, the currently authorised POM product containing ipratropium bromide for nasal application provides 21µg of ipratropium per spray and is indicated for the symptomatic relief of rhinorrhea in allergic and non-allergic rhinitis in adults and children over 12 years of age; the dose is two sprays (42µg) in each nostril administered 2 - 3 times a day and it is available as a 15 ml (180 metered sprays) or a 30 ml (380 metered sprays) pump.

The dose of ipratropium in Otrivine Extra Dual Relief is twice that of the currently authorised POM product (84µg compared to 42µg). This is because the proposed combination product is authorised for short term use in common colds, whereas the prescription medicine is indicated for a milder chronic rhinitis which may require a longer term lower dose.

Xylometazoline hydrochloride applied topically, causes vasoconstriction in the nasal mucosa, leading to a decrease in nasal blood flux and shrinking of the nasal mucosa with a corresponding reduction in the nasal airway resistance. Xylometazoline is approved worldwide for the symptomatic treatment of nasal congestion associated with conditions such as common cold, hay fever or other allergic rhinitis, sinusitis and

has a well-established safety profile, which has been marketed for OTC use for many years.

Combination product

The safety profile of these two active ingredients can be regarded as well-established for nasal application. In a literature review of ipratropium and xylometazoline alone and as a fixed combination, the authors concluded that the combination product should be used as first-line treatment – before any oral treatment – in the symptomatic relief of nasal congestion and rhinorrhoea due to common cold, especially due to the lack of systemic side effects. The combination provides effective relief of nasal congestion and rhinorrhoea by a topical, local action, and avoids unnecessary systemic drug exposure compared to oral alternatives.

In the common cold, the two main symptoms are nasal congestion and rhinorrhoea.

Otrivine Extra Dual Relief Nasal Spray offers the benefit to treat simultaneously these two lead symptoms of common cold as compared to available mono therapies.

The applicant proposes to introduce a fixed combination product containing both these well-established ingredients, as a Pharmacy (P) medicine, for the relief of symptoms of the common cold in adults. This combination provides effective relief of nasal congestion and rhinorrhoea by a topical, local action, and avoids unnecessary systemic drug exposure compared to oral alternatives.

Rationale for availability as a Pharmacy Medicine

The common cold in adults is a well characterised and familiar infection. The condition does not normally require consultation with a physician and a myriad of medicinal products are available without medical prescription to alleviate symptoms.

The two main symptoms of common cold (rhinorrhea and nasal congestion) are of short duration and easily self-diagnosed by patients. Otrivine Extra Dual Relief Nasal is being proposed as suitable for supply through pharmacies for self-medication for short term treatment. The common cold indication is suitable for non-prescription use

since patients easily recognise the symptoms of a cold, the risks of misdiagnosis are small and the infection is self-limiting. Furthermore this product has a simple dosage regimen with a short-term duration of treatment, the systemic absorption of the active ingredients is very low and side-effects are well known and generally well tolerated.

The prevalence of the infection and frequency of episodes can vary greatly but on average adults experience two to four colds per year with the infection typically lasting for a week. Although the infection is generally mild in nature, the symptoms of nasal stuffiness, runny nose, sneezing, headache, sore throat and a cough can be a discomfort and interfere with sleeping, eating and exercise patterns. This leads to many sufferers seeking relief quickly in the form of an over the counter remedy.

The availability of this product from pharmacists would give consumers more access points and a wider choice of treatment options with advice for the most appropriate product for their symptoms.

Regulation 62(3)) of the Human Medicines Regulations 2012 requires a medicine to be supplied by a prescription (POM) only if it:

- is likely to present a direct or indirect danger to human health, even when used correctly, if used without the supervision of a doctor
- is frequently and to a very wide extent used incorrectly, and as a result is likely to present a direct or indirect danger to human health
- contains substances or preparations of substances of which the activity requires, or the side effects require, further investigation
- is normally prescribed by a doctor for parenteral administration (that is, by injection).

The applicant has carefully considered these criteria for reclassification of Otrivine Extra Dual Relief Nasal Spray.

Criterion 1: Evaluation of danger to health when used correctly

“Medicinal products shall be subject to medical prescription when they are likely to present a danger either directly or indirectly even when used correctly, if utilised without medical supervision”.

Direct danger

Ipratropium and xylometazoline have a low toxicity and no relevant reproductive toxicity, genotoxic or carcinogenic properties were found. Adverse reactions during clinical use are well documented and are generally mild in nature. Topical application of the two active substances to the nasal mucosa results in a very low systemic absorption thus there is a limited potential for known and dose-dependent systemic, anticholinergic or sympathomimetic effects.

Xylometazoline was first registered in Switzerland on 8 December 1958 and is currently approved in 128 countries worldwide.

Both ipratropium and xylometazoline have been authorised for use in the indication proposed and have well-established safety profiles at the doses recommended. In addition, it has to be noted that nasal ipratropium is approved as OTC in combination with xylometazoline in other member states of the European Union. The risk of appearance of any rare and unknown adverse event is therefore very low, in particular since clinical studies have shown that no interactions between the active ingredients are expected.

Risks identified in the Risk Management Plan relating to possible drug interactions are well described in the patient information leaflet, with the advice to consult a doctor or pharmacist before using the product if in doubt about taking concomitant medicines. Such interactions are rare and are unlikely to lead to serious adverse reactions.

The information on when the product should not be used is detailed to patients in the product packaging and in pack leaflet such as:

- patients with known hypersensitivity to the active ingredients or other constituents or
- patients with glaucoma.
- Patients are also advised to discuss with their doctor or pharmacist if they have narrow-angle glaucoma or heart disease, thus addressing the identified risk of increased intraocular pressure, atrial fibrillation and laryngospasm & pharyngeal oedema.

The applicant has proposed additional risk minimisation measures as for this product due to the wider exposure through pharmacy supply. These are discussed in more detail in the Risk Management Plan and a summary is provided below.

Otrivine Extra Dual Relief nasal Spray is proposed as pharmacy only (P) product. Pharmacists are already familiar with recommending Xylometazoline containing products.

The applicant will provide educational materials for pharmacists and pharmacy counter assistants.

The objective of the training materials is to provide the pharmacist/pharmacy counter assistant with additional knowledge and understanding in respect of the specific additional risks identified for OTC availability in the UK of this combination product, and how best to mitigate those risks, including:

- confusion with other Otrivine brand products and other brands of OTC xylometazoline nasal spray
- confusion with the existing ipratropium bromide product available as prescription only medicine
- higher dose of ipratropium bromide than previously available in the UK being available as a P product
- exceeding the 7 day max period of use
- off-label use in the paediatric population
- unknown safety in pregnant and lactating women

Indirect danger

The symptoms of rhinorrhoea and nasal congestion associated with a cold are common and easily recognised. These symptoms are of short duration and the risk that symptomatic treatment would mask more serious underlying conditions, requiring medical attention and supervision, is low. This risk is further reduced by limiting treatment duration to a maximum of 7 days that is informed through the SmPC and Patient Information leaflet.

The potential of xylometazoline to induce rebound congestion is very low if used as directed.

There is no evidence from clinical trials or post marketing safety data that wider use of these two active ingredients would increase the risk of pharmacological resistance.

Risk of misuse

Post marketing surveillance indicates that intentional misuse of xylometazoline and ipratropium is rare. Results from an in-use study also confirm the safety of the product when contraindications were not fully respected. The danger to health is small if the patient uses the product when it is not indicated, uses it for longer periods than recommended, exceeds the recommended dose or fails to heed warnings or contraindications. No serious health consequences are likely if use of the product results in a delay in the patient seeking further medical advice for these symptoms.

Criterion 2: Evaluation of danger to health when used incorrectly.

“Medicinal products shall be subject to medical prescription when they are frequently and to a very wide extent used incorrectly, and as a result are likely to present a direct or indirect danger to human health”.

There is no evidence to suggest that the ingredients of the product are frequently used incorrectly. The pharmacy-based, in-use study demonstrates that patients are able to use the product safely as an OTC medication. No formal comparison was made of the incidence of adverse reactions between patients using the product incorrectly versus

correctly. However, neither the incidences nor the types of reported adverse reactions differ between off-label users and those who used the product according to the labelling.

The applicant is of the opinion that the risk of incorrect use leading to harmful effects is very low.

Criterion 3: Contains substances thereof the activity and/or side effects of which require further investigation

“Medicinal products shall be subject to medical prescription when they contain substances or preparations thereof the activity and/or side effect of which require further investigation”.

The activity and safety profile of the active ingredients used as single agents for the symptoms of the common cold are well established and have been in use for decades. The patient exposure to xylometazilne and ipratropium in combination is extensive at 10.5 million packs sold since market launch to 31 Mar 2013. The post-marketing data does not indicate any difference in safety from that of the individual actives. In addition the efficacy profile has been established in clinical trials. The product does not meet this criterion.

Criterion 4: parenteral administration

“Medical products shall be subject to medical prescription when they are normally to be administered parenterally (for injection)”.

This criterion is not applicable to this product.

4. Support for Reclassification

This is a company application only.

5. Specific OTC Requirements

There are no specific OTC requirements.

6. Safety Profile

Both ipratropium and xylometazoline have been authorised in combination for use in the indication proposed and have well-established safety profiles as single actives and in combination at the doses recommended. The safety profile of the product can be considered to be established for nasal use and generally well tolerated.

The assessment of the post-marketing safety data with 6.2 million patients exposed to the drug since first launch in 2006 did not reveal any unexpected events. The risk of appearance of any rare and unknown adverse event is therefore very low. Adverse reactions to the product are mild to moderate in general and usually resolve upon treatment discontinuation. There were no treatment related serious adverse events and no complications were reported. The adverse event reporting rate, estimated at 1 case report every 31, 800 patients is considered to be very low. This post marketing experience further supports the safety results obtained from clinical investigations detailed in the application dossier.

The product is not known to be associated with abuse.

The negligible systemic absorption associated with topical administration minimises the potential for systemic adverse events and drug-drug interactions. The estimated degree of systemic exposure with the proposed topical regimen is minimal. Systemic symptoms following accidental ingestion or overdose are therefore unlikely.

In conclusion, the safety profile of the combination product has been shown to be comparable to the well-established safety profiles of the single active ingredients. Extensive exposure has not identified any unknown serious adverse events and not identified any new adverse events. The applicant is therefore of the opinion that nasal administered xylometazoline and ipratropium fixed combination have a favourable risk-benefit-ratio and the product be considered for classification as a non-prescription medicinal product.

Overall conclusion

Human Medicines Regulations 2012, states that a medicine may only be supplied by prescription if it meets criteria specified in regulation 62(3).

It is the view of the applicant that a) ipratropium bromide 0.6 mg/ml as a monotherapy and b) ipratropium bromide 0.6 mg/ml in combination with xylometazoline hydrochloride, 0.5 mg/ml does not meet the criterion specified in regulation 62(3) and should not be subject to a prescription and is justified in being re-classified as being supplied by a pharmacist (P).

The common cold is a relatively mild, easily recognisable, self-limiting disease that is routinely self-diagnosed. The risk of misdiagnosis is limited. This indication is proven suitable for OTC treatment. Patients are instructed to seek medical advice if the symptoms do not respond to treatment within 7 days or worsen.

The product has demonstrated a good efficacy and safety profile in clinical studies in adult patients with the common cold. The fixed combination offers the benefit to treat both major symptoms of a common cold (rhinorrhoea and nasal congestion). The favourable risk-benefit profile is further supported by the observational, pharmacy-based in-use study and by post-marketing surveillance data for the actives in combination as well as single actives.

Assessment of the risks in relation to the criteria for prescription control indicates that this product is well suited for self-medication for this therapeutic indication. The labelling and patient information leaflet provides comprehensive instructions and appropriate warnings and precautions to ensure safe use without medical supervision.

PACKAGE LEAFLET: INFORMATION FOR THE USER



Otrivine[®]

Extra Dual Relief

0.5 mg/ml + 0.6 mg/ml

Nasal spray

Xylometazoline hydrochloride/lpratropium bromide

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

Always use this medicine exactly as described in this leaflet or as your doctor or pharmacist have told you.

- Keep this leaflet. You may need to read it again.
- Ask your pharmacist if you need more information or advice.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.
- You must talk to a doctor if you do not feel better or if you feel worse.

What is in this leaflet:

1. What Otrivine Extra Dual Relief is and what it is used for
2. What you need to know before you use Otrivine Extra Dual Relief
3. How to use Otrivine Extra Dual Relief
4. Possible side effects
5. How to store Otrivine Extra Dual Relief
6. Contents of the pack and other information

1. WHAT OTRIVINE[®] EXTRA DUAL RELIEF IS AND WHAT IT IS USED FOR

Otrivine Extra Dual Relief is a combination medicinal product consisting of two different substances. One of the active ingredients helps with runny nose, the other has a decongesting effect.

Otrivine Extra Dual Relief is used for the treatment of nasal congestion with runny nose (rhinorrhea) in connection with common colds.

2. WHAT YOU NEED TO KNOW BEFORE YOU USE OTRIVINE[®] EXTRA DUAL RELIEF**Do not use Otrivine Extra Dual Relief**

- In children below 18 years of age, as adequate information on safety and efficacy is not available

- If you are allergic to Xylometazoline hydrochloride or ipratropium bromide or any of the other ingredients of this medicine (listed in section 6)
- If you are allergic to atropine or similar substances, e.g. hyoscyamine and scopolamine
- If you had your pituitary gland removed by surgery carried out through the nose
- If you have had brain surgery where the operation was carried out through the nose or mouth
- If you suffer from glaucoma (increased pressure in the eye)
- If you have a very dry nose (inflammatory nasal dryness, rhinitis sicca).

Warnings and precautions

Talk to your doctor or pharmacist before using Otrivine Extra Dual Relief if you suffer from:

- Heart disease and/or raised blood pressure
- Diabetes
- An overactive thyroid gland (hyperthyroidism)
- Difficulty in urinating and/or an enlarged prostate gland
- Narrow-angle glaucoma
- A tendency to have nosebleeds
- Obstruction of the gut (small intestine)
- Cystic fibrosis
- Benign tumour of the adrenal gland that produces high amounts of adrenaline and nor-adrenaline (phaeochromocytoma) or a particular sensitivity to adrenaline and nor-adrenaline as you may experience dizziness, tremor, rapid heart rate, raised blood pressure and sleeplessness.

Immediate hypersensitivity (allergic reaction) may occur in rare cases. This may be seen as itchy red rash with raised inflammation of the skin (hives), difficulty breathing or speaking, difficulty swallowing due to swelling of the lips, face or throat. These symptoms may appear individually or all combined as a severe allergic reaction. If this occurs, immediately STOP using this medicine (see section 4).

Otrivine Extra Dual Relief should not be used for more than 7 consecutive days. If symptoms persist, consult a doctor. Prolonged or excessive use may cause stuffiness in the nose to return or worsen and swelling of the nasal mucosa.

Avoid spraying Otrivine Extra Dual Relief in or around the eyes. If this happens thoroughly rinse the eyes with cold water. Your vision may become temporarily blurred and the eye irritated, painful and red. If this happens contact your doctor for advice. Worsening of narrow-angle glaucoma may also occur.

Children and adolescents

Otrivine Extra Dual Relief is not recommended for use in children and adolescents below 18 years as adequate information on safety and efficacy is not available.



Other medicines and Otrivine Extra Dual Relief

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

It is particularly important that you mention the following:

- Monoamine oxidase inhibitors (used for treatment of depression). If you are taking or have taken these in the last two weeks, dangerous rises of the blood pressure may occur
- Tri-cyclic and tetra-cyclic antidepressants (if you are taking or have taken these in the last two weeks)
- Medicines used for travel sickness (medicines containing anticholinergic substances)
- Medicines used for gut disorders (particularly those for abnormal motility) (medicines containing anticholinergic substances).

If you use any of the above medicines, consult a doctor before using Otrivine Extra Dual Relief.

Pregnancy and breast-feeding

Otrivine Extra Dual Relief should not be used during pregnancy unless your doctor recommends it.

During breast-feeding Otrivine Extra Dual Relief should not be used unless your doctor decides the advantages outweigh the potential risks to the infant.

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Driving and using machines:

Visual disturbances (including blurred vision and dilation of the pupil), dizziness and fatigue have been reported with Otrivine Extra Dual Relief. If affected, you should avoid driving, operating machinery or taking part in activities where these symptoms may put yourself or others at risk.

3. HOW TO USE OTRIVINE® EXTRA DUAL RELIEF

Always use this medicine exactly as described in this leaflet or your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

The recommended dose is:

Adults: One puff in each nostril as needed, up to 3 times daily for maximum 7 days. Leave at least 6 hours between two doses. Do not exceed 3 applications daily into each nostril.

It is recommended that you stop treatment with Otrivine Extra Dual Relief as soon as your symptoms improve, even if this is sooner than 7 days, in order to minimise the risk of adverse reactions.

If you think the effect of this medicine is too strong or too weak, consult your doctor or pharmacist.

Instructions for use:

- Always blow your nose before using the nasal spray
- Remove the dust cap
- Do not cut the nozzle. The metered dose spray is ready to prime before use



- Before the first application, prime the pump by pumping 4 times. Once primed the pump will normally remain charged throughout regular daily treatment periods. Should the spray not be ejected during the full actuation stroke, or if the product has not been used for longer than 6 days, the pump will need to be reprimed with 4 pumps as initially performed
- Hold the bottle upright
- Bend your head slightly forward
- Close one nostril by placing your finger against the side of your nose and insert the spray tip into the other nostril. Press the pump quickly while inhaling through the nose
- Repeat this procedure in the other nostril

The effect occurs within 5-15 minutes.

Avoid spraying Otrivine Extra Dual Relief in or around the eyes.

If you use more Otrivine Extra Dual Relief than you should:

If you, or someone else, have taken more medicine than you should, contact your doctor, hospital or emergency room for assessment of the risk. It is advisable to take this leaflet, bottle or pack with you. This is particularly important for children who are more likely to develop adverse events than adults.

Symptoms of overdose are severe dizziness, sweating, severely lowered body temperature, headache, slow heart beat, rapid heart beat, impaired breathing, coma, convulsion, hypertension (high blood pressure) which may be followed by hypotension (low blood pressure).

Other symptoms may be dry mouth, difficulties focusing with the eye and hallucinations.

4. POSSIBLE SIDE EFFECTS

Like all medicines, this medicine can cause side effects, although not everybody gets them.

STOP using Otrivine Extra Dual Relief and seek medical help immediately if you have any of the following:

- Palpitations and increased heart rate (affects less than 1 in 100 people)
- Signs of an allergic reaction as difficulty breathing, speaking or swallowing; swelling of the face, lips, tongue or throat; severe itching of the skin, with a red rash or raised bumps (frequency not known cannot be estimated from available data)
- Disturbances of vision (including blurred vision, worsening of glaucoma or increased pressure in the eye), rainbow-coloured circles/halos around bright lights and/or eye pain (frequency not known cannot be estimated from available data).

The most common side effects are nose bleeding and nasal dryness. Many of the side effects reported are also symptoms of common cold.

Very common side effects (may affect more than 1 in 10 people):

- Nose bleeding, nasal dryness.

Common side effects (may affect up to 1 in 10 people):

- Nasal discomfort, congestion of the nose, dry and irritated throat, pain in the nose
- Dry mouth
- Altered taste sensation, headache.

Uncommon (may affect up to 1 in 100 people):

- Nasal ulcer, sneezing, pain in the throat, cough, hoarseness
- Stomach upsets, nausea
- Altered smell sensation, dizziness, shakiness
- Discomfort, tiredness
- Sleeplessness
- Irritation of the eyes, dry eyes

Rare (may affect up to 1 in 1,000 people):

- Runny nose

Frequency not known (cannot be estimated from available data):

- Rash, hives
- Discomfort around the nose
- Discomfort in the chest, thirst
- Sudden spasm of throat muscle
- Irregular pulse
- Difficulties focusing with the eyes, dilation of the pupils
- Itching
- Difficulties emptying the bladder.

In order to minimise the risk of side effects such as nose bleeding and other effects on the nose, it is recommended that you stop treatment with Otrivine Extra Dual Relief when your symptoms improve even if this is sooner than 7 days.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet.

You can also report side effects directly via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard

By reporting side effects you can help provide more information on the safety of this medicine.

5. HOW TO STORE OTRIVINE® EXTRA DUAL RELIEF

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label after EXP. The expiry date refers to the last day of that month.

Do not freeze.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What Otrivine® Extra Dual Relief contains

The active substances are xylometazoline hydrochloride and ipratropium bromide.

1 ml contains 0.5 mg xylometazoline hydrochloride and 0.6 mg ipratropium bromide.

1 puff contains 70 micrograms xylometazoline hydrochloride and 84 micrograms ipratropium bromide.

The other ingredients are disodium edetate, glycerol (85%), purified water, sodium hydroxide and hydrochloric acid.

What Otrivine Extra Dual Relief looks like and contents of the pack

Otrivine Extra Dual Relief is a clear solution.

The bottle contains approximately 70 puffs.

Otrivine Extra Dual Relief is available as a 10 ml nasal spray with a metered-dose spray pump.

Marketing Authorisation Holder and Manufacturer

Novartis Consumer Health UK Limited

Trading as Novartis Consumer Health

Park View

Riverside way

Watchmoor Park

Camberley, Surrey

GU15 3YL

This medicinal product is authorised in the Member States of the EEA under the following names:

AT	Otrivin Duo 0,5 mg/ml + 0,6 mg/ml Nasenspray, Lösung
BE	Otrivine Duo 0,5mg/ml + 0,6mg/ml neusspray oplossing
BG	Otrivin Extra 0.5 mg/ml + 0.6 mg/ml nasal spray, solution
CY	Otrivin Advance
CZ	Otrivin Rhinostop
DE	Otriven Duo mit Xylometazolin und Ipratropium
DK	Otrivin Comp næsespray, opløsning
EE	Otrivin Total
EL	Otrivin Advance
ES	Otriduo 0,5mg/ml + 0,6mg/ml pulverizacion nasal
FI	Otrivin Comp 0,5mg/ml + 0,6mg/ml nenäsümute, liuos
HU	Otrivin Plus 0,5mg/ml + 0,6mg/ml oldatos orrspray
IE	Otrivine Extra Dual Relief 0.5mg/ml, 0.6mg/ml Nasal Spray
IS	Otrivin Comp 0,5mg/ml + 0,6mg/ml nefuoi lausn
IT	Otriduo 0,5mg/ml + 0,6mg/ml spray nasale, soluzione

LT	OtriDuo 0,5 mg/ml + 0,6 mg/ml nosies purškalas, tirpalas
LU	Otrivine Duo
LV	Otrivin Total 0,5 mg/ml + 0,6mg/ml nasal spray solution
MT	Otrivine Extra Dual Relief 0.5mg/ml, 0.6mg/ml Nasal Spray
NL	Otrivin Duo Xylometazoline hydrochloride & Ipratropium bromide, 0,5/0,6 mg/ml, neusspray, oplossing
NO	Otrivin Comp 0,5mg/ml + 0,6mg/ml nesessay, oppløsning
PL	Otrivin Ipra MAX
PT	Otrifar 0.5mg/ml + 0.6mg/ml solução para pulverização
RO	Vibrocil Duo 0,5mg/ml + 0,6mg/ml spray nazal, solutie
SE	Otricomb 0,5mg/ml + 0,6 mg/ml nässpray lösning
SI	Otrivin Duo 0,5 mg/0,6 mg v 1 ml pršilo za nos, raztopina
SK	Otrivin Complete
UK	Otrivine Extra Dual Relief 0.5mg/ml, 0.6mg/ml Nasal Spray

This leaflet was last revised on May 28, 2014.

Otrivine® is a registered trademark of Novartis AG.

GB 308882 – XXXXXX

 **NOVARTIS**





Otrivine®
Extra Dual Relief
 Nasal spray
 0.5 mg/ml + 0.6 mg/ml
 Xylometazoline hydrochloride/
 Ipratropium bromide



GB 308880

Otrivine®

Extra Dual Relief

0.5 mg/ml + 0.6 mg/ml

Nasal spray

Xylometazoline hydrochloride/
 Ipratropium bromide



Works in minutes
 Lasts up to 6 hours

Nasal spray, solution 10ml.

Otrivine® Extra Dual Relief 0.5 mg/ml + 0.6 mg/ml nasal spray provides relief from the symptoms of nasal congestion and a runny nose due to colds.

Each application delivers a measured dose which works within minutes to clear a blocked nose and helps stop excessive nasal secretions for up to six hours.

Directions:

For nasal use.
 For nasal congestion and rhinorrhea.

Read the package leaflet before use.

Dosage

Adults over 18 years: One spray dose in each nostril maximum 3 times daily for maximum 7 days. At least 6 hours should elapse between two doses.

Do not use continuously for more than seven consecutive days. If symptoms persist consult your doctor.

Warning: Do not exceed the stated dose.

Otrivine®

Extra Dual Relief

0.5 mg/ml + 0.6 mg/ml

Nasal spray

Xylometazoline hydrochloride/
 Ipratropium bromide

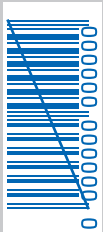


Works in minutes
 Lasts up to 6 hours

Active ingredient:
 1 ml contains, xylometazoline hydrochloride 0.5 mg, ipratropium bromide 0.6 mg. 1 puff contains 70 micrograms xylometazoline hydrochloride and 84 micrograms ipratropium bromide.

Also contains: Disodium edetate, glycerol (85%), purified water, as well as hydrochloric acid and sodium hydroxide (to adjust pH).
 Keep out of the sight and reach of children.

Each Otrivine pack should be used by one person only to prevent any cross infection. Do not use after the expiry date given. Do not freeze.



PL 00030/0462

P

10 ml

Novartis Consumer Health,
 Camberley, GU15 3YL, UK

NOVARTIS

XX 11111
 ALUFIN
 (Special de Vior)
 P 2945 C
 P 485 C
 P 7417 C
 Black

Lot/Exp.:

40 x 30 x 110



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Paediatric Chief Pharmacists Group
Patients Association
Pharmacy and Medicines Division (Scotland)
PSNC
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Terrence Higgins Trust
The Association of Independent Multiple Pharmacies
The Royal College of Radiologists
UK Homeopathic Medical Association
UK Inter-professional Group
UKCPA
WHICH
Women in medicine