APPLICATION FOR RECLASSIFICATION
NASACORT (triamcinolone acetonide)
55 mcg/ actuation
aqueous nasal spray

PART A

1. International non-proprietary name: triamcinolone acetonide

2. Proprietary name: Nasacort AQ Nasal Spray

3. Name of company requesting reclassification: Aventis Pharma Limited

4. Dose form and strength: Nasal Spray, 55 mcg/ actuation aqueous nasal spray

5. Pack size: 120 metered doses per pack

6. Indications for which change is sought:

   Current Restricted Medicine indication
   "Prophylaxis and treatment of seasonal allergic rhinitis in adults and children aged 12 years and over."

   Indication proposed for rescheduling to Pharmacy Medicine
   "Prophylaxis and treatment of allergic rhinitis in adults and children aged 12 years and over."

7. Present classification:

   Classified as a restricted medicine for the short-term treatment or prophylaxis of seasonal allergic rhinitis in adults and children aged 12 years and over. The maximum recommended daily dose is no greater than 220 mcg in a primary pack containing 120 actuations or less.

8. Classification sought

   This application seeks to reschedule triamcinolone acetonide nasal spray to Pharmacy Medicine and to expand the indications to include perennial allergic rhinitis, thereby becoming 'allergic rhinitis'. We request that the same pack size and dose restrictions that have been applied for Part III of the schedule, namely, a maximum recommended daily dose which is no greater than 220 mcg and maximum pack size of 120 actuations.

9. Classification status in other countries

Intranasal triamcinolone acetonide is classified as a Prescription Only Medicine in several countries, including Canada, Sweden and the USA. In the UK an application seeking Pharmacy Status was submitted in December 1999, this was subsequently approved (a copy of the Summary of Product Characteristics is provided in Appendix 2). In Australia, an application seeking Pharmacy status was submitted in October 2003 for consideration at the February 2004 NDPSC meeting.

10. Extent of usage in NZ and elsewhere

Although not currently marketed in New Zealand or Australia, intranasal triamcinolone acetonide is registered in 64 countries throughout the world. The approval dates of intranasal triamcinolone in New Zealand and other recognised countries are listed in Table 1.

Table 1: Approval dates for intranasal triamcinolone acetonide

Country	**Date of Approval**
Australia	7 October 1998
Austria	13 January 1998
Canada	28 February 1996
Denmark	1 December 1997
Finland	17 November 1997
France	19 February 1997
Germany	16 December 1997
Greece	8 December 1997
Netherlands	5 November 1997
New Zealand	16 February 1999
Russia	28 October 1998
South Africa	12 July 1996
Sweden	19 December 1997
Switzerland	29 November 1996
UK	28 February 1997
USA	20 May 1996

11. Proposed Labelling:

A copy of the proposed labelling for NASACORT AQ, Pharmacy Medicine, is provided in Appendix 3.

12. Proposed Warning Statements:

The specific warning statements for "Corticosteroids as aqueous solutions for nasal inhalation", outlined in the New Zealand Regulatory Guidelines for Medicines, Volume 1, section 12.10.6, will be included in the leaflet provided in packs of NASACORT, Pharmacy Medicine.

13. Other products containing the same active ingredient and which would be affected by the proposed change.

A tabulated summary of products registered in New Zealand containing triamcinolone acetonide as an active ingredient is provided in Table 2.

Table 2: Products registered in New Zealand containing triamcinolone acetonide

Tradename	**Active**	**Indication**
ARISTOCORT Cream & Ointment (Prescription Medicine)	triamcinolone acetonide 0.02%, 0.05%	Inflammatory Dermatoses
NASACORT AQ Nasal Spray (Prescription Medicine)	triamcinolone acetonide 55 mcg/ actuation	Allergic Rhinitis
ORACORT Dental Paste Prescription Medicine (≤ 5g Restricted Medicine).	triamcinolone acetonide 0.1%	Oral inflammatory lesions
VIADERM KC Cream and Ointment (Prescription Medicine)	triamcinolone acetonide 0.1% gramicidin 0.025% neomycin0.25%, nystatin100 000 U	Topical treatment of superficial bacterial infections, cutaneous candidosis and dermatological conditions

PART B

Reasons for Requesting Change

1. A Statement of the benefits from the proposed change

   The reclassification of Nasacort Nasal Spray as Pharmacy Medicine would allow consumers easier access to a safe treatment for allergic rhinitis. The safety and efficacy profile of intranasal triamcinolone acetonide is equivalent to other nasal steroids such as beclomethasone and budesonide.

   The treatment of allergic rhinitis is already regarded as a condition which is appropriate for self-diagnosis. This is evident from the numerous therapies already available without pharmacist supervision.

   Although the current scheduling for intranasal triamcinolone acetonide allows for consumer access without a prescription, the requirement for pharmacist supervision prevents it being made available concurrently with other allergic rhinitis therapies currently available as Pharmacy Medicine. This is particularly significant for an indication such as allergic rhinitis, in which therapeutic agents are often self-selected by consumers.

   The efficacy of intranasal triamcinolone acetonide in the adult population has been well demonstrated in clinical trials and safety studies have revealed a low incidence of adverse events following prolonged intranasal exposure. Several studies noted an absence of systemic glucocorticoid effects such as HPA-axis suppression. Substantial international post-marketing experience has been provided, and data gathered from this exposure have not revealed any new findings, trends or increased reporting frequency for intranasal triamcinolone acetonide.

   Most of the adverse events experienced with intranasal triamcinolone are readily recognisable and low to moderate in severity. Furthermore, safety data gathered post-marketing have not revealed any new findings, trends or increased reporting frequency for intranasal triamcinolone acetonide.

   In conclusion, we believe that intranasal triamcinolone acetonide does not warrant supervision by a pharmacist when used for the short-term prophylaxis and treatment of allergic rhinitis (thereby including perennial allergic rhinitis) in adults and adolescents (≥12 years) and request that it be rescheduled from a Restricted Medicine to Pharmacy Medicine.

2. Ease of Diagnosis

Due to the high prevalence of allergic rhinitis, the symptoms are often readily identifiable by the patient. Allergic rhinitis is already regarded as a condition which is appropriate for self-diagnosis as is evident from the numerous therapies already available without pharmacist supervision. In most instances patients learn to identify the symptoms of their allergies and in some cases are even able to isolate the cause of their allergies. Misdiagnosis would appear unlikely as patients will have usually presented to a medical practitioner for an initial diagnosis.

3. Relevant comparative data for like compounds

Extensive clinical trials have demonstrated that intranasal triamcinolone acetonide is as effective as intranasal beclomethasone twice daily or intranasal budesonide once daily in adults & adolescents (≥ 12 years) for the treatment of seasonal and perennial allergic rhinitis. In Part IV of the New Zealand Registration Dossier submitted for the registration of Nasacort, 13 clinical studies involving the safety and efficacy of triamcinolone acetonide nasal spray for the approved indications were submitted for assessment. Twelve of these clinical trials were placebo-controlled, double blind studies while one study was a long term open-label study. In addition to placebo, Nasacort was compared to aqueous formulations of beclomethasone dipropionate (2 studies) and budesonide (1 study). Furthermore 17 clinical studies were performed using the Nasacort nasal aerosol. Eight of these trials were double blind studies versus placebo, four were open label long term studies and five were performed double blind or single blind against active control treatments (beclomethasone dipropionate, flunisolide, fluticasone propionate, astemizole and loratadine). Additionally, the data on the efficacy and safety of Nasacort in paediatric patients included the results of eight double blind, placebo controlled clinical trials.

Grubbe et al. (1996) conducted a single masked, randomised, controlled, multi-centre, parallel group study to compare the efficacy, tolerability and treatment related side effects of 4 week intranasal therapy with 220μg once daily dose of triamcinolone acetonide aerosol versus 168μg twice daily beclomethasone dipropionate aqueous spray in 313 patients with perennial allergic rhinitis. The authors concluded that the study shows comparable efficacy and tolerance between the once daily administration of the starting dose of triamcinolone acetonide aerosol and the twice daily administration of the maximum recommended dose of beclomethasone dipropionate aqueous nasal spray.

4. Local data or special considerations relating to NZ

There is no local data separately available for Nasacort. Aventis Pharma is not aware of any additional special considerations in New Zealand for Nasacort.

5. Interactions with other medicines

Due to the intranasal route of administration and therefore minimal systemic absorption after intranasal use, triamcinolone acetonide is unlikely to interact with other medicines unlike many oral antihistamines which are presently available for allergic rhinitis. Additionally, intranasal corticosteroids are not associated with the potentially significant sedative side effects associated with first generation treatments for allergic rhinitis.

6. Contraindications

As per the datasheet, Nasacort is contraindicated in patients with known hypersensitivity to any constituents of the formulation.

7. Possible resistance

Progressive improvement in efficacy is shown to occur throughout the treatment period, indicative of a lack of tolerance or tachyphylaxis.

8. Adverse events

Clinical Trials

The overall conclusion of the extensive clinical trial development program described in the registration dossier was that intranasal triamcinolone acetonide for the treatment of allergic rhinitis was well tolerated. Within the dose range studied and up to twice the maximum adult therapeutic dose recommended (ie. twice the 220μg/day dose) and up to four times the paediatric therapeutic dose (ie. 110μg/day dose), intranasal triamcinolone acetonide did not have any effect on the HPA function (ie. growth function), which indicates the absence of a systemic effect with this aqueous nasal formulation. Additionally, HPA axis suppression has not been reported with the use of therapeutic doses of triamcinolone acetonide.

Clinical safety results in paediatric patients aged 4 to12 years also showed intranasal triamcinolone acetonide to be well tolerated. Epistaxis, a particularly frequent event in this patient population, was reported at a comparable frequency to the placebo control groups. In a review of clinical trials involving triamcinolone acetonide nasal sprays, the most common adverse events reported to intranasal triamcinolone acetonide included nasal irritation, sneezing, dry mucous membranes, headache and epistaxis. A 1 year study using an aerosol formulation of triamcinolone acetonide in 93 patients using 110 to 440μg/day, the only treatment-related adverse events reported were headache (n=1) and epistaxis (n=5) (Jeal & Faulds, 1997). Those adverse events possibly or probably related to the topical application of the drug treatment were few, not dose related and occurred at a frequency not higher than the placebo controls.

Schenkel et al. (1997) investigated the use of triamcinolone acetonide aqueous nasal spray for the treatment of seasonal allergic rhinitis (SAR) in 223 children aged 6 to 11 years in a multi-centre, double-blinded, parallel group study. The numbers of patients reporting adverse events was comparable for the three treatment groups: 16.2% (12/74) for triamcinolone acetonide 110μg: 23.3% (17/73) for the triamcinolone acetonide 220μg; and 18.4% (14/76) for the placebo group. There were no serious adverse events reported during the study and no patient discontinued use because of an adverse event. Headache and epistaxis were the most frequently reported adverse event. Headache was reported in 7% of patients taking triamcinolone acetonide 110μg, 3% of patients taking the 220μg, and 4% of patients taking placebo. One percent of patients in the 110μg group and 7% of patients in the placebo group reported epistaxis. The topical effects of the study medication were assessed by comparing the overall number of nasal adverse events (nasal irritation, dry mucous membranes, nasosinus congestion, throat discomfort, sneezing, epistaxis and upper respiratory tract infection) and no dose related trends were found between treatment groups. The authors concluded that the effectiveness, tolerability and once daily dosing supports the use of intranasal triamcinolone acetonide as first line therapy for the relief of SAR symptoms in children.

Nayak et al (1998) conducted a double blind, placebo-controlled study, which compared the effect of once daily triamcinolone acetonide nasal spray (220μg or 440μg) with placebo on adrenocortical function after 6 weeks of treatment in paediatric patients with allergic rhinitis. The study concluded that triamcinolone acetonide nasal spray is effective and well tolerated for the short and long term treatment of symptoms associated with perennial and seasonal allergic rhinitis, with demonstrated results in both the adult and paediatric population. The findings from this trial demonstrated that a therapeutic dose (220μg/day) and a higher dose (440μg/day) of triamcinolone acetonide nasal spray do not measurably alter adrenocortical function in paediatric patients with allergic rhinitis.

Post-Marketing Experience

Recent PSURs covering February 2000 to February 2003, are enclosed in the present application (Appendix 4). These updates contain information on all adverse events from all sources reported to Aventis Pharma in association with triamcinolone acetonide for nasal spray use. Extensive safety data gathered from this exposure have not revealed any new findings, trends or increased reporting frequency for intranasal triamcinolone acetonide.

9. Potential for abuse or misuse

Triamcinolone acetonide is non-sedating, non-addictive and not associated with any mood altering effects. Therefore, there is minimal potential for misuse or abuse. Triamcinolone also has a wide therapeutic index. Extensive preclinical studies have shown that it is poorly absorbed in all species when administered as an oral suspension.

APPENDICES

REFERENCES

Grubbe, R., Adelglass, J.M et al. (1996). "Intranasal therapy with once daily triamcinolone acetonide aerosol vs twice daily beclomethasone dipropionate aqueous spray in patients with perennial allergic rhinitis." Current Ther Research 57(11): 825-837.

Jeal, W. & Faulds, D. (1997). "Triamcinolone acetonide: A review of its pharmacological properties and therapeutic efficacy in the management of allergic rhinitis." Drugs 53(2)): 257-280.

Nayak, A.S., Ellis, M.H et al. (1998). "The effects of triamcinolone acetonide aqueous nasal spray on adrenocortical function in children with allergic rhinitis." J Allergy Clin Immunol 101: 157-62.

Schenkel, E.J., Gross, G.M. et al. (1997). "Triamcinolone acetonide aqueous nasal inhaler for the treatment of spring grass seasonal allergic rhinitis in children." Pediatric Asthma, Allergy & Immunology 11(2): 129-136.

APPENDICES

Appendix 1 References

Appendix 2 Nasacort AQ Summary of Product Characteristics

Appendix 3 Proposed labelling for NASACORT AQ, Pharmacy Medicine

Appendix 4

Periodic Safety Update Report for triamcinolone acetonide February 2000 to February 2001 (attachments not included)

Periodic Safety Update Report for triamcinolone acetonide February 2001 to February 2002 (attachments not included)

Periodic Safety Update Report for triamcinolone acetonide February 2002 to February 2003 (attachments not included)

Appendix 5 NASACORT AQ - Current Data Sheet

Appendix 6 NASACORT AQ - Proposed Data Sheet