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Interventions for adult Eustachian tube dysfunction (HTA No. 12/43/01)

Research Protocol 1.0
5 October 2012

1. Title of the Project

Interventions for adult Eustachian tube dysfunction (ETD): a systematic review

2. Name of TAR team and project lead

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3. Plain English summary

The Eustachian tube is a narrow tube which links the back of the nose to the middle ear. It is normally closed but opens when we swallow, yawn or chew. The Eustachian tube has three main functions: it protects the middle ear from pathogens; it allows air to flow into the middle ear, which can help to keep the air pressure equal on either side of the eardrum, enabling the eardrum to work and vibrate properly; and it has a drainage function, clearing secretions away from the middle ear.

The precise function of the Eustachian tube is not fully understood. The definition of Eustachian tube dysfunction (ETD), its mechanism and its underlying causes are also debated. ETD can occur when the Eustachian tube is swollen or cannot open properly. It can cause muffled hearing, pain, a feeling of fullness in the ear, tinnitus (ringing or buzzing in the ear), or problems with balance. ETD typically happens after a cold, or a nose, sinus, ear or throat infection.

Symptoms are often mild and generally do not last beyond a few days. Simple actions such as swallowing, yawning, chewing or blowing against a closed mouth and nose may stop the symptoms. However, symptoms sometimes last several weeks or more, in which case treatment may be considered. In the long-term, ETD has been linked with damage to the middle-ear and the eardrum and it may lead to infection of the middle ear, glue ear, or retraction of the eardrum.

There are several treatment options. Decongestant nasal sprays or drops may be used for colds or other causes of nasal congestion. Antihistamine tablets or nasal sprays may be advised for allergies such as hay fever. Steroid nasal sprays may also be used for allergies or when other causes of persistent inflammation in the nose are suspected. If symptoms

persist, or if the cause of ETD is not clear, an assessment with an ear specialist may be needed. In some cases, surgery may be considered. Currently, the main technique involves inserting a ventilation tube into the eardrum through a small incision. There are also newer surgical techniques that are mainly used in the context of research.

Currently there are no comprehensive guidelines for the treatment of ETD in adults. The purpose of this project is to assess the benefits and safety of different treatments options for ETD in adults.

4. Decision problem

4.1 Background

The Eustachian tube is a narrow tube which links the back of the nose to the middle ear. It is normally closed but opens when we swallow, yawn or chew. The Eustachian tube has three main functions: to protect the middle ear from pathogens; to ventilate the middle ear, which can help to keep the air pressure equal on either side of the eardrum, enabling the eardrum to work and vibrate properly; and to help drain secretions from the middle ear cleft.

Eustachian tube dysfunction (ETD) is the inability of the Eustachian tube to adequately perform these functions. However, the precise function and mechanisms of the Eustachian tube and the underlying causes of dysfunction are complex and not fully understood.[1] From a diagnostic perspective ETD is also poorly defined.

ETD may occur when the tube is swollen, does not open or close properly.[2] If the tube is dysfunctional, symptoms such as muffled hearing, pain, tinnitus, a feeling of fullness in the ear or problems with balance may occur. Abnormal patency (patulous Eustachian tube) is a separate condition, in which the Eustachian tube remains intermittently open, causing an echoing sound of the person's own heartbeat, breathing, and speech.

The Eustachian tube typically becomes swollen or dysfunctional following the onset of an infectious or inflammatory condition such as an upper respiratory tract infection, allergic rhinitis or chronic rhinosinusitis.[3, 4] Dysfunction of the Eustachian tube may also be related to failure of the muscles associated with Eustachian tube opening and malformations such as cleft palate. Extrinsic compression of the Eustachian tube due to inflammation of the adenoids, tumour or trauma may also result in ETD,[2, 5] although these conditions and their management are beyond the scope of this review. Other risk factors include tobacco smoke, reflux and radiation exposure.[6-8]

Long-term ETD has been associated with damage to the middle-ear and the eardrum. Complications include chronic otitis media (middle ear infection), serous otitis media (glue ear), and middle ear atelectasis (retraction of the eardrum).[1, 9] However, its role in the development of other middle ear conditions is not fully understood.[1]

There is limited data on ETD prevalence and incidence, which may notably be due to the lack of consensus regarding ETD definition. There appears to be no association with gender,[1] although it has been suggested that ethnicity and geographical factors (such as proximity to the poles) are associated with increased incidence and prevalence. [10 1] The incidence of ETD is disproportionately high in patients with cleft palate.[5]

Diagnosis and Management

ETD symptoms are common. They are often mild and generally resolve after a few days. Simple actions such as swallowing, yawning, chewing or forced exhalation against a closed

mouth and nose can help to equalise pressure in the middle ear and resolve symptoms. However, symptoms sometimes persist, in which case treatment may be required.

There are no comprehensive guidelines on diagnosis of ETD.[11] Diagnosis is generally based on clinical examination and medical history to identify potential underlying causes.[11] Common diagnostic factors include the inability to 'clear' or 'pop' the ear with changes in barometric pressure. Negative middle ear pressure often indicates ETD, although patients with ETD may have normal middle ear pressure. Evidence on the predictive value of Eustachian tube function tests is limited, and several tests may be needed for a reliable and comprehensive assessment of ET function.[12] Tympanometry and nasal endoscopy are initial test options.

There are a number of non-surgical and surgical treatment options aimed at improving Eustachian tube function, but there is limited consensus about management. Management strategies include:

- Active observation, which involves monitoring the symptoms to determine whether they naturally resolve.
- Supportive care, which includes advice about self-management such as to swallow, yawn, or chew to help equalise the pressure in the middle ear.
- Autoinflation, which is a technique whereby the Eustachian tube is reopened by raising the pressure in the nose. This can be achieved in several ways, including forced exhalation against a closed mouth and nose (Valsalva manoeuvre). Other methods include blowing up a balloon through each nostril or using an anaesthetic mask.[13] The aim is to introduce air into the middle ear, via the Eustachian tube, equalising the pressures and allowing better fluid drainage.
- Nasal douching, in which the nasal cavity is washed with a saline solution to flush out excess mucus and debris from the nose and sinuses.
- Decongestants, antihistamines, nasal or oral corticosteroids which are aimed at reducing nasal congestion and/or inflammation.
- Antibiotics, for the treatment of chronic rhinosinusitis which may be affecting the opening of the ET.
- Simethicone, which is currently being investigated in adults to assess whether it can help break up the bubbles that may block the opening of the Eustachian tube in the back of the nose during a cold, allowing air to pass between the nose and middle ear.[14]

Currently, the main surgical treatment in the UK is:

- A pressure equalising tube (also known as tympanostomy tube, ventilation tube or grommet) which is inserted into the eardrum through a small incision. Pressure equalising tubes typically extrude after 6 to 9 months, and repeated tube insertions may be necessary. Long-acting tubes are occasionally used, although these may be prone to crusting, infection, obstruction and permanent tympanic membrane perforation.

Newer surgical methods which are mainly used in the context of research include:

- Balloon dilatation of the Eustachian tube (or tympanostomy tube, myringotomy tube), a procedure which aims to dilate the Eustachian tube and improve its function. It consists of introducing a balloon catheter into the Eustachian tube through the nose, under transnasal endoscopic vision. The balloon is filled with saline. Pressure is maintained for approximately two minutes, following which the balloon is emptied and removed. The procedure is usually performed under general anaesthesia.

- Transtubal application of fluids, an emerging and minimally invasive approach for the application of fluids to the middle ear via the Eustachian tube. The transtubal application approach involves placing a microendoscope within the Eustachian tube under local anaesthesia via its epipharyngeal opening. Subsequently, fluids are applied through an additional working channel after microendoscopic evaluation.[15]
- Eustachian tuboplasty, an emerging treatment in which a laser or rotary cutting tool is used to strip away enlarged mucous membranes and cartilage to clear obstruction to the Eustachian tube. Tuboplasty has been used in patients with chronic ETD as an alternative to pressure equalising tubes which may have extruded on numerous occasions.[16] The intervention may also be used for middle ear atelectasis or serous effusion.[17]

There is no consensus on the optimal timing of the interventions. Surgical interventions are generally (though not exclusively) used where ETD is resistant to other interventions. A step-up approach is usually adopted, from primary to secondary and tertiary care settings. Treatment choice is based primarily on aetiology, severity and persistence of symptoms, as well as the degree of invasiveness of the treatment.

Existing research

A rapid appraisal of the review and guideline literature has been undertaken to inform the project. We searched key resources for published systematic reviews and guidelines on ETD, including the Cochrane Library, PROSPERO, SIGN guidelines, National Guidelines Clearinghouse (USA), NIHR HTA website, the NICE website, HSTAT, TRIP, Clinical Evidence, NHS Evidence and the NHS Clinical Knowledge Summaries database. Results of the rapid appraisal searches can be found in Appendix A. One literature review[18] and one interventional procedure guidance[19] of relevance were identified.

A review of the literature by van Heerbeek[18] published in 2002 focused on interventions aimed at improving Eustachian tube function, but was of limited relevance. Although this was a broad review including a range of interventions and a broad population (including animals, children and adults), the searches were relatively limited (MEDLINE and PubMed only) and require updating.[20]

NICE issued guidance on balloon dilatation of the Eustachian tube in November 2011,[19] based on a rapid review of literature[21] which included three case series,[16, 22, 23] of which two were only published as conference abstracts.[16, 23] The guidance concluded that current evidence on the efficacy and safety of the procedure is inadequate in quantity and quality. NICE recommended that the intervention should only be used in the context of research; future research should address the efficacy of the procedure in the short and longer term, report data on safety outcomes, clearly describe which parts of the Eustachian tube are treated and report subjective measurements of symptom improvement as well as objective measurements of Eustachian tube function.

As highlighted in the commissioning brief, although websites such as BMJ Best Practice offer diagnostic and treatment suggestions, there is a lack of comprehensive treatment guidelines and no recent systematic review assessing the effectiveness of interventions for ETD. The commissioning brief requests a wide systematic review including best available evidence that will provide primary care practitioners with evidence about the value of referral, advise surgeons on the effectiveness of surgical interventions and inform recommendations for future research.

A key challenge in undertaking the review is that ETD is an ill-defined condition and consensus about its diagnostic criteria is lacking. In order to provide an informative overview

of the evidence on interventions for ETD, a pragmatic approach will be taken regarding how the condition is defined.

4.2 Research objectives

The aim of the research project is to determine the clinical effectiveness of interventions for adult Eustachian tube dysfunction (ETD) and to identify gaps in the evidence.

5. Methods for synthesis of clinical evidence

We will undertake a systematic review to evaluate the clinical effectiveness of interventions for the management of ETD. The systematic review will be conducted and reported following the general principles recommended in CRD's guidance[24] and the PRISMA statement.[25] The research protocol will be registered on PROSPERO.

Search strategy

Both published and unpublished literature will be identified from systematic searches of electronic sources, hand searching, consultation with experts in the field, and reference checking. The following databases will be searched: MEDLINE, MEDLINE In-Process, Cumulative Index to Nursing & Allied Health (CINAHL), EMBASE, Science Citation Index, BIOSIS, Cochrane Database of Systematic Reviews (CDSR), Database of Abstracts of Reviews of Effects (DARE), Health Technology Assessment (HTA) database, Cochrane Central Register of Controlled Trials (CENTRAL), PASCAL, and Latin American and Caribbean Health Sciences (LILACS). In addition, information on studies in progress, unpublished research or research reported in the grey literature will be sought by searching a range of relevant databases including Conference Proceedings Citation Index: Science, Inside Conferences, Dissertation Abstracts, ClinicalTrials.gov, Controlled Clinical Trials, WHO International Clinical Trials Registry Platform portal, EU Clinical Trials Register, National Research Register Archive, US Food and Drug Administration (FDA), UK Medicines and Healthcare products Regulatory Agency (MHRA) and the European Medicines Agency (EMA).

A draft search strategy has been developed on Ovid MEDLINE which can be found in Appendix B. This strategy will be further developed and converted to run appropriately on other databases. The strategy combines terms for Eustachian tube and terms for interventions used to treat ETD. No language or date limits will be applied to the search strategy and study design filters will not be used.

The Clinical Practice Research Datalink (CPRD) will be investigated to establish whether it contains any relevant information on the epidemiology and natural history of ETD.

Study selection

Abstracts of studies identified by the searches will be independently assessed for inclusion by two reviewers using the criteria outlined below. Disagreements will be resolved through discussion and, where necessary, by consultation with a third reviewer. For abstracts and titles of potential relevance, full papers will also be assessed independently by two reviewers with disagreements resolved by the same procedure.

Inclusion and exclusion criteria

Participants

Adults (18 years or older) with a clinical diagnosis of ETD will be included. Given the current lack of consensus on diagnostic criteria for ETD, a strict definition of ETD will not be applied and primary study definitions of ETD will be accepted, provided that they are based on symptomatology, and/or tests such as tympanometry or otoscopy. Studies of patients with known patulous Eustachian tube or nasopharyngeal tumours will be excluded as these

populations are distinct and are likely to require different management options. Studies with mixed populations of patients with and without ETD will be included if separate outcome data are available for the population of interest.

Interventions
Interventions explicitly aimed at treating ETD will be eligible. A list of eligible interventions and examples of specific treatments is provided in Table 1 below.

Table 1: Eligible treatments

Treatment	**Examples**
Active observation	Monitoring to determine whether the condition resolves naturally
Supportive care	Advice on self-management strategies such as advice to swallow, yawn, or chew
Auto-inflation	Valsalva manoeuvre
Nasal douching	Sodium chloride
Topical nasal decongestants	Xylomethazoline
Antihistamines	Clemastine
Intranasal corticosteroids	Fluticasone propionate, Budesonide, Mometasone
Oral corticosteroids	Prednisolone
Leukotriene receptor antagonists (LTRAs)	Montelukast, Zafirlukast
Antibiotics	Doxycycline
Simethicone	Gas-X
Surgery	Pressure equalisation tubes Balloon dilatation of the ET Transtubal application of fluids Laser Eustachian tuboplasty

Comparators
Any comparator (placebo, no intervention or another eligible treatment) will be considered for inclusion.

Setting
Primary, secondary and tertiary care.

Outcomes
There is currently no consensus regarding the most appropriate measure of treatment success. Change in severity and/or frequency of symptoms will be treated as the primary outcome as this is likely to be relevant to patients. Other outcomes of interest will include: quality of life; improvement in middle ear function based on measurement tools such as tympanometry (reported as a categorical or continuous outcome); improvement in hearing based on audiometry (reported as a categorical or continuous outcome); tympanic membrane mobility; clearance of middle ear effusion; need for additional treatment, e.g. requirement for surgical procedure (including re-intervention); early tube extrusion (for pressure equalising tubes); adverse events of interventions; and complications related to ETD (e.g. atelectasis).

Study design
The review will include experimental trials (randomised and quasi-randomised) as well as observational studies with a control group. Uncontrolled observational studies (e.g. case series) including at least 10 patients will also be considered for interventions where no controlled studies are found. Studies without a control group have considerable limitations, particularly where the condition may naturally resolve and where there are limited data

available on the natural history of the condition. This study design will be included to provide as broad an overview as possible of current research in this field and in order to help inform any recommendations for future research.

Due to the lack of consensus on definitions of ETD there is likely to be variability across countries in the types of interventions in use and searches for studies in other languages are likely to identify interventions that are not relevant to the NHS. For instance, two Polish language studies on vibro-aerosols and vibro-pressure massage were identified in the scoping searches.[26, 27] Therefore, only English language studies will be included.

Data extraction

Data relating to study design, population characteristics, inclusion criteria (including method of diagnosing ETD), intervention and comparator, details of outcome measures used and results will be extracted by one reviewer using a piloted and standardised data extraction form. Dichotomous outcomes will be extracted as relative risks and continuous outcomes as mean differences (with 95% confidence intervals). We will record whether studies present outcome data by participants or by ear. Extracted data will be checked for accuracy by a second reviewer. Disagreements will be resolved through consensus, and if necessary, a third reviewer will be consulted. Authors will be contacted for clarification and missing data as necessary. Data from studies with multiple publications will be extracted and reported as a single study.

Quality assessment

RCTs will be assessed using the Cochrane Risk of Bias Tool.[29] Tools used by the TAR group in previous reviews will be adapted and employed for the assessment of comparative non-randomised studies[30, 31] and the assessment of case-series.[30] The assessment will be performed independently and in duplicate by two reviewers. Disagreements will be resolved through consensus, and, if necessary, a third reviewer will be consulted.

Methods of analysis and synthesis

In the first instance, study characteristics and quality assessment will be presented in a series of structured tables. We anticipate that it is unlikely that there will be sufficient data available for a quantitative synthesis or sophisticated subgroup analysis. If this is the case a narrative synthesis will be undertaken, with studies grouped by intervention and then outcome and duration of follow-up. Results will be interpreted in the context of the quality of the individual studies and clinical heterogeneity. Where there are sufficient clinically homogeneous data, data will be pooled and statistical heterogeneity will be investigated using appropriate methods.[28, 29] Should a quantitative synthesis be possible, an analysis plan will be specified prior to undertaking any analysis to reduce the risk of introducing bias.

Subgroups

Analysis of specific subgroups will be undertaken where sufficient data are available. Key characteristics of interest are definition of ETD used, duration of ETD, associated conditions and severity of ETD symptoms at baseline.

6. Expertise in this TAR team and authors contributions

The Centre for Reviews and Dissemination (CRD) undertakes systematic reviews of research about the effects of interventions used in health and social care (www.york.ac.uk/inst/crd). Recent studies include a systematic review and cost-effectiveness analysis on the management of frozen shoulder,[30] a systematic review and cost-effectiveness analysis on low-intensity psychological interventions for the secondary prevention of relapse after depression,[32] and a systematic review of the clinical effectiveness of EOS 2D/3D X-ray imaging system for the evaluation and monitoring of scoliosis and other relevant orthopaedic conditions.[33]

Melissa Harden has contributed to the protocol and will undertake the literature searches for the systematic review and the associated bibliographic management. She is an information specialist with 6 years experience in the design, conduct and reporting of literature searches and has supported numerous systematic reviews and health technology assessments.

Alexis Llewellyn, Research Fellow, CRD, has worked on several systematic reviews, including for NICE, the HTA programme and other agencies. He has contributed to the study protocol and will provide input at all stages of the review.

Catriona McDaid, Senior Research Fellow, CRD, has ten years experience in systematic reviews and systematic review methodology. She has worked on systematic reviews for NICE, the HTA programme, AGNSS and other agencies. She will be responsible for managing the review. She has contributed to the protocol and will provide input at all stages of the review.

Gill Norman, Research Fellow, CRD, has eight years experience in systematic reviews and related areas. She has worked on systematic reviews and related technology appraisals for NICE, the HTA and other agencies. She has contributed to the protocol and will be involved in all aspects of the review process.

Clinical advice for the review will be provided by Mr Andrew Coatesworth, Consultant ENT Surgeon, York Foundation Trust, Professor Anne Schilder, Professor of Paediatric Otorhinolaryngology and Director of ENT Clinical Trials Programme, University College London Partners and Dr Daniel Kimberling, GP with an interest in ENT, Gale Farm Surgery, Acomb, York. They have contributed to the protocol, will comment on the draft report and provide advice on clinical aspects as necessary during the project.

7. Project timetable and milestones

The key milestones are as follows:

Draft protocol	14 September 2012
Approval of protocol by HTA	5 October 2012
Commence literature searches and screening	8 October 2012
Commence data extraction and quality assessment	29 October 2012
Progress report to HTA	30 November 2012
Commence synthesis and report writing	3 December 2012
Final report	8 February 2013

8. Competing interests of authors

None of the authors have any competing interests to declare.

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Appendix A

Rapid appraisal search of high level sources to identify existing and in progress systematic reviews and guidelines.

Source	Number of records identified
Cochrane Database of Systematic Reviews (CDSR) http://www.thecochranelibrary.com/	2
Database of Abstracts of Reviews of Effects (DARE) http://www.crd.york.ac.uk/crdweb/	4
PROSPERO: international prospective register of systematic reviews http://144.32.150.25/PROSPERO/	0
Health Technology Assessment (HTA) Database http://www.crd.york.ac.uk/crdweb/	0
SIGN Guidelines http://www.sign.ac.uk/	0
National Guideline Clearinghouse http://www.guidelines.gov/	5
NIHR Health Technology Assessment Programme http://www.hta.ac.uk/	0
NICE http://www.nice.org.uk/	2
Health Services/Technology Assessment Text (HSTAT) http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=hstat	0
TRIP http://www.tripdatabase.com	47
Clinical Evidence http://clinicalevidence.bmj.com/ceweb/conditions/index.jsp	0
NHS Evidence http://www.evidence.nhs.uk/default.aspx	2
NHS Clinical Knowledge Summaries http://www.cks.nhs.uk/home	3

Appendix B

The following search strategy was designed to identify studies of interventions to treat Eustachian tube dysfunction. The strategy will be adapted to run on other databases.

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present>

Date of search: 8th October 2012

1 Eustachian Tube/ (2702)
2 ((eustachian or auditory or pharyngotympanic) adj3 tub$).ti,ab. (2960)
3 (eustachian adj2 (canal or orifice$)).ti,ab. (67)
4 (middle ear adj3 dysfunction$).ti,ab. (121)
5 (middle ear adj3 pressure$).ti,ab. (823)
6 or/1-5 (4399)
7 exp Adrenal Cortex Hormones/ (322423)
8 exp Steroids/ (672905)
9 exp Anti-Inflammatory Agents/ (381776)
10 (adrenal cort$ adj2 hormone$).ti,ab. (864)
11 (corticosteroid$ or cortico steroid$ or corticoid$).ti,ab. (75248)
12 steroid$.ti,ab. (171724)
13 glucocorticoid$.ti,ab. (48091)
14 (anti inflam$ or antiinflam$).ti,ab. (91002)
15 (fluticason$ or flixonase or flonase or flovent or cultivate or flixotide or atemur or axotide or beconase or cci 18781 or cci18781 or cutivat$ or flixovate or flunase or fluspiral or flutide or flutinase or flutivate or fluxonal or gr 18781 or gr18781 or zoflut).ti,ab,rn. (4575)
16 (budeson$ or pulmicort or horacort or rhinocort or bidien or budecort or budicort or CCRIS 5230 or cortivent or entocort or micronyl or noex or preferid or respules or rhinosol or spirocort or symbicort or uceris).ti,ab,rn. (4372)
17 (mometason$ or sch 32088 or nasonex or rinelon or elocon or allermax aqueous or asmanex or danitin or dermotasone or dermovel or ecural or elica or elocom or elocone or elocyn or elomet or elosalic or eloson or flumeta or mefurosan or metaspray or momate or mometAid or monovel or morecort or motaderm or nosorex or novasone or propel or rimelon or rivelon or uniclar).ti,ab,rn. (1512)
18 (triamcinolone acetonide or tricinolon or cinonide or kenalog or azmacort or kenacort or acetospan or adcortyl A or allerNaze or aristocort or aristoderm or aristogel or CCRIS 5231 or coupe-A or flutex or flutone or kenalone or NSC 21916 or nasacort or omcilon A or oracort or oralone or polcortolon or rineton or solodelf or tramacin or tri-nasal or triacet$ or triacort or triam-Injekt or triamonide or trianex or triatex or triderm or triesence or trivaris or trymex or volon A).ti,ab,rn. (7767)
19 (dexameth$ or adrenocot or aflucoson$ or alfalyl or Anaflogistico or Aphtasolon or arcodexan$ or artrosone or Auxiron or Azium or bidexol or Bisu DS or Calonat or CCRIS 7067 or cebedex or cetadexon or colofoam or corsona or Corsone or cortastat or cortidex$ or cortidron$ or Cortisumman or dacortina fuerte or dacortine fuerte or dalalone or danasone or Decacortin or decadeltoson$ or Decaderm or decadion or decadran or decadron$ or decaesadril or Decagel or decaject or Decalix or decameth or Decasone or decaspray or decasterolone or decdan or decilone or decofluor or Dectancyl or Dekacort or delladec or deltafluoren$ or Dergramin or Deronil).ti,ab,rn. (56163)
20 (desacort or desacortone or Desadrene or desalark or desameton$ or Deseronil or desigdron or dexa cortisyl or dexa dabrosan or dexa korti or Dexa Mamallet or dexa scherosan or dexa scherozon$ or Dexacort$ or Dexa-Cort$ or dexadabroson or dexadecadrol or Dexadeltone or dexadrol or Dexafarma or dexagel or dexagen or dexahelvacort or dexakorti or dexalien or dexalocal or Dexalona or dexame$ or Dexametasona or dexan or dexane or dexano or Dexapolcort or Dexapos or dexapot or Dexaprol or dexascheroson or Dexa-Scheroson or dexascherozon$ or Dexa-sine or Dexason$ or Dex-ide or Dexinolon or Dexinoral or dexionil or dexona or Dexone or dexpak or Dextelan).ti,ab,rn. (55444)
21 (dextrasone or Dezone or dibasona or Dinormon or doxamethasone or esacortene or exadion$ or firmalone or fluormethyl prednisolon$ or fluormethylprednisolon$ or Fluormone or

Fluorocort or fluorodelta or Fortecortin or Gammacorte$ or grosodexon$ or hexadecadiol or hexadecadrol or hexadiol or hexadrol or Isopto Dex or isopto maxidex or isoptodex or isoptomaxidex or Lokalison F or Loverine or Luxazone or marvidione or maxidex or Mediamethasone or megacortin or mephameson$ or metasolon$ or methazon$ ion or methazonion$ or metisone lafi or mexasone or Mexidex or millicorten$ or Mymethasone or nisomethasona or novocort or NSC 34521 or nsc34521).ti,ab,rn. (74)
22 (Ocu-trol or oftan-dexa or opticorten or opticortinol or oradexan or oradexon$ or orgadrone or Ozurdex or pidexon or Policort or Prednisolon F or prodexon$ or sanamethasone or santenson or santeson or sawasone or solurex or spoloven or sterasone or thilodexine or triamcimetil or vexamet or visumetazone or visumethazone or adrecort or Aeroseb or dexacen or isnacort or methylfluorprednisolone or posurdex).ti,ab,rn. (44)
23 (beclomet$ or aerobec or afifon or Alanase or Aldecin$ or anceron or apo-beclomethasone or ascocortonyl or asmabec clickhaler or Atomase or atomide or beceze or Beclacin or beclamet or beclate or Beclazone or beclo asma or beclo AZU or beclo rhino or becloasma or beclocort or becloforte or beclojet or beclone or beclorhinol or beclosol or beclotaide or becloturmant or becloturmat or beclovent or becodisk$ or beconase or beconasol or becotide or belax or bemedrex).ti,ab,rn. (3437)
24 (Benconase or bronchocort or bronconox or chf 1514 or chf1514 or Clenil or decomit or ecobec or Entyderma or filair or Inalone or junik or Korbutone or Menaderm or miflasone or nasobec aqueous or nexxair or nobec or orbec or prolair or propaderm or qvar or ratioallerg or respocort or rhinivict or Rhino Clenil or Rhinosol or rinaze or rynconox or sanasthmax or sanasthmyl or "sbn 024" or sbn024 or Sch 18020W or Turbinal or vancenase or vanceril or ventolair or viarex or viarin or Viaro or xiten).ti,ab,rn. (141)
25 (betamethasone or betamethason or betnesol or bentelan or rinderon$ or celestone phosphate or beta corlan or beta methasone or betam-ophtal or diprospan or durabetason or etnesol or inflacor or linolosal or linosal or NSC 90616 or solucelestan).ti,ab,rn. (6266)
26 (apo-flunisolide or inhacort or nasalide or ratio-flunisolide or rhinalar or RS-3999 or syntaris or aeroBid or nasarel or aerospan or bronalide or cyntaris or flunitec or flunisolid$ or gibiflu or locasyn or lokilan or lunibron-a or lunis or nisolid or rs3999 or sanergal or soluzione or synaclyn or val 679 or val679).ti,ab,rn. (355)
27 (prednison$ or Adasone or ancortone or Apo-Prednisone or biocortone or Cartancyl or CCRIS 2646 or colisone or Cortan or Cortancyl or cortidelt or cortiprex or Cotone or Cutason or dacorten or Dacortin or de cortisyl or decortancyl or decortin$ or Decortisyl or Dehydrocortisone or dekortin or delitisone or dellacort or delta cortelan or delta Cortisone or delta dome or delta e or delta prenovis or delta-1-Cortisone or delta-1-Dehydrocortisone or deltacort$ or delta-dome or Deltasone or deltison$ or deltra or di adreson or diadreson or drazone or Econosone or Encorton$).ti,ab,rn. (43824)
28 (Enkortolon or enkorton or fernisone or Fiasone or hostacortin or HSDB 3168 or Incocortyl or insone or IN Sone or Juvason or Kortancyl or Liquid Pred or Lisacort or lodotra or Lodtra or me-korti or meprison or metacortandracin or Meticorten or meticortine or NCI-C04897 or nisona or Nizon or Novoprednisone or nsc 10023 or nsc10023 or Nurison or Orasone or orisane or Panafcort or Panasol or paracort or Parmenison or pehacort or precort or precortal).ti,ab,rn. (135)
29 (Predni Tablinen or prednicen-m or prednicorm or Prednicort or prednicot or Prednidib or Prednilonga or Predniment or prednitone or Prednizon or Prednovister or Presone or pronison or Pronisone or pronizone or pulmison or Rectodelt or Retrocortine or servisone or SK-Prednisone or steerometz or Sterapred or Supercortil or U 6020 or Ultracorten$ or urtilone or Winpred or Wojtab or Zenadrid).ti,ab,rn. (50)
30 (methylprednisolon$ or adlone-40 or adlone-80 or A-Methapred or Artisone-wyeth or Besonia or BRN 2340300 or dep medalone 80 or depmedalone or depoject-80 or Depo-Medrol or depopred or Dopomedrol or esametone or firmacort or HSDB 3127 or Lemod or Medesone or medixon or med-jec-40 or Medlone 21 or mednin or medralone 80 or medrate or Medrol or medrone or meprednisolone or mesopren or Metastab or methacort 40 or methacort 80 or methylcotol or methylcotolone or Methyleneprednisolone or methylpred dp or methylsterolone or metidrol).ti,ab,rn. (19994)
31 (Metilbetasone or Metilprednisolon$ or Metipred or metrisone or Metrocort or metycortin or metypred or metypresol or Metysolon or Moderin or neomedrone or Nirypan or Noretona or nsc 19987 or nsc19987 or Predni N Tablinen or prednol or Promacortine or Reactenol or Sieropresol or solomet or solu decortin or Solu-medrol or Summicort or Suprametil or U 7532 or U-67 590A or Urbason or Urbasone or Wyacort).ti,ab,rn. (195)
32 (Prednisolon$ or adelcort or antisolon or antisolone or aprednislon or aprednislone or benisolon or benisolone or berisolon or berisolone or BRN 1354103 or Bubbli-Pred or caberdelta or capsoid or CCRIS 980 or co hydeltra or codelcortone or CO-Hydeltra or compresolon or Cordrol or cortadeltona

or cortadeltone or cortalone or cortelinter or cortisolone or Cotogesic or cotolone or dacrotin or ecaprednil or decortril or dehydro cortex or dehydro hydrocortisone or dehydro hydrocortisone or dehydrocortex or dehydrocortisol or dehydrocortisole or dehydrohydrocortison).ti,ab,rn. (36518)
33 (dehydrohydrocortisone or delcortol or delta cortef or delta cortril or delta ef cortelan or delta f or delta hycortol or delta hydrocortisone or delta hydrocortisone or delta ophticor or delta stab or delta1 dehydrocortisol or delta1 dehydrohydrocortisone or delta1 hydrocortisone or deltacortef or delta-cortef or Deltacortenol or deltacortenolo or deltacortil or deltacortoil or deltacortril or deltaderm or delta-Ef-Cortelan or deltaglycortril or deltahycortol or deltahydrocortison or deltahydrocortisone or deltaophticor or deltasolone or deltastab or deltidrosol or deltisilone).ti,ab,rn. (750)
34 (deltisolon or deltisolone or deltolasson or deltolassone or deltosona or deltosone or depo-predate or dermosolon or Derpo PD or Dexa-Cortidelt or hostacortin H or dhasolone or diadresone f or DiAdresonF or dicortol or domucortone or Donisolone or Dydeltrone or Eazolin D or encortelon or encortelone or encortolon or Erbacort or Erbasona or Estilsona or Fernisolone or glistelone or hefasolon or HSDB 3385 or hydeltra or hydeltrone or hydrelta or hydrocortancyl or hydrocortidelt or hydrodeltalone or hydrodeltisone or hydroretrocortin or hydroretrocortine or inflanefran).ti,ab,rn. (22)
35 (insolone or K 1557 or keteocort or key-pred or lenisolone or Lentosone or leocortol or liquipred or lygal kopftinktur or mediasolone or meprisolon or meprisolone or metacortalon or metacortalone or metacortandralon or metacortandralone or metacortelone or meti derm or meticortelone or metiderm or meti derm or morlone or mydrapred or neo delta or nisolon or nisolone or nsc 9120 or nsc9120 or opredsone or Orapred or panafcortelone or panafort or paracortol or Paracotol or Pediapred or phlogex or PRDL or pre cortisyl).ti,ab,rn. (34)
36 (preconin or precortalon or precortancyl or Precortilon or precortisyl or predacort 50 or predaject-50 or predalone 50 or predartrina or predartrine or Predate or predeltilone or predisole or predisyr or pred-ject-50 or predne dome or prednecort or prednedome or Predne-Dome or prednelan or predni coelin or predni h tablinen or Prednicen or prednicoelin or prednicortelone or prednifor drops or predni-helvacort or Prednilíderm or predniment or predniretard or prednis or prednisil or prednivet or prednorsolon or prednorsolone or Predonin or Predonine or predorgasolona or predorgasolone).ti,ab,rn. (28673)
37 (prelon or prelone or prenilone or prenin or prenolone or preventan or prezolon or Rolisone or rubycort or scherisolon or scherisolona or serilone or solondo or solone or solupren or soluprene or spiricort or spolotane or Steran or sterane or sterolone or supercortisol or supercortizol or taracortelone or Ulacort or walesolone or wysolone).ti,ab,rn. (64)
38 or/7-37 (1058233)
39 6 and 38 (106)
40 exp Nasal Decongestants/ (15904)
41 Imidazoles/ (38412)
42 Nasal Sprays/ (108)
43 (xylometazolin$ or Balkis or Chlorohist-LA or Decongest or espa-rhin or Gelonasal or Idasal or Idril N or Nasan or Imidin or NasenGel or NasenTropfen or NasenSpray or Novorin or Otradrops or Otraspray or Otrivin or Otriven$ or Rapako or schnupfen endrine or Snup or stas or Amidrin or Neo-Synephrine II or Olynth or Otrivine or Rhinactin or ba 11391 or ba11391 or "brn 0180524" or brufasol or otrovin hcl or servilaryn or tixycold or xylometarzoline or xylometazonolin$ or xylomethazoline or xilometazolin$ or zylometazoline or otrix).ti,ab,rn. (464)
44 (cirazolin$ or LD 3098).ti,ab,rn. (408)
45 (naphazolin$ or Afazol Grin or AK Con or AKCon or Albalon or albasol or All Clear or allersol or alpha-Naphthylmethyl imidazoline or antan or benil or "BRN 0151864" or cefasan or Ciba 2020 or Clear Eyes or Clearine or coldan or Colirio Alfa or comfort eye drops or dazolin or degest 2 or derinox or Idril or imidin or minha or Miraclar or mirafrin or Nafazair or Nafazolin$ or naphacel ofteno or naphasal or Naphcon or naphozoline hydrochloride or naphtears or naphthazoline or naphthizine).ti,ab,rn. (665)
46 (naphthyzin or nastizol or nazil ofteno or niazol or ocu-zoline or opcon or Optazine or Privin$ or Proculin or rhinantin or rhinazin or rhinoperd or rimidol or sanorin or sanotin or Siozwo or strictylon or Tele Stulln or TeleStulln or Vasoclear or Vasocon or Vasoconstrictor Pensa or VasoNit or vistalbalon or vistobalon).ti,ab,rn. (15396)
47 (Oxymetazolin$ or afrazine or afrin or atomol or bayfrin or "BRN 0886303" or dristan or drixine or duramist plus or H 990 or Hazol or HSDB 3143 or Iliadin or iliadine or Nafrine or nasivin or Navisin or Nezeril or nostrilla or ocuclear or Oximetazolin$ or Oxylazine or Oxymethazoline or Rhinofrenol or rhinolitan or rhinosan or sch 9384 or Sinerol or sinex long last or sinex or visine).ti,ab,rn. (991)
48 (Phenylephrin$ or adrianol or af-taf or Ah-Chew or AI3-02402 or ak-dilate or albalon relief or alconefrin or almefrin or biomidrin or biomydrin or CCRIS 8464 or derizene or despec-sf or disneumon

pernasal or dristan nasal mist or drosin or efrin-10 or efrisel or fenylephrine or HSDB 3383 or idrianol or isonefrine or isophrin or isopto frin or isoptofrin or l meta synephrine or lexatol or m synephrine or mesaton$ or meta sympathol or meta synephrine or metaoxedrin$).ti,ab,rn. (19182)
49 (Metasympatol or metasynephrine or Mezaton or m-Methylaminoethanolphenol or m-Oxedrine or m-Sympathol or m-Sympatol or m-Synephrine or mydfrin or nefrin-ofteno or Neo Synephrine or neofrin or neooxedrine or neophryn or neosynephrin or neosynephrine or neosynesin or neosynesine or ocu-phrin or oftan-metaoksedrin or op-isophrin or optistin or phenoptic or phenylefrine or phenylephedrine or prefrin or pupiletto forte or rectasol or rhinall 10 or slv 325 or slv325 or sucraphen or visadron or vistafrin or vistosan).ti,ab,rn. (212)
50 (Phenylpropanolamin$ or acutrim or apodrine or apoephedrine or apophedrine or appedrine or BRN 3196918 or descon or Dexatrim or dexatrim or diet gard or dietac premeal or HSDB 6485 or kontexin or monydrin or Mucron or mydriatin or nobese or Norephedrine or NSC 9920 or phenyl propanolamine or phenylpropanolamide or PPA or pressedrine or procol or Prolamine or propadine or propadrine or Propagest or Rhindecon or Super Odrinex or trimolet).ti,ab,rn. (4543)
51 (Pseudoephedrin$ or acunaso or afrinol or Besan or dimetapp or d-Isoephedrine or drixora or Ephedrine or HSDB 3177 or Isoephedrine or isofedrine or isophedrine or logicin plus or monofed or nasa-12 or novafed or otrinol or pseudo ephedrine or pseudo-12 or Pseudoefedrina or pseudono or Psi-ephedrin or repedrina or rhinalair or sch 4855 or sch4855 or sinumed or sinutab or subulin or Sudafed or sudomyl or sudosian or symptofed or tiptipot).ti,ab,rn. (5861)
52 (Synephrin$ or Sympaethamin$ or Oxedrine or aetaphen or asthma spray spofa or pentedrine or vasoton or Analeptin or DL-Synephrine or Ethaphene or NSC 166285 or NSC 170956 or Parakorper or Parasympatol or S 38537-9 or Simpalon or Simpatol or Sympathol or Sympatol or Synefrin or Synthenate or p-Hydroxyphenylmethylaminoethanol or p-Methylaminoethanolphenol or p-Oxedrine or p-Synephrine).ti,ab,rn. (8094)
53 (tetrahydrozolin$ or tetryzoline or Caltheon or Collyrium Fresh or Diabenyl T or Eye-Sine or Eye-Zine or Murine Plus or Murine Sore Eyes or Ophtalmin or Optazine Fresh or Optigene or Rhinopront or Tetra-Ide or Tetraclear or Tetrilin or Tyzine or Vasopos or Visine or Yxin or Vispring or Berberil N or "BRN 0011442" or HSDB 7471 or Tetrizolin$ or Tyzanol or clarine or insto or murine tears or murine-2 or nasan or nazane or nazine or necor tyzine or octilia or ophthalmin-n or opsil-a or optizoline or rhinoprout or stilla drops or visina or visolin).ti,ab,rn. (192)
54 (brompheniramine or Bromfed or Lodrane or Dimetapp).ti,ab,rn. (354)
55 (decongestant$ or decongestive$).ti,ab. (1474)
56 ((nasal or nose) adj2 (spray$ or mist or aerosol$)).ti,ab. (2359)
57 or/40-56 (92301)
58 6 and 57 (71)
59 exp Histamine Antagonists/ (53989)
60 (anti histamin$ or antihistamin$).ti,ab. (10920)
61 (histamine adj3 (antagonist$ or block$)).ti,ab. (5986)
62 ((H1 or H2 or H3 or H4) adj2 (antagonist$ or block$)).ti,ab. (10245)
63 (acrivastin$ or semprex or semprex-D or benadryl or prolert or BW 825C or BW825C or BW A825C).ti,ab,rn. (365)
64 (bilastine or bilaxten or f 96221 bm1 or f96221 bm1).ti,ab,rn. (35)
65 (Cetirizin$ or acidrine or adezio or agelmin or Alercet or Alergex or Alerid or Alerlisin or Alertisin or alertop or alerviden or aletir or alled or Allergy relief or Alleroff or allertec or alltec or alzytec or Apo-Cetirizine or betarhin or cerazine or cerini or cerotec or cesta or Cetalerg or Ceterifug or cethis or Ceti TAD or Cetiderm or Cetidura or Cetil von ct or CetiLich or cetimin or cetin or Ceti-Puren or cetirax or Cetirigamma or cetirin or Cetirlan or cetizin or Cetriler or cetrimed or Cetrine or cetrizet or cetrizin or Cetryn or cetymin or Cetzine or Cezin or cistamine or deallergy or falergi or finallerg or Formistin or histazine or histica or Hitrizin or HSDB 7739).ti,ab,rn. (1453)
66 (incidal-od or lergium or nosemin or nosmin or ozen or "P 071" or P071 or prixlae or razene or Reactine or Ressital or rhizin or risima or Riztec or ryvel or Ryzen or Salvalerg or sancotec or selitex or Setir or Setiral or setizin or simtec or Stopaler or Sun mark all day allergy or sutac or symitec or terizin or terzine or Topcare all day allergy or Triz or "UCB-P 071" or vick-zyrt or Virdos or Virlix or Voltric or Xero-sed or zenriz or zensil or zeran or zertine or Zetir or zicet or zinex or Ziptek or zirtec or Zirtek or Zirtin or zyllergy or zymed or zyrac or zyrazine or zyrcon or zyrlex or Zyrtec or Zyrtec-D or zyrtek or Zyrzine).ti,ab,rn. (1556)
67 (desloratadine or clarinex or aerius or neoclarityn or azomyr or denosin or SCH 34117 or allex or aviant or claramax or dasselta or decarbethoxyloratadine or desalex or descarboethoxyloratadine or deslor or neoclaritine or sch34117 or supraler).ti,ab,rn. (465)

68 (fexofenadine or allegra or telfast or Carboxyterfenadine or MDL 16455A or mdl 16455 or mdl16455).ti,ab,rn. (684)
69 (levocetirizine or xusal or xyzal).ti,ab,rn. (251)
70 (loratadin$ or aerotina or Alarin or Alavert or alerfast or alernitis or Alerpriv or alertadin or allerta or Allertidin or allertyn or allohex or ambrace or analergal or anhissen or anlos or ardin or Bactimicina allergy or Biloina or bonalerg or caradine or carin or civeran or clalodine or claratyne or clarid or Clarinase or Claritin or claritine or clarityn or clarityne or Clarium or cronitin or cronopen or curyken or demazin anti-allergy or ezasmin or ezede or finska or frenaler or fristamin or genadine or halodin or hislorex or histalor or histaloran or HSDB 3578 or j-tadine or klarihist or klinset or laredine or lergia or Lergy or lertamine or Lesidas or lindine or lisino or lisono or lobeta or lodain or lorabasics or loracert or loraclar or loraderm or loradex).ti,ab,rn. (3041)
71 (Loradif or loradin or lorahist or loralerg or lora-lich or lorano or loranox or Loranox or Lorantis or lorastine or lora-tabs or loratadura or loratan or loratazine or loratidin or loratidine or loraton or loratrim or loratyne or Loraver or loreen or lorfast or lorihis or lorin or lorita or Loritine or lotadine or lotarin or lowadina or mosedin or noratin or notamin or Nularef or onemin or optimin or polaratyne or proactin or pylor or restamine or Rhinase or ridamin or rihest or rinityn or Rinomex or rityne or roletra or rotifar or Sanelor or Sch 29851 or Sch29851 or sensibit or Sinhistan Dy or sohotin or Tadine or Talorat Dy or tidilor or tirlor or Topcare or toradine or velodan or versal or voratadine or zeos).ti,ab,rn. (93)
72 (mizolastin$ or zolistan or mistamine or mistalin or mizollen or zolim or mizolen or "SL 85 0324" or CCRIS 8410 or mkc 431 or sl 850324).ti,ab,rn. (115)
73 (rupatadine or rupafin or UR 12592 or UR12592).ti,ab,rn. (70)
74 (Chlorphenamin$ or 4-Chloropheniramine or ahiston or alerfin or alergical or alergidryl or alergitrat or alermine or aller or Aller-Chlor or Allerclor or allerfin or Allergican or Allergin or Allergisan or allergyl or allermin or allerphen or Alunex or analerg or anaphyl or Antagonate or antamin or apomin or barominic or cadistin or Carbinoxamide maleate or CCRIS 1418 or Chlo-Amine or chlometon or chlor trimeton or Chlor-100 or chloramate unicelles or chlorleate or Chlormene or chlorophenamine maleate or Chloropheniramine or Chlorophenylpyridamine or Chloropiril).ti,ab,rn. (4230)
75 (Chloroprophenpyridamine or chloroton or Chlorpheniramin$ or chlorpheno or chlorphenon or Chlorpro or Chlorprophenpyridamine or chlorpyrimine or Chlorspan 12 or Chlortab-4 or chlortrimeton or Chlor-Trimeton or chlortripolon or Chlor-Tripolon or Clorfenamina or Clorfeniramina or cloro trimeton or cloroalergan or Cloropiril or clorotrimeton or Cloro-Trimeton or C-Meton or cohistan or com-trimeton or Dehist or dl-Chlorpheniramine maleate or Efidac 24).ti,ab,rn. (13363)
76 (clemastin$ or meclastin$ or neclastine or mecloprodin or tavist or tavegyl or HS 592 or HS592).ti,ab,rn. (463)
77 (cyproheptadine or adekin or Antergan or antisemin or apeton 4 or astonin or BRN 1685976 or CCRIS 5232 or ciplactin or cipractin or ciproeptadine or Ciproheptadina or ciproral or ciprovit-a or cryoheptidine or crypoheptadine or cyheptine or cylat or cypraheptidine or cypro h or cyproatin or cyprogin or cyprohaptadi$ or cypromin or cyprono or cyprosian or cytadine or Dihexazin or Dronactin or Eiproheptadine or ennamax or glocyp or heptasan or HSDB 3048 or ifrasal or istam-far or klarivitina or kulinet or MK 141 or nuran or Periact$ or Peritol or petina or pilian or pronicy or sinapdin or trimetabol or Viternum).ti,ab,rn. (2968)
78 (ketotifen$ or ketotiphen$ or zaditen or zaditor or BRN 3983897 or HC 20 511 or hc 20511 or HSDB 7283).ti,ab,rn. (1472)
79 (Prometh$ or 3277 RP or A-91033 or adgan or Allerfen or allergan or Anergan 25 or Anergan 50 or antiallersin or antinaus 50 or Aprobit or Atosil or Avomine or baymethazine or Bonnox or "BRN 0088554" or Camergan or CCRIS 5873 or CCRIS 7056 or Closin or dimapp or Dimethylamino-isopropyl-phenthiazin or Diphergan or Diprasine or Diprazin$ or diprozin or Dorme or Duplamin or Eusedon Mono or fargan or Farganesse or Fellozine or fenazil or fenazine or Fenergan or Fenetazin$ or Frinova or Ganphen or Hibechin or hiberna or Histantil or Histargan or HL 8700 or HSDB 3173 or insomn-eze or Isophenergan or Isopromethazine or Kinetosin or lercigan or Lergigan or lergigan or "Lilly 01516" or Lilly 1516 or Metaryl or Mymethazine Fortis or NCI-C60673 or NSC 231688).ti,ab,rn. (4507)
80 (NSC 30321 or Pelpica or pentazine or phargan or Phenadoz or Phenargan or Phencen or Phenergan or Phenerzine or phenoject-50 or Phensedyl or Pilothia or Pipolfen or Pipolphen$ or Plletia or pm 284 or Primine or Pro-50 or Proazamine or procit or promacot or Promantine or promazinamide or Prome or Promergan or Promesan or Promet or Prometazin or Prometazina or Prometh$ or Promezathine or Promine or Proneurin or Prorex or protazine or Prothazin or Prothiazine or prothazine or provigan or Provigan or Pyrethia or Pyrethiazine or Remsed or Romergan or rp 3277

or rp 3389 or Rumergan or sayomol or SKF 1498 or Soporil or tanidil or thiergan or V GAN or vallergine or WY 509 or Zipan-25 or Zipan-50).ti,ab,rn. (4091)
81 or/59-80 (82509)
82 6 and 81 (45)
83 Simethicone/ (270)
84 (simethicone or Antifoam A or Antifoam AF or DC antifoam A or Disflatyl or Gas-X or gas relief or HSDB 3906 or Mylanta or mytab gas or Phazyme or Sab Simplex or Simeticone or dimethicone or digel or flatulex or infacol or lefax or minifom or mylicon or silain or Alka-Seltzer Anti-Gas or Colic Drops or Colicon or Degas or Gas Aide or Genasyme or Maalox Anti-Gas or Majorcon or Micon-80 or Mylaval or SonoRx or WindEze or Wind-Eze).ti,ab,rn. (513)
85 83 or 84 (513)
86 6 and 85 (0)
87 exp Nasal Lavage/ (960)
88 Therapeutic Irrigation/ (14655)
89 ((nasal or nose) adj3 (douch$ or irrigat$ or lavage)).ti,ab. (1345)
90 (saline adj3 (douch$ or irrigat$ or lavage)).ti,ab. (1689)
91 or/87-90 (17313)
92 6 and 91 (37)
93 Leukotriene Antagonists/ (2568)
94 (leukotriene adj3 (antagonist$ or block$ or inhibitor$)).ti,ab. (2975)
95 (montelukast or Singulair or Montelo-10 or montair or montek or montus or romilast or "MK 0476" or mk 476 or mk0476 or mk476 or l 706631 or l706631).ti,ab,rn. (1580)
96 (zafirlukast or Accolate or accoleit or Olmoran or Aeronix or respix or vanticon or zafirst or zuvair or ICI 204,219 or ICI 204219).ti,ab,rn. (492)
97 (pranlukast or azlaire or ultair or ONO 1078 or SB 205312 or SB205312 or ONO RS 411 or rs411 or rs 411).ti,ab,rn. (404)
98 (zileuton$ or A 64077 or A64077 or Abbot 64077 or cgs 23622 or cgs23622 or Zyflo or Leutrol).ti,ab,rn. (518)
99 or/93-98 (5395)
100 6 and 99 (0)
101 Chewing Gum/ (1895)
102 Xylitol/ (1868)
103 (Xylitol or BRN 1720523 or Eutrit or HSDB 7967 or Kannit or Klinit or NSC 25283 or Newtol or Xylite or Xylitol or Xyliton or xylit).ti,ab,rn. (2740)
104 or/101-103 (4411)
105 6 and 104 (0)
106 exp Anti-Infective Agents/ (1191754)
107 (anti bacterial$ or antibacterial$ or anti biotic$ or antibiotic$ or anti mycobacterial$ or antimycobacterial$ or bacteriocid$).ti,ab. (241072)
108 (anti infective$ or antiinfective$ or anti microbial$ or antimicrobial$ or microbicide$).ti,ab. (84764)
109 (doxycyclin$ or adoxa or alpha-Doxycycline or amermycin or atrax or azudoxat or bactidox or banndoclin or basedillin or bassado or biocolyn or biodoxi or bmy 28689 or bmy28689 or bronmycin or bu 3839t or bu3839t or cloran or cyclidox or dentistar or deoxycycline or deoxymycin dispersal or deoxymykoin or deoxyoxytetracycline or desoxy oxytetracycline or desoxycycline or doinmycin or doryx or dosil or Dossiciclina or dotur or doxaciclin or doxacycline or doxat or doxatet or doxibiotic or Doxiciclina or doxicycline or doxilin or doximed or doximycin or doxin or doxine or doxi-sergo).ti,ab,rn. (11242)
110 (Doxitard or Doxivetin or doxocycline or doxsig or doxy or doxy-1 or doxybiocin or doxy-caps or doxycen or doxychel or doxycin or doxycydine monohydrate or doxylag or doxylin or doxymycin or doxypuren or Doxy-Puren or Doxysol or doxytec or Doxytetracycline or doxytrim or dumoxin or duracycline or esdoxin or etidoxina or gewacyclin or gs 3065 or HSDB 3071 or hydramycin or ibralene or idocyclin or idocyklin or interdoxin or investin or Liviatin or longamycin or lydox or magdrin or medomycin or mespafin or mildox or miraclin or monodox or nordox or novum vibramycin).ti,ab,rn. (7033)
111 (nsc 56228 or oracea or paldomycin or pernox gel or radox or remycin or respidox or Ronaxan or roximycin or serodoxy or servidoxine or servidoxyne or siadocin or siclidon or sigadoxin or spanor or supracyclin or supramycina or tenutan or tolexine or torymycin or tsurupioxin or unidox or veemycin or viadoxin or vibra$ or viradoxyl-n or wanmycin or zadorin).ti,ab,rn. (42398)

112 (amoxicil$ or a gram or abdimox or acilina or acimox or actimoxi or adbiotin or agerpen or agram or a-gram or alfamox or alfoxil or almodan or almorsan or alphamox or amagesen solutab or ameclina or amocillin or amoclen or amodex or amo-flamisan or amoflux or amohexal or amolin or amonex or amopen or Amopenixin or amophar ge or amosine or amoval or amoxa or amoxal or amoxapen or amoxaren or amoxcil or amoxcillin or amoxcin or Amoxi or amoxi-basan or Amoxicaps or amoxiclin or amoxicot or amoxidal or Amoxiden or amoxidin or amoxidrops or amoxihexal or amoxil$).ti,ab,rn. (19750)
113 (Amoxi-Mast or amoxipen or amoxipenil or amoxisol or amoxivan or amoxivet or Amoxivet or amoxy or Amoxycillin$ or amoxy-diolan or amoxypen or AMPC or ampliron or Ampy-Penyl or Anemolin or apo-amoxi or ardine or aroxin or Aspenil or azillin or bacihexal or bactamox or bactox ge or beamoxy or betamox or bimox or bintamox or biomox or biotamoxal or bioxidona or bioxyllin or BLP 1410 or bristamox or brl 2333 or brl2333 or broadmetz or cabermox or Cemoxin or cilamox or clamox or clamoxyl or clearamox or clonamox or coamoxin or damoxicil or D-Amoxicillin or Delacillin).ti,ab,rn. (4247)
114 (dispermox or doxamil or draximox or edamox or Efpenix or erphamoxy or eupen or farconcil or fisamox or flemoxin or fluamoxina or foxolin or fullcilina or gexcil or gimalxina or glamox or glassatan or gomcillin or grinsul or grunamox or hamoxillin or hiconcil or hidramox or hipen or Histocillin or hosboral or HSDB 3204 or Hydroxyampicillin or ibamox or ibiamox or ikamoxil or imacillin or imaxilin or inamox or infectomycin or intermox or isimoxin or izoltil or julphamox or jutamox or kamoxin or ladoxillin or lamoxy or larocilin or larocin or larotid or macromox or magnimox or maxamox or maxcil).ti,ab,rn. (21)
115 (medimox or meixil or Metafarma or metifarma or mopen or morgenxil or moxacin or Moxal$ or moxarin or Moxatag or moxilen or moxilin or moximar or moxitab or moxtid or moxylin or moxypen or moxyvit or neogram or novabritine or novamox or novamoxin or novenzymin or novoxil or NSC 277174 or nuvosyl or optium or ospamox or pamocil or pamoxicillin or pamoxin or panvilon or pasetocin or penamox or penbiosyn or pentyloxycillin or pharmoxyl or p-Hydroxyampicillin or piramox or polymox or pondnoxcill or rancil or ranmoxy or ranoxil or ranoxyl or Ro 10-8756).ti,ab,rn. (1540)
116 (robamox or romoxil or ronemox or saltermox or sawacillin or sawamezin or Sawamox PM or servamox or shamoxil or sia-mox or sigamopen or silamox or sil-a-mox or simoxil or solpenox or sumox or superpeni or teramoxyl or tolodina or tormoxin or triafamox or triamoxil or trifamox or trimox or Unicillin or uro clamoxyl or uroclamoxyl or utimox or vastamox or velamox or Vetramox or vistrep or widecillin or winpen or wymox or Wymox or Wymox or xiltrop or zamocillin or zamox or zamoxil or zerrsox or zimox).ti,ab,rn. (14)
117 (clarith$ or A 56268 or A56268 or abbotic or abbott 56268 or Adel or aeroxina or Astromen or bactirel or baxin filmtab or Biaxin or biclar or bicrolid or binoklar or bremon or carimycin or c-clarin or CCRIS 8833 or celex or clacin or clacine or clambiotic or clapharma or claribid or Claricide or claridar or clarimac or claripen or claritrol or Claritromicina or claroma or Clathromycin or clormicin).ti,ab,rn. (7366)
118 (crixan or cylind or Cyllid or cyllind or dicupal or DRG-0099 or er 36469 or er36469 or gervaken or hecobac or Helas or heliclar or helitic or klacid or klacina or klaciped or klaribac or klaricid or Klarid or klaridex or klaridia or klarin or Klax or klerimed or kofron or lagur or Mabicrol or macladim or macladin or maclar or mavid or monozeclar or naxy or "TE 031" or TE031 or veclam or zeclar).ti,ab,rn. (101)
119 (moxif$ or Actira or Avalox or avelon or Avelox or Avolex or BAY 12 8039 or BAY 128039 or bay128039 or CCRIS 8690 or Izilox or megaxin or moxeza or Octegra or Proflox or vigamox).ti,ab,rn. (2639)
120 (Telithromycin or Ketek or RU 66647 or HMR 3647 or HMR3647 or levviax or ru 647 or ru 66647 or ru647 or ru66647).ti,ab,rn. (855)
121 (azithromycin$ or Aritromicina or aruzilina or atizor or Azadose or azasite or azenil or azimin or azithral or Azitrocin or azitromax or Azitromicine or aziwok or azomyne or aztrin or Azythromycin or BRN 5387583 or CCRIS 1961 or cp 62933 or cp62933 or DRG-0104 or forcin or Goxal or Hemomycin or HSDB 7205 or inedol or isv 401 or isv401 or kromicin or macrozit or mezatrin or Misultina).ti,ab,rn. (5129)
122 (Mixoterin or octavax or Setron or Sumamed or sunamed or Tobil or tobyl or Toraseptol or tromix or Trulimax or Ultreon or Vinzam or xithrone or xz 450 or xz450 or zaret or zarom or Zentavion or Zeto or zibramax or zifin or zimericina or zistic or Zithrax or Zithromax or zithrox or zitrim or zitrobifan or Zitromax or Zitrotek or Zmas or zmax or Z-Pak).ti,ab,rn. (401)
123 or/106-122 (1349743)
124 6 and 123 (270)
125 Balloon Dilation/ (13893)

126 Dilatation/ (7905)
127 Dilatation, Pathologic/ (8128)
128 Catheterization/ (31341)
129 Catheterization, Peripheral/ (5862)
130 catheter$.ti,ab. (142557)
131 dilat$.ti,ab. (101802)
132 (BET or BDET).ti,ab. (4975)
133 tuboplast$.ti,ab. (182)
134 exp Laser Therapy/ (46697)
135 exp Lasers/ (36258)
136 laser$.ti,ab. (163455)
137 LETP.ti,ab. (5)
138 Middle Ear Ventilation/ (1984)
139 (tympanostom$ or tympanotom$).ti,ab. (1435)
140 grommet$.ti,ab. (453)
141 ((ventilat$ or aerat$) adj4 ear$).ti,ab. (1472)
142 ((ventilat$ or aerat$) adj4 tub$).ti,ab. (2404)
143 (pressur$ adj3 tub$).ti,ab. (1460)
144 ear tube$.ti,ab. (67)
145 PE tube$.ti,ab. (43)
146 T tube$.ti,ab. (2251)
147 (transtubal or trans tubal).ti,ab. (60)
148 (myringotom$ or myringocentesis).ti,ab. (1163)
149 (paracentesis or tympanocentesis).ti,ab. (2556)
150 ((eardrum$ or ear drum$ or tympan$) adj3 (punctur$ or tap$)).ti,ab. (23)
151 or/125-150 (459729)
152 6 and 151 (931)
153 Valsalva Maneuver/ (3361)
154 Insufflation/ (1366)
155 Yawning/ (533)
156 Mastication/ (7711)
157 Deglutition/ (6665)
158 Watchful Waiting/ (561)
159 valsalva$.ti,ab. (6721)
160 (autoinflat$ or auto inflat$).ti,ab. (73)
161 (insufflat$ or autoinsufflat$ or auto insufflat$).ti,ab. (5159)
162 (inflat$ adj4 ear$).ti,ab. (117)
163 Politzer$.ti,ab. (124)
164 ((equalis$ or equaliz$ or normalis$ or normaliz$) adj5 pressure$).ti,ab. (3810)
165 (yawn$ or swallow$ or chew$ or masticat$ or deglutition).ti,ab. (36922)
166 (watch$ adj2 wait$).ti,ab. (1809)
167 (wait adj2 see).ti,ab. (873)
168 (active$ adj2 observ$).ti,ab. (1012)
169 conservative.ti,ab. (68251)
170 (management adj2 (decision$ or option$ or choice$)).ti,ab. (9031)
171 (support$ adj4 (care or caring)).ti,ab. (19380)
172 ((standard or usual) adj3 care).ti,ab. (23669)
173 (advice or advis$).ti,ab. (69192)
174 or/153-173 (247702)
175 6 and 174 (603)
176 39 or 58 or 82 or 86 or 92 or 100 or 105 or 124 or 152 or 175 (1562)
177 exp animals/ not humans/ (3791654)
178 176 not 177 (1345)