A/prov

U.S. PATENT AND TRADEMARK OFFICE
PROVISIONAL APPLICATION FOR PATENT COVER SHEET

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 C.F.R. §1.53(c).

Atty. Docket: HALLGREN=1

INVENTOR(s)/APPLICANT(s)			
LAST NAME	FIRST NAME	MIDDLE INITIAL	RESIDENCE (CITY AND EITHER STATE OR FOREIGN COUNTRY)
HALLGREN FELLSTROM	Roger Bengt		Balinge, Sweden Knivsta, Sweden

[ ] Additional inventors are being named on separately numbered sheets attached hereto.

TITLE OF THE INVENTION (280 characters max)

NEW THERAPY IN GLOMERULONEPHRITIS

CORRESPONDENCE ADDRESS

BROWDY AND NEIMARK, P.L.L.C.
419 Seventh Street, N.W., Suite 300
Washington, D.C. 20004

ENCLOSED APPLICATION PARTS (check all that apply)

[XX] Specification Number of Pages 13 [ ] Small Entity Statement

[ ] Drawing(s) Number of Sheets ____ [ ] Other (specify) _____

METHOD OF PAYMENT (check one)

[X] A check no. 18338 is enclosed to cover the Provisional filing fee of
[X] $150 large entity [ ] $75 small entity

[X] The Commissioner is hereby authorized to charge any deficiency in the filing fees and credit any overpayment to Deposit Account Number 02-4035.

The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.

[XX] No [ ] Yes, the name of the U.S. Government agency and the Government contract number are:

_____

Respectfully submitted,

BROWDY AND NEIMARK, P.L.L.C.

By: _____
Sheridan Neimark
Registration No.: 20,520

Date: 01 April 1998

SN:bcs
f:\user3\98apr\hall.ptr

NEW THERAPY IN GLOMERULONEPHRITIS

Field of Invention

The present invention provides a new treatment for glomerulonephritis.

Background to the Invention

The functional units of the kidney, such as the glomeruli may suffer from inflammation. An inflammatory attack in the glomeruli is termed glomerulonephritis and can be classified into subgroups such as membraneous glomerulonephritis, focal segmental glomerulosclerosis, mesangial diffuse proliferative glomerulonephritis, endocapillary or extracapillary proliferative glomerulonephritis. Using histopathological techniques these subgroups vary with respect to microscopical or immunhistochemical picture. One cause of inflammation is due to the deposition of immunoglobulin A (IgA) in glomeruli. This condition is termed IgA nephropathy (1-3), which is the most common form of glomerulonephritis in a global perspective.

Assessment of the degree of severity of glomerulonephritis is based on different investigation results. The most important findings are 1) the degree of urinary excretion of protein (proteinuria) and 2) the filtering function of the kidney, which can be assessed by serum creatinine (s-creatinine). Histological examination of material from kidney (renal biopsy) yields information about the type of renal damage as well as the severity of the injury. The outcome of a glomerulonephritis is variable and is dependent upon the histological and the immunhistochemical findings in a renal biopsy. Patients with IgA nephropathy having a constant proteinuria often develop renal failure and uraemia after 5 to 20 years of illness (4).

Various treatments for glomerulonephritis are known. For example substances which act on the immune system, e.g. Cyclophosphamide, Azathioprine and Cyclosporine have been used. Glucocorticoids have also been used (mainly prednisone or prednisone

acetate) which may be administered orally or by venous infusion (5, 6). Unfortunately, these treatments cause severe side effects and are not particularly effective. Other suggested treatments include ACE inhibitors (7), polyunsaturated fatty acid preparations (8) and vitamin E (9). The treatment results for these therapies for IgA nephropathy have been quite disappointing and it has been concluded that an effective treatment against progressive IgA nephropathy is basically missing (10). For this reason, a substantial number of patients with IgA nephropathy, 20-30%, will eventually develop renal insufficiency and uraemia (1-4). The available treatment for uraemia today is dialysis or kidney transplantation. Renal transplant patients who have been transplanted because of uraemia due to glomerulonephritis frequently suffer from recurrence of glomerulonephritis in the transplant and subsequently a gradual loss of transplant function (11, 12). This is most common in patients who previously suffered from IgA nephropathy. Today there is no effective treatment against recurrence of glomerulonephritis in a transplant.

The glucocorticoids that have been used in IgA nephropathy and in other types of glomerulonephritis are characterised by a substantial gastrointestinal absorption after oral administration, aiming to exert a direct effect on circulating leukocytes and cells that have infiltrated the kidney or the renal transplant, thus having a systemic effect. Such a systemic effect is also achieved if glucocorticoids are administered as an intravenous infusion. Systemic administration of glucocorticoids may have influenced the outcome of IgA nephropathy in some cases.

It has now surprisingly been found that a glucocorticoid substance which has a minimal systemic effect, but exerts its effect preferably in the intestinal wall of a certain part of the gut (the lower third of the small intesitne and the upper fourth of the large intestine), is effective in controlling IgA nephropathy in a native kidney or a kidney transplant. It would not be expected that treatment of an apparently healthy intestine has an effect on an inflamed kidney. This discovery represents a breakthrough in the treatment of

glomerulonephritis since it has the advantage of reduction of severe side effects on the body, including effects on skeleton, metabolism and muscles, caused by systemic glucocorticiods.

Summary of the Invention

According to the invention there is provided the use of a glucocorticoid substance which has a minimal systemic effect in the manufacture of a medicament for oral or rectal administration for use in the treatment of glomerulonephritis.

According to the invention there is further provided a method of treating a patient suffering from glomerulonephritis which comprises administering orally or rectally to the patient a therapeutically effective amount of a glucocorticoid substance which has a minimal systemic effect.

According to the invention there is further provided a pharmaceutical composition comprising a glucocorticoid substance which has a minimal systemic effect for oral or rectal administration in association with a pharmaceutically acceptable diluent, adjuvant or carrier, which composition is for use in the treatment of glomerulonephritis.

Detailed Description of the Invention

The invention is preferably used to treat a patient who suffers from acute or chronic glomerulonephritis. Glomerulonephritis may be divided into subtypes such as membranous glomerulonephritis, focal segmental proliferative glomerulonephritis, diffuse mesangioproliferative glomerulonephritis, endocapillary or extracapillary proliferative glomerulonephritis, depending on where the inflammation is located. This invention is preferably used to treat the IgA nephropathy type of glomerulonephritis. The invention is particularly suitable for treating patients who have suffered form glomerulonephritis (particularly IgA nephropathy), had a transplant, and suffered from a recurrence of glomerulonephritis (particularly IgA nephropathy) in the transplanted kidney.

The glucocorticoid substance used in the present invention is preferably one which has a first pass metabolism of at least 90% for the minimisation of the systemic effects. The first pass metabolism of a glucocorticoid substance can be determined using the method disclosed previously (13). More preferably it is budesonide, rofleponide or derivatives thereof, belcomethasone dipropionate, belcomethasone monopropionate, ciclesonide, tipredane, flunisolide, traimcinolone acetonide or flutiscasone propionate. Budesonide, which is a 16,17-bytylidenedioxy-11β,21-dihydroxypregna-1,4-diene-3,20-dione, is particularly prefered.

The glucocorticoid substance when administered orally is generally administered in the form of tablets, pills, capsules, syrups, powders or granulates and when it is administered rectally, is in the form of foams, suppositories or enemas.

The glucocorticoid substance may be administered on its own or as a pharmaceutical composition in combination with a pharmaceutically acceptable diluent, adjuvant or carrier. particularly preferred are compositions not containing material capable of causing an adverse, e.g. an allergic reaction.

The glucocorticoid substance may be admixed with an adjuvant or a carrier, e.g. lactose, saccharose, sorbitol, mannitol, starches such as potato starch, corn starch or amylopectin, cellulose derivatives, a binder such as gelatine or polyvinlypyrrolidone, and a lubricant such as magnesium stearate, calcium stearate, polyethylene glycol, waxes and/or paraffin, and then compressed into tablets. If coated tablets are required, the cores, prepared as described above, may be coated with a concentrated sugar solution which may contain e.g. gum arabic, gelatine, talcum and/or titanium dioxide. Alternatively, the tablet may be coated with a suitable polymer dissolved in a readily volatile organic solvent. The tablet

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.