



SCLERODERMA MEDICATIONS GUIDE (Canada)

Scleroderma Quebec™

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Symptoms and treatments

- ▶ Raynaud's Phenomenon
- ▶ Gastrointestinal Symptoms
- ▶ Joint & Tendon Pain
- ▶ Pulmonary Fibrosis/Intersitial Lung Disease
- ▶ Pulmonary Arterial Hypertension
- ▶ Renal Crisis/New Onset Hypertension
- ▶ Skin Fibrosis
- ▶ Sjögren's Syndrome
- ▶ Localized Scleroderma
- ▶ Skin Itching (Pruritus)/Dryness

For full consultation of the Scleroderma Medications Guide, visit Sclerodermie Quebec's website at www.en.sclerodermie.ca.



Although there isn't a cure for scleroderma, there are effective treatment options that can help alleviate symptoms and slow down disease progression. Current prescription and over-the-counter medication are designed to treat scleroderma by targeting:

- ▶ Inflammation
- ▶ Autoimmunity
- ▶ Vascular disease
- ▶ Tissue fibrosis

As a medical doctor or health care professional caring for persons with scleroderma, it is important to ensure patients understand the nature of the medications they may be prescribed and how they work to help control disease symptoms from progressing. Patient knowledge is powerful, as it reduces fear and increases compliance, resulting in a higher percentage of successful treatment.

The following guide includes a list of drugs commonly prescribed by doctors in Canada to treat patients with scleroderma. The list is provided for informational purposes only, and is not to be taken as an endorsement of any drug by Scleroderma Quebec.

Many of these drugs are prescribed by doctors, but have not been proven useful and should be used only with caution and supervision. It is important to consider, that not every medication is appropriate for every patient. The treating physician, who is familiar with the patient's medical history, health status and disease progression, will be able to determine the most appropriate treatment options.

RAYNAUD'S PHENOMENON

Raynaud's is present in up to 95% of people with scleroderma. Whitening of fingers and/or toes triggered by cold or severe stress. The whiteness phase can be followed by a blue phase and then a red phase.

CALCIUM CHANNEL BLOCKERS

- NIFEDIPINE (ADALAT[®])
- AMLODOPINE (NORVASC[®])
- DILTIAZEM (CARDIZEM[®])
- FELODIPINE (PLENDIL[®])

Action - Relax blood vessels

Side Effects

Flushing, headache, dizziness, constipation, low blood pressure, swelling in the legs, palpitations.

PHOSPHODIESTERASE TYPE 5 INHIBITORS

- SILDENAFIL (REVATIO[®])

Action - Relax blood vessels

Side Effects

Headache, flushing, indigestion, nose bleed, vision abnormalities, nasal congestion, diarrhea, insomnia.

- TADALAFIL (ADCIRCA[®])

Action - Relax blood vessels

Side Effects

Headache, myalgia, flushing, indigestion, nausea, nasal congestion.

ANGIOTENSIN II RECEPTOR ANTAGONISTS

- LOSARTAN (COZAAR[®])

Action - Block constriction of blood vessels

Side Effects

Headache, respiratory tract infection, dizziness, tiredness, dry cough.



TOPICAL NITRATES

- NITROGLYCERIN OINTMENT

Action - Relax blood vessels

Side Effects

Flushing, headache, dizziness, low blood pressure, palpitations, reflux.

PROSTAGLANDIN DERIVATIVES

- EPOPROSTENOL (FLOLAN[®], CARIPUL[®])
- TREPROSTINIL (REMODULIN[®])

Actions - Relax blood vessels

Used for severe, refractory or complicated Raynaud's

Side Effects

See section of Pulmonary Arterial Hypertension page 8.

ALPHA-ADRENERGIC BLOCKERS

- PRAZOSINE (MINIPRESS[®])

Action - Relax blood vessels

Side Effects

Dizziness, headache, drowsiness, tiredness, light-headedness, palpitations, nausea.

OTHER

- PENTOXIFYLLINE (TRENTAL[®])

Action - Unclear

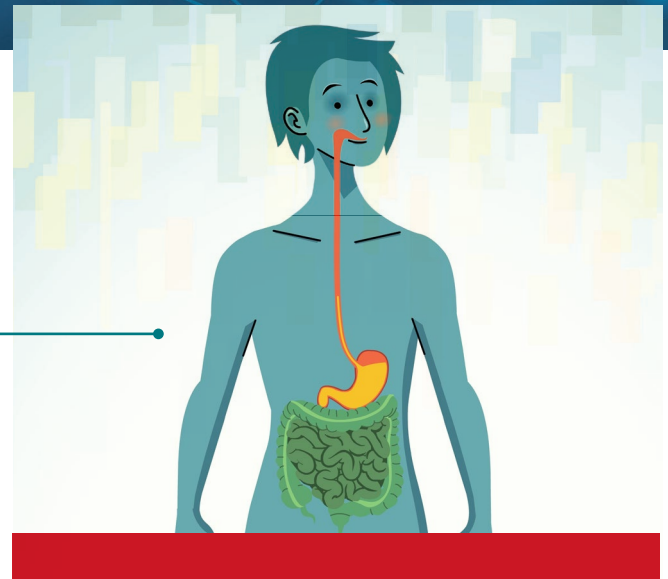
Side Effects

Nausea, dizziness, headache, vomiting.



GASTROINTESTINAL SYMPTOMS

Gastrointestinal disorders affect the vast majority of patients. Gastric reflux is a common symptom that manifests itself by a burning sensation radiating up to the throat after meals and may cause inflammation of the lining of the esophagus (esophagitis reflux) if left untreated.



GASTROESOPHAGEAL REFLUX DISEASE (GERD)

ANTIACIDES

- DIOVOL[®], GAVISCON[®],
- ROLAIDS[®], TUMS[®]

Action - Neutralize stomach acidity

Side Effects

Abdominal cramping, chalky taste, nausea, vomiting, diarrhea, constipation, pale stool.

HISTAMINE H2-RECEPTOR BLOCKERS

- CIMETIDINE
- RANITIDINE (ZANTAC[®])
- FAMOTIDINE (PEPCID[®])
- NIZATIDINE (AXID[®])

Action - Inhibit stomach acid secretion

Side Effects

Mental confusion (Cimetidine only), drowsiness, dizziness, headache, nausea, vomiting.



PROTON PUMP INHIBITORS

- OMEPRAZOLE (LOSEC[®])
- LANSOPRAZOLE (PREVACID[®])
- DEXLANSOPRAZOLE (DEXILANT[®])
- ESOMEPRAZOLE (NEXIUM[®])
- RABEPRAZOLE (PARIET[®])
- PANTOPRAZOLE (PANTOLOC[®])

Action - Inhibit stomach acid secretion

Side Effects

Headache, diarrhea, abdominal cramping, flatulence, nausea, dizziness.

OTHER

- SUCRALFATE (SULCRATE[®])

Action - Coat esophagus & stomach; forms protective barrier

Side Effects

Headache, constipation, abdominal cramping, nausea, diarrhea.

SCLERODERMA MEDICATIONS GUIDE (CANADA) GASTROINTESTINAL SYMPTOMS

SWALLOWING DIFFICULTIES

GI STIMULANTS

- METOCLOPRAMIDE (METONIA®)

Action - Stimulate intestinal muscle contractions, may improve heartburn

Side Effects

Abdominal cramping, diarrhea, dizziness, headache, drowsiness and tiredness, cardiac arrhythmias.

- DOMPERIDONE (MOTILIUM®)

Action - Stimulate intestinal muscle contractions, may improve heartburn

Side Effects

Abdominal cramping, diarrhea, dizziness, headache, palpitations, cardiac arrhythmias.

- ERYTHROMYCINE

Action - Stimulate intestinal muscle contractions

Side Effects

Abdominal cramping, diarrhea, dizziness, headache, palpitations, cardiac arrhythmias.

- OCTREOTIDE ACETATE (SANDOSTATIN®)

Action - An injectable medication. Can be helpful in very severe cases for improving bowel motility

Side Effects

Diarrhea, abdominal cramping, flatulence, flu-like symptoms, anemia, constipation, headache, low heart rate, cardiac arrhythmias.



CONSTIPATION

BULKING AGENTS

- CALCIUM POLYCARBOPHIL (PRODIEM®)

- PSYLLIUM HYDROPHILIC MUCILLOID (METAMUCIL®)

Action - Improve stool consistency, shorten colon transit time and increase frequency of bowel movements

Side Effects

Abdominal bloating, flatulence, constipation.

SOFTENING AGENTS

- DOCUSATE CALCIUM (SOFLAX C®, CALAX®)

- DOCUSATE SODIUM (COLACE®)

Action - Soften stool

Side Effect

Mild abdominal cramping.

OSMOTIC AGENTS

- LACTULOSE

Action - Keep liquids inside bowels to soften stools

Side Effects

Mild abdominal cramping, diarrhea, flatulence, nausea, vomiting.

- POLYETHYLENE GLYCOL (LAX-A-DAY®, PEGALAX®, RELAXA®, RESTORALAX®)

Action - Keep liquids inside bowels to soften stools

Side Effects

Cramping, diarrhea, abdominal bloating, flatulence, nausea.

SMALL INTESTINE DYSFUNCTION: BACTERIAL OVERGROWTH/DIARRHEA



Broad Spectrum Antibiotic use is the mainstay of treatment for this complication. There are many potential approaches to this therapy. For example: Antibiotics are given in 2–3 week courses followed by a 1–2 week drug holiday. Generally a few cycles of this treatment can allow for quiet periods of a few months to a few years. However, some persons may require almost continuous antibiotics.

Alternating antibiotics and increasing the antibiotic-free period will decrease the development of resistant strains of bacteria.

Note: Prolonged use of Broad Spectrum Antibiotics may be complicated by superinfection.



BROAD SPECTRUM ANTIBIOTICS

Action - Decrease bacterial overgrowth

EXAMPLES INCLUDE:

- **TETRACYCLIN, AMPICILLIN**

Side Effects

Nausea, vomiting, diarrhea, abdominal pain, photosensitivity, skin rash.

- **METRONIDAZOLE (FLAGYL®)**

Side Effects

Metallic taste, headache, diarrhea, reduced appetite, dizziness, nausea.

- **CIPROFLOXACINE (CIPRO®)**

Side Effects

Drowsiness, dizziness, nausea, vomiting, diarrhea.

- **AMOXICILLIN/CLAVULANATE (CLAVULIN®)**

Side Effects

Diarrhea, nausea, vomiting, abdominal discomfort, skin rash, vaginitis, pseudomembranous colitis.

- **CLARITHROMYCIN (BIAXIN®)**

- **AZITHROMYCIN (ZITHROMAX®)**

Side Effects

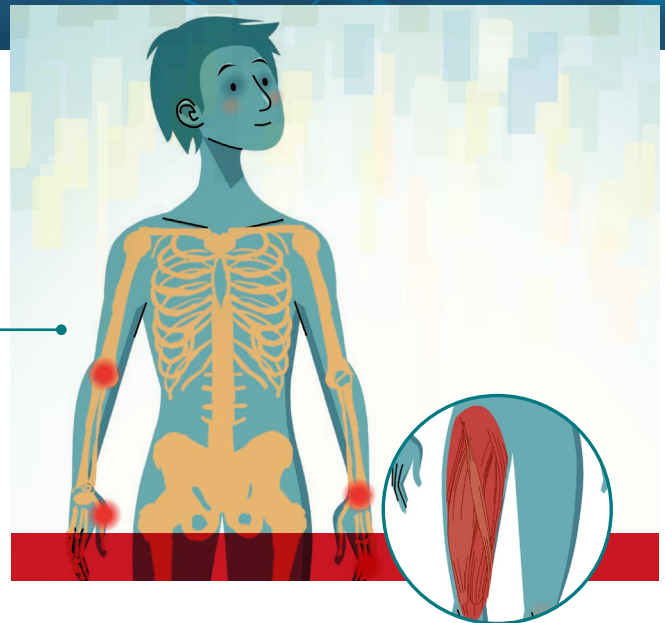
Altered taste (dysgeusia), diarrhea, nausea, heartburn, abdominal pain.



JOINT AND TENDON PAIN

Joint pain is common. It is caused by inflammation of the joints and tendons, which quite often leads to joint swelling and stiffness that can become quite debilitating.

Muscular pain (myalgia) can be intermittent or continuous. It can also be associated with muscle weakness (myositis). Symptoms include difficulty in climbing stairs, lifting objects and getting up, and also difficulty swallowing.



NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS)

- DICLOFENAC (VOLTAREN®)
- DICLOFENAC & MISOPROSTOL (ARTHROTEC®)
- DICLOFENAC SODIUM (VOLTAREN®)
- FLURBIPROFEN (ANSAID®)
- IBUPROFEN (MOTRIN®, ADVIL®)
- KETOPROFEN
- KETOROLAC (TORADOL®)
- MELOXICAM (MOBICOX®)
- NABUMETON (RELAFEN®)
- NAPROXEN (NAPROSYN®, ANAPROX®, ALEVEV®)
- OXAPROZIN
- PIROXICAM
- SULINDAC

Action - Suppress inflammation

Side Effects

Abdominal pain and cramping, gastric irritation and stomach ulcers, high blood pressure, impaired kidney function, bleeding and bruising, cardiovascular disease, increased liver enzymes.

COX-2 INHIBITORS

- CELECOXIB (CELEBREX®)

Action - Suppress inflammation

Side Effects

Abdominal pain and cramping, gastric irritation and stomach ulcers, high blood pressure, impaired kidney function, bleeding and bruising, cardiovascular disease, increased liver enzymes.

ANTALGICS

- ACETAMINOPHEN (TYLENOL®)

Action - Relieve pain

Side Effects

Anemia, skin rash, metabolic disorder. Overdosage manifestations include: nausea, vomiting, elevated liver enzymes, jaundice, hepatic impairment, renal toxicity.

- TRAMADOL (ULTRAM®)

Action - Relieve pain

Side Effects

Nausea, dizziness, headache, drowsiness, constipation, vomiting, flushing, itching.



PULMONARY FIBROSIS/ INTERSTITIAL LUNG DISEASE

A potentially serious complication where normal lung tissue is gradually replaced by scarred fibrotic tissue, making it difficult to breathe and deliver needed oxygen to the body. Pulmonary fibrosis causes shortness of breath and also sometimes a dry cough.



IMMUNOSUPPRESSANTS

- MYCOPHENOLATE MOFETIL (CELLCEPT®)
- MYCOPHENOLATE SODIUM (MYFORTIC®)

Action - Suppress immune response; anti-fibrotic effect

Side Effects

Abdominal pain, diarrhea, nausea, vomiting, decreased appetite, headache, increased susceptibility to infections, anemia.

- CYCLOPHOSPHAMIDE (PROCYTOX®)

Action - Suppress immune response

Side Effects

Hair loss, decreased appetite, bladder inflammation, bone marrow damage, nausea, diarrhea, vomiting, mouth ulcers, increased susceptibility to infections, increased cancer risk.

- RITUXIMAB (RITUXAN®, RIXIMYO®, RUXIENCE®, TRUXIMA®, RIABNI®)

Action - Suppress immune response

Side Effects

Infusion reaction, cardiac arrhythmias, skin rash, increased susceptibility to infections.

- TOCILIZUMAB (ACTEMRA®)

Action - Suppress immune response

Side Effects

Infusion or injection site reaction, GI perforation, dyslipidemia, elevated liver enzymes.

- AZATHIOPRINE (IMURAN®)

Action - Suppress immune response

Side Effects

Nausea, vomiting, diarrhea, decreased appetite, increased susceptibility to infections, pancreatitis, increased cancer risk, anemia.

- CYCLOSPORINE (NEORAL®, SANDIMMUNE®)

Action - Suppress immune response

Side Effects

Tremor, hypertension, hirsutism, renal failure, headache, nausea, vomiting, infections.

ANTI-FIBROTIC DRUGS

- NINTEDANIB (OFEV®)

Action - Blocks the activity of fibroblasts which contribute to tissue fibrosis

Side Effects

Diarrhea, nausea, vomiting, abdominal pain, decreased appetite, weight loss, elevated liver enzymes, bleeding.



PULMONARY ARTERIAL HYPERTENSION

Increased pressure in the pulmonary arteries due to the narrowing of small arteries in the lungs. Blood flow to the lungs is significantly restricted, making the heart work harder to pump blood through the lungs.

Patients diagnosed with pulmonary arterial hypertension should be referred to a pulmonary hypertension center for experienced evaluation and management of this serious scleroderma complication.

ENDOTHELIN RECEPTOR ANTAGONISTS

- AMBRISENTAN (VOLIBRIS®)

Action - Act on blood vessels

Side Effects

Peripheral edema, headache, decreased hemoglobin, nasal stuffiness, palpitations.

- BOSENTAN (TRACLEER®)

Action - Act on blood vessels

Side Effects

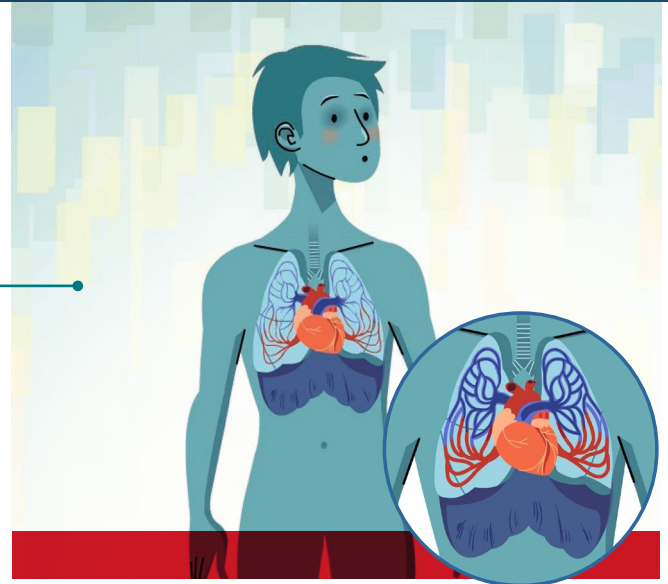
Headache, nasal stuffiness, flushing, liver function abnormality, pulmonary edema, low blood pressure.

- MACITENTAN (OPSUMIT®)

Action - Act on blood vessels

Side Effects

Nasal stuffiness, headache, anemia, bronchitis, sore throat.



PROSTACYCLIN DERIVATIVES

- EPOPROSTENOL (FLOLAN®, CARIPUL®)

Action - Act on blood vessels, inhibit platelet aggregation

Side Effects

Headache, dizziness, flushing, jaw pain, diarrhea, bone pain, potential serious infection associated with central line catheter in the chest wall.

- TREPROSTINIL (REMODULIN®)

Side Effects

Pain at infusion site, headache, cough, diarrhea, nausea, flushing, jaw pain, skin rash, edema.

PROSTACYCLIN RECEPTOR AGONIST

- SELEXIPAG (UPTRAVI®)

Action - Act on blood vessels

Side Effects

Headache, diarrhea, jaw pain, nausea, vomiting, muscle pain, flushing.

SCLERODERMA MEDICATIONS GUIDE (CANADA) PULMONARY ARTERIAL HYPERTENSION

SOLUBLE GUANYLATE CYCLASE STIMULATOR

- RIOCIGUAT (ADEMPAS®)

Action - Act on blood vessels

Side Effects

Headache, dizziness, nausea, diarrhea, edema, low blood pressure, palpitations, bleeding.

PHOSPHODIESTERASE TYPE 5 (PDE5) INHIBITOR

- SILDENAFIL (REVATIO®)

Action - Act on blood vessels

Side Effects

Headache, flushing, dyspepsia, nosebleeds, vision change, nasal stuffiness, diarrhea, insomnia.

- TADALAFIL (ADCIRCA®)

Action - Act on blood vessels

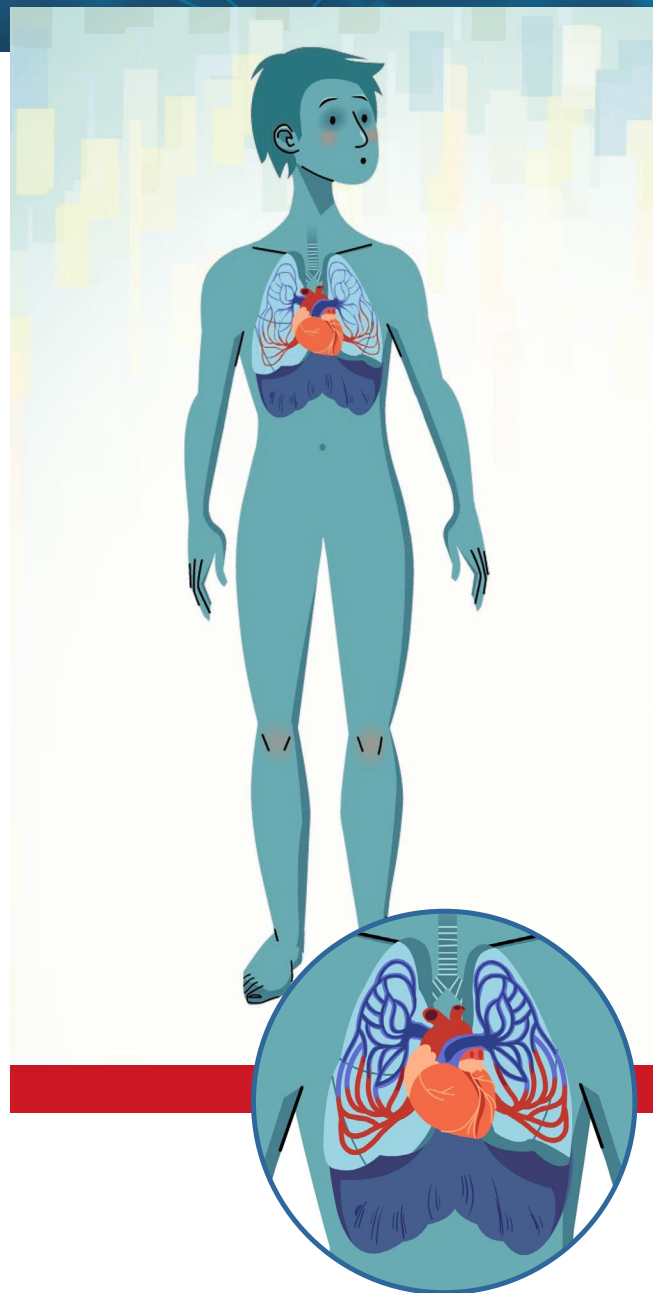
Side Effects

Headache, muscle pain, flushing, stomach upset, nausea, respiratory tract infection, nasal stuffiness.

COMBINATION OF TREATMENTS

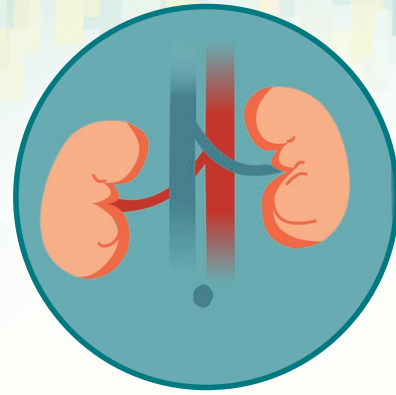
- MACITENTAN AND TADALAFIL (OPSYNVI®)

Actions and side effects - See sections on individual drugs above.



RENAL CRISIS/NEW ONSET HYPERTENSION

A renal crisis, which is due to an acute obstruction of arterioles and capillaries in the kidneys, leads to a sudden and sharp increase in arterial blood pressure. The symptoms are those of a hypertensive crisis: new and severe headaches, marked shortness of breath (left heart failure), and even epileptic seizures (convulsions). This is a very serious complication which requires urgent medical attention. Often during a scleroderma renal crisis, the kidneys stop functioning and dialysis (filtering the blood to avoid uremia) is then needed.



ANGIOTENSIN CONVERTING ENZYME INHIBITORS

- CAPTOPRIL
- ENALAPRIL (VASOTEC®)
- LISINAPRIL (PRINIVIL®, ZESTRIL®)
- QUINAPRIL (ACCUPRIL®)
- RAMIPRIL (ALTACE®)
- FOSINOPRIL (MONOPRIL®)
- BENAZEPRIL (LOTENSIN®)
- TRANDOLAPRIL (MAVIK®)

Action - Block constriction of blood vessels

Side Effects

Low blood pressure, dizziness, increased blood-potassium level, headache, dry cough, tiredness, photosensitivity.

If taking corticosteroids, monitor your blood pressure frequently, and report changes to your healthcare provider immediately.

Warning About Corticosteroids and Renal Crisis

Corticosteroids, such as Prednisone and Medrol, have been used to treat several complications of systemic scleroderma, such as pulmonary fibrosis, pruritus (itchy skin), and joint pain.

Recent findings indicate that corticosteroids can be implicated in precipitating renal crisis.

Therefore, the medical community has concluded corticosteroids should be used cautiously, in a carefully screened patient population.

For example: to manage patients who also have myositis (muscle inflammation).

Anyone taking corticosteroids should monitor blood pressure frequently, and report changes to the healthcare provider immediately.



SKIN FIBROSIS

Thickening and loss of elasticity of the skin on different parts of the body. Hence the name «scleroderma», which means hard skin.

IMMUNOSUPPRESSANTS

- METHOTREXATE

Action - Suppress immune response

Side Effects

Diarrhea, decreased appetite, liver and kidney disorder, nausea, mouth sores, skin rash.

- MYCOPHENOLATE MOFETIL (CELLCEPT®)

- MYCOPHENATE SODIUM (MYFORTIC®)

Action - Suppress immune response and anti-fibrotic effect

Side Effects

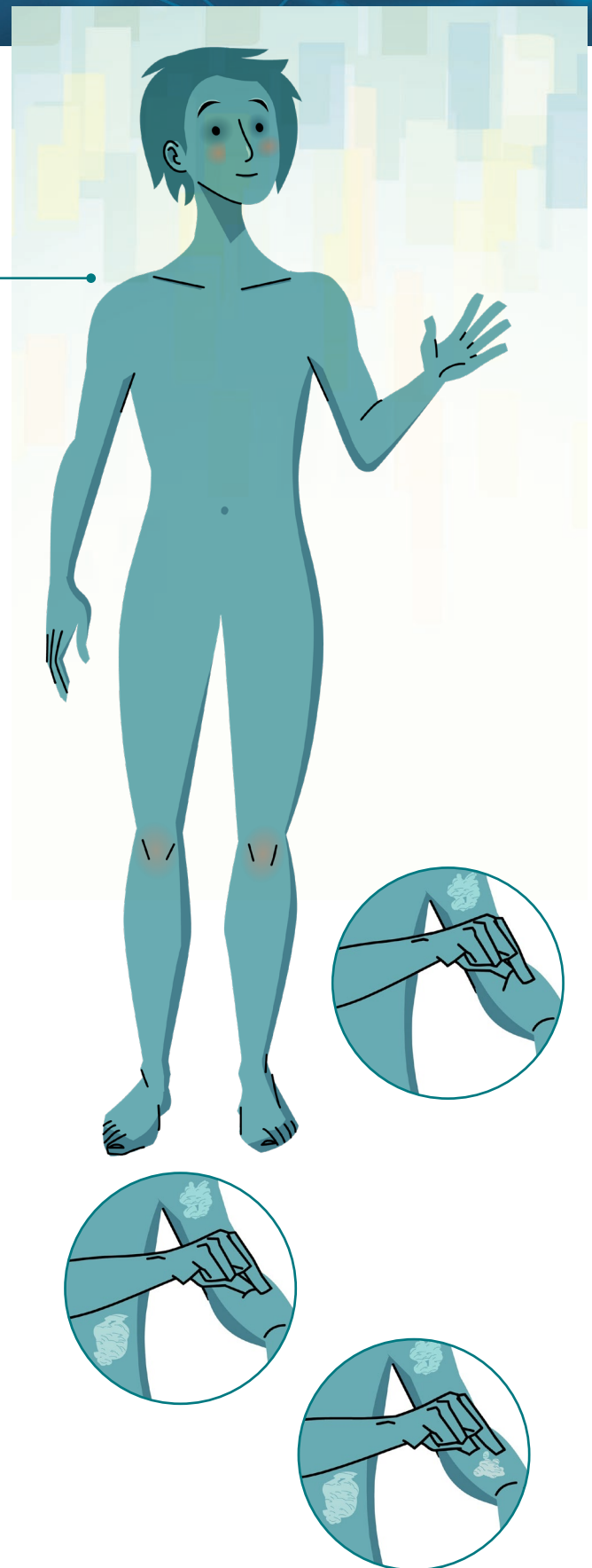
Abdominal pain, diarrhea, nausea, vomiting, decreased appetite, headache, increased susceptibility to infections, anemia.

- CYCLOPHOSPHAMIDE (PROCYTOX®)

Action - Suppress immune response

Side Effects

Hair loss, decreased appetite, bladder inflammation, bone marrow damage, nausea, diarrhea, vomiting, mouth ulcers, increased susceptibility to infections, increased cancer risk.



SJÖGREN'S SYNDROME

Sjögren's syndrome is an autoimmune disease affecting mainly lacrimal glands (which produce tears) and salivary glands. This syndrome is characterized by symptoms of dry mouth and dry eyes. Sjögren's syndrome can coexist with systemic sclerosis.



PRESCRIPTION DRUGS

- PILOCARPINE HYDROCHLORIDE (SALAGEN®)

Action - Improves dry mouth symptoms

Side Effects

Sweating, nausea, shiver, dizziness, headache, flushing, urinary frequency, tiredness, hypertension.

- ANETHOLTRITHIONE (SIALOR®)

Action - Stimulate saliva secretion

Side Effects

Soft feces, yellow urine.

OVER-THE-COUNTER PRODUCTS

DRY MOUTH

- MOUTH KOTE ORAL MOISTURIZER®

- BIOTENE ORAL BALANCE®

- MOISTURIZING GEL®

- BIOTENE DRY MOUTH – GUM®

- BIOTENE DRY MOUTH – TOOTHPASTE®

- BIOTENE DRY MOUTH – MOUTHWASH®

Action - Saliva substitute, alleviate dry mouth

Side Effect

No significant side effect observed.



DRY EYES

- ARTIFICIAL TEARS

Available in the form of solutions, gels or ointments. Products without preservatives are preferable.

Action - Provide tear-like lubrication

Side Effects

Mild stinging, temporary blurred vision.



LOCALIZED SCLERODERMA

Localized scleroderma is a fibrotic disease of the skin and sometimes of the underlying tissues, but does not affect internal organs. It affects mostly children, but can also occur in adulthood. There are several forms of localized scleroderma, including circumscribed or plaque morphea (involving one or multiple well-defined, oval to round areas of skin thickening), generalized morphea (when at least 4 plaques involving at least 2 anatomical sites are present), linear scleroderma (characterized by tight, thick bands, frequently affecting extremities) and scleroderma en coup de sabre (a type of linear scleroderma that affects the forehead and scalp area on one side of the head, with resemblance to the cut of a saber). Raynaud's phenomenon is usually absent in localized scleroderma.

MEDICATIONS

(None proven in controlled trials; the following have been used)

LOCAL TREATMENTS

- TOPICAL STEROIDS

Action - Anti-inflammatory and anti-fibrotic effects

Side Effects

Skin atrophy, hypopigmentation, erythema, rash, acne rash, local irritation, skin dryness, skin infection, skin photosensitivity with certain agents.

- INTRALESIONAL STEROIDS

Action - Anti-inflammatory and anti-fibrotic effects

Side Effects

Skin atrophy, pain at the injection site, bleeding, infection, allergic reaction, a kind of meshwork on the skin due to the dilation of the capillaries (= definition of telangiectasia), changes in skin pigmentation.

- TOPICAL TACROLIMUS

Side Effects

Burning, itching, erythema, acne, folliculitis, headaches, skin infection, hypersensitivity reaction.

- TOPICAL VITAMIN D ANALOGUES (CALCIPOTRIOL)

Side Effects

Skin irritation, itching, tingling sensation, local erythema, dermatitis, skin dryness, skin photosensitivity.

PHOTOTHERAPY

Action - Decrease skin thickening

Side Effects

Burning, itching, nausea, skin aging.

SYSTEMIC TREATMENTS

- METHOTREXATE

Action - Suppress immune response

Side Effects

Diarrhea, decreased appetite, liver and kidney disorder, nausea, mouth sores, skin rash.

- MYCOPHENOLATE MOFETIL (CELLCEPT®)

- MYCOPHENATE SODIUM (MYFORTIC®)

Action - Suppress immune response and anti-fibrotic effect

Side Effects

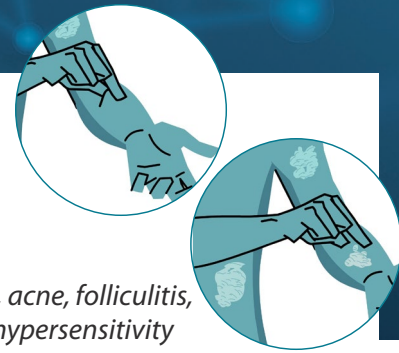
Abdominal pain, diarrhea, nausea, vomiting, decreased appetite, headache, increased susceptibility to infections, anemia.

- PREDNISON

Action - Suppress inflammation

Side Effects

Dyspepsia, insomnia, nervousness anxiety, increased appetite, hyperglycemia, hypertension, headache, dizziness, glaucoma, cataracts, bruising.



SKIN ITCHING (PRURITUS)/DRYNESS

Itch (pruritus) and skin dryness are frequent symptoms in systemic sclerosis. They are usually caused by skin irritation due to inflammation and fibrosis. Pruritus can also sometimes be a sign of liver disease associated with systemic sclerosis (primary biliary cholangitis).



To relieve dry itchy skin, it is necessary to moisturize often. Also, the skin must be protected from harsh detergents, hot water, and the cold winter air, all of which will rob moisture from the skin. Using a humidifier in the home during the cold winter heating months to replace much-needed moisture into the air may be helpful. Not everyone will have the same response to every product. A few products may need to be tried until one is found to work for the patient.

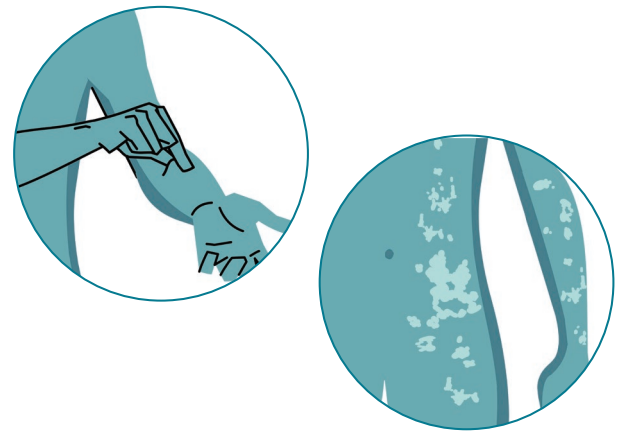
OVER-THE-COUNTER SKIN LOTIONS

- KERICREAM®
- LUBRIDERM®
- EUCERIN® MOISTURIZING CREAMS AND LOTIONS
- NIVEA®
- ULTRADERM®
- ALPHA KERI® BATH OIL
- AVEENO® BATH OIL & MOISTURIZER
- DIPHENHYDRAMINE (BENADRYL®)
- CETIRIZINE (REACTINE®)

Action - Moisturize skin

Side Effect

No significant side effect observed.



ANTIHISTAMINES (PRESCRIPTION)

- HYDROXYZINE (ATARAX®)

Action - Block histamine response, thereby decreasing itching

Side Effects

Drowsiness, dry mouth, nausea, fatigue, dizziness, headaches, agitation, increased appetite, weight gain, blurred vision.



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