Safety and Efficacy Issues

Tolvaptan: risk of liver injury

United States of America — Healthcare professionals have been notified of significant liver injury associated with the use of tolvaptan (Samsca®).

In a double-blind, placebo-controlled trial in about 1400 patients with autosomal dominant polycystic kidney disease (ADPKD) and its open-label extension trial, three patients developed significant increases in serum alanine aminotransferase with concomitant, clinically significant increases in serum total bilirubin. In the trials, the maximum daily dose administered (90 mg in the morning and 30 mg in the afternoon) was higher than the maximum 60 mg daily dose approved for the treatment of hyponatraemia.

Tolvaptan is a selective vasopressin V2-receptor antagonist indicated for the treatment of clinically significant hypervolaemic and euvolaemic hyponatraemia. Samsca® is not approved for the treatment of ADPKD.

Most of the liver enzyme abnormalities were observed during the first 18 months of therapy. Following discontinuation of treatment, all three patients improved. An external panel of experts assessed these cases as being either probably or highly likely to be caused by tolvaptan. These findings indicate that tolvaptan has the potential to cause irreversible and potentially fatal liver injury. These data are not adequate to exclude the possibility that patients receiving tolvaptan for its indicated use of clinically significant hypervolaemic and euvolaemic hyponatraemia are at a potential increased risk for irreversible and potentially fatal liver injury.

Healthcare providers should perform liver tests promptly in patients who report symptoms that may indicate liver injury, including fatigue, anorexia, right upper abdominal discomfort, dark urine or jaundice. If hepatic injury is suspected, tolvaptan should be promptly discontinued, appropriate treatment should be instituted, and investigations should be performed to determine probable cause. Tolvaptan should not be reinitiated in patients unless the cause for the observed liver injury is definitively established to be unrelated to treatment with tolvaptan.


Roflumilast: risk of suicidal behaviour

United Kingdom — Roflumilast (Daxas®) is a phosphodiesterase-type-4 (PDE4) inhibitor used for maintenance treatment of severe chronic obstructive pulmonary disease (COPD) associated with chronic bronchitis. It is indicated for adult patients with a history of frequent exacerbations as an add-on to bronchodilator treatment. The recommended dose is one 500 microgram tablet daily.

From clinical trial data, roflumilast is known to be associated with an increased risk of psychiatric disorders such as insomnia, anxiety, nervousness and depression. Rare instances of suicidal ideation and behaviour, including completed suicide, have also been observed. A recent review of postmarketing data (unpublished) has found that cases of suicidal behaviour have also
been reported in patients with and without a history of depression, usually in the first weeks of treatment.

If patients have existing psychiatric symptoms, or if concomitant treatment is intended with other medicines likely to cause psychiatric symptoms, roflumilast treatment should only be started or continued after careful assessment of the benefits and risks.


### Sodium picosulfate/magnesium citrate: convulsions

**Canada** — Pico-Salax® contains sodium picosulfate and magnesium citrate (also referred to as citric acid and magnesium oxide) and is available as a nonprescription oral purgative indicated for the clearance of the bowel prior to x-ray examination, endoscopy or surgery (1). In addition to Pico-Salax®, there are four other marketed medications containing sodium picosulfate/magnesium citrate in Canada: Picodan®, Purg-Odan®, Picoflo® and Oral Purgative®.

Pico-Salax® acts as an osmotic laxative, stimulates peristalsis and has a powerful washing out effect within 3 to 6 hours or less of administration (1). The diarrhoea produced by the medication can lead to dehydration and loss of electrolytes, particularly sodium which may result in hyponatraemia and convulsions (1–3). Elderly and debilitated individuals are particularly at risk. Pico-Salax® may also decrease the absorption of oral medications due to an increase in gastrointestinal transit rate, and may be associated with convulsions in patients taking anticonvulsants (1).

As of 30 June 2012, Health Canada has received 11 reports of convulsions suspected of being associated with Pico-Salax®. Several articles in the literature reported incidents of seizures and hyponatraemia or emphasized the risk of electrolyte disturbances when using sodium picosulfate/magnesium citrate (4–7). It is important to replace electrolytes as well as fluids when rehydrating (8). Both the risk of hyponatraemia and decreased drug absorption are well described in the prescribing and consumer information for Pico-Salax® (1).

Extracted from the Canadian Adverse Reaction Newsletter, Volume 23, Number 1, January 2013 at http://www.hc-sc.gc.ca/dhp-mpbs/medeff/bulletin/carn-bcei_v23n1-eng

**References**


Risperidone and rhabdomyolysis

Canada — Risperidone is an atypical antipsychotic agent indicated for the treatment or management of schizophrenia, inappropriate behaviour associated with severe dementia and manic episodes associated with Bipolar I disorder (1). All atypical antipsychotics marketed in Canada can trigger neuroleptic malignant syndrome (NMS), and rhabdomyolysis can be part of this syndrome.

Rhabdomyolysis refers to the disintegration of striated muscle and the consequent release of muscular cell contents such as myoglobin into extracellular fluid and circulation. Myoglobin is normally bound to plasma globulins, of which a small amount may be excreted in the urine. When a massive amount of myoglobin is released, and the binding capacity of plasma proteins is surpassed, myoglobin is filtered by the glomeruli and eventually reaches the tubules, where it can cause obstruction and may lead to renal failure (2). Clinical signs and symptoms of rhabdomyolysis include muscle pain, weakness, and dark red-coloured urine. Typically, serum creatine phosphokinase (CPK) levels are also markedly elevated and can be used to assess the presence and intensity of muscle damage (2–3).

Other atypical antipsychotics including clozapine, olanzapine, quetiapine, aripiprazole and one paliperidone product are currently labelled for the risk of rhabdomyolysis independent of NMS, as well as part of NMS, in their respective Canadian product monographs (4–8). Risperidone and ziprasidone are not labelled for the risk of rhabdomyolysis independent of NMS (1, 9).

As of 30 June 2012, Health Canada has received five reports of rhabdomyolysis independent of NMS suspected of being associated with risperidone. All but one patient had recovered at the time of reporting. No deaths were reported. Reports of significant and transient elevation of CPK in stable patients without the presence of NMS involving risperidone and other antipsychotics have been described in the literature (3, 10, 11). However, the exact pathophysiological mechanism that mediates this association remains unclear. There are individual vulnerability factors involved in the development of rhabdomyolysis in the presence of antipsychotics (12). It has also been proposed, based on animal studies, that the accumulation of serotonin in skeletal muscle can play a role in the development of muscle injury (11).

Health professionals should be aware of the risk of rhabdomyolysis without the presence of NMS suspected of being associated with the use of risperidone.

References


**Docetaxel: serious respiratory-related adverse reactions**

Canada — Docetaxel (Taxotere®) is an injectable chemotherapy drug that was first marketed on 31 December 1995. It is currently indicated for the treatment of cancer: breast, non-small cell lung, ovarian and prostate, as well as squamous cell carcinoma of the head and neck (1). Currently, there is one generic product marketed in Canada.

Docetaxel belongs to a group of antineoplastic medicines known as taxanes which act by disrupting the microtubular network essential for cell division (1). Specifically, it promotes the assembly and stabilization of microtubules and leads to the production of microtubule bundles without normal function, resulting in the inhibition of mitosis in cells.

Several antineoplastic drugs, including docetaxel, have been known to induce pulmonary toxicity, which may result in a variety of pathological syndromes ranging from unspecified dyspnea to pulmonary pneumonitis that may lead to permanent pulmonary fibrosis and possible death (2–3). This type of drug-associated lung injury typically occurs as a result of cellular dysfunction which can trigger apoptosis or by impairing the cell and tissue repair sequence (4).

As of 31 July 2012, Health Canada has received 31 reports of respiratory-related adverse reactions suspected of being associated with docetaxel involving pneumonitis, interstitial lung disease (ILD), lung infiltration or respiratory failure. Among these cases, 23 patients required hospitalization. A fatal outcome was reported in nine cases.

Several cases of serious respiratory-related adverse reactions in patients using docetaxel, either alone or in combination with other antineoplastic agents, have been reported in the literature. Reported adverse reactions include pneumonitis or interstitial pneumonitis, pulmonary infiltrates, acute respiratory distress syndrome, respiratory failure, ILD, interstitial infiltrates and pneumocystis pneumonia. Some of these cases resulted in fatal outcomes (5).

Extracted from the Canadian Adverse Reaction Newsletter, Volume 23, Number 1, January 2013 at http://www.hc-sc.gc.ca/dhp-mps/medeff/bulletin/carn-bcei_v23n1-eng

**References**


than for men. The FDA has prepared a list of questions and answers as an overview of this safety issue.


Combination treatment with telaprevir, peginterferon alfa and ribavirin: serious skin reactions

United States of America — The Food and Drug Administration (FDA) has received reports of serious skin reactions, some fatal, in patients taking the hepatitis C drug telaprevir (Incivek®) in combination with the drugs peginterferon alfa and ribavirin (Incivek® combination treatment). Significantly, some patients died when they continued to receive Incivek® combination treatment after developing a worsening, or progressive rash and systemic symptoms. As a result, FDA has added a boxed warning to the drug label stating that Incivek® combination treatment must be immediately stopped in patients experiencing a rash with systemic symptoms or a progressive severe rash. Consideration should also be given to stopping any other medications that may be associated with serious skin reactions. Typical systemic symptoms and signs may include fever, nausea, diarrhoea, mouth sores or ulcers, facial edema, red or inflamed eyes, swelling or hepatitis. All patients with serious skin reactions should also receive urgent medical care.

Incivek® is a hepatic C virus NS3/4A protease inhibitor indicated in combination with peginterferon alfa and ribavirin for the treatment of genotype 1 chronic hepatitis C in adult patients with compensated liver disease, including patients who have cirrhosis, are treatment-naïve, or who have been previously received interferon-based treatment. Incivek® must always be used in combination with peginterferon alfa and ribavirin.
Serious skin reactions, including drug rash with eosinophilia and systemic symptoms (or DRESS) and Stevens-Johnson Syndrome (SJS) have been previously reported in patients taking Incivek® combination treatment. If serious skin reactions occur, all three components of Incivek® combination treatment must be immediately discontinued.


Dabigatran etexilate mesylate: not for patients with mechanical prosthetic heart valves

United States of America — Healthcare professionals have been notified that the anticoagulant dabigatran etexilate mesylate (Pradaxa®) should not be used to prevent major thromboembolic events in patients with mechanical heart valves, also known as mechanical prosthetic heart valves. The RE-ALIGN clinical trial conducted in Europe (1) was recently stopped because Pradaxa® users were more likely to experience strokes, heart attacks, and blood clots forming on the mechanical heart valves than were users of the anticoagulant warfarin. There was also more bleeding after valve surgery in Pradaxa® users than in the warfarin users.

Dabigatran is approved to reduce the risk of stroke and systemic embolism in patients with non-valvular atrial fibrillation. It is not approved for patients with atrial fibrillation caused by heart valve problems. The FDA is requiring a contraindication of dabigatran for patients with mechanical heart valves. Healthcare professionals should promptly transition any patient with a mechanical heart valve who is taking dabigatran to another medication.

The use of dabigatran in patients with another type of valve replacement made of natural biological tissue, known as a bioprosthetic valves, has not been evaluated and cannot be recommended.

References


Sodium oxybate with alcohol or drugs: respiratory depression

United States of America — The Food and Drug Administration (FDA) is reminding healthcare professionals and patients that the combined use of sodium oxybate (Xyrem®) with alcohol or central nervous system (CNS) depressant drugs can markedly impair consciousness and may lead to respiratory depression.

The use of alcohol with Xyrem® is a new contraindication added to the label, which already contraindicates its use with insomnia drugs. Use with other CNS depressant drugs such as opioid analgesics, benzodiazepines, sedating antidepressants or antipsychotics, general anesthetics, and muscle relaxants should be avoided.

Sodium oxybate is approved to reduce cataplexy and treat daytime sleepiness in patients with narcolepsy. Sodium oxybate is also known as gamma-hydroxybutyrate (GHB). GHB is a known drug of abuse associated with central nervous system (CNS) adverse events, including death. Even at recommended doses, Xyrem® can cause confusion, depression, and other neuropsychiatric events.

WHO Drug Information Vol. 27, No. 1, 2013

Statins: risk of increased blood sugar levels and diabetes

Canada — Health Canada has announced a labelling update for all statins regarding the risk of increased blood sugar levels and a small increased risk of diabetes among patients already at risk for the disease.

Based on the review of all available data, Health Canada concluded that the risk of diabetes appears to be mainly in patients with pre-existing risk factors for diabetes, such as high levels of glucose or triglycerides, obesity or high blood pressure. Health Canada continues to believe the overall cardiovascular benefits of statin drugs in reducing blood cholesterol outweigh their risks.

A new warning about increased blood sugar levels and the risk of diabetes, including information on how to identify high-risk patients, has been added to the drug labels for the six statins currently marketed in Canada: atorvastatin, lovastatin, rosuvastatin, simvastatin, pravastatin and fluvastatin.


Immunomodulatory medicines: progressive multifocal leukoencephalopathy

Australia — Immunomodulatory medicines have been associated with the development of progressive multifocal leukoencephalopathy. Awareness of risk factors and early recognition of symptoms is important as early diagnosis is likely to improve the prognosis (1).

Progressive multifocal leukoencephalopathy (PML) is a rare, but often fatal, demyelinating disease of the central nervous system. PML lesions are typically asymmetrical demyelinated plaque areas with irregular borders, surrounded by macrophages and irregular astrocytes with large, multiple nuclei (2). Patients with PML can have a variety of symptoms including muscle weakness, sensory deficit, cognitive dysfunction, language impairment and/or coordination and gait difficulties (3).

PML is caused by a human polyomavirus, the JC virus. Approximately 50% of the world’s population are infected with the virus by the time they reach age 20, although most remain asymptomatic (4). After initial virus infection, the virus remains quiescent in the kidneys, bone marrow and lymphoid tissue (3).

In immunocompromised individuals the quiescent virus can reactivate, enter the bloodstream and then gain entry to the central nervous system where it infects oligodendrocytes and astrocytes. Infection of these cells leads to cell death, and the resulting demyelination produces the neurological signs and symptoms of PML (5). Viruses isolated from the brains of individuals with PML have a genomic rearrangement in the regulatory region that is not found in the strains responsible for initial infection (4,5).

Cell-mediated immunity disorders are the major immunological disorders that predispose individuals to the development of PML (4). Cases have been reported in patients with HIV, lymphoproliferative disorders, malignancies, patients on immunosuppressive therapy after solid organ transplantation and in rheumatic diseases such as systemic lupus erythematosus (6,7).

Immunosuppressive medications that have been associated with PML include cyclophosphamide, corticosteroids, mycophenolate mofetil and monoclonal antibodies including natalizumab, rituximab and alemtuzumab (8).

The early signs of PML are often related to cognitive dysfunction, manifesting...
as mental slowness, disorientation and behavioral changes (2). Motor and sensory disturbance, characterized by lack of coordination, gait disturbance, ataxia, hemiparesis or visual deficits may also be found at the time of presentation (2). Seizures, language difficulties and headaches can occur but are less common. These signs and symptoms progress over the course of a few weeks and death can occur weeks to months after diagnosis.

**Australian and New Zealand reports of PML associated with immunomodulatory medicines (to 30 November 2012)**

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rituximab*</td>
<td>13</td>
</tr>
<tr>
<td>Natalizumab</td>
<td>13</td>
</tr>
<tr>
<td>Alemtuzumab</td>
<td>1</td>
</tr>
<tr>
<td>Cyclophosphamide*</td>
<td>1</td>
</tr>
<tr>
<td>Prednisolone*</td>
<td>1</td>
</tr>
<tr>
<td>Mycophenolate mofetil#</td>
<td>1</td>
</tr>
<tr>
<td>Tacrolimus#</td>
<td>1</td>
</tr>
<tr>
<td>Dexamethasone#</td>
<td>1</td>
</tr>
</tbody>
</table>

* Co-suspect medicines in same report.
# Co-suspect medicines in same report.

Improved chance of survival is associated with early diagnosis, younger age at diagnosis and if the disease is limited to one lobe of the brain (1). Current treatment of PML is limited and is generally supportive in nature. A treatment strategy for PML in HIV-negative patients is to restore the host adaptive immune response by stopping or decreasing immunosuppression (3).

Recovery of the immune system can trigger immune reconstitution inflammatory syndrome (IRIS). In HIV-negative patients with PML-IRIS, the current treatment is corticosteroids to reduce the inflammatory response (3).

**References**


**Thyroxine and fractures**

**Australia** — Health professionals are advised that the product information for thyroxine (Eutroxsig® and Oroxine®) has recently been updated to include a precaution about the increased risk of osteoporotic fracture associated with excessive thyroxine doses. Control of hypothyroidism should be monitored regularly, especially in the elderly, and the thyroxine dose adjusted accordingly.

Chronic hyperthyroidism promotes bone turnover, characterized by increases in bone resorption and in urinary excretion of calcium and phosphorus. Increased
bone resorption may result in osteoporosis and an increased risk of fracture. A similar risk appears to exist for hypothyroid patients receiving higher-than-needed doses of thyroxine. The elderly may be at particularly increased risk, since thyroxine replacement needs decrease with age, and age is an additional risk factor for osteoporosis (1).

**Fracture risk with thyroxine replacement therapy**

Two recent large studies have examined the risk of fracture in patients on long-term thyroxine replacement. A nested case-control study in 213,511 Canadian thyroxine users aged over 70 followed patients for a mean of 3.8 years (1) and an observational cohort study in 17,684 Scottish thyroxine users aged 18 and over, was conducted with a median follow-up of 4.5 years (2). Although neither study measured both thyroxine and TSH levels, each found an association between either high or excessive (as measured by TSH suppression) thyroxine dose and fracture. As well as increasing the risk of osteoporosis, excess thyroxine may also increase the risk of falls secondary to arrhythmia or muscle weakness, particularly in the elderly (1).

The Product Information for thyroxine (Oroxine®, Eutroxsig®) has recently been updated with a new precaution about the effects of thyroxine on bone mineral density. It is recommended that patients receiving thyroxine are given the minimum dose necessary to achieve the desired clinical and biochemical response. Prescribers should keep in mind that replacement thyroxine needs decrease in the elderly and serum TSH should be monitored regularly and thyroxine doses adjusted accordingly. The risk of fracture may be greater in patients with other risk factors for osteoporosis, including postmenopausal women, those with a family history or past history of fracture or osteoporosis, smokers, and patients with vitamin D deficiency.

**References**


**Oral bowel cleansing products: serious electrolyte disturbances**

*Australia* — The use of oral bowel cleansing products is part of the preparation for a number of medical, diagnostic and surgical procedures. These products create a cathartic effect by osmotic action, resulting in a transfer of fluid and electrolytes to the gut lumen. Marked dehydration, electrolyte abnormalities and associated complications may occur as a result in otherwise well patients. The Therapeutic Goods Administration (TGA) has previously alerted prescribers to the risk of severe electrolyte disturbances in association with the use of sodium picosulfate-containing products (1).

Since January 2002, the TGA has received a total of 51 adverse event reports for these products of which 18 were reports of serious electrolyte disturbances. While it is known that the elderly, the frail and those with cardiac failure or renal impairment are potentially at higher risk of an adverse event, health professionals are reminded that serious adverse events can occur in patients under the age of 60 years who are otherwise fit and healthy, and that this should be considered when prescribing/dispensing these products.

All patients should be reminded of the importance of hydration and electrolyte
The risk of venous thromboembolism with these medicines is low but well known and warnings are included in the product information to alert patients and prescribers to the risks. The PRAC will evaluate all available evidence on the benefits and risks of these medicines and give a recommendation on whether marketing authorization should remain as at present, be varied, suspended or revoked, in the interest of all patients in the European Union.

The PRAC has also formally started a review of combined contraceptives containing chlormadinone, desogestrel, dienogest, drospirenone, etonogestrel, gestodene, nomegestrol, norelgestromin and norgestimate, often referred to as third and fourth generation contraceptives.


Fibrin sealant spray: gas embolism

European Union — The European Medicines Agency’s Committee for Medicinal Products for Human Use (CHMP) has recommended a number of new instructions for healthcare professionals using the fibrin sealants Tisseel®, Tissucol®, Artiss® and Beriplast P® (and associated names) to optimize the safe use of these medicines when applied as spray during surgery.

This follows the CHMP advice on two other fibrin sealants, Evicel® and Quixil®, adopted in November 2012.

Fibrin sealants are used in a wide range of surgical procedures to help reduce local bleeding. They can be applied by dripping or spraying the solution onto bleeding tissue, where they form a fibrin clot, stopping bleeding and thereby helping to wound to heal.


Combined contraceptives: venous and arterial thromboembolism

European Union — The European Medicines Agency’s Pharmacovigilance Risk Assessment Committee (PRAC) has formally started a safety review of Diane 35® (cyproterone acetate 2 mg, ethiny-lestradiol 35µg), associated names and its generics at its February 2013 meeting.

The Europe-wide review has been initiated at the request of the French medicines regulatory agency (ANSM), following the announcement of its plan to suspend the marketing authorizations for Diane 35® and its generics for acne treatment in France over the next three months. This was the result of an analysis of known data, including reports of venous and arterial thromboembolism recorded in the French national pharmacovigilance database in association with Diane 35® and its generics over a period of more than 20 years.

These medicines have been authorized at the level of individual Member States for many years. They are widely used across Europe. However, their authorized uses differ between Member States. In many countries they are authorized as a contraceptive in women with hormone-related conditions such as acne, hirsutism and alopecia. In France, they are only authorized for the treatment of acne, but ANSM has noted widespread off-label use as a contraceptive.


Safety and Efficacy Issues
The review of fibrin sealants was initiated following reports of gas embolism with Evicel® and Quixil® in association with the use of spray devices that use a pressure regulator to administer these medicines. These events appear to be related to the use of the spray device at higher-than-recommended pressures and/or in closer-than-recommended proximity to the tissue surface.

The Committee recommended that:

• The product information should be updated with clear and consistent advice for healthcare professionals regarding recommended pressure and distance to use during spraying application.

• Marketing authorization holders for these medicines should ensure that they are used with pressure regulators that do not exceed the maximum pressure required to deliver the fibrin sealant, and that they contain labels stating the recommended pressure and distance.

• The product information should include a warning that the risk of gas embolism appears to be higher when fibrin sealants are sprayed using air, as compared to CO2, and patients should be closely monitored for signs of gas embolism.

• Healthcare professionals in the European Union (EU) will receive a letter outlining the updated information on the safe use of these medicines.

However, for Beriplast P® (and associated names), the CHMP concluded that there is no risk associated with this product because it does not require a gas-assisted spray device during application, therefore there is no risk of gas embolism with this product when used in accordance with prescribing advice and with the recommended device.


Corticosteroids: musculoskeletal adverse events

New Zealand — Healthcare professionals are reminded that corticosteroids are associated with multiple musculoskeletal adverse reactions including avascular necrosis of the bone, osteoporosis and tendinopathies (1).

Avascular necrosis of the bone is an uncommon adverse reaction associated with corticosteroids (1, 2). Higher doses of corticosteroids are associated with a greater risk of avascular necrosis even when used for short periods (2). Importantly, avascular necrosis has also been reported with topical application of corticosteroids (3).

Osteoporosis is a common adverse reaction associated with long-term corticosteroid treatment, where up to 50% of patients are affected (1, 4). Bone loss is more rapid during the early stages of therapy, is dose-dependent and primarily occurs in trabecular bone (1, 4, 5). Daily doses of greater than 7.5 mg prednisolone (or equivalent) have been associated with a higher risk of fracture than daily doses of less than 2.5 mg prednisolone (or equivalent) (5).

Tendinopathies associated with corticosteroid use are predominantly reported in the Achilles and patellar tendons (6). Tendon ruptures have also been reported. Tendinopathies have been associated mainly with oral and intra-articular corticosteroid use (6).

In New Zealand, 40 reports of musculoskeletal adverse events associated with corticosteroids were reported to the Centre for Adverse
Reaction Monitoring (CARM) between January 2000 and June 2012. The majority of the reports were associated with prednisone (30 reports).

The remaining reports were associated with dexamethasone (nine reports), triamcinolone (two reports) and methylprednisolone (one report). In two cases, the patient was on more than one corticosteroid. It is worth noting that in all but one case of tendon rupture the patient was also taking a quinolone antibiotic (7).

The types of musculoskeletal adverse reactions reported in these 40 reports are shown below. Avascular necrosis (55.6%) and osteonecrosis (13.3%) were the most commonly reported musculoskeletal adverse reactions. Of the reported cases of avascular necrosis, two-thirds reported avascular necrosis of the femoral head.

<table>
<thead>
<tr>
<th>CARM reports of musculoskeletal adverse reactions associated with corticosteroids for the period January 2000 to June 2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avascular necrosis</td>
</tr>
<tr>
<td>Osteonecrosis</td>
</tr>
<tr>
<td>Tendon rupture</td>
</tr>
<tr>
<td>Myalgia</td>
</tr>
<tr>
<td>Arthritis</td>
</tr>
<tr>
<td>Septic arthritis</td>
</tr>
<tr>
<td>Osteoporosis</td>
</tr>
<tr>
<td>Fracture pathological</td>
</tr>
</tbody>
</table>

Healthcare professionals are encouraged to educate patients about possible adverse reactions associated with corticosteroid use and to ensure treatment and dose is regularly reviewed. Use of more than one medicine with the potential to cause adverse musculoskeletal effects is likely to increase the risk of an adverse reaction, such as avascular necrosis, osteoporosis and tendon disorders.


References


