Annex 2: Model Information Letter for the Primary-Care Physician

Evidence Based Medicine | Official recommendations | Expert opinion

....., ...

Dear Colleague,

You will soon receive a visit from your patient M (Ms) .....

born on..... in whom we recently started tocilizumab (RoActemra®) treatment for rheumatoid arthritis.

What is tocilizumab?

Tocilizumab is a monoclonal antibody that inhibits the receptor for interleukin-6. Tocilizumab has been proven effective in improving the symptoms and structural disease progression in patients with rheumatoid arthritis (RA).

Based on this evidence of efficacy, tocilizumab was granted a marketing licence in 2009 for active moderate-to-severe RA in patients having failed one or more DMARDs or TNF antagonists, as add-on treatment to methotrexate or as monotherapy in the event of intolerance to methotrexate or when further methotrexate therapy would be inappropriate.

The first tocilizumab infusion was given intravenously in a dosage of ..... in the department of ..... (Dr .....), on .....

An infusion will be given once monthly, in the same dosage, in the absence of pregnancy, infection, surgery, or adverse events.

A DMARD was prescribed in combination with tocilizumab.

❏ YES (specify the nature and dosage of the DMARD) .....

❏ NO (tocilizumab monotherapy)

Effectiveness of tocilizumab therapy

The effect of tocilizumab therapy on the signs and symptoms of RA usually becomes apparent gradually over the first few treatment months.

The final evaluation of the effectiveness of tocilizumab therapy is usually performed after 6 months of treatment.

What are the risks associated with tocilizumab therapy?

Intolerance (a reaction) to the molecule during the infusion or within the next few

hours is very rare. In most cases, simple symptomatic measures suffice. However, admission on an emergency basis is required in patients with constitutional symptoms, respiratory manifestations, cardiovascular manifestations, or diffuse skin lesions.

Infections may occur in tocilizumab-treated patients. Pneumonia and bronchitis are the most common forms, although cellulitis, pyelonephritis, and diverticulitis have been reported also. In tocilizumab-treated patients, infections may fail to elevate the levels of CRP, other markers for inflammation, or leukocytes.

In the absence of signs of a serious infection, prompt initiation of appropriate antimicrobial therapy is warranted. Patients with constitutional symptoms or complications should be admitted on an emergency basis.

Other adverse events have been reported such as blood pressure changes (hypertension, hypotension), hepatic cytolysis (without severe hepatitis), neutropenia (reversible), hypercholesterolemia, and headaches.

Despite this non-exhaustive list of adverse events, it should be borne in mind that the overall safety record of tocilizumab so far is very good.

Interactions may occur between tocilizumab and drugs metabolized via the cytochrome P450 enzymes such as some of the statins (atorvastatin, simvastatin), calcium channel inhibitors, theophylline, warfarin, cyclosporine, benzodiazepines, and phenytoin. These interactions may require dosage adjustment at tocilizumab initiation or discontinuation (dosage increase at tocilizumab initiation and dosage decrease 1 to 2 weeks after tocilizumab discontinuation).

Practical considerations

➤ The infusions will be given once every 4 weeks during brief hospital stays (1 hour to a few hours).

➤ The effectiveness and safety of tocilizumab therapy will be monitored during a rheumatologist visit at least 3 months after the initiation of tocilizumab therapy, but the patient may ask to see you in the event of unusual symptoms, whose possible link to tocilizumab will have to be evaluated.

Please contact one of the members of our team if you are unsure about anything.

➤ The rheumatologist must evaluate the patient at least once every 3 months to assess the clinical effectiveness of tocilizumab therapy (based on the DAS (Disease Activity Score) and the effect on laboratory tests (ESR-CRP)).

➤ We provide most of the monitoring required to assess safety. The only laboratory tests required by tocilizumab therapy are blood cell counts, serum transaminase assays, and serum lipid assays, at 3-month intervals. Additional tests should be performed as indicated by the concomitant medications (e.g., methotrexate and corticosteroids).

Before the first tocilizumab infusion, we checked your patient's immunisation records.

❏ Immunisation against ..... was performed on ...../...../.....

❏ No immunisations were deemed necessary.

If immunisation or re-immunisation with an inactivated vaccine (e.g., influenza) is required, it may be performed during tocilizumab treatment. Administration of the influenza vaccine is recommended once a year.

In contrast, live vaccines (oral poliomyelitis, MMR, varicella-zoster, yellow fever, and BCG) are contraindicated during tocilizumab therapy and during the first 70 days after treatment discontinuation.

➢ In the current state of our knowledge, pregnancy is contraindicated during and until 3 months after tocilizumab therapy. No data are available on potential effects of tocilizumab therapy on the foetus.

➢ In patients who require elective surgery, the recommended interval between the last tocilizumab infusion and the surgical procedure is 4 weeks at least. This interval may be modulated depending on the nature of the surgical procedure (as the risk of postoperative infection varies across procedures), any co-morbidities and patient-related factors, the severity of the joint disease, and the extent of disease control.

If emergency care is required, the appropriateness of prophylactic antibiotics should be discussed on a case-by-case basis.

➢ When routine dental care is needed (cavities, scaling), prophylactic antimicrobial therapy can be suggested, with no change in the treatment regimen for the joint disease.

When dental procedures that carry a risk of infection are required (extraction, apical granuloma, abscess...), the tocilizumab infusion should be postponed as with surgical procedures and prophylactic antimicrobial therapy should be offered.

➢ The patient may travel provided no live vaccines (e.g., yellow fever) are required, as live vaccines can be given only after discontinuing tocilizumab therapy. As with all travellers, measures aimed at preventing infections should be followed scrupulously. Standard antimalarial prophylaxis can be used.

An information sheet explaining all these points was given to the patient before the tocilizumab infusion.

Sincerely,

Physician in charge:

Dr.....

Telephone:.....

Stamp: