January 20, 2011

Dear Patient,

This letter is to let you know about a change in the way you receive the medicine **Eprex** (EPO, epoetin alfa).

Right now you receive this medicine into a vein (intravenous) through your dialysis machine. Before 2003, we used to give Eprex under the skin (subcutaneous) to patients receiving hemodialysis. In 2003, we changed the way we give this medicine because of an increase in pure red cell aplasia (PRCA). PRCA is a rare condition where the body produces fewer red blood cells. We now know that the increase in PRCA is not caused by the way you give the medicine. Health Canada has also removed the warning on giving these medicines under the skin. All Renal Health Clinic (predialysis) patients, and patients receiving peritoneal dialysis (PD), get Eprex under the skin.

Making this change has the following benefits:

- For most patients we can give the Eprex one to two times a week under the skin instead of two to three times a week into the vein.

- We can give you 20-30% less Eprex. Eprex is still a very expensive medicine and giving it under the skin will help save significant money for health care in Manitoba. For this reason, other hemodialysis units in Canada have also switched patients to Eprex under the skin.

- You can take the medicine on your own in the unit if you'd prefer, just as you did before starting hemodialysis, or your dialysis nurse will administer it to you.

The disadvantage to this change is that we recognize that some people may not be happy to get another needle. We have carefully considered all the issues and we have decided to give all our patients Eprex under the skin. This will begin mid-February through March 2011. The doctors, pharmacists and nurses in the Manitoba Renal Program will be working together to make this change. All patients will be monitored closely to make sure their Eprex is working well. If you have any questions, please feel free to ask your doctor, pharmacist or nurse in your dialysis unit or clinic.

Thank you for your cooperation.

Yours truly,

Mauro Verrelli, MD, FRCPC
Medical Director, Manitoba Renal Program

Manitoba Renal Program IV to Subcutaneous Epoetin alfa Conversion Table

Hgb (g/dL) on IV Epoetin alfa	Percent of IV dose to be given subcutaneously*
Less than 10	125%
10-10.4	100%
10.5-11.6 stable	75%
10.5-11.6 and decreasing	100%
11.6-11.9	75%
Greater than 11.9	66%

Hgb target range: 10-12 g/dL

Dosing Frequency:

Once weekly – stable, in target patients. Maximum once weekly dose = 10,000 units*

2 times weekly - patients who are not stable

3 times weekly – patients on larger doses who cannot be dosed 2x/week because the available pre-filled syringe strengths will not accommodate their doses.

MRP maximum epoetin alfa dose is 30,000 units subcut per week.

The goal is to have the majority of MRP patients on 1-2x/week subcutaneous dosing.

Available pre-filled syringe strengths:
1,000 units
2,000 units
3,000 units
4,000 units
5,000 units
6,000 units
8,000 units
10,000 units
20,000 units**
30,000 units**

Order writing reminder: subcutaneous should be written as "subcut" or "subcutaneous" as other abbreviations are not considered safe.

*Calculated doses should be rounded to the nearest pre-filled syringe strength that makes sense. For example, 13,000 units/week could be rounded down to 6,000 units subcut twice weekly on Mon and Fri.

Odd doses that require 2 syringes to administer should not be prescribed (e.g. 7,000 units, 11,000 units).

Try to avoid prescribing different doses in the same week if possible. (e.g. Instead of 5,000 units on Mon and 6,000 units on Fri. considering rounding dose down to 5,000 units 2x/week or rounding dose up to 6,000 units 2x/week).

*The published studies on once weekly epoetin alfa in hemodialysis only enrolled stable, in target patients. The doses needed to maintain target Hgb (range of target Hgb used was anywhere from 9-12 g/L) were in 90-100 units/kg/week range. So even a 100 kg person would only receive up to 10,000 units once weekly.

** These high strength epoetin alfa syringes are available at contract prices but are not currently wardstock. They could be added to wardstock by the renal pharmacist should it be decided to dose higher dose patients at 2x/week. The 40,000 unit syringe should not be used as the MRP maximum dose is 30,000 units/week.

NOTICE FOR DIALYSIS NURSES

CHANGE TO SUBCUTANEOUS EPOETIN ALFA (EPREX) ADMINISTRATION IN HEMODIALYSIS

WHY IS THIS CHANGE HAPPENING?

Eprex administered subcutaneously (subcut) results in a 20-30% dose decrease versus IV administration. This results in decreased costs for this expensive drug to our healthcare system. It is predicted that we will save close to 1 million dollars by making this change in the route of administration. Other hemodialysis units in Canada and the U.S. have also switched patients to subcut injections for this reason.

WHAT ARE OTHER ADVANTAGES TO THIS CHANGE?

For most patients we can give the Eprex less frequently – 1-2 times a week subcut instead of 2-3 times a week IV because subcut Eprex stays around longer in the body than IV Eprex. The patient can administer their own subcut Eprex in the unit if they want to do this. Otherwise, the dialysis nurse will administer it.

The disadvantage to this change is that we recognize that some people may not be happy to get another needle.

HOW WILL PATIENTS BE INFORMED OF THIS CHANGE?

A patient letter will be distributed in the hemodialysis units at the beginning of Feb. 2011. This letter closely follows that used at St. Paul's Hospital in Vancouver where the change to subcutaneous dosing went quite smoothly from a patient perspective.

DIDN'T WE ADMINISTER EPREX SUBCUTANEOUSLY IN THE PAST?

Yes, before 2003 we used to give Eprex subcut to patients receiving hemodialysis. In 2003, we changed the way we give this medicine because of an increase in pure red cell aplasia (PRCA). PRCA is a rare condition where the body produces fewer red blood cells. We now know that the increase in PRCA was not caused by the route of administration and Health Canada has removed the warning on giving Eprex subcut. An investigation found that leachates from uncoated rubber stoppers in the pre-filled syringes may have been the cause of the increase in PRCA. The risk of PRCA with subcut administration of Eprex has returned to baseline levels (~0.5 case per 10,000 patient years' exposure) since coating the rubber stopper in the prefilled syringes. (CSN Anemia Guidelines)
All Renal Health Clinic (predialysis) and patients receiving peritoneal dialysis (PD) have always received Eprex subcut.

WHEN WILL THIS CHANGE OCCUR?

The Renal Pharmacists will begin switching patients to subcut Eprex starting in mid-Feb. 2011 and continuing into March 2011. All Eprex orders will be rewritten by the Renal Pharmacists as the dose, route, and frequency of administration of Eprex will change with subcut dosing.

WHAT SHOULD NURSES BE AWARE OF?

Double check the Eprex order for the route of administration. There will be a period of time (until all patients in all units are converted) that some patients will be on subcut Eprex and others will be on IV Eprex. This is especially true now that patients often transfer back and forth between units. The doses are different so Eprex should be given by the route specified in the drug order.

Prefilled syringes will continue to be used as the multi-dose vial of Eprex is no longer available in Canada. The dose of Eprex will be changed to a corresponding prefilled syringe strength. Odd doses which require 2 syringes will no longer be prescribed (e.g. 7,000 units, 12,000 units).

HOW WILL PATIENT CONCERNS BE HANDLED?

To be fair to all patients, unless there are "extenuating circumstances" (to be determined on a case by case by the hemodialysis physician and reviewed with the pharmacist), all patients will receive subcutaneous injection; we would otherwise we will be creating a double standard. This is the message patients should receive if the issue comes up. Patients who were previously in Renal Health Clinic or PD could also be gently reminded that this is how they used to receive their Eprex (this is included in the patient letter) or how their insulin is administered.

Hopefully our experience will be similar to that of St. Paul's Hospital in Vancouver where only a handful of emaciated patients experienced a lot of pain with the injections and were accommodated with IV Eprex.

WHAT ABOUT PATIENTS WHO RECEIVE DARBEPOETIN (ARANESP) INJECTIONS?

These patients will remain on IV dosing as Aranesp IV and subcut. dosing are equivalent. However, this is not a reason to switch patients to Aranesp as we pay full price for this ESA. The MRP only had 12 HD patients receiving Aranesp as of Sept. 30, 2010.

OTHER QUESTIONS?

Please ask your Renal Pharmacist, Nurse Educator, or Nephrologist.

Winnipeg Regional Health Authority
Caring for Health
Office régional de la santé de Winnipeg
À l'écoute de notre santé

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Briefing Note
Manitoba Renal Program Proposed Change from Intravenous to Subcutaneous Administration of EPO

Senior Management:	**For Information**	☐	**Date** _____
	For Discussion	☐	**Date** _____
	For Approval	**X**	**Date November 29, 2010**
Manitoba Health:	**For Information**	☐	**Date** _____
	For Discussion	☐	**Date** _____
	For Approval	☐	**Date** _____

Issue:
The Manitoba Renal Program (MRP) proposes to change the erythropoietin (EPO) administration from intravenous (IV) to the subcutaneous (SC) route for hemodialysis (HD) patients in Manitoba. The main incentive for this change is a substantial cost reduction due to the lower doses required when EPO is dosed subcutaneously.

Background (Include Manitoba Health's Involvement to Date):
EPO is a protein naturally produced by functioning kidneys, which stimulates the bone marrow to produce red blood cells. Without adequate EPO an individual can become anemic leaving patients tired and lethargic and unable to perform work and other tasks. Since dialysis patients have little or no kidney function, this is often a concern. Fortunately there are EPO drugs that can be prescribed to prevent the onset of anemia in renal patients.

EPO that is given subcutaneously results in a 20-26% dose decrease versus IV administration. The MRP average EPO dose in hemodialysis is 13,000 units/week IV (with a range of 2,000-36,000 units/week IV).

EPO can be given either intravenously or subcutaneously. However, EPO administered by the intravenous route requires an increased dosage to achieve similar hemoglobin targets when compared with the subcutaneous route. Studies in Canadian hemodialysis patients have demonstrated a 20–26% increase in the dose of EPO when iron-replete patients were switched from subcutaneous to intravenous EPO.

Options (Including Analysis/Rationale):

Financial Impact:
The Manitoba Renal Programs annual EPO cost is [redacted]. Hemodialysis patients represent 79.6% of the patient population with the remaining 20.4% being Peritoneal Dialysis patients. The estimate of the savings potential is in the range of 20 to 26% of the net cost for the EPO administered to the hemodialysis patients. This amounts to [redacted] to [redacted] on an annualized basis. With [redacted] year and [redacted] months remaining on the contract if the Manitoba Renal Program made the switch as of January 1, 2011 this would be a savings over the remainder of the current contract in the range of [redacted].

Human Resource Impact:
No anticipated impact.

Operational Impact:
Bedside hemodialysis nurses will inject the medication instead of the current intravenous administration of the medication. No anticipated significant impact.

Benchmarking Data:
Subcutaneous injection of EPO in hemodialysis patients was standard practice within the MRP until 2002 when a higher than usual international incidence of EPO associated pure red blood cell aplasia (PRCA) was noted.

Canadian and American Renal Pharmacists list-servs were polled by one of the MRP Pharmacy coordinators and found that many of the American hemodialysis units have changed to subcutaneous EPO due to their new reimbursement system.

British Columbia converted from IV to SC EPO in January 2007. Personal communication to the MRP pharmacist from the B.C. renal pharmacist notes that “less than a handful of patients complained of pain” with the switch.

Recommended Option:
Given the above the Manitoba Renal Program recommends that the program commences with the switch of approximately 986 hemodialysis patients from intravenous administration to subcutaneous administration of EPO. The MRP will continue to evaluate the relative costs using renal and pharmacy resources as we move forward and gain additional experience.

Ethical Considerations:
Subcutaneous injection of Eprex (with a very small needle) from once to thrice weekly may incur some patient discomfort not present via the intravenous administration as it is injected directly into the dialysis line.

Communication Considerations:
All affected patients shall be given a letter explaining the reason for the change.

Impact on Patient Care:
Patient Issues & Once Weekly Dosing:
The change to subcutaneous EPO may not be well received by some hemodialysis patients. The Manitoba Renal Program will draft a patient letter explaining the reason for the change. In addition, more studies have come out examining the use of once weekly subcutaneous injections of EPO in stable target hemodialysis patients. Although hemoglobin targets can be maintained on once weekly administration a small increase in EPO dose may be needed (12 units/kg/week in 1 study). Many centers in the U.S. are giving EPO once weekly subcutaneously in stable patients who are in the target range. This is a little more challenging in Canada as we no longer have a multi-dose vial of EPO available and we are limited to the prefilled syringe strengths but most patients should be able to be dosed 1-2x weekly.

PRCA:
The risk of PRCA with subcutaneous administration of EPO has returned to baseline levels (~0.5 case per 10,000 patient years' exposure) since coating the rubber stopper in the prefilled syringes.

Consultation and Engagement:
An email notification of the proposed change has been sent out to the MRP Nephrologists, Program Directors, Hemodialysis Unit Managers, and MRP Pharmacy Coordinators requesting that they voice any questions or concerns regarding the change.

Cautionary Notes:
As noted above the change to subcutaneous EPO may not be well received by some hemodialysis patients as subcutaneous injection of Eprex may incur some patient discomfort not present via the intravenous administration.

Submitted By:
Dr. Mauro Verrelli, WRHA Manitoba Renal Program Medical Director
on behalf of the Manitoba Renal Program Team

Date:
November 29, 2010