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(Ministry Of Health Malaysia)
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Ruj. Kami : KKM-55/104/012/01 Jld.IT (6)

Tarikh : 8 Januari 2016

SENARAI EDARAN

YBhg. Datin/Tuan/Puan,

GARIS PANDUAN UNTUK PEMANTAUAN KESELAMATAN PRODUK *ERYTHROPOETIN STIMULATING AGENTS* (ESAs) DAN PELAPORAN KESAN ADVERS *PURE RED CELL APLSIA* (PRCA)

Saya dengan hormatnya merujuk kepada perkara di atas.

2. Untuk makluman, beberapa aduan berkaitan kesan advers *Pure Red Cell Aplasia (PRCA)* yang melibatkan penggunaan *Erythropoetin Stimulating Agents (ESAs)* dari fasiliti Kementerian Kesihatan Malaysia (KKM) telah diterima oleh Biro Pengawalan Farmaseutikal Kebangsaan pada tahun 2014. Sepertimana YBhg. Datin/Tuan/Puan sudah maklum, definasi PRCA adalah seperti di bawah:

'Epoiten-associated pure red cell aplasia (PRCA) is characterized by severe anemia, low reticulocyte count, erythroblasts absence, epoetin non-response, and neutralizing antibodies against erythropoietin (EPO). PRCA is a rare adverse effect resulting from antibodies to Erythropoetin Stimulating Agents (ESAs) that cross-react with endogenous erythropoietin.'

3. Sehubungan itu, Bahagian ni telah mengambil inisiatif menyediakan garis panduan supaya pemantauan aktif terhadap produk ESAs dan pelaporan kejadian advers PRCA dapat dibuat (sila rujuk kepada lampiran yang disertakan). Dimohon supaya penggunaan produk ESA dapat dipantau dari masa ke semasa mengikut garis panduaan yang disertakan.

4. Bahagian ini memohon kerjasama YBhg. Dato'/Datin/Tuan/Puan menyampaikan maklumat ini kepada pegawai-pegawai farmasi yang bertugas di bawah jagaan masing-masing. Sekiranya terdapat sebarang pertanyaan lanjut, sila hubungi Puan Angeline Tan Meng Wah (angelinemengwah@gmail.com/angeline_tan@moh.gov.my) di talian 03-78413254, atau Pn. Noraini bt. Mohamad (norainimohd@moh.gov.my) di talian 03 -7841 3338.

Sekian, terima kasih.

"BERKHIDMAT UNTUK NEGARA"

Saya yang menurut perintah,

ROSMINAH BINTI MOHD DIN
Timbalan Pengarah Klinikal & Teknikal
Bahagian Perkhidmatan Farmasi
Kementerian Kesihatan Malaysia

(ABIDA HAQ BINTI SYED M. HAQ)
Pengarah Amalan dan Perkembangan Farmasi
Bahagian Perkhidmatan Farmasi
Kementerian Kesihatan Malaysia

RMD/NM/ATMW

SENARAI EDARAN

Timbalan Pengarah Kesihatan Negeri (Farmasi)
Perlis

Timbalan Pengarah Kesihatan Negeri (Farmasi)
Kedah

Timbalan Pengarah Kesihatan Negeri (Farmasi)
Pulau Pinang

Timbalan Pengarah Kesihatan Negeri (Farmasi)
Perak

Timbalan Pengarah Kesihatan Negeri (Farmasi)
Selangor

Timbalan Pengarah Kesihatan Negeri (Farmasi)
Negeri Sembilan

Timbalan Pengarah Kesihatan Negeri (Farmasi)
Melaka

Timbalan Pengarah Kesihatan Negeri (Farmasi)
Johor

Timbalan Pengarah Kesihatan Negeri (Farmasi)
Pahang

Timbalan Pengarah Kesihatan Negeri (Farmasi)
Terengganu

Timbalan Pengarah Kesihatan Negeri (Farmasi)
Kelantan

Timbalan Pengarah Kesihatan Negeri (Farmasi)
Sabah

Timbalan Pengarah Kesihatan Negeri (Farmasi)
Sarawak

Timbalan Pengarah Kesihatan Negeri (Farmasi)
W.P Labuan

Timbalan Pengarah Kesihatan Negeri (Farmasi)
W.P Kuala Lumpur dan Putrajaya

Ketua Pegawai Farmasi
Hospital Kuala Lumpur

Ketua Pegawai Farmasi
Institut Kanser Negara

PROSES KERJA PENGENDALIAN & PEMBEKALAN ERYTHROPOEITIN STIMULATING AGENT DI FASILITI KEMENTERIAN KESIHATAN MALAYSIA

Lampiran 1 – *Counseling Checklist on Erythropoietin Stimulating Agents*
Lampiran 2 – *Hemoglobin (Hb) Monitoring Card*
Lampiran 3 – *Pure Red Cell Aplasia (PRCA) Monitoring Guide for Hospital Pharmacist*
Lampiran 4 – *Flowchart of Pure Red Cell Aplasia (PRCA) ADR Reporting*
Lampiran 5 – Administrasi Agen Perangsang Erythropoiten (ESA) Di Unit Hemodialisis
Lampiran 6 – Pendispensan Agen Perangsang *Erythropoeitin* (ESA) Di Jabatan Farmasi Pesakit Luar (FPL)

BIL	PROSES KERJA	TANGGUNGJAWAB
1	**PENGENDALIAN UBAT**	
1.1	Menerima ubat dari stor ubat	Pegawai Farmasi/Staf Dialisis
1.2	Memastikan kuantiti ubat betul dan dalam keadaan yang baik	
1.3	Menyimpan semua ubat di dalam peti sejuk mengikut *First Expiry First Out* (FEFO)	
1.4	Suhu peti sejuk perlu sentiasa dipantau dan *Cold Chain* dikekalkan.	
2.	**MEMPRESKRIPSI**	
2.1	Mengenalpasti pesakit yang dipreskrip dengan ESA.	Pegawai Farmasi/Staf Dialisis
2.2	Kepilkan ***Lampiran 1*** bersama-sama dengan preskripsi serta merujuk pesakit berkenaan kepada pegawai farmasi/ Staf dialysis untuk sesi kaunseling.	
3.	**SARING DAN DISPEN**	
3.1	Terima dan saring preskripsi ESA Hubungi preskriber sekiranya terdapat masalah.	Pegawai Farmasi/Staf Dialisis
3.2	Kepilkan ***Lampiran 2*** kepada pesakit.	
4.	**KAUNSELING** ***Dikendalikan oleh unit yang membekalkan ESA kepada pesakit***	
4.1	**Kaunseling Pertama** - Beri kaunseling kepada pesakit apabila ESA dibekalkan pada kali pertama. - Isikan ***Lampiran 1*** dan simpankan rekod kaunseling di dalam profil pesakit. **Kaunseling Susulan** - Menilai pengetahuan pesakit dan memantau sebarang kesan sampingan - Memantau nilai dan corak Hb pesakit (Rujuk ***Lampiran 2***) - Sekiranya mendapati nilai Hb kian merosot, hubungi preskriber untuk penilaian selanjutnya.	Pegawai Farmasi/Staf Dialisis Pegawai Farmasi/ Staf Dialisis

	- Laporkan *Adverse Drug Reaction* (ADR) jika perlu. (rujuk ***Lampiran 4***)	
4.2	Membekalkan beg sejuk bersama dengan pek ais kepada pesakit yang dipreskrip dengan ESA kali pertama. (Rujuk ***Lampiran 6)***	Pegawai Farmasi/Staf Dialisis
5	**DOKUMENTASI**	
5.1	Rekod semua pembekalan ubat	Pegawai Farmasi/Staf Dialisis
5.2	Failkan semua rekod kaunseling di dalam profil pesakit.	Pegawai Farmasi/Staf Dialisis
5.3	Bagi pembekalan susulan, semak rekod kaunseling pesakit dan memberi kaunseling sekiranya terdapat perubahan dos/jenama/hentian ubat	Pegawai Farmasi

** Nota:*

Contoh ESA: Eprex/Binocrit/Recormon/Mircera

Lampiran 1

COUNSELING CHECKLIST FOR ERYTHROPOIETIN STIMULATING AGENTS

This checklist is intended as a reference document for use by pharmacists and/or nursing staff to counsel EVERY PATIENT who are prescribed with Erythropoetin Stimulating Agents (ESAs). The completed counselling form should be kept in the respective patient's file and/or pharmacy counselling folder for future reference.

Name: **Unit:**

		Yes	No	Remarks
1.	**What is EPO & why is it important for you?** Erythropoietin is a hormone produced by healthy kidneys. It is important to produce red blood cells. When kidneys fail, the production of erythropoietin is reduced. Hence, you need to inject erythropoietin to maintain your hemoglobin level 10-11.5g/dl *Target Hb may be changed according to latest evidence			
2.	**What EPO has the doctor prescribed for you?** The erythropoietin that the doctor prescribed for you is ..... **Dose / frequency/ timing ESA** - .....units..... time(s) a week/month. Inject preferably at the same time of the day on the scheduled day.			
3.	**Possible/ Common side effects of ESA** Experiencing side effects from medication is not unusual. Side effects from ESA is generally not serious. The common ones are: - Irritation at injection site - Headache - Joint / muscle pain - High blood pressure *Note: BP cut off point for ESA administration is individualized for each patient. Generally ESA is witheld if BP >160/100 mmHg . Patient has to be informed on their BP cut off point to either withold or continue ESA at home.*			
4.	**What can you do if you experience side effects that you cannot tolerate?** - Seek advice from the out patient pharmacy department or the dialysis unit			
5.	**Storage & Transport of ESA from hospital to home** - Transport of ESA is only allowed in cool box with ice packs. - Preferably to return home immediately after you get your ESA from pharmacy to facilitate fast storage. - ESA is very sensitive to light and temperature. Protect ESA from light. Store ESA in refrigerator, do not freeze. Keep in 2-8 degree celcius. Avoid fridge door, and the vegetable compartment. Ensure there is proper air circulation around your ESA.			
6.	**Preparing your ESA before injection** Do not take out your ESA from the fridge UNLESS it is time for use.If you have accidentally left your ESA outside the fridge, it has to be used ASAP before the ESA is damaged. **Product** — **Maximum period before damage once out from the fridge** **Recormon** — 3 days **Binocrit** — 3 days **Mircera** — 1 month **Eprex** — 7 days			
7.	How to use the injection? Please refer to section B or C.			

Section B & C: Injection Technique For Recormon and Mircera

B	INJECTION TECHNIQUE FOR SUBCUTANEOUS RECORMON	Done(√)
1.	Remove one syringe and check that the solution is clear, colorless and free from visible particles.	
2.	Allow Recormon to reach room temperature.	
3.	Wash your hand.	
4.	Remove the cap from the syringe.	
5.	Remove one needle from the pack, fix it on the syringe and remove the protective cap from the needle.	
6.	Expel air from the syringe and needle by holding the syringe vertically and gently pressing the plunger upwards.	
7.	Clean the skin at the site of injection using an alcohol wipe.	
8.	Form a skin fold by pinching the skin between thumb and forefinger.	
9.	Insert the needle into the skin fold with a quick, firm action.	
10.	Inject Recormon solution.	
11.	Withdraw the needle quickly and apply pressure over the injection site with a dry, sterile pad.	
12.	Dispose the empty syringe in special wastes container.	
C	INJECTION TECHNIQUE FOR SUBCUTANEOUS MIRCERA	
1.	Remove the box containing the Mircera pre-filled syringe from the refrigerator.	
2.	Keep the syringe in the box to protect it from light and allow it to reach room temperature for at least 30 minutes.	
3.	Remove the plastic tray of the Mircera pre-filled syringe from the box without peeling back the protective film.	
4.	Disinfect the hands well with soap and warm water or hands sanitizer.	
5.	Peel back the protective film from the plastic tray and remove the needle and the syringe.	
6.	Holding the syringe by the middle of the body without touching the release clip to avoid premature release of the safety device.	
7.	Grasp the packaged needle firmly in both hands.	
8.	Break the seal of the needle, using a twisting motion, and remove the needle cap. Do not remove the needle shield that protects the needle.	
9.	Grasp the syringe and the rubber tip cap firmly and remove the rubber tip cap from the syringe (bend and pull).	
10.	Attach the needle to the syringe by pushing it firmly onto the syringe.	
11.	Hold the syringe firmly with one hand and pull off the needle shield with the other hand.	
12.	Throw away the needle shield in the puncture-resistant container or sharps container.	
13.	Hold the syringe with the needle pointing up and tap the syringe gently to bring any bubble to the top. Push the plunger up slowly to the correct dose.	
14.	Clean the chosen injection site area using an alcohol pad.	
15.	Pinch a fold of loose skin at the clean injection site.	
16.	Fully insert the needle into the skin in a quick, "dart-like" motion.	
17.	Slowly push the plunger with the thumb while holding the syringe with the forefinger and middle finger against the finger grips until all the medicine is injected.	
18.	Take the needle out of the skin without releasing the plunger.	
19.	Release the plunger, allowing the needle guard to protect the needle.	
20.	Dispose the empty syringe in special wastes container.	
* Refer to Mircera product insert for graphic illustration if needed.		
Remarks: Reviewed by: Name and Signature (assessor) Date:		

Lampiran 2

Hemoglobin (Hb) Monitoring Card

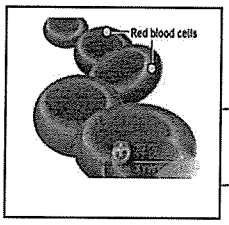
Name :
Age :
Type of Dialysis: HD / PD
Type of ESA :

MRN / IC No. :
Gender: Male / Female

No. of Visit	Date	Hb Level (g/dL)	Route (IV /SC)	Dose (unit)	Remark(s)**
1					
2					
3					
4					
5					
6					
7					
8					
9					
10					

***E.g. ADR detected, change in brand etc.*

Target Hemoglobin Range : 10 – 11.5 g/dL (Target may change according to latest evidence)



PURE RED CELL APLASIA (PRCA)

MONITORING *guide for hospital pharmacists*

WHAT IS PRCA?

PRCA is caused by neutralising anti-erythropoietin antibodies, leading to the reduction of very young red blood cells in the bone marrow. This has been reported to be in association with erythropoietin (EPO) therapy e.g. Eprex, Recormon, Binocrit & Mircera.

WHY MONITOR PRCA?

PRCA is a severe adverse reaction and may be fatal. Patients who are suspected or confirmed to have PRCA should have their EPO therapy discontinued and should not be switched to other types of EPO.

HOW TO DETECT PRCA?

PRCA is confirmed by a positive Anti-EPO antibody test. However, a patient is suspected to have PRCA when the following parameters are present:

1. Fall in haemoglobin of about 0.5 – 1.0 g/dl/week AND
2. Absolute reticulocyte count below 10,000/ul AND
3. No major changes in white cell, platelet or differential leucocyte counts

Eventhough there are no significant symptoms for PRCA, some patients may complain of joint/ muscle pain, sudden tiredness, dizziness or sudden shortness of breath – this should prompt further investigation.

WHAT TO DO IF PRCA IS SUSPECTED?

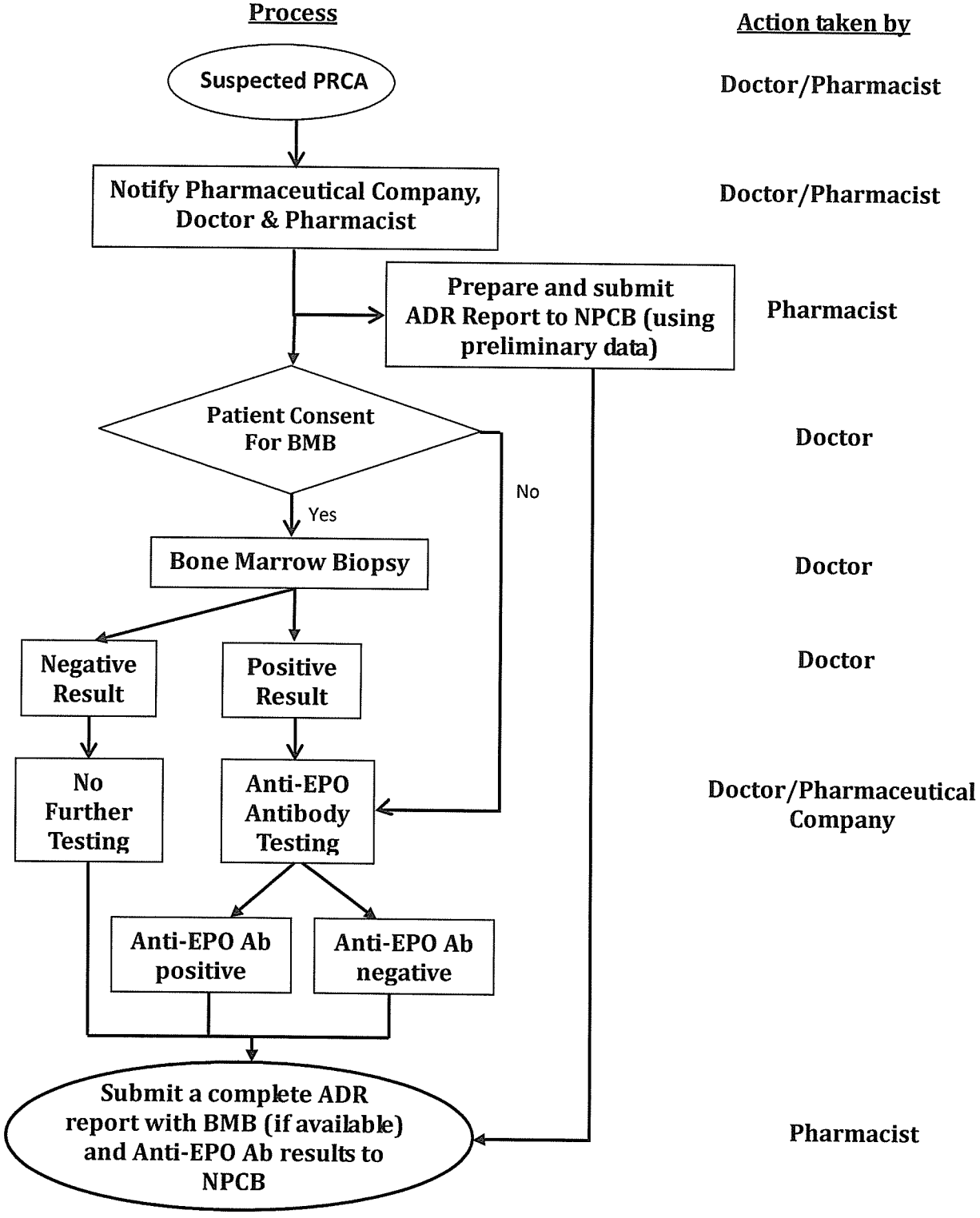
All adverse events should be notified to the prescriber for further investigation and an ADR report should be followed once there is clinical suspicion (with/without bone biopsy result). The National Pharmaceutical Control Bureau (NPCB) should be notified within 48 hours.

Reference:
1. Adapted from KDIGO Clinical Practice Guideline For Anemia in Chronic Kidney Disease 2012
2. Ministry of Health, Renal Replacement Therapy Guideline 2009, 3rd Edition

Updated April 2015

Lampiran 4

Flowchart of Pure Red Cell Aplasia (PRCA) Adverse Drug Reaction (ADR) Reporting



Definition of PRCA:

- Fall in haemoglobin of about 0.5 – 1.0g/dl/week AND
- Absolute reticulocyte count below 10,000 /uL AND
- No major changes in white cell count, platelet count, or differential leukocyte count

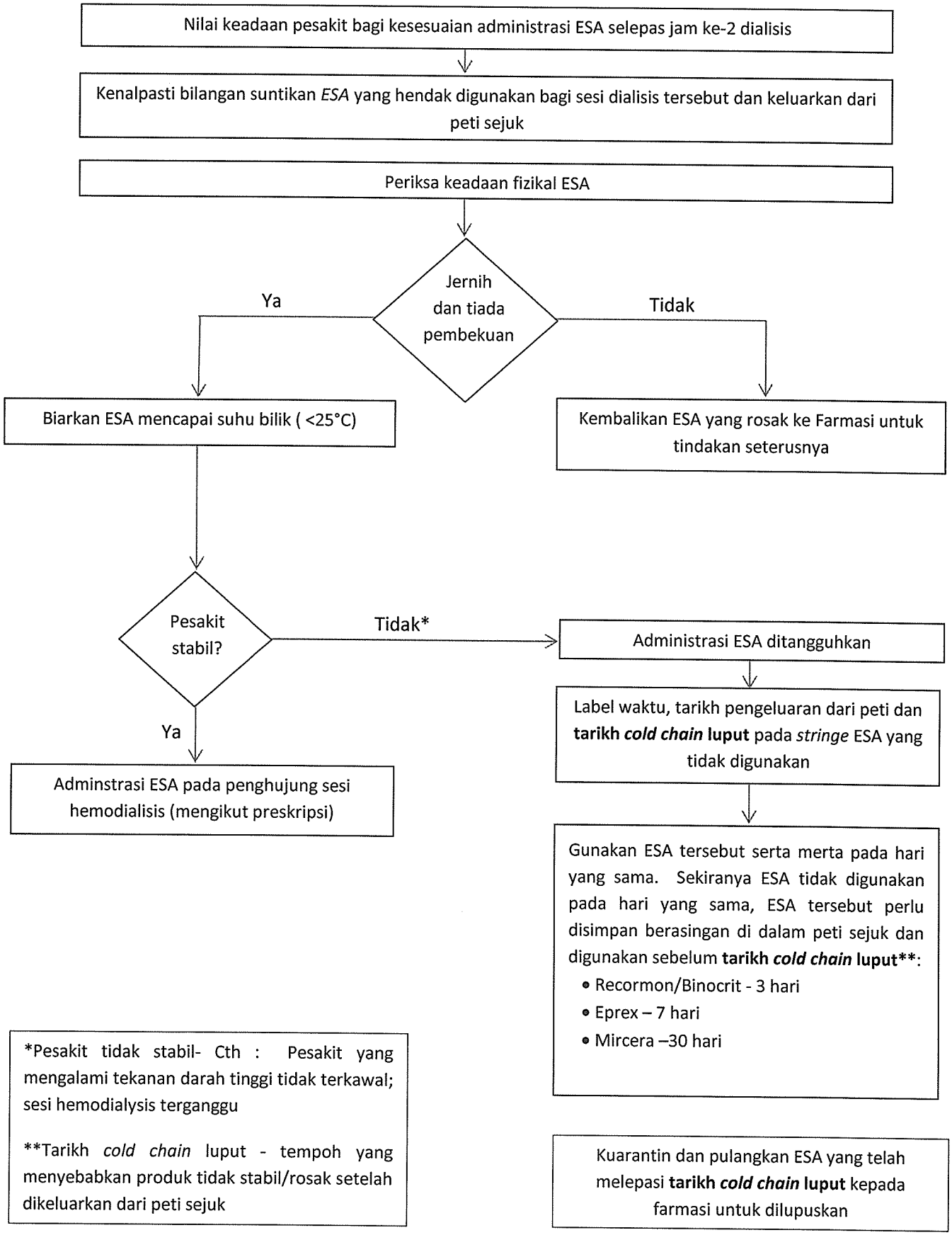
BMB – Bone Marrow Biopsy; EPO – Erythropoietin; Ab – Antibody

Reference:

1. Adapted from KDIGO Clinical Practice Guideline For Anemia in Chronic Kidney Disease 2012
2. Ministry of Health, Renal Replacement Therapy Guideline 2009, 3rd Edition

Lampiran 5

Administrasi Agen Perangsang Erythropoietin (ESA) di Unit Hemodialisis



Updated April 2015

Pendispensan Agen Perangsang Erythropoietin (*ESA*) Di Jabatan Farmasi Pesakit Luar (FPL)