SONO MEDICAL

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ID: 4200102400007 PDV: 200102400007 PB: 01703390

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Broj: 057 / 16
Datum: 07.06.2016.

09-026-2899/16

N/r. Svim korisnicima Tosoh reagenasa u BiH

PREDMET: HITNO sigurnosno obavještenje za korisnike ST AIA – PACK hsE2 Kataloški broj 0025225 i ST AIA – PACK iE2 Kataloški broj 0025224

Poštovani,

Obavještavamo Vas da Tosoh Europe NV pokreće korektivnu sigurnosnu akciju o kojoj su obaviještene i Europske vlasti za **ST AIA – PACK hsE2 Kataloški broj 0025225 i ST AIA – PACK iE2 Kataloški broj 0025224** vezanu za **uzajamnu reaktivnost na Fulvestrant.**

Fulvestrant je komercijalno dostupan pod imenom FASLODEX koji se dobija na recept i propisuje ga liječnik i koristi se za tretiranje receptora hormona – pozitivni metastatski karcinom dojke kod žena koje su prošle kroz menopauzu.

Tosoh korporacija je provela vlastitu istragu i došla do sljedećih rezultata uzajamne reaktivnosti Tosoh Estradiol testa. Uzorci su mjereni bez i sa Fulvestrantom. Ukupan rezultat je prikazan u sljedećoj tabeli

	Kataloški broj	Estradiol rezultat čistog uzorka	Estradiol rezultat sa dodanim fulvestrantom(*2)		% uzajamna reaktivnost (*3)
		pg/ml (*1)	pg/mL	pmol/L	
ST AIA-PACK hsE2	0025225	< 7	329	1207	1.5
ST AIA-PACK iE2	0025224	< 20	148	543	0.66

Bilješka: (*1) 7 pg/mL i 20 pg/mL: donji limit raspona mjerenja ST AIA-PACK hsE2 i ST AIA-PACK iE2, odnosno.
(*2) Uzorak sa dodanih 50,000 pg/mL (82,404 pmol/L) Fulvestranta.
(*3) %Uzajamna reaktivnost = ((promjena estradiol rezultata u pmol/L) / (koncentacija fulvestranta ubačenog u pmol/L)) x 100

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Rizik za zdravlje

Rizik za zdravlje postoji kod svih pacijenata koji su tretirani sa lijekom fulvestrant. Uzajamna reaktivnost može dovesti do pogrešno određenih rezultata estradiol testa koji može dovesti do neprikladne kliničke procjene estrogenskog statusa.

Estradiol sa LH i FSH u serumu koristi se da dođemo do saznanja da li je pacijent u pre ili post menopauzi. Fulvestrant se daje isključivo ženama u postmenopauzi. Klinička slika može biti nejasna ako menstrualna krvarenja prestanu kod žena tokom kemoterapije ili pod tretmanom temoxifen-om. Najčešće se ovaj test radi prije nego se krene sa tretmanom fulvestrant-om tako da nikakva uzajamna reakcija neće biti prisutna. Šta više tretman se obavlja sa jednom mjesečnom injekcijom koncentracija će biti niska kao i uzajamna reaktivnost. Pošto se klasifikacija takođe radi sa LH i FSH rizik pogrešne klasifikacije pre ili post menopauze je minimalan. Ukoliko je došlo do greške klasifikacije tretman sa Fluvestrantom neće početi.
Bitno je da zapamtite da koncentracija estradiola kod žena tratiranih fulvestrant-om treba biti mjerena isključivo testom koji pokazuje zanemarivu uzajamnu reakciju sa fulvestrant-om.

Akcije koje treba preuzeti:

1. Molimo Vas podijelite ovo pismo sa vašim doktorima, biokemičarima i laborantima
2. Ne koristite navedene Tosoh estradiol testove kada provjeravate nivoe estradiola kod pacijenata koji primaju Fulvestrant tretman, već koristite alternativne metode koje imaju zanemarivu uzajamnu reakciju na lijek
3. Ispunite povratni dokument i pošaljite ga najkasnije do 30.06.2016

Molimo Vas da osigurate da ovo pismo dođe do svih zainteresiranih osoba u vašoj organizaciji ili do organizacije gdje su pogođeni proizvodi proslijeđeni.

Ova sigurnosna obavijest (FSN) je upućena svim zainteresiranim stranama.

Iskreno se izvinjavama zbog neugodnosti. Cijenimo vaše razumjevanje i kooperaciju i zahvaljujemo vam se na lojalnosti našoj kompaniji.

Ukoliko imate bilo kakva dodatna pitanja vezana za ovu sigurnosnu obavijest, molimo Vas da se obratite lokalnom Tosoh distributeru.

S poštovanjem,

Damir Bajrić

SONO MEDICAL
Društvo za trgovinu i usluge doo
Sarajevo

Dr Igor Kuljak

TOSOH

TOSOH EUROPE N.V.

URGENT Field Safety Notice

Products affected: 0025224 ST AIA-PACK iE2
0025225 ST AIA-PACK hsE2

FSCA Reference: NC 38409 FSCA

Type of action: Advice on Product Use

Date Issued: Wednesday, 8th June 2016

Dear Customer,

Tosoh Europe NV is initiating a Field Safety Corrective Action for the ST AIA-PACK iE2 and ST AIA-PACK hsE2 (Respective Catalogue Numbers 0025224 and 0025225) regarding cross reactivity of Fulvestrant. Fulvestrant is commercially available under the name Faslodex® and is a prescription medicine used to treat hormone receptor-positive metastatic breast cancer in women who have gone through menopause.

Tosoh Corporation has performed investigations to determine the impact of the cross reactivity in the Tosoh Estradiol Assays. Samples were measured neat and spiked with fulvestrant. A summary of the investigation results is shown in the below table.

Cross reactivity of Fulvestrant in Tosoh Estradiol assays

	Catalogue Number	Estradiol result of neat sample	Estradiol result of Spiked sample (*2)		%Cross reactivity (*3)
		pg/mL (*1)	pg/mL	pmol/L	
ST AIA-PACK hsE2	0025225	< 7	329	1207	1.5
ST AIA-PACK iE2	0025224	< 20	148	543	0.66

Notes: (*1) 7 pg/mL and 20 pg/mL: the lower limit of measuring range of ST AIA-PACK hsE2 and STAIA-PACK iE2, respectively.
(*2) Sample was spiked with 50,000 pg/mL (82,404 pmol/L) Fulvestrant.
(*3) %Cross reactivity = ((change of estradiol result in pmol/L) / (concentration of Fulvestrant spiked in pmol/L)) X 100

Risk to Health
The risk to health applies to all patients being treated with the drug fulvestrant. The cross reactivity could lead to falsely elevated estradiol test results which could lead to an inappropriate clinical assessment of oestrogen status.
Estradiol, along with LH and FSH in serum is used to clarify, whether the patient is pre- or postmenopausal. Fulvestrant is only given to post-menopausal women. It might not be clear from the clinical situation, as menstrual bleeding stops in many women during chemotherapy or under tamoxifen treatment. However, usually this test is done before the start of fulvestrant treatment so no cross reactivity would be present. Moreover as the treatment is done with a monthly injection the

concentration will be low and thus also the cross reactivity would be low. As the classification will also be done with LH and FSH the risk of misclassification pre/post-menopausal is minimal. When there is a misclassification the treatment with Fulvestrant will not be started.
It is important to note that estradiol concentrations in fulvestrant-treated women should only be measured by an assay that demonstrates negligible cross reactivity with fulvestrant.

Action to be Taken:

1) Please **review this letter with your Clinician(s)**.
2) Do not use the listed Tosoh estradiol assays when monitoring estradiol levels in patients receiving Fulvestrant treatment but use an alternative method that has negligible cross reactivity of the drug.
3) Fill out the enclosed **RETURN SHEET** and to send it to our QA/RA department by **June 30th 2016** latest.

Please ensure distribution of this notice to all those who need to be aware within your organisation or to any organisation where the affected product has been transferred to.
This Field Safety Notice (FSN) has been notified to all concerned competent authorities.

We sincerely apologise for the inconvenience. We appreciate your understanding and cooperation and we would like to thank you for your loyalty to our company.

Please do not hesitate to contact your local Tosoh representative if you have any further questions referring to the content of this Field Safety Notice.

Sincerely,
Kirsten Van Garsse
Quality Assurance and Regulatory Affairs Manager EMEA
Tosoh Europe NV